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Synthesis and Insecticidal Activity of New 4-Hydroxy-2H-1-benzopyran-2-one Derivatives

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Abstract Several stable and storable anticoagulant rodenticides involving both merits of acute and chronic rodenticides have been synthesized (Holbrook et al. in Arch Intern Med 165:1095–1106, 2005; Baglin et al. in Br J Haematol 132:277–285, 2006). The structures of synthesized compounds were confirmed by IR, ^{1}H NMR. The compounds were also evaluated for their anticoagulant and acute biologic activity (Lipton et al., JAMA 252:3004–3005, 3).

Keywords Anticoagulant rodenticide · 4-Hydroxy-2H-1-benzopyran-2-one · Cinnamoyl chloride · 4-Bromodiphenyl · Synthesis

Introduction

Nowadays, the continuous search for new anticoagulant rodenticide compounds, driven by resistance problems, speed of action, and the need for environmentally safe rodenticides, has focused recently on the modification of second-generation anticoagulant rodenticides [1–6]. In our lab, we tried to synthesize three novel rodenticides (**N**, **P**, **Q**) by introducing fluoride acetyl group into second-generation anticoagulant rodenticides, and our results showed that the acute toxicity of the compounds were increased, and fluoride acetyl played a magical role to make mice die in the light.

Synthesis of Anticoagulant Rodenticides N, P, Q

Compound **N**, **P**, **Q** were synthesized according to the route of Fig. 1.

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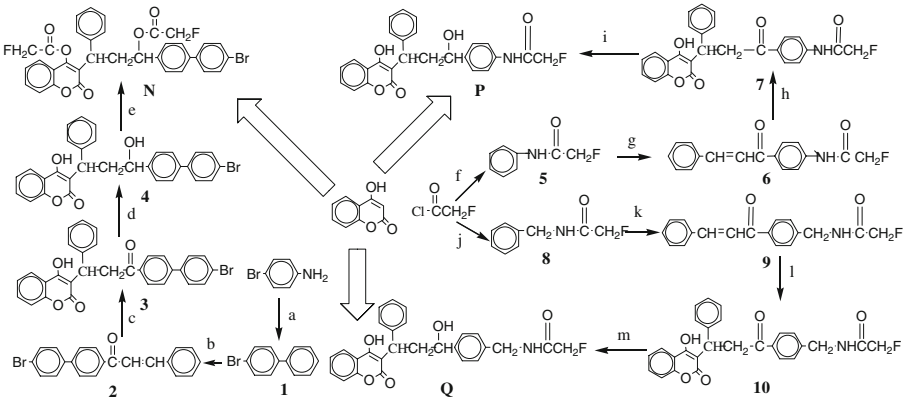

Fig. 1 Synthesis of anticoagulant rodenticide **N**, **P**, **Q**. Reagents and conditions: *a* $HCl/NaNO_2$, C_6H_6, 0~5 °C; *b* cinnamon chloride, $AlCl_3$, 10~15 °C; *c* 4-hydoxycoumarin, 1,4-dioxane, piperidine, reflux; *d* $NaBH_4$, 35 °C; *e* THF, fluoroacetyl chloride, 20 °C; *f* fluoroacetyl chloride, −5~0 °C; *g* aluminum chloride anhydrous, cinnamoyl chloride, reflux; *h* 4-hydoxycoumarin, piperidine, 1,4-dioxane, reflux; *i* $NaBH_4$, 30~33 °C; *j* piperidine, fluoroacetyl chloride, −5~0 °C; *k* aluminum chloride anhydrous, cinnamoyl chloride, reflux, 8 h; *l* 4-hydoxycoumarin, piperidine, 1,4-dioxane, reflux; *m* $NaBH_4$, 25~28 °C

Fluoroacetyl Chloride

PCl_5 (125 g) was stirred for 10 min at 0 °C, and then sodium hydroxide (50 g) was added dropwise. The resulting mixture was stirred at −5~0 °C under the protection of ice bath. After removing the ice bath, the mixture reacted for further 3 h. Distil the mixture by oil bath to collect the distillate before 78 °C and subsequently rectify it to get the distillate between 72 and 73 °C: bp, 72~73 °C; yield, 70.6%.

