Supporting Information for

Synthesis of 4-trifluoromethyl pyridazines via annulation of pyridinium ylides with trifluoroacetyl diazoester

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**General information**

$^1$H NMR, $^{19}$F NMR and $^{13}$C NMR spectra were recorded using Bruker AVIII 400 spectrometer. $^1$H NMR and $^{13}$C NMR chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane and $^{19}$F NMR chemical shifts were determined relative to CFCl$_3$ as the external standard and low field is positive. Coupling constants ($J$) are reported in Hertz (Hz). The residual solvent peak was used as an internal reference: $^1$H NMR (CDCl$_3$ $\delta$ 7.26), $^{13}$C NMR (CDCl$_3$ $\delta$ 77.0), $^1$H NMR (DMSO-$d_6$ $\delta$ 2.50) and $^{13}$C NMR (DMSO-$d_6$ $\delta$ 39.50). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate (I),$^1$ ethyl 2-diazo-3-oxobutanoate (I'),$^2$ N-(acylmethyl)pyridinium bromides (2a – 2u),$^3$ 2-(2-(4-bromophenyl)-2-oxoethyl)isoquinolin-2-ium bromide (2s-1),$^4$ 2-(4-bromophenyl)-$N,N,N$-triethyl-2-oxoethan-1-aminium bromide (2s-2),$^5$ and (2-(4-bromophenyl)-2-oxoethyl)dimethylsulfonium bromide (2s-3)$^6$ were prepared according to the published procedures. Other reagents were received from commercial sources. Solvents were freshly dried and degassed according to the published procedures prior to use. Column chromatography was performed on silica gel 200–300 mesh obtained from Qingdao Haiyang Chemical.

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General procedure of the synthesis of 4-(trifluoromethyl) pyridazines 3a–3u

To an oven-dried 5 mL pressure tube was added N-(acylmethyl)pyridinium bromides 2 (0.30 mmol, 1.0 equiv), NaOAc (124.0 mg, 1.50 mmol, 5.0 equiv), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate 1 (126.0 mg, 0.60 mmol, 3.0 equiv), and toluene (2.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The crude mixture was diluted with ethyl acetate (6 mL) and a saturated ammonium chloride solution (4 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting 4-(trifluoromethyl) pyridazine product was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.
Procedure for gram scale reaction for synthesis of 3c

To an oven-dried 100 mL pressure tube was added 1-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)pyridinium bromide 2c (3.5 g, 10.0 mmol, 1.0 equiv), NaOAc (2.5 g, 30.0 mmol, 5.0 equiv), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate 1 (4.4 g, 20 mmol, 2.0 equiv), and toluene (30.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The crude mixture was diluted with ethyl acetate (50 mL) and a saturated ammonium chloride solution (30 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate to give 2.0 g of ethyl 5,6-di([1,1'-biphenyl]-4-carbonyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3c) (70% yield).
Mechanistic studies

(i) Synthesis of intermediate ethyl-2-(2-(1,4-di([1,1'-biphenyl]-4-yl)-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-4,4,4-trifluoro-3-oxobutanoate (4)

To an oven-dried 50 mL pressure tube was added 1-(2-((1,1'-biphenyl)-4-yl)-2-oxoethyl)pyridinium bromide 2c (212.0 mg, 0.60 mmol, 1.0 equiv), NaOAc (246.0 mg, 3.0 mmol, 5.0 equiv), ethyl 2-diazo-4,4,4-trifluoro-3-oxobutanoate 1 (252.0 mg, 1.2 mmol, 2.0 equiv), and toluene (10.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 12 h. The crude mixture was diluted with ethyl acetate (25 mL) and a saturated ammonium chloride solution (5 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting trifluoroacetylated hydrazone 4 was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.

(ii) Intramolecular cyclization of 4
To an oven-dried 5 mL pressure tube was added ethyl (E)-2-(2-((E)-1,4-di[[1,1'-biphenyl]-4-yl]-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-4,4,4-trifluoro-3-oxobutanoate 4 (30.0 mg, 0.05 mmol, 1.0 equiv), NaOAc (21.0 mg, 0.25 mmol, 5.0 equiv), and toluene (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The crude mixture was diluted with ethyl acetate (10 mL) and a saturated ammonium chloride solution (5 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting residue was purified by column chromatography on silica gel with petroleum ether/ethyl acetate to give 25.0 mg of 3c (87% yield).

