EXPERIMENTAL SECTION

Table S1. Composition and concentration of reaction group and control group

Component and concentration of reaction group 1		**Component and concentration of reaction group 2**	
component	**concentration**	**control group component**	**concentration**
Tris-HCl pH7.5	50 mM	Tris-HCl pH7.5	50 mM
Sodium Chloride	50 mM	Sodium Chloride	50 mM
Magnesium Chloride	5 mM	Magnesium Chloride	5 mM
DTT	1 mM	DTT	1 mM
Manganese Sulfate	0.5 mM	Manganese Sulfate	0.5 mM
CHAPS	1 mM	CHAPS	1 mM
Probe Oligo	50 nM	Probe Oligo	50 nM
PA Protein	250 nM	BSA Protein	250 nM
Total volume	50 μL	Total volume	50 μL

Table S2. Composition and concentration of reaction group and control group

Component and concentration of compound group (A)		**Component and concentration of positive control group (B)**		**Composition and concentration of negative control group (C)**	
Reaction group component	**concentration**	control group component	**concentration**	control group component	**concentration**
Tris-HCl pH7.5	50 mM	Tris-HCl pH7.5	50 mM	Tris-HCl pH7.5	50 mM
Sodium Chloride	50 mM	Sodium Chloride	50 mM	Sodium Chloride	50 mM
Magnesium Chloride	5 mM	Magnesium Chloride	5 mM	Magnesium Chloride	5 mM
DTT	1 mM	DTT	1 mM	DTT	1 mM
Manganese Sulfate	0.5 mM	Manganese Sulfate	0.5 mM	Manganese Sulfate	0.5 mM
CHAPS	1 mM	CHAPS	1 mM	CHAPS	1 mM

Probe Oligo	50 nM	Probe Oligo	50 nM	Probe Oligo	50 nM
PA Protein	250 nM	PA Protein	250 nM	BSA Protein	250 nM
Compound inhibitor	8 gradient	Compound inhibitor	Nothing	Compound inhibitor	Nothing
Total volume	50 μL	Total volume	50 μL	Total volume	50 μL

Experimental data of related compounds

I-1 (R) - 12-diphenylmethyl-7-hydroxy-3,4,12,12a-tetrahydro-1H - [1,4]oxazinyl [3,4-c] pyridyl [2,1-f] [1,2,4] triazine-6,8-dione

Diphenyl alcohol (3.27 g, 10 mmol) and compound **a** (2.02 g,11 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture. After nitrogen displacement, the react at 100 ℃ for 12 hours. When the reaction was completed, 60 mL of ice water was added into the reaction mixture, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate. 6.27 g of light yellow solid was obtained by filter and evaporation, 1.95 g of light yellow solid was obtained by column chromatography (DCM: CH3OH=30:1) in a yield of 39.56%.

1.95 g of the above solids and 1.66 g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate, 5.89 g of oil was yielded by filter and evaporation. 680 mg of pale yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 42.66% and in a content of 96.18. THE content was 99.91% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{23}H_{21}N_3O_4$: 404.4305. Found: 404.1615 $[M+H]^+$.

^{1}H NMR (600 MHz, DMSO-d_6, 25 ℃, TMS): δ 3,02-3.08 (m, 1H), 3.38-3.43 (m, 2H), 3.58-3.66 (m, 2H), 3.94 (dd, 1H), 4.39 (d, 1H), 4.56-4.58 (m, 1H), 5.44 (t, 1H), 5.67-5,71 (m, 1H), 7.19 (d, 2H), 7.23 (d, 1H), 7.29 (d, 2H), 7.36 (dd, 1H), 7.45 (t, 2H), 7.66 (d, 2H), 11.64 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 45.21, 65.56, 67.87,71.28, 72.34, 115.75, 127.51, 128.25, 128.32, 128.50, 129.17, 129.28, 152.68, 160.92, 170.95.

I-2(R)-12-(2(4-methoxyphenyl)methyl)-7-Hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

4,4 '- dimethoxydiphenyl alcohol (2.68 g, 11 mmol) and compound **a** (3.27 g ,10 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture. replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 60 mL of ice water was added into the reaction mixture, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate. 6.02g of light yellow solid was obtained by filter and evaporation. 3.93 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 71.07%.