Cinnamoyl Chloride

Cinnamic acid (25 g) and thionyl chloride (45 g) were added to a 100-mL three-necked flask and stirred for 0.5 h. Superfluous thionyl chloride was braised by reducing the pressure of water pump and cut fraction of 1.47×10^3 Pa and 131 °C was collected: bp, 131 °C; yield, 95.3%; IR (KBr, cm^{-1}) 1,770, 1,600, 1,450, 1,380, 1,230, 780, 710, 430 cm^{-1}; ^1H NMR ($CDCl_3$, δ ppm) 7.14–7.30, (m, 5H, Ph-H), 7.66, (d, H, J =7.4 Hz, CH), 6.28, (d, H, J =9.4 Hz, COCH).

4-Bromodiphenyl (**1**)

4-Bromoaniline (17.2 g) was stirred in 8 mL water. Then, hydrochloric acid was added dropwise, and the resulting mixture was cooled to 0~5 °C. Subsequently, sodium nitrate (7.2 g) dissolved in water (14 mL) was added dropwise into the mixture. Then, the reaction was removed to a 500-mL beaker and cooled by ice bath. Sodium hydroxide (18 mL) was added dropwise into the reaction to get **1**: mp, 90 °C; yield, 89.4%; IR (KBr, cm^{-1}) 1,600, 1,460, 1,380, 1,060, 1,000, 820, 780, 700, 480 cm^{-1}; ^1H NMR ($CDCl_3$, δ ppm) 7.37–7.49, (m, 4H, BrPh-H), 7.23–7.33, (m, 5H, Ph-H).

4-Bromine-4′-cinnamoyl biphenyl (**2**)

4-Bromodiphenyl (23.3 g), cinnamoyl chloride (20 g), and $AlCl_3$ (18 g) were stirred in a 500-mL flask for 1–2 h at 10~15 °C. And then, the reaction was stirred for another 4 h at 20~30 °C. The reactor was subsequently poured into the mixture of hydrochloric acid and ice water to delaminate. After removing organic phase, the remainder was extracted two to three times by ethanol to get **2**: mp, 260 °C; yield, 77.5%; IR (KBr, cm^{-1}) 1,770, 1,600, 1,490, 1,050, 830, 680 cm^{-1}; ^1H NMR ($CDCl_3$, δ ppm) 7.36–7.49, (m, 4H, BrPh-H), 7.67–7.87, (m, 4H, BrPh-Ph-H), 7.13–7.19 (d, 2H, J=7.9 Hz, COCH═CH), 7.15–7.30 (m, 5H, Ph-H).

3-(4-Hydroxyl-2H-1-benzopyran-2-ketone)-3-phenyl-1-(*p*-bromodiphenyl)-1-propyalcohol (**4**)

4-Hydoxycoumarin (8.9 g) was added to a solution of piperidine (5 mL) in 100 mL of 1,4-dioxane. After stirring for 1 h, **2** (18.2 g) was added, and the mixture was refluxed for further 7 h. The reaction mixture was evaporated, and the remainder was washed with ethanol and water and dried over magnesium sulfate to get **3**. Then, compound **3** (10.5 g) and sodium borohydride (0.78 g) were added to a 150-mL flask and heated to reflux for 1 h. Water was added, and the remainder was extracted by chloroform, ethanol to get **4**: mp, 180 °C; yield, 41.5%; IR (KBr, cm^{-1}) 3,583, 3,219, 2,917, 1,667, 1,619, 1,491, 1,110, 810, 710, 700 cm^{-1}; ^1H NMR ($CDCl_3$, δ ppm) 15.0, (s, 1H, OH-H), 7.01–7.27, (m, 4H, (4-hydroxy-2H-1-benzopyran-2-one)-H), 7.12–7.21, (m, 5H, Ph-H), 7.37–7.49, (m, 4H, BrPh-H), 7.26–7.41, (m, 4H, BrPh-Ph-H), 2.10, (d, H, J=7.9 Hz, CH-H), 2.0, (s, H, OH-H).

Anticoagulation Rodenticide (**N**)

A solution of fluoroacetyl chloride (12.50 g) was added in portions to a solution of **4** (10.00 g) in dry tetrahydrofuran (100 mL). Subsequently, the reaction mixture was stirred and refluxed for 4 h at 20 °C. The reaction mixture was evaporated, and remainder was washed with sodium hydroxide and water and dried over magnesium sulfate to get **N**; mp, 190 °C; yield, 78.5%; IR (KBr, cm^{-1}) 2,920, 1,760, 1,680, 1,600, 1,460, 1,360, 1,200, 1,100, 1,050, 800, 780 cm^{-1}; ^1H NMR ($CDCl_3$, δ ppm) 7.01–7.13, (m, 4H, (4-hydroxy-2H-1-benzopyran-2-one)-H), 7.10–7.21, (m, 5H, Ph-H), 7.37–7.49, (m, 4H, BrPh-H), 7.26–7.41, (m, 4H, BrPh-Ph-H), 5.24, (s, H, OCH-H), 5.03–5.05, (s, 2H, CH_2F), 3.45, (s, H, CH-H).