(iii) Synthesis of ethyl -2-(2-(1,4-dioxo-1,4-diphenylbut-2-en-2-yl)hydrazineylidene)-3-oxobutanoate (4')

![Chemical Reaction Diagram]

To an oven-dried 50 mL pressure tube was added 1-(2-([1,1'-biphenyl]-4-yl)-2-oxoethyl)pyridinium bromide 2c (212.0 mg, 0.60 mmol, 1.0 equiv), NaOAc (246.0 mg, 3.0 mmol, 5.0 equiv), ethyl 2-diazo-3-oxobutanoate 1' (187.0 mg, 1.2 mmol, 2.0 equiv), and toluene (10.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The crude mixture was diluted with ethyl acetate (25 mL) and a saturated ammonium chloride solution (5 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting
intermediate $4'$ was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.

(iv) Synthesis of ethyl $(E)$-2-(2-((E)-1,4-bis(4-bromophenyl)-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-3-oxo-3-phenylpropanoate ($4''$)

![Chemical structure diagram]

To an oven-dried 50 mL pressure tube was added 1-(2-(4-bromophenyl)-2-oxoethyl)pyridin-1-ium $2s$ (355 mg, 1.0 mmol, 1.0 equiv), NaOAc (410.0 mg, 5.0 mmol, 5.0 equiv), ethyl 2-diazo-3-oxo-3-phenylpropanoate $1''$ (440.0 mg, 2.0 mmol, 2.0 equiv), and toluene (10.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The crude mixture was diluted with ethyl acetate (25 mL) and a saturated ammonium chloride solution (5 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting intermediate $4''$ was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.

(v) Intramolecular cyclization of $4'$ or $4''$
To an oven-dried 5 mL pressure tube was added 4' (11.0 mg, 0.20 mmol, 1.0 equiv) or 4'' (12.0 mg, 0.20 mmol, 1.0 equiv), NaOAc (8.0 mg, 1.0 mmol, 5.0 equiv), and toluene (1.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 80 °C for 24 h. The \(^1\)H-NMR indicated no formation of 3c' or 3s'.

\[ \text{\(4'(42\%)\)} \]
Synthetic transformation of 3

(i) Transformation of 3a to amide-derivative 5a

To an oven-dried 25 mL pressure tube was added ethyl 5,6-dibenzoyl-4-(trifluoromethyl)pyridazine-3-carboxylate 3a (43.0 mg, 0.10 mmol, 1.0 equiv), aqueous ammonia (14.8 M, 0.14 mL, 1.0 mmol, 10.0 equiv), and MeOH (10.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at room temperature for 3 h. The crude mixture was diluted with ethyl acetate (25 mL) and a saturated ammonium chloride solution (5 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting 5a was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.

(ii) General procedure of the synthesis of 4-(trifluoromethyl)pyridazino[4,5-c]pyridazines 6
To an oven-dried 5 mL pressure tube was added 4-(trifluoromethyl) pyridazine 3 (0.10 mmol, 1.0 equiv), spherical 4 Å molecular sieve (50 mg), a 85% hydrazine hydrate solution (12 mg, 0.20 mmol, 2.0 equiv), and toluene (2.0 mL). The tube was sealed with Teflon screw cap and the solution was stirred at 110 °C for 12 h. The crude mixture was diluted with ethyl acetate (6 mL) and a saturated ammonium chloride solution (3 mL). The organic phase was extracted and dried over anhydrous sodium sulfate, filtered, and the solvent was removed by rotary evaporation. The resulting 4-(trifluoromethyl)pyridazino[4,5-c]pyridazine 6 was purified by column chromatography on silica gel with petroleum ether/ethyl acetate.
Data for compounds

![Diagram of ethyl 5,6-dibenzoyl-4-(trifluoromethyl)pyridazine-3-carboxylate (3a)]

**ethyl 5,6-dibenzoyl-4-(trifluoromethyl)pyridazine-3-carboxylate (3a)**

Obtained as a yellow solid in 71% yield (64 mg). Mp: 150–152 °C. \( R_f \) (petroleum ether : ethyl acetate = 5 : 1) = 0.55. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.99 (d, \( J = 7.8 \) Hz, 2H), 7.76 (d, \( J = 7.7 \) Hz, 2H), 7.69 – 7.59 (m, 2H), 7.55 – 7.45 (m, 4H), 4.61 (q, \( J = 7.1 \) Hz, 2H), 1.48 (t, \( J = 7.1 \) Hz, 3H). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -56.3 (s, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 190.0, 189.9, 163.0, 157.2, 151.5 (q, \( J = 1.8 \) Hz), 138.1 (q, \( J = 2.0 \) Hz), 135.6, 134.8, 134.7, 134.4, 131.3, 129.3, 129.0, 128.6, 125.5 (q, \( J = 35.5 \) Hz), 121.3 (q, \( J = 278.3 \) Hz), 64.0, 13.9. IR (ATR): \( \nu \) 3063, 2986, 1744, 1671, 1597, 1582, 1519, 1450, 1380, 1360, 1296, 1264, 1224, 1154, 1124, 1098, 1073, 1012, 1001, 984, 956, 934, 878, 861, 842, 817, 756, 729, 708, 686, 675, 632, 615, 588, 537, 492, 456, 423 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for C\(_{22}\)H\(_{16}\)F\(_3\)N\(_2\)O\(_4\) [M + H]\(^+\): 429.1057; found: 429.1057.