3.93 g of the above solids and 2.97 g of anhydrous lithium chloride were added into 20 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, yellow solid was obtained by extract and filter. 2.04 g of pale yellow solid was obtained by recrystallization of methanol in a yield of 88.70% and in a content of 93.92%. The content was 99.94% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{25}H_{25}N_3O_6$: 463.4825. Found:487.3614$[M+Na+H]^+$. ^{1}H NMR (600 MHz, DMSO-d_6, 25 ℃, TMS): δ 2.87 (s, 1H), 3.12-3.18 (m, 1H), 3.21 (s, 1H), 3.50-3.65 (m, 2H), 3.74 (dd, 6H), 3.83-3.87 (m, 1H), 4.35-4.37 (m, 1H), 5.10 (s, 1H), 6.74 (dd, 2H), 6.85 (dd, 2H), 6.93 (dd, 2H), 7.15-7.20 (m, 2H), 7.43-7.45 (m, 2H), 11.53 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 46.19, 54.90, 54.99, 55.07, 55.10,

113.36, 113.66, 114.53, 128.33, 128.61, 128.65, 128.84, 157.24, 157.54, 158.87, 159.08.

I-3(R)-12-(2(4-Fluorophenyl)methyl)-7-hydroxyl**-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone**

4,4 '- difluorodiphenyl alcohol (2.42 g, 11 mmol) and compound **a** (3.27 g ,10 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 60 mL of ice water was added into the reaction mixture, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate. 7.13 g of light yellow solid was obtained by filter and evaporation. 2.63 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 49.56%.

2.63 g of the above solids and 2.07 g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate, 5.45 g of oil was yielded by filter and evaporation. 873 mg of pale yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 40.04% and in a content of 97.44%. The content was 99.98% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{23}H_{19}F_2N_3O_4$: 439.1344. Found:440.1425$[M+H]^+$.

^{1}H NMR (600 MHz, DMSO-d_6, 25 ℃, TMS): δ 3.12 (s, 1H), 3.40 (td, 1H), 3.62-3.68 (m, 2H), 3.93 (dd, 1H), 4.37 (d, 1H), 4.54-4.57 (m, 1H), 5.52 (d, 1H), 7.04 (t, 2H), 7.13-7.14 (m, 1H), 7.25-7.34 (m, 5H), 7.71 (dd, 2H), 11.60 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 45.14, 65.66, 67.84, 70.44, 71.08, 115.13, 116.00, 129.57, 129.62, 131.40, 131.45, 139.32, 152.68, 160.85, 171.00.

I-4(12aR)-12-((4-bromobenzene)(benzene)methyl)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

(4-bromophenyl) (phenyl) methanol(2.62 g, 11 mmol) and compound **a** (3.27 g ,10 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 60 mL of ice water was added into the reaction mixture, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate. 9.03g of light yellow solid was obtained by filter and evaporation. 1.37 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 24.00%.

1.37 g of the above solids and 1.01g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 100 mL×2 dichloromethane was used to extraction, the organic phase was combined, and its was washed with 20 mL of saturated sodium chloride solution, and dried with anhydrous sodium sulfate, 5.08 g of oil was yielded by filter and evaporation. 860 mg of pale yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 74.78% and in a content of 95.86%. The content was 99.24% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{23}H_{20}BrN_3O_4$: 481.0637/483.0617. Found: 482.0636 $[M+H]^+$/484.1425$[M+H]^+$. ^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 0.67 (d, 2H), 0.85 (d, 1H), 1.04-1.07 (m, 1H), 1.23 (d, 2H), 4.02 (dd, 1H), 4.54-4.58 (m, 1H) 5.73 (ddd, 1H), 6.20 (s, 1H), 7.20 (s, 2H), 7.28-7.29 (m, 3H), 7.45 (s, 2H), 7.63 (dd, 2H), 11.61 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 46.19, 62.89, 67.91, 71.49, 73.52, 119.70, 126.21, 126.40, 126.60, 126.87, 128.02, 128.15, 128.32, 128.43, 128.64, 128.83, 130.93， 137.66, 142.55, 145.16, 145.23, 169.59.

II-1(R)-12-(5H-Dibenzo[a,d][7]Cycloheptene-5-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

dibenzocycloheptanol (2.29 g, 11 mmol) and compound **a** (3.27 g ,10 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 4 g of light yellow solid was obtained by distillation. 2.4 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 46.42%.

2.4 g of the above solids and 1.90 g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 1.98g of light yellow solid compound II-1 was obtained by recrystallization. in a yield of 100% and in a content of 94.49%. The content was 99.93% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{25}H_{21}N_3O_4$: 427.4519. Found: 428.3532$[M+H]^+$.

