

新型嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶衍生物的合成与除草活性林海^a 聂会祥^a 赵安林^a 王涛^{*,a} 罗劲^{*,b}^(a)江西师范大学化学化工学院 江西省化学生物学重点实验室 南昌 330022)^(b)江西师范大学分析测试中心 南昌 330022)

摘要 为了寻找结构新颖且具有优异除草活性的含氮稠杂环化合物,以 2-烷硫基-5-氰基-6-硫甲基嘧啶-4-胺为原料合成了 42 个新型的嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶衍生物消旋体(**I-1**~**I-42**),其结构经熔点、¹H NMR、¹³C NMR、红外吸收光谱法(IR)和高分辨质谱(HRMS)确证。初步的除草活性测试表明,在浓度为 100 mg/L 时,大部分化合物对单子叶植物(小麦、稗草和高粱)和双子叶植物(萝卜、油菜和黄瓜)表现出显著的除草活性,特别是化合物 **I-13**, **I-14**, **I-23**, **I-25** 和 **I-30**~**I-42** 对 6 种供试植物的根和茎长抑制率都达到了 100%。

关键词 嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶;合成;除草活性

Synthesis and Herbicidal Activity of Novel Pyrimido[5,4-*e*]-[1,2,4]triazolo[1,5-*c*]pyrimidine DerivativesLin, Hai^a Nie, Huixiang^a Zhao, Anlin^a Wang, Tao^{*,a,b} Luo, Jin^{*,b}^(a) Jiangxi Province Key Laboratory of Chemical Biology, College of Chemistry and Chemical Engineering, Jiangxi Normal University, Nanchang 330022)^(b) Analytical and Testing Center, Jiangxi Normal University, Nanchang 330022)

Abstract To discover *N*-containing fused heterocyclic compounds with novel structure and excellent herbicidal activity, forty-two pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine derivatives (**I-1**~**I-42**) were synthesised using 2-(alkylthio)-5-carbonitrile-6-(methylthio)pyrimidine-4-amino as starting materials. Their structures were clearly confirmed by melting point, ¹H NMR, ¹³C NMR, infrared absorption spectroscopy (IR), and high-resolution mass spectra (HRMS). The preliminary bioassay indicated that many target compounds exhibited remarkable herbicidal activities against the monocotyledons (*Triticum aestivum* L., *Echinochloa crusgalli*, and *Sorghum bicolor*) and dicotyledons (*Raphanus sativus*, *Brassica campestris*, and *Cucumis sativus*) at the concentration of 100 mg/L. Especially, compounds **I-13**, **I-14**, **I-23**, **I-25** and **I-30**~**I-42** showed excellent herbicidal activities against the roots and stalks of the six test plant at 100 mg/L with 100% inhibition rates.

Keywords pyrimido[5,4-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine; synthesis; herbicidal activity

含氮杂环化合物是一类重要的有机化合物,在生物化学和药物化学的发展中起着至关重要的作用。含氮杂环广泛分布在自然界中,并且是维生素、核酸、抗生素和染料等的重要结构单元^[1-5]。在过去的几十年里,探索和开发具有优异生物和药理活性的含氮杂环化合物一直是研究热点^[6-11]。有关含氮杂环化合物的研究也趋向于结构复杂的双杂环和多杂环化合物^[12-17]。

作为一类含氮稠杂环化合物,嘧啶并三唑并嘧啶衍生物受到的关注比较少,只有少数文献报道了它们的合

成及生物活性。Giudice 等^[18]以 4-氨基-5-氰基嘧啶为原料合成了 4 个嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶化合物。Rahimizadeh 等^[19]利用嘧啶并嘧啶中间体与三乙基原酸酯的乙酸溶液在回流下反应得到了一系列嘧啶并[4,5-*d*][1,2,4]三唑并[4,3-*a*]嘧啶衍生物,这些化合物表现出很好的荧光性能。2016 年,Abdelhamid 等^[20]通过 7-硫酮-5,6,7,8-四氢嘧啶并[4,5-*d*]嘧啶-二酮与氯代脒在氯仿为溶剂、三乙胺为催化剂、回流的条件下反应,制备了 2 个嘧啶并[5,4-*e*][1,2,4]三唑并[4,3-*a*]嘧啶化合物,并

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测试了它们的抗菌活性. 尽管这些课题组成功地合成了一些嘧啶并三唑并嘧啶衍生物, 但关于这类化合物, 特别是嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶的研究仍然缺乏. 因此, 嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶衍生物的合成和生物活性具有广阔的研究价值.

嘧啶是一类重要的含氮杂环化合物, 具有广谱的生物活性, 如杀虫、杀菌、除草、抗癌和抗病毒等被广泛地应用于医药和农药领域^[21]. 目前, 含嘧啶结构的除草剂非常多, 包括乙酰乳酸合成酶(ALS 酶)抑制剂嘧草硫醚、环酯草醚、氯吡嘧磺隆、双氯磺草胺、磺草唑啉以及唑嘧磺草胺等. 含嘧啶结构的除草剂具有高效低毒、环境友好等特点, 一直备受关注, 相关报道也层出不穷. 本课题组^[22-24]曾以 2-烷硫基-5-氰基-6-硫甲基嘧啶-4-胺为原料, 制备了数十个含 1,2,4-三唑的嘧啶化合物, 并发现有些化合物表现出较好的除草活性. 为了继续寻找具有超高效除草活性的含氮稠杂环化合物, 本工作应用生物活性亚结构拼接原理, 将嘧啶亚结构和三唑并嘧啶亚结构合并到一个分子中, 设计合成了一系列嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶衍生物消旋体, 测试了它们的除草活性, 并讨论了构效关系.

1 结果与讨论

1.1 目标化合物的合成

中间体和目标化合物的合成路线如 Scheme 1 所示. 中间体 **1**、**2** 和 **3** 根据本课题组以前的文献报道合成^[21-23]. 为了得到高收率的目标化合物, 根据文献报道^[25], 本工作以 2-乙硫基-6-甲硫基-5-[3-(3-三氟甲基苯氧甲基)-1*H*-1,2,4-三唑]-嘧啶-4-胺(**3a**)和丙醛为模板, 筛选了金属盐催化剂、溶剂、温度及时间对反应的影响, 结果见表 1.

首先, 考察了金属盐催化剂对反应的影响. 结果显

示, 四氯化锆的催化下得到产物的收率为 85% (Entry 7, 表 1), 而其他的催化剂如氯化铜、硫酸铜、氯化铁和氯化亚铁等收率比较低(Entries 1~6, 表 1). 接着, 考察了溶剂对反应的影响. 当溶剂为四氢呋喃、二氯甲烷、丙酮和乙腈时, 产物收率比乙醇为溶剂时都要低很多(Entries 8~11, 表 1). 最后, 考察了温度和时间对反应的影响. 温度低于 80 °C 及延长或缩短反应时间, 产物的收率都会下降(Entries 12~16, 表 1). 因此, 得出模板反应的最佳反应条件是: 以四氯化锆为催化剂, 乙醇为溶剂, 80 °C 和 5 h. 在最佳反应条件下共合成了 42 个未见文献报道的嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶化合物消旋体(**I-1**~**I-42**).

1.2 波谱分析

以目标化合物 **I-2** 为例, 在 ¹H NMR 中, 化学位移 δ 6.93 处的单峰对应于嘧啶环上的氮氢, 而化学位移 δ 6.07 处的多重峰对应于嘧啶环上的碳氢, 氧亚甲基氢的化学位移在 δ 5.27 呈单峰, 硫甲基氢的化学位移在 δ 2.62 为单峰. ¹³C NMR 中, δ 63.96 处的峰对应于氧亚甲基碳, 硫甲基碳的吸收峰在 δ 13.01, 硫乙基碳的吸收峰在 δ 14.76 和 25.41, 嘧啶上丙基碳的吸收峰在 δ 13.48, 16.36 和 39.29. ¹⁹F NMR 中, -62.65 处的峰对应于三氟甲基. 高分辨质谱(HRMS)计算值(m/z 497.1405)和实测值(m/z 497.1411)误差在 $m/z \pm 0.0010$ 以内.

1.3 除草活性

按照文献[26]描述的离体培养平皿法测试了目标化合物在浓度为 10 和 100 mg/L 时对单子叶植物(小麦、稗草和高粱)和双子叶植物(萝卜、油菜和黄瓜)茎长和根长的抑制率(%), 对照药为除草剂唑嘧磺草胺, 结果见表 2.