Fluoride Acetanilide (**5**)

Frozen aniline (42 g) was added to 100 mL cold benzene. Fluoroacetyl chloride (41 g) was added dropwise by constant pressure filter, and the mixture was stirred for 2 h at 0 °C. After evaporation of solvent, the remainder was purified with acetone and water and dried to get **5**: mp, 80 °C; yield, 29.5%; IR (KBr, cm^{-1}) 3,356, 2,360, 2,343, 1,676.5, 1,607, 1,541, 1,500, 1,446, 1,327, 1,047, 754, 696 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 8.01 (s, 1H, NH), 7.06–7.70 (m, 5H, ArH), 4.97 (d, 2H, J=32.0 Hz, CH_2F).

4-Cinnamic Acid-Fluoride Acetanilide (**6**)

Fluoride acetanilide (15 g), $AlCl_3$ (133 g), and cinnamoyl chloride (33 g) were added to 150 mL dried CS_2. Then, ice bath was removed, and the mixture was heated slowly to reflux for 1 h. The mixture was kept still for 3 h. Then, organic phase of CS_2 was removed,

and red residues were extracted with cold hydrochloric acid (10 mL), purified with ethanol and water, and dried over magnesium sulfate to get **6**: mp, 105 °C; yield, 63.4%; IR (KBr, cm^{-1}) 3,355, 1,760, 1,686, 1,528, 1,221, 1,039, 973, 766, 691 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 8.01 (s, 1H, NH), 7.06–7.70 (m, 5H, ArH), 4.97 (d, 2H, J=32.0 Hz, CH_2F).

3-{2-[4-(4-Fluoroacetamidomethyl)phenyl]
benzoyl-1-phenylethyl}-4-hydroxy-2H-1-aniline-2-one (**7**)

4-Hydroxycoumarin (3.5 g) was added to a solution of piperidine (5 mL) in 100 mL of 1,4-dioxane and stirred for 1 h. Then, 4-cinnamic acid-fluoride acetanilide **6** was added to the mixture and refluxed for further 9 h. The reaction mixture was evaporated, and the remainder was recrystallized with ethanol, washed with saturated brine, and dried over magnesium sulfate to get **7**: mp, 121~122 °C; yield, 57.7%; IR (KBr, cm^{-1}) 3,330, 1,770, 1,689, 1,552, 1,495, 1,452, 1,039, 965, 840, 758, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 14.8 (s, 1H, OH), 8.0 (s, 1H, NH), 7.03–7.74 (m, 13H, J=7.2, ArH), 4.99 (d, 2H, J=33.2 Hz, CH_2F), 3.98 (t, 1H, J=7.5 Hz, CH), 2.76–3.02 (d, 2H, J= 7.2 Hz, CH_2).

Anticoagulation Rodenticide (**P**)

Compound **7** (25 g) was dissolved in 100 mL of dried ethanol. Sodium hydroxide (0.3 g) was added quickly at 15 °C, and mixture was stirred for 15 min. Then, $NaBH_4$ (4.5 g) was added dropwise, and the resulting mixture was stirred for a further 3 h at 30~33 °C. The remainder was purified with low concentration hydrochloric acid to pH 2 and subsequently poured into ice water and stayed still for 24 h. Then, organic phase was extracted three times with ethanol, washed with brine, and dried over magnesium sulfate to get final product **P**: mp, 135~136 °C; yield, 59.6%; IR (KBr, cm^{-1}) 3,411, 3,060, 1,700, 1,681, 1,530, 1,493, 1,452, 1,110, 1,037, 965, 840, 758, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 15.0 (s, 1H, OH), 8.0 (s, 1H, NH), 7.03–7.58 (m, 13H, J=7.2 Hz, ArH), 5.02 (d, 2H, J=33.2 Hz, CH_2F), 4.51 (t, 1H, J=7.5 Hz, CH), 2.1 (d, 2H, J=11.2 Hz, CH_2),2.0 (s, 1H, OH).