^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 2.82 (d, 1H), 3.08 (dd, 1H), 3.54 (s, 1H), 3.95-3.97 (m, 2H), 4.00 (d, 1H), 5.01 (d, 1H), 5.10 (s, 1H), 6.69 (dd, 1H), 7.10 (dd, 1H), 7.23 (d, 1H), 7.28 (dd, 1H), 7.34-7.42 (m, 3H), 7.47 (dd, 1H), 7.55-7.62 (m, 3H), 7.69 (t, 1H), 11.11 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 50.15, 50.53, 66.02, 68.09, 73.27, 126.32, 127.91, 128.66, 130.11, 131.03, 131.42, 132,56, 133.82, 134,11, 134,47, 135.66, 142.24, 161.14, 170.08.

(II-2(R)-12-(5H-Dibenzo[a,d][7]Cycloheptane-5-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

dibenzocycloheptanol (2.10 g, 10mmol) and compound **a** (3.27 g ,10 mmol) were added into a 100 mL thick wall pressure flask, then 20 mL of T_3P ethyl acetate

solution (mass fraction 50%) and 20 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 2.72 g of light yellow solid was obtained by distillation. 3.14 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 60.62%.

3.14 g of the above solids and 1.90 g of anhydrous lithium chloride were added into 20 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 2.59 g of light yellow solid was obtained by recrystallization in a yield of 100% and in a content of 92.08%. The content was 99.11% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{25}H_{23}N_3O_4$: 429.4678. Found: 430.1771$[M+H]^+$.

^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 2.84-2.89 (m, 2H), 3.59 (t, 1H), 3.76 (t, 2H), 3.98 (dd, 3H), 4.27 (d, 1H), 4.29 (s, 1H), 5.44 (dd, 2H), 6.85 (dd, 1H), 6.91 (d, 1H), 7.18-7.21 (m, 2H), 7.34 (s, 1H), 7.37-7.38 (m, 2H), 7.43 (s, 2H), 8.66 (d, 1H), 11.80 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 30.98, 31.87, 45.39, 65.57, 68.24, 69.89, 74.72, 110.13, 115.50, 125.83, 128.64, 128.83, 129.17, 129.51, 130.89, 131.00, 131.10, 131.36, 133.63, 135.03, 139.92, 140.29, 153.13, 161.38, 171.00.

II-3 (12aR)-12-(10,11-Difluoride-7,12-Dihydrobenzo[e]Naphthyl[1,2-b]Evil genu in-7-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

10,11-difluoro-7,12-dihydrobenzo [e] naphthaleno [1,2-b] oxheptan-7-alcohol (1.29 g, 4.3 mmol) and compound **a** (1.40 g ,4.3 mmol) were added into a 100 mL thick wall pressure flask, then 10 mL of T_3P ethyl acetate solution (mass fraction 50%) and 10 mL of ethyl acetate were added into reaction mixture, replace with nitrogen,

and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 2.66 g of light yellow solid was obtained by distillation. 0.64 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 24.43%.

0.64 g of the above solids and 0.44 g of anhydrous lithium chloride were added into 10 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 0.5 g of light yellow solid was obtained by recrystallization in a yield of 100% and in a content of 93.44%. The content was 99.85% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{28}H_{21}F_2N_3O_5$: 517.4802. Found: 518.1528$[M+H]^+$.
^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 3.56 (s, 1H), 3.67 (d, 1H), 3.86 (dd, 1H), 4.00 (dd, 1H), 4.46-4.53 (m, 2H), 5.16-5.25 (m, 1H), 5.55 (dd, 2H), 5.72 (d, 1H), 7.37-7.40 (m, 2H), 7.44 (d, 1H), 7.48 (d, 1H), 7.51-7.57 (m, 2H), 7.61 (dd, 2H), 7.90 (d, 1H), 8.25 (dd, 1H), 11.81 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 46.66, 61.79, 65.95, 68.58, 71.09, 113.51, 114.33, 121.66, 123.03, 126.69, 126.89, 127.85, 128.22, 128.80, 129.11, 129.31, 130.12, 130.58, 134.13, 135.10, 152.93, 162.11.