由表 2 数据可知: 浓度为 100 mg/L 时, 大部分目标

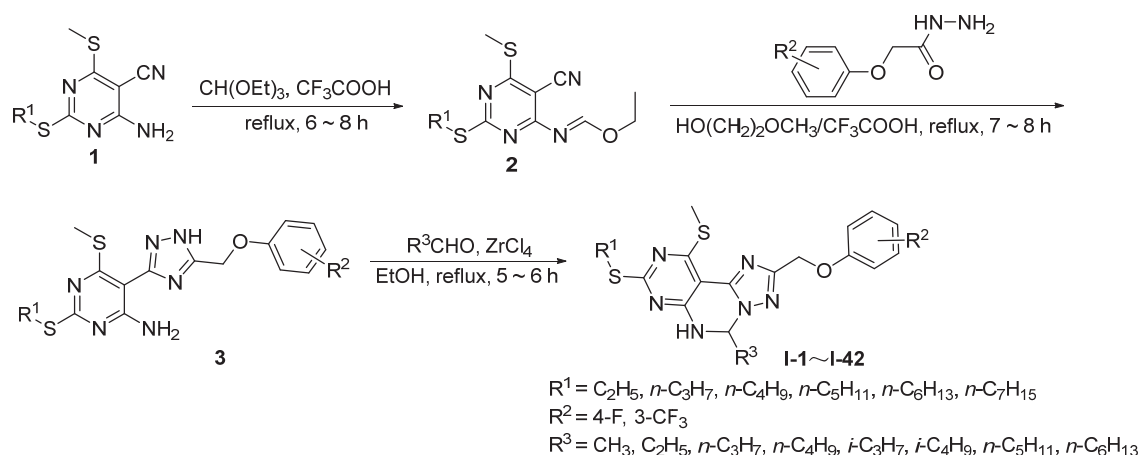
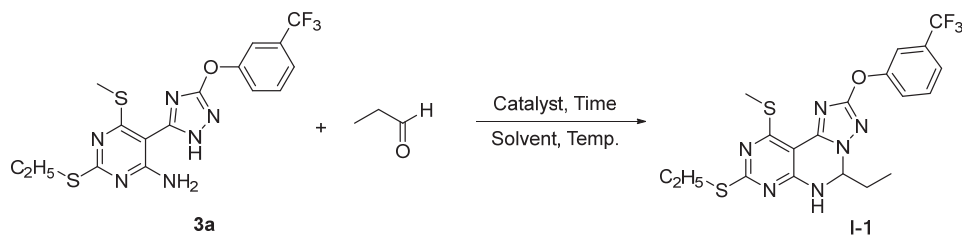


图 1 目标化合物 **I-1**~**I-42** 的合成路线
Scheme 1 Synthetic route of the target compounds **I-1**~**I-42**

表 1 反应条件的筛选^a
Table 1 Screening of reaction conditions



Entry	Catalyst	Solvent	<i>T</i> /°C	<i>t</i> /h	Yield ^b /%
1	—	乙醇	80	5	0
2	氯化铜	乙醇	80	5	26
3	硫酸铜	乙醇	80	5	0
4	醋酸铜	乙醇	80	5	0
5	氯化亚铁	乙醇	80	5	18
6	氯化铁	乙醇	80	5	31
7	四氯化锆	乙醇	80	5	85
8	四氯化锆	二氯甲烷	80	5	46
9	四氯化锆	四氢呋喃	80	5	69
10	四氯化锆	丙酮	80	5	51
11	四氯化锆	乙腈	80	5	43
12	四氯化锆	乙醇	60	5	28
13	四氯化锆	乙醇	40	5	10
14	四氯化锆	乙醇	80	6	84
15	四氯化锆	乙醇	80	7	82
16	四氯化锆	乙醇	80	4	73

^a Reaction conditions: **3a** (1.0 mmol), propanal (1.5 mmol), solvent (10 mL), metal catalyst (0.1 mmol). ^b Isolated yields.

化合物对单子叶植物(小麦、稗草和高粱)和双子叶植物(萝卜、油菜和黄瓜)的根和茎的抑制效果非常明显,其中, **I-13**, **I-14**, **I-23**, **I-25** 和 **I-30~I-42** 对 6 种供试植物的根和茎的抑制率都达到了 100%; **I-1**, **I-3~I-12**, **I-16**, **I-17**, **I-19**, **I-20~I-22**, **I-24**, **I-26** 和 **I-28** 对油菜的根和茎的抑制率达到了 100%; **I-10**, **I-20**, **I-21** 和 **I-24** 对稗草的根和茎的抑制率达到了 100%; **I-4**, **I-7**, **I-8**, **I-11**, **I-12**, **I-16**, **I-20~I-22**, **I-24**, **I-26**, **I-27** 和 **I-29** 对黄瓜的根和茎的抑制率达到了 100%; **I-3**, **I-4**, **I-6~I-12**, **I-15~I-22**, **I-24**, **I-26**, **I-27** 和 **I-29** 对小麦的根和茎的抑制率达到了 100%; **I-3**, **I-4**, **I-7**, **I-10~I-12**, **I-16**, **I-17**, **I-19**, **I-22**, **I-24**, **I-26** 和 **I-29** 对高粱的根和茎的抑制率达到了 100%; **I-1~I-12**, **I-15~I-17**, **I-19**, **I-20**, **I-22** 和 **I-26~I-29** 对萝卜的根和茎的抑制率达到了 100%; **I-2** 对油菜的根和茎的抑制效果优于阳性对照药唑啉磺草胺。浓度为 10 mg/L 时, 供试化合物的除草活性均明显下降, 只有少数化合物表现出很好的除草活性, 如 **I-3**, **I-7** 和 **I-18** 对油菜的根和茎的抑制率高达 100%; **I-19** 完全抑制了稗草的根和茎的生长; **I-4** 和 **I-9** 对萝卜的根和茎的抑制率达到了 100%; **I-15** 完全抑制了高粱和萝卜的根和茎的生

长; **I-16** 完全抑制了油菜和稗草的根和茎的生长; **I-21** 对高粱和油菜的根和茎呈现出 100%抑制; **I-5** 和 **I-22** 对油菜和萝卜的根和茎达到了 100%抑制; **I-35** 和 **I-37** 对黄瓜和萝卜的根和茎的抑制率也达到了 100%; **I-38** 对小麦和高粱的根和茎达到了 100%抑制; **I-2**, **I-4**, **I-6**, **I-8~I-10**, **I-12~I-15**, **I-23**, **I-32**, **I-33**, **I-38**, **I-39** 和 **I-41** 对油菜的根的抑制率高于阳性对照药; **I-5**, **I-6**, **I-9~I-11**, **I-13~I-15** 和 **I-21** 对稗草的根的抑制率比阳性对照药高; **I-6** 和 **I-17** 对黄瓜的根的抑制作用比阳性对照药好; **I-18** 对萝卜的根达到了 100%抑制。总体上看, 高浓度时抑制效果比低浓度时更好, 对根的抑制作用普遍优于对茎的抑制作用。

由构效关系可知, 浓度为 100 mg/L 时, R^1 为 *n*-Bu、 R^2 为 3- CF_3 、 R^3 为 *n*- C_5H_{11} 或 *n*- C_6H_{13} 时, R^1 为 Et、 R^2 为 4-F、 R^3 为 Et 或 *n*-Bu 时, R^1 为 *n*-Pr~*n*- C_7H_{15} 、 R^2 为 4-F、 R^3 为 Me~*n*- C_6H_{13} 时, 目标化合物对单双子叶植物的根和茎的抑制活性优于其他化合物且为非选择性; 当 R^2 为 4-F 时, 目标化合物的除草活性明显比 3- CF_3 好; R^1 为乙基和丙基、 R^2 为 3- CF_3 时, 目标化合物对稗草、黄瓜、小麦和高粱的抑制活性相对较差。浓度为 10 mg/L

表2 化合物 I-1~I-42 对单、双子叶植物的除草活性抑制率(%)
Table 2 Inhibition percentage (%) of compounds I-1~I-42 to monocotyledons and dicotyledons

Compd.	R ¹	R ²	R ³	浓度/(mg·L ⁻¹)	油菜根/茎	稗草根/茎	黄瓜根/茎	小麦根/茎	高粱根/茎	萝卜根/茎
I-1	Et	3-CF ₃	Et	100	100/100	70/—25	61/—10	52/20	69/16	100/100
				10	76/—112	54/—10	45/30	29/2	80/27	35/—2
I-2	Et	3-CF ₃	<i>n</i> -Pr	100	87/100	45/—19	46/20	40/14	64/22	100/100
				10	61/—141	64/—34	58/5	22/2	68/28	100/100
I-3	Et	3-CF ₃	<i>n</i> -Bu	100	100/100	73/11	77/11	100/100	100/100	100/100
				10	100/100	64/—13	51/34	31/7	84/45	13/—5
I-4	<i>n</i> -Pr	3-CF ₃	Et	100	100/100	94/31	100/100	100/100	100/100	100/100
				10	91/—167	80/—20	58/19	69/7	85/2	100/100
I-5	<i>n</i> -Pr	3-CF ₃	<i>i</i> -Pr	100	100/100	84/16	69/32	66/—17	82/30	100/100
				10	100/100	86/—26	43/10	—20/—5	73/24	100/100
I-6	<i>n</i> -Pr	3-CF ₃	<i>i</i> -Bu	100	100/100	80/12	64/5	100/100	90/27	100/100
				10	78/—90	100/11	85/5	45/—5	48/6	100/100
I-7	<i>n</i> -Bu	3-CF ₃	Me	100	100/100	90/—7	100/100	100/100	100/100	100/100
				10	100/100	56/—30	54/36	27/24	75/33	37/11
I-8	<i>n</i> -Bu	3-CF ₃	Et	100	100/100	82/8	100/100	100/100	92/61	100/100
				10	84/—107	69/—1	49/20	46/2	83/30	36/—16
I-9	<i>n</i> -Bu	3-CF ₃	<i>n</i> -Pr	100	100/100	87/14	65/13	100/100	91/51	100/100
				10	84/—162	80/10	64/22	10/1	62/16	100/100
I-10	<i>n</i> -Bu	3-CF ₃	<i>n</i> -Bu	100	100/100	100/100	78/—13	100/100	100/100	100/100
				10	81/—107	87/5	45/39	2/7	67/25	63/59
I-11	<i>n</i> -Bu	3-CF ₃	<i>i</i> -Pr	100	100/100	84/5	100/100	100/100	100/100	100/100
				10	53/—183	80/19	37/34	13/—6	64/12	—52/—7
I-12	<i>n</i> -Bu	3-CF ₃	<i>i</i> -Bu	100	100/100	89/21	100/100	100/100	100/100	100/100
				10	64/—114	47/—33	64/37	42/0	57/19	58/—2
I-13	<i>n</i> -Bu	3-CF ₃	<i>n</i> -C ₅ H ₁₁	100	100/100	100/100	100/100	100/100	100/100	100/100
				10	78/—135	71/—7	56/15	46/—1	57/—2	43/8
I-14	<i>n</i> -Bu	3-CF ₃	<i>n</i> -C ₆ H ₁₃	100	100/100	100/100	100/100	100/100	100/100	100/100
				10	74/—107	79/44	69/—4	55/—5	58/16	43/—2
I-15	<i>n</i> -C ₆ H ₁₃	3-CF ₃	<i>n</i> -C ₆ H ₁₃	100	80/—58	85/—13	63/—21	100/100	77/27	100/100
				10	68/—135	85/—43	77/15	43/—15	100/100	100/100
I-16	<i>n</i> -C ₇ H ₁₅	3-CF ₃	Me	100	100/100	86/11	100/100	100/100	100/100	100/100
				10	100/100	100/100	67/16	6/—19	60/8	45/2
I-17	<i>n</i> -C ₇ H ₁₅	3-CF ₃	Et	100	100/100	86/—1	66/36	100/100	100/100	100/100
				10	34/—114	54/—19	86/29	48/6	67/28	24/2
I-18	<i>n</i> -C ₇ H ₁₅	3-CF ₃	<i>n</i> -Pr	100	62/—38	88/23	62/51	100/100	75/6	—19/31
				10	100/100	67/—1	61/1	25/—29	66/13	49/35
I-19	<i>n</i> -C ₇ H ₁₅	3-CF ₃	<i>n</i> -Bu	100	100/100	38/—27	79/58	100/100	100/100	100/100
				10	33/57	100/100	27/49	—58/4	51/39	100/6
I-20	<i>n</i> -C ₇ H ₁₅	3-CF ₃	<i>i</i> -Bu	100	100/100	100/100	100/100	100/100	81/45	100/100
				10	39/—144	52/—42	54/2	48/11	43/16	—49/9
I-21	<i>n</i> -C ₇ H ₁₅	3-CF ₃	<i>n</i> -C ₅ H ₁₁	100	44/—90	100/100	100/100	100/100	22/22	88/83
				10	100/100	58/—42	59/40	19/10	100/100	—19/—31
I-22	<i>n</i> -C ₇ H ₁₅	3-CF ₃	<i>n</i> -C ₆ H ₁₃	100	100/100	75/—71	100/100	100/100	100/100	100/100
				10	100/100	49/—68	53/27	—16/2	69/46	100/100