![Diagram of ethyl 5,6-bis(4-methylbenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3b)]

**ethyl 5,6-bis(4-methylbenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3b)**

Obtained as a white solid in 72% yield (49 mg). Mp: 176–178 °C. \( R_f \) (petroleum ether : ethyl acetate = 5 : 1) = 0.40. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.90 (d, \( J = 8.0 \) Hz, 2H), 7.65 (d, \( J = 7.8 \) Hz, 2H), 7.38 – 7.23 (m, 4H), 4.63 (q, \( J = 7.3 \) Hz, 2H), 2.46 (s, 6H), 1.51 (t, \( J = 7.3 \) Hz, 3H). \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) \( \delta \) -56.3 (s, 3F). \(^{13}\)C NMR
(101 MHz, CDCl$_3$) $\delta$ 189.6, 189.4, 163.2, 157.7, 151.4, 146.1, 138.1, 133.3, 132.0, 131.5, 129.7, 129.5, 129.4, 128.5, 125.3 (q, $J = 35.4$ Hz), 121.3 (q, $J = 278.2$ Hz), 63.9, 21.9, 13.9. IR (ATR): $\nu$ 2959, 2926, 2855, 1747, 1670, 1605, 1572, 1494, 1464, 1409, 1380, 1362, 1297, 1266, 1231, 1211, 1182, 1161, 1124, 1096, 1081, 1019, 960, 881, 849, 820, 754, 745, 700, 587, 527, 496, 460, 429, 421 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{24}$H$_{20}$F$_3$N$_2$O$_4$ [M + H]$^+$: 457.1370; found: 457.1369.

Ethyl 5,6-di([1,1'-biphenyl]-4-carbonyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3c)

Obtained as a yellow solid in 81% yield (70 mg). Mp: 196–198 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.60. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 (d, $J = 8.0$ Hz, 2H), 7.85 (d, $J = 8.0$ Hz, 2H), 7.78 – 7.70 (m, 4H), 7.69 – 7.60 (m, 4H), 7.58 – 7.36 (m, 6H), 4.66 (q, $J = 7.1$ Hz, 2H), 1.53 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -56.2 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 189.6, 189.4, 163.1, 157.4, 151.5 (q, $J = 1.6$ Hz), 147.5, 139.5, 139.4, 138.1 (q, $J = 2.1$ Hz), 134.4, 133.1, 132.0, 129.9, 129.0, 128.7 (d, $J = 2.0$ Hz), 127.6, 127.4, 127.3, 125.5 (q, $J = 35.5$ Hz), 121.3 (q, $J = 277.7$ Hz), 64.0, 13.9. IR (ATR): $\nu$ 3034, 2983, 1747, 1681, 1668, 1602, 1559, 1518, 1486, 1465, 1449, 1407, 1382, 1359, 1314, 1293, 1265, 1233, 1177, 1157, 1124, 1078, 1007, 955, 918, 881, 859, 749, 733, 696, 659, 627, 590, 485 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{34}$H$_{24}$F$_3$N$_2$O$_4$ [M + H]$^+$: 581.1683; found: 581.1685.
ethyl 5,6-di(2-naphthoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3d)

Obtained as a yellow solid in 85% yield (67 mg). Mp: 194–196 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.65. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 8.60 (s, 1H), 8.20 (s, 1H), 8.03 – 7.93 (m, 4H), 7.92 – 7.84 (m, 4H), 7.70 – 7.51 (m, 4H), 4.67 (q, \(J = 7.1\) Hz, 2H), 1.53 (t, \(J = 7.1\) Hz, 3H). \(^1^9\)F NMR (376 MHz, CDCl\(_3\)) δ -56.2 (s, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 190.0, 189.7, 183.1, 157.7, 151.6, 138.3 (q, \(J = 2.0\) Hz), 136.3, 136.2, 135.1, 133.1, 132.4, 132.2, 132.1, 131.7, 130.2, 129.9, 129.6, 129.5, 129.2, 128.7, 128.0, 127.8, 127.3, 127.1, 125.6 (q, \(J = 35.5\) Hz), 125.0, 123.6, 121.4 (q, \(J = 278.3\) Hz), 64.0, 14.0. IR (ATR): ν 3059, 2984, 1747, 1662, 1625, 1595, 1574, 1507, 1467, 1437, 1384, 1277, 1253, 1219, 1193, 1155, 1134, 1109, 1018, 975, 935, 914, 865, 847, 824, 789, 775, 759, 738, 701, 603, 584, 475 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for C\(_{30}\)H\(_{20}\)F\(_3\)N\(_2\)O\(_4\) [M + H]\(^+\): 529.1370; found: 529.1372.