Fluoride Acetyl Benzylamine (**8**)

Benzylamine (32 g) was added to a solution of piperidine (5 mL) in 100 mL of dried benzene after cooling by ice water for 2 h. Fluoroacetyl chloride (26 g) was added dropwise by constant pressure filter, and mixture was stirred for 3 h at −5~0 °C. The remainder was purified with acetone and water and dried over magnesium sulfate to get **8** as a pale yellow solid: mp, 83 °C; yield, 76.3%; IR (KBr, cm^{-1}) 3,312, 2,976, 2,936, 2,365, 1,655, 1,549, 1,358, 1,250, 1,037, 744, 698, 603 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 8.02 (s, 1H, NH), 7.06–7.70 (m, 5H, ArH), 4.99 (d, 2H, J=32.0 Hz, CH_2F), 4.45 (q, 2H, J=6.8 Hz, CH_2).

4-Cinnamic Acid-Fluoride Acetyl Benzylamine (**9**)

Fluoride acetyl benzylamine (15 g), $AlCl_3$ (130 g), and cinnamoyl chloride (35 g) were added to 150 ml of dried CS_2. Then, ice bath was removed, and the mixture was heated slowly to

Table 1 Lab comparison experiment on the efficiency of compounds **N**, **P**, **Q** and notable existing rodenticides.

Time (days)	1% zinc phosphide			0.025% diphacinone			0.025% warfarin			0.005% bromadiolone
	Mortality (%)	LD_{50}	Palatability	Mortality (%)	LD_{50}	Palatability	Mortality (%)	LD_{50}	Palatability	Mortality (%)
1	10	27.9 (mg/kg)	0.60	0	2.5 (mg/kg)	0.38	0	3.0 (mg/kg)	0.64	0
2	80			0			0			0
3	80			0			0			10
4	80			10			10			10
5	80			20			10			30
6	80			60			50			80
7	80			80			70			90

Time (days)	0.005% bromadiolone		0.005% compound **N**			0.005% compound **P**			0.005% compound **Q**		
	LD_{50}	Palatability	Mortality (%)	LD_{50}	Palatability	Mortality (%)	LD_{50}	Palatability	Mortality (%)	LD_{50}	Palatability
1	1.25 (mg/kg)	0.81	0	0.693 (mg/kg)	0.72	0	0.72 (mg/kg)	0.84	0	0.71 (mg/kg)	0.86
2			50			40			40		
3			90			70			60		
4			90			90			80		
5			100			100			90		
6			100			100			100		
7			100			100			100		

reflux for 1.5 h. After removing organic phase, the red residue was extracted with hydrochloric acid (10 mL), purified with ethanol and water and dried over magnesium sulfate to get **9**: mp, 110 °C; yield, 69%; IR (KBr, cm^{-1}) 3,310, 1,765, 1,688, 1,530, 1,358, 1,050, 750, 689 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 8.01 (s, 1H, NH), 7.14–7.70 (m, 9H, ArH), 7.15–7.19 (t, 2H, J=12.0 Hz, CH=CH), 4.99 (d, 2H, J=32.0 Hz, CH_2F), 4.62 (d, 2H, J=26.0 Hz, CH_2).

-{2-[4-(4-Fluoroacetamidomethyl)phenyl]
benzoyl-1-phenylethyl}-4-hydroxy-2H-1-benzopyran-2-one (**10**)

4-Hydroxycoumarin (3.5 g) was added to a solution of piperidine (5 mL) in 100 mL of 1,4-dioxane and stirred for 1 h. Then, **9** was added to the mixture and refluxed for further 8 h. The reaction was evaporated, and the remainder was recrystallized with ethanol, washed with saturated brine, and dried over magnesium sulfate to get **10**: mp, 127~128 °C; yield, 61%; IR (KBr, cm^{-1}) 3,310, 1,769, 1,685, 1,554, 1,496, 1,455, 1,050, 964, 855, 760, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 14.9 (s, 1H, OH), 8.0 (s, 1H, NH), 7.02–7.76 (m, 13H, J=9.2 Hz, ArH), 4.99 (d, 2H, J=27.2 Hz, CH_2F), 4.45 (d, 2H, J=7.2 Hz, CH_2), 3.97 (t, 1H, J=7.5 Hz, CH), 2.75–3.02 (t, 2H, J=7.2 Hz, CH_2).