续表

Compd.	R ¹	R ²	R ³	浓度/(mg·L ⁻¹)	油菜根/茎	稗草根/茎	黄瓜根/茎	小麦根/茎	高粱根/茎	萝卜根/茎
I-23	Et	4-F	Et	100 10	100/100 65/7	100/100 15/-51	100/100 11/15	100/100 48/22	100/100 -31/-20	100/100 32/21
I-24	Et	4-F	<i>n</i> -Pr	100 10	100/100 -12/1	100/100 22/-88	100/100 -12/1	100/100 30/-4	100/100 -6/-38	82/75 -11/30
I-25	Et	4-F	<i>n</i> -Bu	100 10	100/100 49/11	100/100 9/-45	100/100 39/-6	100/100 40/-2	100/100 -5/-21	100/100 3/4
I-26	Et	4-F	<i>n</i> -C ₅ H ₁₁	100 10	100/100 48/-14	64/-47 -1/-30	100/100 48/-14	100/100 58/-16	100/100 -13/-22	100/100 77/32
I-27	Et	4-F	<i>n</i> -C ₆ H ₁₃	100 10	40/-19 37/-37	75/20 13/-91	100/100 9/37	100/100 -1/-1	39/44 -2/-32	100/100 69/14
I-28	<i>n</i> -Pr	4-F	Et	100 10	63/28 22/-38	38/-42 -13/-23	63/28 22/-38	44/12 15/-18	-2/-4 -45/22	100/100 45/7
I-29	<i>n</i> -Pr	4-F	<i>n</i> -Bu	100 10	100/100 44/-48	60/-11 35/-252	100/100 15/-41	100/100 9/-14	100/100 29/-2	100/100 9/5
I-30	<i>n</i> -Pr	4-F	<i>n</i> -C ₅ H ₁₁	100 10	100/100 26/-11	100/100 24/-54	100/100 40/-15	100/100 -9/27	100/100 -82/-67	100/100 55/-2
I-31	<i>n</i> -Pr	4-F	<i>n</i> -C ₆ H ₁₃	100 10	100/100 25/-22	100/100 -16/-91	100/100 -20/-28	100/100 -61/-28	100/100 -76/-94	100/100 -5/14
I-32	<i>n</i> -Bu	4-F	Me	100 10	100/100 70/1	100/100 13/-67	100/100 44/-31	100/100 18/-22	100/100 -52/-6	100/100 38/19
I-33	<i>n</i> -Bu	4-F	Et	100 10	100/100 68/23	100/100 24/-42	100/100 -21/-38	100/100 -30/-12	100/100 -130/-14	100/100 35/-4
I-34	<i>n</i> -Bu	4-F	<i>n</i> -Pr	100 10	100/100 48/-12	100/100 20/-98	100/100 17/-12	100/100 32/-2	100/100 -45/-56	100/100 13/9
I-35	<i>n</i> -Bu	4-F	<i>n</i> -Bu	100 10	100/100 25/7	100/100 38/-85	100/100 100/100	100/100 38/2	100/100 -32/-29	100/100 100/100
I-36	<i>n</i> -C ₅ H ₁₁	4-F	Et	100 10	100/100 48/22	100/100 43/59	100/100 30/-20	100/100 53/-10	100/100 -10/-11	100/100 35/-6
I-37	<i>n</i> -C ₅ H ₁₁	4-F	<i>n</i> -Pr	100 10	100/100 53/44	100/100 56/-11	100/100 100/100	100/100 61/-14	100/100 -41/-57	100/100 100/100
I-38	<i>n</i> -C ₅ H ₁₁	4-F	<i>n</i> -Bu	100 10	100/100 64/7	100/100 38/-73	100/100 -7/-14	100/100 100/100	100/100 100/100	100/100 35/14
I-39	<i>n</i> -C ₅ H ₁₁	4-F	<i>n</i> -C ₅ H ₁₁	100 10	100/100 64/33	100/100 60/-5	100/100 44/-31	100/100 40/-6	100/100 15/17	100/100 56/14
I-40	<i>n</i> -C ₅ H ₁₁	4-F	<i>n</i> -C ₆ H ₁₃	100 10	100/100 61/-23	100/100 42/-30	100/100 42/-31	100/100 43/-18	100/100 -52/-46	100/100 17/-11
I-41	<i>n</i> -C ₆ H ₁₃	4-F	<i>n</i> -Bu	100 10	100/100 80/15	100/100 31/-73	100/100 34/21	100/100 43/-9	100/100 -19/-28	100/100 64/51
I-42	<i>n</i> -C ₇ H ₁₅	4-F	<i>n</i> -C ₅ H ₁₁	100 10	100/100 37/4	100/100 56/-79	100/100 32/-48	100/100 30/-22	100/100 -15/56	100/100 49/-11
唑啉磺草胺				100 10	84/62 62/47	97/89 70/8	92/73 82/61	95/83 83/60	93/86 90/84	90/85 83/77

时, 当 R^1 为 Et 或 n -Pr 或 n -Bu 或 n -C₆H₁₃ 或 n -C₇H₁₅、 R^2 为 3-CF₃、 R^3 为 Me 或 n -Pr 或 n -Bu 或 n -C₅H₁₁ 或 n -C₆H₁₃ 时, 供试化合物对油菜、稗草、高粱和萝卜的根和茎的抑制作用明显高于其他化合物; 而 R^2 为 4-F 时, 只有 R^1 为 n -Bu 或 n -C₅H₁₁、 R^3 为 n -Pr 或 n -Bu, 目标化合物对小麦、高粱和萝卜的表现出优异的除草活性; R^2 为 3-CF₃ 目标化合物的除草活性比 4-F 更好。从化合物的结构上来看, 我们推测其除草活性的作用靶标是 ALS 酶, 进一步活性测试还在探索中。

2 结论

本研究设计合成了 42 个嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶化合物消旋体, 并通过熔点、¹H NMR、¹³C NMR、IR 和 HRMS 确认了它们的结构。除草活性测试结果表明: 大部分化合物特别是 **I-13**, **I-14**, **I-23**, **I-25** 和 **I-30**~**I-42** 在 100 mg/L 浓度下表现出优异的除草活性。这些化合物可作为新型农药先导进一步深入结构优化和除草活性测试。本文研究结果不仅发展了一种合成嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶衍生物的新方法, 而且为含氮稠杂环化合物的新型农药分子设计提供了一定的参考价值。

3 实验部分

3.1 仪器与试剂

熔点测定仪(XT-4 型), 温度未经校正; 傅立叶变换红外光谱仪(Nicolet 6700); 超导核磁共振波谱仪(BRUKER AVANCE 400, CDCl₃ 为溶剂, TMS 为内标); 高分辨质谱联用仪(Sciex TripleTOF6600)。化学试剂均为市售分析纯, 三氟乙酸使用前经干燥处理。中间体 **1**, **2** 和 **3** 根据参考文献[22~24]合成得到。

3.2 目标化合物的合成

向 50 mL 的圆底烧瓶中分别加入中间体 **3** (1.0 mmol)、脂肪醛(1.5 mmol)、催化剂 ZrCl₄ (0.1 mmol) 和 10 mL 无水乙醇, 混合物搅拌加热至 80 °C 反应 5 h。待原料反应完全后, 冷却静置 12 h, 有大量固体析出, 抽滤, 固体经无水乙醇重结晶干燥即得目标化合物消旋体 **I-1**~**I-42**。

2-(3-三氟甲基苯氧基)-5,6-二氢-5-乙基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-1**): 白色固体, 收率 85%。m.p. 203~205 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ : 7.44~7.34 (m, 3H), 7.23 (d, $J=8.2$ Hz, 2H), 6.18~6.10 (m, 1H), 5.28 (s, 2H), 3.27~3.12 (m, 2H), 2.62 (s, 3H), 2.21~2.10 (m, 1H), 2.09~1.97 (m, 1H), 1.42 (t, $J=7.3$ Hz, 3H), 0.87 (t, $J=7.4$ Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ : 170.9, 165.5,

160.4, 158.6, 157.1, 147.4, 131.7 (q, $J=32.4$ Hz), 129.9, 124.0 (q, $J=272.5$ Hz), 118.6, 117.9 (q, $J=3.8$ Hz), 112.1 (q, $J=3.9$ Hz), 95.1, 70.5, 64.0, 30.5, 25.4, 14.8, 13.0, 7.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3229, 2931, 1609, 1549, 1400, 1251, 868, 697 cm⁻¹. HRMS calcd for C₂₀H₂₂F₃N₆OS₂ [M + H]⁺ 483.1249, found 483.1243.