II-4 (12aR)-12-(9,10-Difluoride-8,13-Dihydrobenzo[e]Naphthyl[2,1-b]Evil genui n-13-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

9,10-difluoro-8,13-dihydrobenzo [e] naphthaleno [1,2-b] oxheptane-13-alcohol (1.49 g, 5 mmol) and compound **a** (1.64 g ,5 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T_3P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction,

the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 3.07 g of light yellow solid was obtained by distillation. 1.7 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 56.67%.

1.7 g of the above solids and 1.2 g of anhydrous lithium chloride were added into 10 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 1.1 g of light yellow solid was obtained by recrystallization in a yield of 100% and in a content of 91.26%. The content was 100% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{28}H_{21}F_2N_3O_5$: 517.4802. Found: 518.1528$[M+H]^+$.
^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 2.81 (d, 1H), 3.02 (dd, 1H), 3.32 (d, 2H), 3.94 (d, 1H), 4.85-4.87 (m, 1H), 5.08 (d, 1H), 5.63-5.69 (m, 1H), 6.34 (m, 1H), 7.24 (m, 3H), 7.57 (dd, 2H), 7.84 (d, 2H), 8.14-8.23 (m, 1H), 8.58-8.67 (m, 3H), 11.67 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 53.23, 63.93, 64.40, 65.70, 65.98, 67.77, 122.23, 124.10, 125.15, 126.89, 127.34, 129.64, 130.55, 131.34, 132.56, 133.61, 133.85, 134,15, 155.38, 165.06, 165.20, 165.94, 166.06, 166.20, 169.41, 170.07.

II-5 12-(7,8-Difluoride-6,11-Dihydrodibenzo[b,e]Evil genuin-11-base)-7-hydroxy l-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Tri azine-6,8-diketone

7,8-difluoro-6,11-dihydrodibenzo [b, e] oxheptan-7-alcohol (1.45 g, 5.84 mmol) and compound **a** (1.91 g ,5.84 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T_3P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate

aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 3.55 g of light yellow solid was obtained by distillation. 0.84 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 25.85%.

0.84 g of the above solids and 0.63 g of anhydrous lithium chloride were added into 10 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 0.49 g of light yellow solid was obtained by recrystallization in a yield of 70% and in a content of 92.02%. The content was 100% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{24}H_{19}F_2N_3O_5$: 467.4216. Found: 468.1376$[M+H]^+$. ^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 2.76 (d, 1H), 2.95 (d, 1H), 3.38 (s, 1H), 3.66 (s, 1H), 3.81 (dd, 1H), 3.87-3.88 (m, 1H), 4.46-4.50 (m, 2H), 5.24-5.28 (m, 1H), 5.32 (s, 1H), 6.07-6.12 (m, 1H), 6.77-6.85 (m, 1H), 6.97 (t, 1H), 7.07 (dt, 2H), 7.23-7.26 (m, 1H), 7.33-7.44 (m, 2H), 11.78 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 46.66, 61.08, 65.97, 68.57, 70.11, 71.16, 117.48, 118.16, 120.29, 120.31, 120.61, 121.36, 122.35, 124.97, 126.84, 127.39, 128.80, 129.12, 129.31, 132.24, 133.62, 134.06, 157.13, 157.58.

II-6 (12aR)-12-(7,8-Difluoride-4-Methoxy group-6,11-Dihydrodibenzo[b,e]Evil genuin-11-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

7,8-difluoro-4-methoxy-6,11-dihydrodibenzo [b, e] oxheptan-7-alcohol (1.39 g, 5mmol) and compound **a** (1.64 g ,5 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T_3P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn,

and dried with anhydrous sodium sulfate. 2.88 g of light yellow solid was obtained by distillation. 1.83 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 62.35%.

1.83 g of the above solids and 1.32 g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 1.49 g of light yellow solid was obtained by recrystallization in a yield of 96.13% and in a content of 90.93%. The content was 99.28% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{25}H_{21}F_2N_3O_6$: 497.4475. Found: 498.1641$[M+H]^+$.
^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 3.03 (dd, 1H), 3.07-3.11 (m, 1H), 3.26 (d, 1H), 3.39 (dd, 1H), 3.68 (dd, 1H), 3.72 (d, 3H), 3.82-3.88 (m, 1H), 5.24 (dd, 1H), 5.53 (s, 1H), 5.67 (dd, 1H), 5.72-5.79 (m, 1H), 7.02-7.14 (m, 1H), 7.56 (dd, 1H), 7.60 (dd, 2H), 7.66 (dd, 1H), 7.79 (d, 1H), 7.84 (dd, 1H), 11.66 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 41.63, 52.28, 54.25, 65.12, 68.57, 69.52, 88.22, 113.11, 125.86, 126.25, 126.57, 128.45, 128.61, 128.73, 131.71, 132.27, 132.92, 140.06, 145.56, 148.75, 150.45, 153.94, 164.05, 172.46.