Anticoagulation Rodenticide (**Q**)

Compound **10** (25 g) was dissolved in 100 mL of dried ethanol. Sodium hydroxide (0.3 g) was added quickly at 20 °C, and the mixture was stirred for 15 min. Then, $NaBH_4$ (4.3 g) was added dropwise, and resulting mixture was stirred for a further 2 h at 25~28 °C. The remainder was purified with low concentration hydrochloric acid to pH 2 and subsequently poured into ice water to stay still for 24 h. Then, organic phase was extracted with ethanol, washed with brine, and dried over magnesium sulfate to get final product **Q**: mp, 141~142 °C; yield, 79%; IR (KBr, cm^{-1}) 3,400, 3,050, 1,701, 1,677, 1,543, 1,496, 1,454, 1,110, 1,050, 964, 855, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 300 Hz, δ ppm) 15.0 (s, 1H, OH), 8.0 (s, 1H, NH), 6.98–7.28 (m, 13H, J=7.2 Hz, ArH), 4.99 (d, 2H, J=33.2 Hz, CH_2F), 4.45 (d, 2H, J=11.2 Hz, CH_2), 3.55 (t, 1H, J=7.5 Hz, CH), 2.1 (d, 2H, J=11.2 Hz, CH_2), 2.0 (s, 1H, OH).

Biological Assays

Materials and Methods

Test animals were laboratory-bred, wild-type, white, male and female mice weighing 151–171 g drawn from the Liaoning Center for Disease Control and Prevention (CDC) on standard rat feed [7].

Test chemicals were zinc phosphide, diphacinone, warfarin, and bromadiolone. And, novel anticoagulant rodenticides **N**, **P**, **Q** were synthesized in our laboratory [8].

Table 2 The number of dead rodents found in the light (field test).

Time	1 day	2 days	3 days	4 days	5 days	6 days	7 days
Greenhouse 1	0	0	0	0	1	1	2
Greenhouse 2	0	6	8	6	2	1	0

Table 3 Choice experiment of compound **N**, **P**, **Q**.

Compound **N**						Compound **P**					Compound **Q**				
No.	Bait consumption *g*/20 g weight	No bait consumption *g*/20 g weight	Mortality *P*%	Palatability *K*	Average *k*	Bait consumption *g*/20 g weight	No bait consumption *g*/20 g weight	Mortality *P*%	Palatability *K*	Average *k*	Bait consumption *g*/20 g weight	No bait consumption *g*/20 g weight	Mortality *P*%	Palatability *K*	Average *k*
1	1.21	1.59	100	0.761		1.58	2.32	100	0.74		1.64	2.30	100	0.75	
2	1.11	1.64	100	0.677		1.50	1.87	100	0.8		1.57	1.90	100	0.81	
3	1.09	1.54	100	0.708		1.55	1.89	100	0.82		1.59	1.88	100	0.83	
4	1.26	1.76	100	0.716	0.72	1.62	2.10	100	0.78	0.84	1.65	2.08	100	0.79	0.86
5	1.30	1.80	100	0.72		1.70	1.81	100	0.94		1.73	1.81	100	0.95	
6	1.33	1.82	100	0.731		1.75	1.94	100	0.90		1.77	1.93	100	0.90	
7	1.39	1.89	100	0.740		1.65	2.12	100	0.78		1.69	2.12	100	0.78	
8	1.46	2.12	100	0.69		1.68	1.91	100	0.88		1.69	1.91	100	0.89	
9	1.53	2.09	100	0.73		1.74	2.07	100	0.84		1.79	2.07	100	0.85	

Bioactivity Assays

In the no-choice and choice experiments, compounds **N**, **P**, **Q** were applied as rodenticide bait of laboratory-prepared. Laboratory-bred type, white, male and female mice weighing 151-171 g were drawn from the Liaoning Center for Disease Control and Prevention (CDC) on standard rat feed. In the no-choice experiment of each new compound, mice were divided into ten groups, and each group had five males and five females. Baits comprised about 65% corn, 25% oats, 5% corn oil, and 5% sugar and different ratio of **N**, **P**, **Q** were prepared. In the choice experiment, mice were divided into ten groups, and each group had five males and five females. Baits comprised 65% corn, 25% oats, 5% corn oil, and 5% sugar and 0.005% **N**, **P**, **Q** were prepared. In the comparison experiment of the new compounds to notable existing rodenticides, mice were divided into seven groups, and each group had five males and five females. Baits comprised about 65% corn, 25% oats, 5% corn oil, and 5% sugar and different ratios of zinc phosphide, diphacinone, warfarin, bromadiolone, and **N**, **P**, **Q** were prepared. At first, mice received the same treatment as in the breeding compartments: whole barley, alfalfa, and pieces of carrots, with straw bedding. Then, they were baited with treated or untreated test diet until it was consumed totally. During the baiting period, they had no food or bedding (no-choice experiment), apart from a piece of carrot as a source of water. In each experiment, all the mice were offered identical amount of bait per unit of body weight. To achieve this, all the baits were cut into proper weight. The remaining bait was weighed daily. When the mice finished the dose offered, the ordinary food and bedding were replaced. In the case where the mice did not finish the experimental dose after 96 h, the experimental food was replaced with the ordinary food. The temperature ranged from 15 to 30 °C, with a 12/12-h day/night cycle. In the field test, bromadiolone and compound **N** were tested in two greenhouses, which have similar rodents' density (21% and 20%, respectively). Bromadiolone (0.005%) was used in greenhouse 1, and compound **N** with the same concentration was used in greenhouse 2 [9].