2-(3-三氟甲基苯氧基)-5,6-二氢-5-丙基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-2**): 白色固体, 收率 82%。m.p. 218~219 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ : 7.44~7.34 (m, 2H), 7.26~7.21 (m, 2H), 6.93 (s, 1H), 6.10~6.04 (m, 1H), 5.27 (s, 2H), 3.27~3.14 (m, 2H), 2.62 (s, 3H), 2.11~1.94 (m, 2H), 1.88 (s, 1H), 1.42 (t, $J=7.3$ Hz, 3H), 1.31~1.20 (m, 1H), 0.90 (t, $J=7.3$ Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.6, 160.3, 158.6, 156.7, 147.2, 131.8 (q, $J=32.3$ Hz), 129.9, 124.0 (q, $J=272.4$ Hz), 118.6, 117.9 (q, $J=4.1$ Hz), 112.1 (q, $J=3.6$, 3.1 Hz), 95.2, 69.6, 64.0, 39.3, 25.4, 16.4, 14.8, 13.5, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2928, 1601, 1547, 1459, 1254, 867, 696 cm⁻¹. HRMS calcd for C₂₁H₂₄F₃N₆OS₂ [M + H]⁺ 497.1405, found 497.1411.

2-(3-三氟甲基苯氧基)-5,6-二氢-5-丁基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-3**): 白色固体, 收率 86%。m.p. 216~217 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.35 (m, 2H), 7.23 (d, $J=7.4$ Hz, 2H), 6.82 (s, 1H), 6.06 (t, $J=5.1$ Hz, 1H), 5.27 (s, 2H), 3.29~3.15 (m, 2H), 2.62 (s, 3H), 2.12~2.00 (m, 2H), 1.93 (s, 1H), 1.42 (t, $J=7.3$ Hz, 3H), 1.33~1.26 (m, 2H), 1.23~1.14 (m, 1H), 0.83 (t, $J=7.0$ Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ : 170.9, 165.6, 160.3, 158.6, 156.7, 147.2, 131.8 (q, $J=32.2$ Hz), 129.9, 123.9 (q, $J=272.5$ Hz), 118.5, 117.9 (q, $J=4.0$ Hz), 112.1 (q, $J=3.9$ Hz), 95.2, 69.8, 63.9, 36.9, 25.4, 24.9, 22.1, 14.8, 13.8, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2928, 1609, 1550, 1400, 1256, 866, 698 cm⁻¹. HRMS calcd for C₂₂H₂₆F₃N₆OS₂ [M + H]⁺ 511.1562, found 511.1556.

2-(3-三氟甲基苯氧基)-5,6-二氢-5-乙基-8-丙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-4**): 白色固体, 收率 79%。m.p. 217~218 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ : 7.41 (t, $J=8.0$ Hz, 1H), 7.35 (s, 1H), 7.27~7.19 (m, 2H), 6.21 (t, $J=4.2$ Hz, 1H), 5.28 (s, 2H), 3.31~3.25 (m, 2H), 2.69 (s, 3H), 2.30~2.20 (m,

1H), 2.16~2.06 (m, 1H), 1.88~1.79 (m, 2H), 1.08 (t, $J=7.4$ Hz, 3H), 0.89 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 168.6, 164.3, 160.9, 158.3, 151.5, 145.2, 131.8 (q, $J=32.3$ Hz), 130.0, 123.9 (q, $J=272.3$ Hz), 118.6, 118.2 (q, $J=3.5$ Hz), 112.0 (q, $J=4.0$ Hz), 94.6, 71.1, 63.4, 33.3, 29.8, 22.3, 13.8, 13.3, 6.5; ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.7; IR (KBr) ν : 3217, 2962, 1603, 1544, 1324, 1265, 867, 696 cm^{-1} . HRMS calcd for $\text{C}_{21}\text{H}_{24}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 497.1405, found 497.1400.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-异丙基-8-丙硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-5**): 白色固体, 收率 60%. m.p. 204~206 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform- d) δ : 7.42~7.35 (m, 2H), 7.23 (d, $J=8.2$ Hz, 2H), 7.12 (s, 1H), 5.99~5.96 (m, 1H), 5.28 (s, 2H), 3.20~3.11 (m, 2H), 2.61 (s, 3H), 2.51~2.42 (m, 1H), 1.82~1.77 (m, 2H), 1.05 (t, $J=7.4$ Hz, 3H), 0.97 (d, $J=7.0$ Hz, 3H), 0.79 (d, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 170.9, 165.5, 160.3, 158.6, 157.1, 147.5, 131.8 (q, $J=32.4$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.6, 117.9 (q, $J=3.8$ Hz), 112.1 (q, $J=3.8$ Hz), 95.1, 74.0, 64.0, 35.4, 33.0, 23.0, 16.6, 15.1, 13.5, 13.0; ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.7; IR (KBr) ν : 3233, 2960, 1603, 1545, 1392, 1216, 869, 696 cm^{-1} . HRMS calcd for $\text{C}_{22}\text{H}_{26}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 511.1562, found 511.1556.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-异丁基-8-丙硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-6**): 白色固体, 收率 65%. m.p. 202~204 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform- d) δ : 7.42~7.34 (m, 2H), 7.25~7.21 (m, 2H), 7.02 (s, 1H), 6.10~6.02 (m, 1H), 5.27 (s, 2H), 3.22~3.11 (m, 2H), 2.62 (s, 3H), 2.00~1.92 (m, 1H), 1.84~1.70 (m, 4H), 1.05 (t, $J=7.4$ Hz, 3H), 0.92 (d, $J=5.9$ Hz, 6H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 171.1, 165.6, 160.1, 158.6, 156.6, 147.0, 131.8 (q, $J=32.1$ Hz), 129.9, 123.9 (q, $J=272.3$ Hz), 118.6, 117.9 (q, $J=3.7$ Hz), 112.1 (q, $J=3.9$, 3.3 Hz), 95.5, 68.4, 63.9, 46.0, 33.0, 23.7, 23.0, 22.7, 22.2, 13.5, 13.0; ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.6; IR (KBr) ν : 3218, 2968, 1602, 1544, 1401, 1216, 870, 695 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{28}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 525.1718, found 525.1713.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-甲基-8-丁硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-7**): 白色固体, 收率 79%. m.p. 199~200 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform- d) δ : 7.44~7.35 (m, 2H), 7.25~7.22 (m, 2H), 6.67 (s, 1H), 6.12 (q, $J=5.5$ Hz, 1H), 5.26

(s, 2H), 3.23~3.13 (m, 2H), 2.61 (s, 3H), 1.79 (d, $J=5.9$ Hz, 3H), 1.75~1.70 (m, 2H), 1.50~1.40 (m, 2H), 0.96 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 171.3, 165.7, 160.4, 158.6, 156.5, 147.0, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.6$ Hz), 118.5, 117.9 (q, $J=3.9$ Hz), 112.1 (q, $J=3.8$ Hz), 95.2, 66.4, 63.9, 31.6, 30.8, 23.6, 22.1, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.7; IR (KBr) ν : 3217, 2962, 1603, 1544, 1324, 1265, 867, 696 cm^{-1} . HRMS calcd for $\text{C}_{21}\text{H}_{24}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 497.1405, found 497.1400.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-乙基-8-丁硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-8**): 白色固体, 收率 77%. m.p. 205~206 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform- d) δ : 7.42~7.35 (m, 3H), 7.25~7.21 (m, 2H), 6.17~6.11 (m, 1H), 5.28 (s, 2H), 3.23~3.15 (m, 2H), 2.61 (s, 3H), 2.20~2.10 (m, 1H), 2.08~1.99 (m, 1H), 1.78~1.72 (m, 2H), 1.53~1.43 (m, 2H), 0.96 (t, $J=7.4$ Hz, 3H), 0.87 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 170.9, 165.5, 160.4, 158.6, 157.0, 147.4, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.5, 117.9 (q, $J=3.4$ Hz), 112.1 (q, $J=3.8$ Hz), 95.1, 70.4, 64.0, 31.7, 30.8, 30.5, 22.1, 13.7, 13.0, 7.0. ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.7; IR (KBr) ν : 3232, 2931, 1606, 1550, 1400, 1265, 869, 655 cm^{-1} . HRMS calcd for $\text{C}_{22}\text{H}_{26}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 511.1562, found 511.1556.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-丙基-8-丁硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-9**): 白色固体, 收率 80%. m.p. 216~217 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform- d) δ : 7.43~7.34 (m, 3H), 7.23 (d, $J=8.0$ Hz, 2H), 6.16~6.10 (m, 1H), 5.28 (s, 2H), 3.25~3.15 (m, 2H), 2.64~2.61 (m, 3H), 2.07~1.95 (m, 2H), 1.80~1.70 (m, 2H), 1.52~1.37 (m, 3H), 1.28~1.17 (m, 1H), 0.96 (t, $J=7.4$ Hz, 3H), 0.88 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform- d) δ : 171.0, 165.530, 160.3, 158.6, 156.8, 147.2, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.3$ Hz), 118.5, 117.9 (q, $J=3.8$ Hz), 112.1 (q, $J=3.8$ Hz), 95.2, 69.6, 64.0, 39.5, 31.7, 30.8, 22.1, 16.3, 13.7, 13.5, 13.0; ^{19}F NMR (376 MHz, Chloroform- d) δ : -62.7; IR (KBr) ν : 3227, 2930, 1601, 1545, 1399, 1267, 868, 655 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{28}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 525.1718, found 525.1713.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-丁基-8-丁硫基-10-甲硫基-嘧啶并[5,4- e][1,2,4]三唑并[1,5- c]嘧啶 (**I-10**): 白色固体, 收率 82%. m.p. 210~211 $^{\circ}\text{C}$; ^1H