II-7 (12aR)-12-(7,8-Difluoride-2-Methoxy group-6,11-Dihydrodibenzo[b,e]Evil genuin-11-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Py ridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

7,8-difluoro-2-methoxy-6,11-dihydrodibenzo [b, e] oxheptan-7-alcohol (1.39 g, 5mmol) and compound **a** (1.64 g ,5 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T_3P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn,

and dried with anhydrous sodium sulfate. 2.67 g of light yellow solid was obtained by distillation. 1.72 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 58.60%.

1.72 g of the above solids and 1.24 g of anhydrous lithium chloride were added into 15 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 1.23 g of light yellow solid was obtained by recrystallization in a yield of 84.83% and in a content of 91.66%. The content was 99.84% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{25}H_{21}F_2N_3O_6$: 497.4475. Found: 498.1631$[M+H]^+$.
^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 2.92 (dd, 1H), 3.27 (dd, 1H), 3.38 (dt, 1H), 3.72 (d, 3H), 3.85 (dd, 1H), 4.30-4.41 (m, 1H), 4.44-4.51 (m, 1H), 5.16 (dd, 1H), 5.66 (dd, 1H), 5.74 (d, 1H), 5.81 (d, 1H), 5.99 (dd, 1H), 6.81 (d, 1H), 6.93 (d, 1H), 6.98-7.03 (m, 1H), 7.17 (d, 1H), 7.24 (dd, 1H), 7.44 (ddd, 1H), 11.58 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 45.62, 54.57, 55.40, 65.54, 69.05, 70.79, 91.10, 113.57, 115.91, 116.45, 117.79, 121.37, 122.10, 126.85, 127.75, 131.70, 132.42, 141.12, 148.91, 149.21, 150.02, 153.40, 154.03, 154.54, 172.99.

II-8 12-(4,7,8-Trifluoride-6,11-Dihydrodibenzo[b,e]Evil genuin-11-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

4,7,8-trifluoro-6,11-dihydrodibenzo [b, e] oxheptan-7-alcohol (1.33 g, 5mmol) and compound **a** (1.64 g ,5 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T$_3$P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried

with anhydrous sodium sulfate. 3.2 g of light yellow solid was obtained by distillation. 0.91 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 31.71%.

0.91 g of the above solids and 0.67 g of anhydrous lithium chloride were added into 10 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 0.6 g of light yellow solid was obtained by recrystallization in a yield of 78.95% and in a content of 94.96%. The content was 99.89% after liquid phase purification was preparationed.

HRMS(ESI): m/z Calcd for $C_{24}H_{18}F_3N_3O_5$: 485.4120. Found: 486.1279$[M+H]^+$.
^{1}H NMR (600 MHz, 600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 3.54 (s, 1H), 3.66 (d, 1H), 3.87 (dd, 1H), 3.95-4.07 (m, 1H), 4.46 (dd, 2H), 5.37 (dd, 2H), 5.52 (d, 1H), 5.71 (dd, 1H), 6.18 (t, 1H), 7.06 (dd, 1H), 7.16-7.18 (m, 1H), 7.29 (dd, 1H), 7.35-7.38 (m, 1H), 7.44 (d, 1H), 7.55 (dd, 1H), 11.78 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 45.88, 46.65, 61.78, 65.95, 68.54, 70.54, 118.08, 118.47, 121.10, 122.78, 126.96, 128.43, 128.80, 129.11, 129.31, 133.15, 133.55, 145.21, 145.90, 149.68, 151.64, 154.07, 161.83, 166.11.

II-9 12-(2,7,8-Trifluoride-6,11-Dihydrodibenzo[b,e]Evil genuin-11-base)-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1H-[1,4]oxazinyl[3,4-c]Pyridyl group[2,1-f][1,2,4]Triazine-6,8-diketone

2,7,8-trifluoro-6,11-dihydrodibenzo [b, e] oxheptan-7-alcohol (1.33 g, 5mmol) and compound **a** (1.64 g ,5 mmol) were added into a 100 mL thick wall pressure flask, then 15 mL of T$_3$P ethyl acetate solution (mass fraction 50%) and 15 mL of ethyl acetate were added into reaction mixture, replace with nitrogen, and react at 100 ℃ for 12 hours. When the reaction was completed, 50 mL of ice water was added into the reaction mixture, 120 mL×2 ethyl acetate was used to extraction, the organic phase was combined, and its was washed with 50 mL of saturated sodium bicarbonate aqueous solution and 50 mL of saturated sodium chloride solution in turn, and dried

with anhydrous sodium sulfate. 3.1 g of light yellow solid was obtained by distillation. 1.35 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1) in a yield of 47.04%.