Results and Discussions

The statistics of Tables 1, 2, 3, 4, 5, and 6 demonstrates that the introduction of fluoride acetyl into the bromine position of the bromodialone leads to an enormous increase in the

Table 4 No-choice experiment of compound **N**.

No.	***N***/mg/kg	White mice	Death	Mortality *p* (%)	Survive *g* (%)
1	0.38	10	2	20	80
2	0.60	10	4	40	60
3	0.84	10	5	50	50
4	1.09	10	8	80	20
5	1.55	10	8	90	10
6	1.60	10	9	90	10
7	1.69	10	10	100	0
8	1.71	10	10	100	0
9	1.80	10	10	100	0
10	1.91	10	10	100	0

LD_{50}=0.693 mg/kg

Table 5 No-choice experiment of compound **P**.

No.	*M*/mg/kg	White mice	Death	Mortality *p* (%)	Survive *g* (%)
1	0.39	10	2	20	80
2	0.54	10	4	40	60
3	0.78	10	5	50	50
4	1.10	10	8	80	20
5	1.56	10	8	90	10
6	1.61	10	9	90	10
7	1.65	10	10	100	0
8	1.70	10	10	100	0
9	1.79	10	10	100	0
10	1.90	10	10	100	0

LD_{50}=0.72 mg/kg

acute toxicity. The novel compounds **N**, **P**, **Q** have both merits of acute and chronic rodenticides, and their acute toxicity increases gradually with the decrease of the group connected to fluoride acetyl [10].

The results of oral LD_{50} values for compound **N**, **P**, **Q** are 0.693, 0.72, 0.71 mg/kg, respectively, which mean that the acute toxicity of **N**, **P**, **Q** have been strengthened greatly. The ingestion coefficients are 0.72, 0.84, 0.86, respectively, which suggest that their baits have a good taste to the rodents, and they would be promising candidates of rodenticides. The results of field test showed that these new compounds play a magic role to make mice die in the light [11]. Our further research shows that the principle of this phenomenon is due to the fluoride acetyl group, which causes rodents to suffocate from oxygen and run out of their nests. Our corresponding data also showed that the mortality pattern of new compounds were affected by the increase in concentration, that is, new compounds show both acute and chronic rodenticide advantages in higher concentration, but have obvious chronic traits in low concentration.

Table 6 No-choice experiment of compound **Q**.

No.	*M*/mg/kg	White mice	Death	Mortality *p* (%)	Survive *g* (%)
1	0.40	10	2	20	80
2	0.56	10	4	40	60
3	0.80	10	5	50	50
4	1.14	10	8	80	20
5	1.58	10	8	90	10
6	1.65	10	9	90	10
7	1.67	10	10	100	0
8	1.72	10	10	100	0
9	1.81	10	10	100	0
10	1.90	10	10	100	0

LD_{50}=0.71 mg/kg

Conclusion

Second-generation anticoagulant rodenticides such as bromodialone and diphacinone have been known for almost 40 years to be very active against rodents. In this paper, we have demonstrated that the introduction of fluoride acetyl group into molecular structure of second-generation anticoagulant rodenticide leads to a distinct increase in the rodenticide efficacy. The novel anticoagulant rodenticides **N**, **P**, **Q** researched on the basis of the in-depth optimization study displays outstanding activity against rodents and combined with excellent efficacy on preventing environment pollution. So, these novel rodenticides **N**, **P**, **Q** would be promising candidates of rodenticide in agrochemical market especially in the urban rodent control.

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