NMR (400 MHz, Chloroform-*d*) δ : 7.43~7.35 (m, 2H), 7.25~7.17 (m, 3H), 6.14~6.07 (m, 1H), 5.28 (s, 2H), 3.24~3.15 (m, 2H), 2.62 (s, 3H), 2.08~1.99 (m, 2H), 1.79~1.70 (m, 2H), 1.53~1.43 (m, 2H), 1.30~1.12 (m, 4H), 0.96 (t, $J=7.4$ Hz, 3H), 0.81 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.3, 158.6, 156.8, 147.2, 131.8 (q, $J=32.2$ Hz), 129.9, 123.9 (q, $J=272.5$ Hz), 118.5, 117.9 (q, $J=3.6$ Hz), 112.1 (q, $J=3.6$ Hz), 95.1, 69.8, 63.9, 37.1, 31.7, 30.8, 24.9, 22.1, 13.8, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2930, 1610, 1551, 1401, 1258, 865, 698 cm^{-1} . HRMS calcd for $\text{C}_{24}\text{H}_{30}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 539.1875, found 539.1870.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-异丙基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-11**): 白色固体, 收率 59%. m.p. 183~185 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.48~7.35 (m, 3H), 7.26~7.21 (m, 2H), 6.04~5.99 (m, 1H), 5.29 (s, 2H), 3.25~3.13 (m, 2H), 2.61 (s, 3H), 2.45 (tt, $J=6.9, 3.5$ Hz, 1H), 1.79~1.71 (m, 2H), 1.53~1.43 (m, 2H), 0.99~0.93 (m, 6H), 0.79 (d, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.8, 165.4, 160.3, 158.6, 157.2, 147.6, 131.7 (q, $J=32.4$ Hz), 129.9, 123.9 (q, $J=272.2$ Hz), 118.6, 117.9 (q, $J=3.9$ Hz), 112.1 (q, $J=4.1$ Hz), 95.1, 73.9, 64.0, 35.6, 31.7, 30.8, 22.1, 16.5, 15.2, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3217, 2962, 1603, 1544, 1324, 1215, 867, 696 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{28}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 525.1718, found 525.1713.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-异丁基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-12**): 白色固体, 收率 62%. m.p. 182~183 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.36 (m, 2H), 7.25~7.21 (m, 2H), 7.03 (s, 1H), 6.09~6.03 (m, 1H), 5.27 (s, 2H), 3.24~3.12 (m, 2H), 2.62 (s, 3H), 1.99~1.92 (m, 1H), 1.86~1.70 (m, 4H), 1.52~1.42 (m, 2H), 0.99~0.91 (m, 9H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.1, 165.6, 160.1, 158.6, 156.6, 147.0, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.6$ Hz), 118.6, 117.9 (q, $J=3.8$ Hz), 112.1 (q, $J=3.9$ Hz), 95.5, 68.4, 63.9, 46.0, 31.6, 30.8, 23.7, 22.7, 22.2, 22.1, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.6; IR (KBr) ν : 3217, 2962, 1603, 1544, 1324, 1265, 867, 696 cm^{-1} . HRMS calcd for $\text{C}_{24}\text{H}_{30}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 539.1875, found 539.1869.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-戊基-8-丁硫

基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-13**): 白色固体, 收率 85%. m.p. 201~203 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.35 (m, 2H), 7.25~7.21 (m, 2H), 7.14 (s, 1H), 6.12~6.06 (m, 1H), 5.27 (s, 2H), 3.23~3.15 (m, 2H), 2.62 (s, 3H), 2.10~1.99 (m, 2H), 1.79~1.70 (m, 2H), 1.51~1.36 (m, 3H), 1.25~1.18 (m, 5H), 0.96 (t, $J=7.4$ Hz, 3H), 0.84~0.78 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.3, 158.6, 156.7, 147.2, 131.8 (q, $J=32.2$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.5, 117.9 (q, $J=3.3$ Hz), 112.1 (q, $J=3.8$ Hz), 95.2, 69.8, 63.9, 37.3, 31.7, 31.1, 30.8, 22.6, 22.4, 22.1, 13.8, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2931, 1605, 1548, 1399, 1267, 865, 696 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{32}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 553.2031, found 553.2026.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-己基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-14**): 白色固体, 收率 79%. m.p. 192~194 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.43~7.36 (m, 2H), 7.25~7.21 (m, 2H), 7.15 (s, 1H), 6.11~6.07 (m, 1H), 5.27 (s, 2H), 3.23~3.14 (m, 2H), 2.62 (s, 3H), 2.07~1.98 (m, 2H), 1.79~1.71 (m, 2H), 1.54~1.36 (m, 3H), 1.26~1.14 (m, 7H), 0.96 (t, $J=7.4$ Hz, 3H), 0.82 (t, $J=7.0$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.6, 160.3, 158.6, 156.7, 147.2, 131.8 (q, $J=32.2$ Hz), 129.9, 123.9 (q, $J=272.6$ Hz), 118.5, 117.9 (q, $J=3.7$ Hz), 112.1 (q, $J=3.8$ Hz), 95.2, 69.8, 63.9, 37.3, 31.7, 31.5, 30.8, 28.6, 22.9, 22.4, 22.1, 13.9, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3225, 2930, 1609, 1548, 1326, 1264, 867, 696 cm^{-1} . HRMS calcd for $\text{C}_{26}\text{H}_{34}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 567.2188, found 567.2182.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-己基-8-己硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-15**): 白色固体, 收率 85%. m.p. 182~183 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.44~7.35 (m, 3H), 7.26~7.20 (m, 2H), 6.11 (d, $J=5.3$ Hz, 1H), 5.28 (s, 2H), 3.24~3.11 (m, 2H), 2.62 (s, 3H), 2.09~1.98 (m, 2H), 1.83~1.70 (m, 2H), 1.47~1.30 (m, 7H), 1.26~1.13 (m, 7H), 0.93~0.87 (m, 3H), 0.82 (t, $J=7.0$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 165.5, 160.3, 158.6, 156.8, 147.2, 131.8 (d, $J=32.0$ Hz), 129.9, 123.9 (d, $J=272.3$ Hz), 118.5, 117.9 (d, $J=4.0$ Hz), 112.1 (q, $J=3.0, 2.1$ Hz), 95.2, 69.8, 63.9, 37.3, 31.5, 31.5, 31.1, 29.6, 28.7, 28.7, 22.9, 22.6, 22.5, 14.0, 14.0, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3229, 2927,

1605, 1545, 1325, 1213, 864, 655 cm^{-1} . HRMS calcd for $\text{C}_{28}\text{H}_{38}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 595.2501, found 595.2495.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-甲基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-16**): 白色固体, 收率 75%. m.p. 197~199 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.36 (m, 2H), 7.25~7.21 (m, 2H), 6.14 (q, $J=5.3$ Hz, 1H), 5.26 (s, 2H), 3.22~3.13 (m, 2H), 2.62 (s, 3H), 1.82~1.74 (m, 6H), 1.49~1.40 (m, 2H), 1.35~1.23 (m, 5H), 0.90 (t, $J=6.7$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.1, 165.7, 160.4, 158.6, 156.4, 146.9, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.5, 117.94 (q, $J=3.9$ Hz), 112.1 (q, $J=3.7$ Hz), 95.2, 66.4, 63.9, 31.5, 31.1, 29.6, 28.7, 23.7, 22.6, 14.0, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2931, 1610, 1547, 1319, 1215, 804, 694 cm^{-1} . HRMS calcd for $\text{C}_{24}\text{H}_{30}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 539.1875, found 539.1869.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-乙基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-17**): 白色固体, 收率 79%. m.p. 207~209 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.32 (m, 3H), 7.26~7.21 (m, 2H), 6.17~6.10 (m, 1H), 5.27 (s, 2H), 3.22~3.13 (m, 2H), 2.61 (s, 3H), 2.22~1.98 (m, 2H), 1.81~1.71 (m, 3H), 1.48~1.41 (m, 2H), 1.38~1.21 (m, 5H), 0.92~0.85 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.4, 158.6, 157.0, 147.4, 131.8 (q, $J=32.5$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.6, 117.9 (q, $J=4.2$ Hz), 112.1 (q, $J=6.0, 4.2$ Hz), 95.1, 70.5, 64.0, 31.4, 31.1, 30.5, 29.6, 28.7, 22.6, 14.0, 13.0, 7.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2929, 1608, 1545, 1332, 1222, 866, 698 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{32}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 553.2031, found 553.2026.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-丙基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-18**): 白色固体, 收率 76%. m.p. 187~188 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.35 (m, 2H), 7.26~7.20 (m, 2H), 6.14~6.09 (m, 1H), 5.27 (s, 2H), 3.22~3.13 (m, 2H), 2.62 (s, 3H), 2.10~1.93 (m, 2H), 1.81~1.70 (m, 2H), 1.49~1.38 (m, 3H), 1.36~1.18 (m, 7H), 0.92~0.85 (m, 6H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.3, 158.6, 156.9, 147.2, 131.8 (q, $J=32.3$ Hz), 129.9, 123.9 (q, $J=272.4$ Hz), 118.6, 117.9 (q, $J=3.8$ Hz), 112.1 (q, $J=3.7, 3.2$ Hz), 95.2, 69.6, 64.0, 39.5, 31.7, 31.1, 29.6, 29.0, 28.9, 22.6, 16.3,