1.35 g of the above solids and 0.72 g of anhydrous lithium chloride were added into 10 mL of DMAc, after nitrogen protection, the react at 70 ℃ for 8 hours . 20 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, the filter cake was washed with 10 mL of water after the reaction mixture was filtered , light yellow solid was obtained by dried, 0.78 g of light yellow solid was obtained by recrystallization in a yield of 69.03% and in a content of 94.54%. The content was 99.87% after liquid phase purification.

HRMS(ESI): m/z Calcd for $C_{24}H_{18}F_3N_3O_5$: 485.4120. Found: 486.1280$[M+H]^+$.
^{1}H NMR (600 MHz, DMSO-*d*$_6$, 25 ℃, TMS): δ 3.54 (d, 1H), 3.65-3.67 (m, 1H), 3.85-3.87 (m, 1H), 3.98-4.05 (m, 1H), 4.33-4.35 (m, 2H), 5.18-5.24 (m, 2H), 5.54 (s, 1H), 5.64 (s, 1H), 6.84-6.90 (m, 1H), 7.03-7.11 (m, 2H), 7.24 (dd, 2H), 7.35-7.44 (m, 1H), 7.51-7.55 (m, 1H), 11.78 (s, 1H). ^{13}C NMR (150 MHz, DMSO): δ 45.58, 60.26, 63.93, 64.90, 67.82, 69.16, 107.56, 111.98, 117.27, 118.10, 121.22, 122.19, 125.96, 127.09, 127.72, 128.04, 128.24, 132.03, 137.06, 152.45, 156.66, 160.94, 161.34, 165.05.

III-1 12-((2-Chlorothiazole-5-base)-methyl))-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-diketone

2-chloro-5-chloromethylthiazole (2,34 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 6.27 g of light yellow oil was obtained. 1.46 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids, 816mg of lithium chloride and 10 mL of DMAc were added

into a reaction flask ,the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 2,92 g of light yellow oil was obtained. 180 mg of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 4.89% and in a content of 90.95%. The content was 99.48% after liquid phase purification.

HRMS(ESI): $C_{14}H_{13}ClN_4O_4S$, m/z$[M+Na]^+$: 391.0248;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 3.15-3.16 (m, 1H), 3.25 (d, 1H), 3.40-3.45 (m, 1H), 3.63 (s, 1H), 3.83 (s, 1H), 3.92 (s, 1H), 4.36-4.40 (m, 1H), 4.46 (d, 1H), 5.89 (d, 1H), 7.26 (d, 1H), 7.48 (t, 2H), 11.61 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 65.91, 67.67, 67.74, 70.25, 72.81, 129.14, 132.01, 135.54, 136.38, 138.47, 142.65, 142.81, 143.40, 152.16.

III-2 12-((6-Clopidol-3-base)-methyl))-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-diketone

2-Chloro-5-chloromethylpyridine (2.29 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 8.01 g of light yellow oil was obtained. 2.47 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids, 2.29 g of lithium chloride and 15 mL of DMAc were added into a reaction flask ,the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride

solution in turn, and dried with anhydrous sodium sulfate, 7.10 g of light yellow oil was obtained. 1 g of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 27.62% and in a content of 96.79%. The content was 99.79% after liquid phase purification was preparationed.

HRMS(ESI): $C_{16}H_{15}ClN_4O_4$, m/z$[M+H]^+$: 363.0860;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 3.26 (t, 1H), 3.51 (d, 2H), 3.84-3.93 (m, 2H), 4.37 (dd, 3H), 5.08 (s, 1H), 5.82 (d, 1H), 7.16 (d, 1H), 7.50 (dd, 1H), 7.80 (dd, 1H), 8.28 (t, 1H), 11.67 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 65.35, 111.22, 115.69, 124.09,130.15, 137.95, 141.15, 150.10, 150.87, 152.80, 170.96.