14.1, 13.5, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3226, 2929, 1608, 1548, 1300, 1220, 865, 696 cm^{-1} . HRMS calcd for $\text{C}_{26}\text{H}_{34}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 567.2188, found 567.2182.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-丁基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-19**): 白色固体, 收率 86%. m.p. 179~180 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.35 (m, 2H), 7.25~7.22 (m, 2H), 6.14~6.07 (m, 1H), 5.28 (s, 2H), 3.21~3.14 (m, 2H), 2.62 (s, 3H), 2.10~1.97 (m, 2H), 1.80~1.71 (m, 2H), 1.49~1.19 (m, 12H), 0.92~0.87 (m, 3H), 0.81 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.3, 158.6, 156.8, 147.2, 131.8 (d, $J=32.5$ Hz), 129.9, 123.9 (d, $J=272.3$ Hz), 118.5, 117.9 (q, $J=3.9$ Hz), 112.1 (q, $J=3.5$ Hz), 95.2, 69.8, 64.0, 37.1, 31.7, 31.1, 29.6, 29.0, 28.9, 24.9, 22.6, 22.1, 14.1, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3227, 2929, 1607, 1548, 1326, 1267, 865, 696 cm^{-1} . HRMS calcd for $\text{C}_{27}\text{H}_{36}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 581.2344, found 581.2339.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-异丁基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-20**): 白色固体, 收率 65%. m.p. 163~164 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.42~7.36 (m, 2H), 7.25~7.21 (m, 2H), 7.15 (s, 1H), 6.10~6.04 (m, 1H), 5.27 (s, 2H), 3.21~3.14 (m, 2H), 2.62 (s, 3H), 2.06~1.89 (m, 2H), 1.85~1.72 (m, 4H), 1.48~1.40 (m, 2H), 1.34~1.27 (m, 5H), 0.94~0.88 (m, 9H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.6, 160.1, 158.6, 156.6, 147.0, 131.8 (q, $J=32.2$ Hz), 129.9, 123.9 (q, $J=272.5$ Hz), 118.6, 117.9 (q, $J=3.6$ Hz), 112.1 (q, $J=3.6$ Hz), 95.5, 68.4, 63.9, 46.0, 31.7, 31.1, 29.6, 29.0, 28.9, 23.7, 22.7, 22.6, 22.3, 14.1, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3217, 2928, 1603, 1541, 1326, 1215, 868, 696 cm^{-1} . HRMS calcd for $\text{C}_{27}\text{H}_{36}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 581.2344, found 581.2348.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-戊基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶 (**I-21**): 白色固体, 收率 82%. m.p. 172~173 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.43~7.35 (m, 2H), 7.25~7.19 (m, 3H), 6.12~6.06 (m, 1H), 5.27 (s, 2H), 3.22~3.14 (m, 2H), 2.62 (s, 3H), 2.09~1.96 (m, 2H), 1.79~1.71 (m, 2H), 1.47~1.39 (m, 2H), 1.36~1.16 (m, 12H), 0.91~0.86 (m, 3H), 0.83~0.78 (m, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.3, 158.6,

156.8, 147.2, 131.8 (d, $J=32.3$ Hz), 129.9, 123.9 (d, $J=272.4$ Hz), 118.5, 117.9 (q, $J=3.7$ Hz), 112.1 (d, $J=4.0$ Hz), 95.2, 69.8, 63.9, 37.3, 31.7, 31.5, 31.1, 29.7, 20.0, 28.9, 22.6, 22.6, 22.4, 14.1, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3217, 2928, 1603, 1541, 1326, 1215, 868, 696 cm^{-1} . HRMS calcd for $\text{C}_{28}\text{H}_{38}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 595.2501, found 595.2495.

2-(3-三氟甲基苯氧亚甲基)-5,6-二氢-5-己基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-22**): 白色固体, 收率 76%. m.p. 169~170 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.43~7.35 (m, 2H), 7.25~7.18 (m, 3H), 6.12~6.06 (m, 1H), 5.27 (s, 2H), 3.22~3.13 (m, 2H), 2.62 (s, 3H), 2.09~1.99 (m, 2H), 1.80~1.71 (m, 2H), 1.47~1.40 (m, 2H), 1.35~1.13 (m, 14H), 0.92~0.86 (m, 3H), 0.82 (t, $J=7.0$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.9, 165.6, 160.3, 158.6, 156.7, 147.2, 131.8 (q, $J=32.5$ Hz), 129.9, 123.9 (q, $J=272.5$ Hz), 118.5, 117.9 (q, $J=4.0$ Hz), 112.1 (q, $J=7.2$, 6.1 Hz), 95.2, 69.8, 63.9, 37.3, 31.7, 31.5, 31.1, 29.6, 29.0, 28.9, 28.7, 22.9, 22.6, 22.5, 14.1, 14.0, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -62.7; IR (KBr) ν : 3231, 2922, 1614, 1553, 1327, 1269, 871, 694 cm^{-1} . HRMS calcd for $\text{C}_{29}\text{H}_{40}\text{F}_3\text{N}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 609.2657, found 609.2655.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-乙基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-23**): 黄色固体, 收率 79%. m.p. 210~212 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.43 (s, 1H), 7.02~6.94 (m, 4H), 6.18~6.12 (m, 1H), 5.20 (s, 2H), 3.25~3.14 (m, 2H), 2.62 (s, 3H), 2.18~2.10 (m, 1H), 2.07~1.98 (m, 1H), 1.42 (t, $J=7.3$ Hz, 3H), 0.87 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.7, 165.4, 160.8, 157.6 (d, $J=238.6$ Hz), 157.0, 154.6 (d, $J=2.1$ Hz), 147.2, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 70.4, 64.5, 30.6, 25.4, 14.8, 13.0, 7.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3231, 2972, 1601, 1506, 1249, 827 cm^{-1} . HRMS calcd for $\text{C}_{19}\text{H}_{21}\text{FN}_6\text{NaOS}_2$ $[\text{M}+\text{Na}]^+$ 455.1100, found 455.1094.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丙基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-24**): 黄色固体, 收率 82%. m.p. 233~235 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.05 (s, 1H), 7.02~6.94 (m, 4H), 6.12~6.06 (m, 1H), 5.19 (s, 2H), 3.24~3.15 (m, 2H), 2.62 (s, 3H), 2.08~1.95 (m, 2H), 1.45~1.17 (m, 5H), 0.89 (t, $J=7.3$ Hz, 3H); ^{13}C NMR (100 MHz, Chloro-

form-*d*) δ : 170.8, 165.5, 160.8, 157.6 (d, $J=238.6$ Hz), 156.8, 154.6 (d, $J=2.2$ Hz), 147.1, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.3, 69.6, 64.4, 39.4, 25.4, 16.3, 14.8, 13.5, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3234, 2931, 1601, 1517, 1251, 825 cm^{-1} . HRMS calcd for $\text{C}_{20}\text{H}_{24}\text{FN}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 447.1437, found 447.1432.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丁基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-25**): 黄色固体, 收率 79%. m.p. 218~220 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.13 (s, 1H), 7.03~6.94 (m, 4H), 6.13~6.08 (m, 1H), 5.20 (s, 2H), 3.25~3.15 (m, 2H), 2.62 (s, 3H), 2.08~1.99 (m, 2H), 1.42 (t, $J=7.3$ Hz, 3H), 1.35~1.12 (m, 4H), 0.82 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.8, 165.5, 160.8, 157.5 (d, $J=238.7$ Hz), 156.8, 154.6 (d, $J=2.0$ Hz), 147.1, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 69.7, 64.4, 37.1, 25.4, 24.9, 22.2, 14.8, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3231, 2926, 1608, 1551, 1255, 827 cm^{-1} . HRMS calcd for $\text{C}_{21}\text{H}_{26}\text{FN}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 461.1594, found 461.1591.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-戊基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-26**): 黄色固体, 收率 70%. m.p. 199~202 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.32 (s, 1H), 7.03~6.94 (m, 4H), 6.14~6.09 (m, 1H), 5.20 (s, 2H), 3.26~3.15 (m, 2H), 2.62 (s, 3H), 2.09~1.96 (m, 2H), 1.42 (t, $J=7.3$ Hz, 3H), 1.36~1.10 (m, 6H), 0.81 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.7, 165.4, 160.7, 157.5 (d, $J=238.7$ Hz), 156.8, 154.6 (d, $J=2.0$ Hz), 147.1, 116.1 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.3, 69.7, 64.4, 37.3, 31.1, 25.4, 22.6, 22.4, 14.8, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3228, 2924, 1611, 1552, 1254, 825 cm^{-1} . HRMS calcd for $\text{C}_{22}\text{H}_{27}\text{NaFN}_6\text{OS}_2$ $[\text{M}+\text{Na}]^+$ 497.1570, found 497.1564.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-己基-8-乙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-27**): 黄色固体, 收率 65%. m.p. 189~192 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.17 (s, 1H), 7.02~6.94 (m, 4H), 6.12~6.06 (m, 1H), 5.20 (s, 2H), 3.24~3.15 (m, 2H), 2.62 (s, 3H), 2.07~1.97 (m, 2H), 1.42 (t, $J=7.3$ Hz, 3H), 1.26~1.13 (m, 8H), 0.83 (t, $J=7.0$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.7, 165.5, 160.8, 157.5 (d, $J=238.6$ Hz), 156.7, 154.6 (d, $J=2.0$ Hz), 147.0, 116.1 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.3, 69.7, 64.4, 37.3,

31.5, 28.7, 25.4, 22.9, 22.5, 14.8, 14.0, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3226, 2927, 1607, 1548, 1250, 829 cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{29}\text{NaFN}_6\text{OS}_2$ $[\text{M} + \text{Na}]^+$ 511.1726, found 511.1721.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-乙基-8-丙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-28**): 黄色固体, 收率 83%. m.p. 222~224 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.11 (s, 1H), 7.03~6.95 (m, 4H), 6.13~6.08 (m, 1H), 5.19 (s, 2H), 3.20~3.12 (m, 2H), 2.62 (s, 3H), 2.21~2.00 (m, 2H), 1.83~1.76 (m, 2H), 1.05 (t, $J=7.4$ Hz, 3H), 0.88 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.4, 160.8, 157.6 (d, $J=238.6$ Hz), 156.9, 154.6 (d, $J=2.0$ Hz), 147.3, 116.3 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 70.4, 64.5, 33.0, 30.4, 23.0, 13.5, 13.0, 7.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3227, 2931, 1605, 1517, 1229, 823 cm^{-1} . HRMS calcd for $\text{C}_{20}\text{H}_{24}\text{FN}_6\text{OS}_2$ $[\text{M} + \text{H}]^+$ 447.1437, found 447.1435.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丁基-8-丙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-29**): 黄色固体, 收率 76%. m.p. 223~224 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.03~6.95 (m, 4H), 6.01~5.97 (m, 1H), 5.19 (s, 2H), 3.19~3.11 (m, 2H), 2.62 (s, 3H), 2.10~2.03 (m, 2H), 1.81~1.77 (m, 2H), 1.33~1.23 (m, 4H), 1.06 (t, $J=7.3$ Hz, 3H), 0.86 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.5, 165.6, 160.8, 157.6 (d, $J=238.8$ Hz), 156.3, 154.6 (d, $J=2.0$ Hz), 147.0, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 69.8, 64.4, 36.9, 33.0, 24.9, 22.9, 22.1, 13.8, 13.5, 13.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3105, 2957, 1608, 1518, 1238, 823 cm^{-1} . HRMS calcd for $\text{C}_{22}\text{H}_{27}\text{NaFN}_6\text{OS}_2$ $[\text{M} + \text{Na}]^+$ 497.1570, found 497.1564.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-戊基-8-丙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-30**): 黄色固体, 收率 70%. m.p. 210~212 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.87 (s, 1H), 7.02~6.95 (m, 4H), 6.08 (t, $J=4.8$ Hz, 1H), 5.19 (s, 2H), 3.19~3.12 (m, 2H), 2.62 (s, 3H), 2.11~1.99 (m, 2H), 1.84~1.74 (m, 2H), 1.27~1.16 (m, 6H), 1.05 (t, $J=7.4$ Hz, 3H), 0.82 (t, $J=6.7$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 169.6, 165.8, 160.8, 157.6 (d, $J=238.7$ Hz), 155.5, 154.6 (d, $J=2.0$ Hz), 146.7, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.1, 69.9, 64.4, 37.0, 33.0, 31.1, 22.9, 22.4, 22.4, 13.8, 13.5, 13.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3225, 2935, 1605, 1517, 1225, 823

cm^{-1} . HRMS calcd for $\text{C}_{23}\text{H}_{29}\text{NaFN}_6\text{OS}_2$ $[\text{M} + \text{Na}]^+$ 511.1726, found 511.1730.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-己基-8-丙硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-31**): 黄色固体, 收率 65%. m.p. 208~209 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.12 (s, 1H), 7.04~6.95 (m, 4H), 6.06 (t, $J=5.1$ Hz, 1H), 5.19 (s, 2H), 3.21~3.13 (m, 2H), 2.62 (s, 3H), 2.10~1.99 (m, 2H), 1.85~1.75 (m, 2H), 1.29~1.15 (m, 8H), 1.06 (t, $J=7.3$ Hz, 3H), 0.83 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.5, 165.6, 160.8, 157.5 (d, $J=240.7$ Hz), 154.6 (d, $J=1.8$ Hz), 146.9, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 69.8, 64.4, 37.2, 33.0, 31.5, 28.7, 23.0, 22.9, 22.5, 14.0, 13.5, 13.1; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3224, 2928, 1607, 1548, 1253, 823 cm^{-1} . HRMS calcd for $\text{C}_{24}\text{H}_{32}\text{FN}_6\text{OS}_2$ $[\text{M} + \text{H}]^+$ 503.2063, found 503.2058.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-甲基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-32**): 黄色固体, 收率 83%. m.p. 209~211 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.04~6.96 (m, 4H), 6.91 (s, 1H), 6.18~6.12 (m, 1H), 5.19 (s, 2H), 3.22~3.16 (m, 2H), 2.62 (s, 3H), 1.80~1.74 (m, 5H), 1.51~1.43 (m, 2H), 1.24 (t, $J=7.0$ Hz, 1H), 0.96 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.1, 165.6, 160.8, 157.6 (d, $J=238.9$ Hz), 156.5, 154.6 (d, $J=2.1$ Hz), 146.8, 116.1 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.3, 66.4, 64.4, 31.6, 30.8, 23.8, 22.1, 13.7, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3228, 2928, 1605, 1518, 1259, 824 cm^{-1} . HRMS calcd for $\text{C}_{20}\text{H}_{24}\text{FN}_6\text{OS}_2$ $[\text{M} + \text{H}]^+$ 447.1437, found 447.1441.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-乙基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-33**): 黄色固体, 收率 85%. m.p. 210~212 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.03~6.95 (m, 5H), 6.07 (t, $J=4.7$ Hz, 1H), 5.19 (s, 2H), 3.22~3.15 (m, 2H), 2.62 (s, 3H), 2.10~2.03 (m, 2H), 1.80~1.71 (m, 2H), 1.53~1.42 (m, 2H), 0.96 (t, $J=7.4$ Hz, 3H), 0.90 (t, $J=7.4$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.7, 165.6, 160.9, 157.6 (d, $J=238.7$ Hz), 156.5, 154.6 (d, $J=2.2$ Hz), 147.2, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.1, 70.5, 64.4, 31.6, 30.8, 30.3, 22.1, 13.1, 7.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3231, 2929, 1606, 1507, 1222, 824 cm^{-1} . HRMS calcd for $\text{C}_{21}\text{H}_{25}\text{NaFN}_6\text{OS}_2$ $[\text{M} + \text{Na}]^+$ 483.1413, found 483.1408.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丙基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-34**): 黄色固体, 收率 85%. m.p. 218~220 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.03~6.94 (m, 4H), 6.89 (s, 1H), 6.10~6.04 (m, 1H), 5.19 (s, 2H), 3.22~3.14 (m, 2H), 2.62 (s, 3H), 2.08~1.96 (m, 2H), 1.80~1.70 (m, 2H), 1.52~1.44 (m, 2H), 1.33~1.15 (m, 2H), 0.96 (t, *J*=7.4 Hz, 3H), 0.90 (t, *J*=7.3 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 171.0, 165.5, 160.8, 157.6 (d, *J*=238.8 Hz), 156.7, 154.6 (d, *J*=2.1 Hz), 147.1, 116.2 (d, *J*=8.0 Hz), 115.7 (d, *J*=23.1 Hz), 95.3, 69.6, 64.4, 39.3, 31.6, 30.8, 22.1, 16.4, 13.7, 13.5, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3224, 2872, 1606, 1507, 1266, 825 cm⁻¹. HRMS calcd for C₂₂H₂₈FN₆OS₂ [M+H]⁺ 475.1750, found 475.1745.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-戊基-8-丁硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-35**): 黄色固体, 收率 68%. m.p. 215~217 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.03~6.94 (m, 5H), 6.09~6.05 (m, 1H), 5.19 (s, 2H), 3.22~3.15 (m, 2H), 2.62 (s, 3H), 2.09~1.98 (m, 2H), 1.77~1.72 (m, 2H), 1.53~1.43 (m, 2H), 1.29~1.16 (m, 6H), 0.96 (t, *J*=7.4 Hz, 3H), 0.82 (t, *J*=6.7 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 171.1, 165.4, 160.8, 157.6 (d, *J*=238.5 Hz), 156.8, 154.6 (d, *J*=2.1 Hz), 147.1, 116.2 (d, *J*=8.0 Hz), 115.7 (d, *J*=23.1 Hz), 95.2, 69.7, 64.4, 37.3, 31.7, 31.1, 30.8, 22.6, 22.4, 22.1, 13.8, 13.7, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3222, 2828, 1617, 1506, 1266, 824 cm⁻¹. HRMS calcd for C₂₄H₃₂FN₆OS₂ [M+H]⁺ 503.2063, found 503.2064.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-乙基-8-戊硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-36**): 黄色固体, 收率 79%. m.p. 193~194 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.29 (s, 1H), 7.04~6.95 (m, 4H), 6.16~6.09 (m, 1H), 5.20 (s, 2H), 3.23~3.13 (m, 2H), 2.62 (s, 3H), 2.20~1.99 (m, 2H), 1.81~1.73 (m, 2H), 1.45~1.32 (m, 4H), 0.94~0.86 (m, 6H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 170.9, 165.4, 160.8, 157.6 (d, *J*=238.8 Hz), 156.9, 154.6 (d, *J*=1.9 Hz), 147.3, 116.2 (d, *J*=8.1 Hz), 115.7 (d, *J*=23.1 Hz), 95.2, 70.4, 64.5, 31.2, 31.1, 30.5, 29.3, 22.3, 14.0, 13.0, 7.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3225, 2929, 1606, 823, 562 cm⁻¹. HRMS calcd for C₂₂H₂₇NaFN₆OS₂ [M+Na]⁺ 497.1570, found 497.1564.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丙基-8-戊硫基-10-

甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-37**): 黄色固体, 收率 84%. m.p. 216~217 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.33 (s, 1H), 7.03~6.94 (m, 4H), 6.15~6.09 (m, 1H), 5.19 (s, 2H), 3.20~3.15 (m, 2H), 2.62 (s, 3H), 2.06~1.94 (m, 2H), 1.82~1.70 (m, 3H), 1.43~1.37 (m, 4H), 1.26~1.19 (m, 1H), 0.94~0.86 (m, 6H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 171.0, 165.4, 160.7, 157.6 (d, *J*=238.7 Hz), 156.9, 154.6 (d, *J*=2.0 Hz), 147.1, 116.2 (d, *J*=8.1 Hz), 115.7 (d, *J*=23.1 Hz), 95.3, 69.6, 64.5, 39.5, 31.2, 31.1, 29.3, 16.3, 14.0, 13.5, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3226, 2928, 1606, 825, 562 cm⁻¹. HRMS calcd for C₂₃H₂₉NaFN₆OS₂ [M+Na]⁺ 511.1726, found 511.1721.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丁基-8-戊硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-38**): 黄色固体, 收率 63%. m.p. 220~221 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.03~6.94 (m, 5H), 6.09~6.05 (m, 1H), 5.19 (s, 2H), 3.22~3.14 (m, 2H), 2.62 (s, 3H), 2.05~2.00 (m, 2H), 1.81~1.71 (m, 2H), 1.45~1.26 (m, 8H), 0.92 (t, *J*=7.0 Hz, 3H), 0.83 (t, *J*=7.1 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 170.8, 165.5, 160.8, 157.6 (d, *J*=238.7 Hz), 156.6, 154.6 (d, *J*=1.8 Hz), 147.0, 116.2 (d, *J*=8.0 Hz), 115.7 (d, *J*=23.1 Hz), 95.2, 69.8, 64.4, 37.0, 31.2, 31.1, 29.3, 24.9, 22.3, 22.1, 14.0, 13.8, 13.1; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3221, 2928, 1606, 825, 561 cm⁻¹. HRMS calcd for C₂₄H₃₂FN₆OS₂ [M+H]⁺ 503.2063, found 503.2058.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-戊基-8-戊硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-39**): 黄色固体, 收率 67%. m.p. 208~210 °C; ¹H NMR (400 MHz, Chloroform-*d*) δ: 7.04~6.94 (m, 5H), 6.09~6.04 (m, 1H), 5.19 (s, 2H), 3.21~3.14 (m, 2H), 2.62 (s, 3H), 2.07~1.99 (m, 2H), 1.80~1.72 (m, 2H), 1.44~1.33 (m, 5H), 1.26~1.20 (m, 5H), 0.92 (t, *J*=7.1 Hz, 3H), 0.82 (t, *J*=6.0 Hz, 3H); ¹³C NMR (100 MHz, Chloroform-*d*) δ: 171.0, 165.5, 160.8, 157.6 (d, *J*=238.8 Hz), 156.7, 154.6 (d, *J*=2.1 Hz), 147.1, 116.2 (d, *J*=8.1 Hz), 115.7 (d, *J*=23.1 Hz), 95.2, 69.7, 64.4, 37.2, 31.2, 31.1, 31.1, 29.3, 22.6, 22.4, 22.3, 14.0, 13.8, 13.0; ¹⁹F NMR (376 MHz, Chloroform-*d*) δ: -123.5; IR (KBr) ν: 3222, 2927, 1607, 825, 561 cm⁻¹. HRMS calcd for C₂₅H₃₃NaFN₆OS₂ [M+H]⁺ 539.2039, found 539.2034.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-己基-8-戊硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-40**): 黄色固体, 收率 63%. m.p. 199~202 °C; ¹H NMR (400

MHz, Chloroform-*d*) δ : 7.31 (s, 1H), 7.03~6.95 (m, 4H), 6.13~6.07 (m, 1H), 5.20 (s, 2H), 3.21~3.14 (m, 2H), 2.62 (s, 3H), 2.07~1.97 (m, 2H), 1.80~1.73 (m, 2H), 1.46~1.32 (m, 6H), 1.25~1.16 (m, 6H), 0.92 (t, $J=7.0$ Hz, 3H), 0.82 (t, $J=6.9$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 170.9, 165.4, 160.8, 157.6 (d, $J=238.7$ Hz), 156.8, 154.6 (d, $J=1.8$ Hz), 147.1, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.3, 69.7, 37.4, 31.5, 31.2, 31.1, 29.3, 28.7, 22.9, 22.4, 22.3, 14.0, 14.0, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3222, 2927, 1607, 825, 561 cm^{-1} . HRMS calcd for $\text{C}_{26}\text{H}_{35}\text{NaFN}_6\text{OS}_2$ $[\text{M}+\text{Na}]^+$ 553.2196, found 553.2193.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-丁基-8-己硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-41**): 黄色固体, 收率 79%. m.p. 200~203 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.03~6.94 (m, 4H), 6.85 (s, 1H), 6.08~6.04 (m, 1H), 5.19 (s, 2H), 3.20~3.14 (m, 2H), 2.62 (s, 3H), 2.12~1.98 (m, 3H), 1.79~1.72 (m, 2H), 1.48~1.42 (m, 2H), 1.35~1.27 (m, 7H), 0.90 (t, $J=6.6$ Hz, 3H), 0.83 (t, $J=7.1$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.0, 165.5, 160.8, 157.6 (d, $J=238.6$ Hz), 156.6, 154.6 (d, $J=2.2$ Hz), 147.1, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 69.8, 64.4, 36.9, 31.4, 31.1, 29.6, 28.7, 24.9, 22.6, 22.1, 14.0, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3230, 2928, 1607, 823, 617 cm^{-1} . HRMS calcd for $\text{C}_{25}\text{H}_{34}\text{FN}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 517.2220, found 517.2220.

2-(4-氟苯氧亚甲基)-5,6-二氢-5-戊基-8-庚硫基-10-甲硫基-嘧啶并[5,4-*e*][1,2,4]三唑并[1,5-*c*]嘧啶(**I-42**): 黄色固体, 收率 64%. m.p. 194~196 $^{\circ}\text{C}$; ^1H NMR (400 MHz, Chloroform-*d*) δ : 7.02~6.94 (m, 4H), 6.76 (d, $J=16.9$ Hz, 1H), 6.05 (d, $J=5.1$ Hz, 1H), 5.19 (s, 2H), 3.22~3.13 (m, 2H), 2.61 (s, 3H), 2.07~1.98 (m, 2H), 1.78~1.68 (m, 4H), 1.47~1.41 (m, 2H), 1.30~1.20 (m, 10H), 0.91~0.87 (m, 3H), 0.84 (t, $J=6.8$ Hz, 3H); ^{13}C NMR (100 MHz, Chloroform-*d*) δ : 171.3, 165.4, 160.8, 157.6 (d, $J=238.6$ Hz), 156.7, 154.6 (d, $J=2.3$ Hz), 147.2, 116.2 (d, $J=8.0$ Hz), 115.7 (d, $J=23.1$ Hz), 95.2, 69.7, 64.5, 36.9, 31.7, 31.1, 29.6, 29.0, 24.9, 22.6, 22.1, 14.0, 13.8, 13.0; ^{19}F NMR (376 MHz, Chloroform-*d*) δ : -123.5; IR (KBr) ν : 3227, 2926, 1610, 823, 617 cm^{-1} . HRMS calcd for $\text{C}_{26}\text{H}_{36}\text{FN}_6\text{OS}_2$ $[\text{M}+\text{H}]^+$ 531.2376, found 531.2371.

3.3 除草活性测试

挑选六种供试植物种子包括单子叶植物(小麦、稗草和高粱)和双子叶植物(萝卜、油菜和黄瓜)。通过离体

培养皿法^[26]测试目标化合物 **I-1**~**I-42** 对这些供试植物的除草活性。在培养皿中铺上 2 层 90 mm 的圆形滤纸, 再均匀撒入 15 粒左右的植物种子, 每种植物种子分别用 100, 10 mg/L 的样品溶液处理培养(加入 6 mL 的样品溶液)。蒸馏水作为空白对照, 除草剂唑啶磺草胺作为阳性对照。将培养皿置于人工培养箱中, 温度设置为 25 $^{\circ}\text{C}$; 待植物种子长出叶片, 打开光照灯, 定时设置每天光照时长为 8 h, 8 d 后进行测试, 用刻度尺测量根和茎的生长情况, 每个浓度测 10 株的数据, 取平均值来计算抑制率。

$$\text{抑制率}/\% = [1 - (\text{处理平均长度} / \text{空白平均长度})] \times 100\%$$

辅助材料(Supporting Information) 目标化合物 **I-1**~**I-42** 的 ^1H NMR、 ^{19}F NMR 和 ^{13}C NMR 谱图。这些材料可以免费从本刊网站(<http://sioc-journal.cn/>)上下载。

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