III-3 7-hydroxyl-12-((5-methyl-2-Phenyloxazole-4-base)-methyl))-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-diketone

4-Chloromethyl-5-methyl-2-phenyloxazole (2.89 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 4.27 g of light yellow oil was obtained. 2.23 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids, 1.88 g of lithium chloride and 15 mL of DMAc were added into a reaction flask ,the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 6.95 g of light yellow oil was obtained. 1.02 g of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 25% and in a content of 95.16%. The content was 98.54% after liquid phase purification.

HRMS(ESI): $C_{21}H_{20}N_4O_5$, m/z$[M+H]^+$: 409.1511;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 2.07 (s, 3H), 3.22 (t, 1H), 3.53 (d, 2H), 3.84-3.98 (m, 2H), 4.25 (dd, 3H), 5.18 (d, 1H), 5.90 (d, 1H), 7.18 (d, 1H), 7.51 (dd, 3H), 7.89-7.99 (m, 2H), 11.67 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 9.37, 65.37, 111.33, 125.61, 126.60, 129.01, 129.75, 130.38, 137.92, 148.43, 152.59, 158.94, 169.46, 171.00.

III-4 12-((3,5-Dimethylisoxazole-4-base)-methyl))-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-dikétone

4-Chloromethyl-3,5-dimethylisoxazole (2.04 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 8.20 g of light yellow oil was obtained. 4.22 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids, 4.06 g of lithium chloride and 25 mL of DMAc were added into a reaction flask ,the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 10.24 g of light yellow oil was obtained. 1.16 g of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 33.52% and in a content of 96.93. The content was 99.85% after liquid phase purification.

HRMS(ESI): $C_{21}H_{20}N_4O_5$, m/z$[M+H]^+$: 409.1511;

HRMS(ESI): $C_{16}H_{18}N_4O_5$, m/z$[M+H]^+$: 347.1353;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 2.05 (s, 3H), 2.14 (s, 3H), 3.25 (s, 1H), 3.58 (d,

2H), 3.84-3.86 (m, 2H), 4.13 (s, 2H), 4.42 (s, 1H), 5.04 (s, 1H), 5.89 (s, 1H), 7.07 (s, 1H), 11.76 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 9.95, 10.65, 49.92, 62.08, 66.05, 73.15, 82.55, 101.00, 108.75, 111.98, 138.69, 153.60, 160.11, 168.98, 171.61, 174.39.

III-5 4'-((7-hydroxyl**-6,8-diketone-3,4-Dihydrogen-1*H*-[1,4]-oxazinyl[3,4-c[Pyridyl group[2,1-f][1,2,4]Triazine-12(6H,8H,12aH)-**base**)methyl)-[1,1'-Biphenyl]-4-Acetonitrile**

2-Cyano-4 '- bromomethylbiphenyl (3.80 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 8 g of light yellow oil was obtained. 3.60 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids, 2.93 g of lithium chloride and 30 mL of DMAc were added into a reaction flask, the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 14.72 g of light yellow oil was obtained. 1.72 g of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 40.18% and in a content of 91.42%. The content was 99.65% after liquid phase purification was preparationed.

HRMS(ESI): $C_{24}H_{20}N_4O_4$, m/z$[M+H]^+$: 429.1563;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 3.32 (s, 1H), 3.57 (d, 2H), 3.84-3.95 (m, 2H), 4.38 (s, 3H), 5.06 (s, 1H), 5.81 (d, 1H), 7.13 (d, 1H), 7.46 (d, 2H), 7.54 (d, 2H), 7.61 (dd, 2H), 7.80 (t, 1H), 7.96 (d, 1H), 11.69 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 65.39, 110.15, 118.32, 128.24, 128.75, 129.97, 133.44, 133.74, 137.71, 143.96, 152.83, 170.93.

III-6 12-((5-Chlorothiophene-2-base)-methyl))-7-hydroxyl-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-diketone

2-Chloro-5-chloromethylthiophene (2.33 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 6.27 g of light yellow oil was obtained.

The above solids, 3.81 g of lithium chloride and 30 mL of DMAc were added into a reaction flask, the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 6.74 g of light yellow oil was obtained. 1.16 g of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 16.35% and in a content of 99.16%. The content was 99.95% after liquid phase purification.

HRMS(ESI): $C_{15}H_{14}ClN_3O_4S$, m/z$[M+H]^+$: 368.0469;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 3.21 (td, 1H), 3.49-3.83 (m, 2H), 3.90 (dd, 2H), 4.27 (s, 1H), 4.47 (dd, 2H), 5.07 (d, 1H), 5.88 (t, 1H), 6.79 (d, 1H), 6.97 (d, 1H), 7.21 (d, 1H), 11.66 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 54.81, 65.34, 111.24, 115.43, 126.69, 129.38, 129.53, 136.09, 137.71, 152.80, 170.96.

III-7 7-hydroxyl-12-((5-Methylisoxazole-3-base)-methyl))-3,4,12,12a-Tetrahydrogen-1*H*-[1,4] -oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6,8-diketone

3-Chloromethyl-5-methylisoxazole (1.84 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70

mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 6.27 g of light yellow oil was obtained.

The above solids, 2.11 g of lithium chloride and 15 mL of DMAc were added into a reaction flask, the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 4.46 g of light yellow oil was obtained. 830 mg of light yellow solid was obtained by column chromatography(DCM:CH_3OH=30:1) in a yield of 25% and in a content of 97.23%. The content was 99.85% after liquid phase purification.

HRMS(ESI): $C_{15}H_{16}N_4O_5$, m/z$[M+H]^+$: 333.1190;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 2.50 (d, 3H), 3.21 (td, 1H), 3.52 (dt, 2H), 3.83-3.94 (m, 2H), 4.38 (dt, 3H), 5.09 (d, 1H), 5.92 (d, 1H), 6.31 (s, 1H), 7.30 (d, 1H), 11.58 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 65.28, 102.31, 111.52, 115.14, 137.75, 152.67, 158.73, 170.11, 171.02.

III-8 ((4'-(1*H*-Tetrazole-5-base)-[1,1'-Biphenyl]-4base)methyl)-7-hydroxyl-3,4,12, 12a-Tetrahydrogen-1*H*-[1,4]oxazinyl[3,4-c[Pyridyl group[2,1-f] [1,2,4]Triazine-6, 8-diketone

2-Cyano-4 '- bromomethylbiphenyl (3.80 g, 14 mmol), compound **a** (3.27 g ,10 mmol) , potassium carbonate (1.93 g, 14 mmol) and DMF(30 mL) were added into a reaction flask , react at 50 ℃ for 8 hours with turning on the stirring. When the reaction was completed, 50 mL of water was added into the reaction mixture, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate. 8 g of light yellow oil was obtained. 3.60 g of light yellow solid was obtained by column chromatography(DCM: CH3OH=30:1).

The above solids (1.80 g, 3.5 mmol) and 20 mL of diethylene glycol dimethy were

added into a reaction flask , zinc chloride and sodium azide were added after solution was clarified, after nitrogen protection, the react at 125 ℃ for 35 hours. When the reaction was completed, cool to 10 ℃into the reaction liquid, 30 mL of $NaNO_2$ solution and 30 mL of water were added, 1.5 g of light yellow solid was obtained by filtered and dried.

The above solids,(1.27 g , 30 mmol)of lithium chloride and 30 mL of DMAc were added into a reaction flask, the react at 70 ℃ for 8 hours with turning on the stirring. 50 mL of water was droped into the reaction liquid, 1 M diluted hydrochloric acid was used to adjust the pH of the reaction solution to about 6, 70 mL×2 dichloromethane was used to extraction, and its was washed with water and saturated sodium chloride solution in turn, and dried with anhydrous sodium sulfate, 1.07 g of light yellow oil was obtained. A yield of 26.12% was obtained by column chromatography(DCM:CH_3OH=30:1) in a content of 92.60%.The content was 99.91% after liquid phase purification.

HRMS(ESI): $C_{15}H_{16}N_4O_5$, m/z$[M+H]^+$: 333.1190;

^{1}H-NMR (600 MHz, DMSO-d_6): δ 3.26 (s, 1H), 3.52 (s, 1H), 3.67 (s, 1H), 3.84 (s, 1H), 3.95 (d, 1H), 4.38 (t, 3H), 5.90 (s, 1H), 6.38 (s, 1H), 7.13 (d, 1H), 7.46 (d, 2H), 7.55 (d, 2H), 7.60-7.62 (m, 2H), 7.80 (t, 1H), 7.96 (d, 1H), 11.69 (s, 1H). ^{13}C-NMR (150 MHz, DMSO): δ 65.39, 110.15, 118.32, 128.24, 128.75, 129.97, 133.44, 133.74, 135.41, 137.71, 143.96, 152.83, 169.46, 170.93.