ethyl 5,6-bis(4-methoxybenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3e)

Obtained as a yellow solid in 63% yield (47 mg). Mp: 152–154 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.55. \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ 7.98 (d, \(J = 8.2\) Hz, 2H), 7.72 (d, \(J = 7.7\) Hz, 2H), 7.00 – 6.92 (m, 4H), 4.62 (q, \(J = 7.1\) Hz, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 1.50 (t, \(J = 7.1\) Hz, 3H). \(^1^9\)F NMR (376 MHz, CDCl\(_3\)) δ -56.4 (s, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) δ 188.4, 188.1, 165.0, 164.8, 163.2, 157.9, 151.3,
138.0, 133.9, 131.9, 128.9, 127.5, 125.1 (q, \(J = 35.3\) Hz), 121.3 (q, \(J = 276.9\) Hz), 114.3, 114.0, 63.9, 55.7, 55.6, 13.9. IR (ATR): \(\nu\) 2982, 2938, 2843, 1745, 1662, 1594, 1573, 1511, 1444, 1424, 1402, 1381, 1360, 1317, 1250, 1234, 1166, 1123, 1023, 983, 956, 880, 847, 810, 785, 766, 740, 702, 642, 608, 515, 477, 448, 424, 410 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for \(\text{C}_{24}\text{H}_{20}\text{F}_{3}\text{N}_{2}\text{O}_{6}\) [M + H]^+: 489.1268; found: 489.1269.

ethyl 5,6-bis(3-methoxybenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3f)

Obtained as a yellow solid in 58% yield (43 mg). Mp: 152–154 °C. \(R_f\) (petroleum ether : ethyl acetate = 5 : 1) = 0.53. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.04 (d, \(J = 7.8\) Hz, 1H), 7.63 – 7.54 (m, 3H), 7.12 (t, \(J = 7.5\) Hz, 1H), 7.04 (t, \(J = 7.5\) Hz, 1H), 6.97 (d, \(J = 8.3\) Hz, 1H), 6.94 (d, \(J = 8.5\) Hz, 1H), 4.59 (q, \(J = 7.1\) Hz, 2H), 3.68 (s, 3H), 3.55 (s, 3H), 1.48 (t, \(J = 7.1\) Hz, 3H). \(^1^9\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -56.9 (s, 3F). \(^1^3\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 191.5, 188.0, 163.6, 159.6, 159.5, 156.1, 151.3, 140.0, 136.5, 135.1, 131.3, 130.4, 125.9, 124.9, 123.0 (q, \(J = 35.8\) Hz), 121.8 (q, \(J = 277.2\) Hz), 121.3, 120.8, 112.1, 112.0, 63.5, 55.9, 55.5, 13.9. IR (ATR): \(\nu\) 2927, 2843, 1746, 1670, 1598, 1582, 1519, 1485, 1466, 1450, 1438, 1402, 1380, 1359, 1282, 1248, 1221, 1159, 1132, 1047, 1017, 987, 958, 879, 861, 841, 796, 754, 729, 709, 687, 671, 651, 588, 535, 523, 495, 442, 427, 414 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for \(\text{C}_{24}\text{H}_{20}\text{F}_{3}\text{N}_{2}\text{O}_{6}\) [M + H]^+: 489.1268; found: 489.1267.
ethyl 5,6-bis(3,4-dimethoxybenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3g)

Obtained as a yellow solid in 52% yield (43 mg). Mp: 170–172 °C. $R_f$ (petroleum ether : ethyl acetate = 3 : 1) = 0.44. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J = 8.5$ Hz, 1H), 7.56 (s, 1H), 7.51 (s, 1H), 7.11 (d, $J = 7.7$ Hz, 1H), 6.92 (d, $J = 8.5$ Hz, 1H), 6.87 (d, $J = 8.3$ Hz, 1H), 4.63 (q, $J = 7.1$ Hz, 2H), 3.99 (s, 3H), 3.96 (s, 3H), 3.95 (s, 3H), 3.91 (s, 3H), 1.50 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -56.4 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 188.4, 188.1, 163.2, 157.9, 155.1, 154.9, 151.3 (q, $J = 1.6$ Hz), 149.5, 149.3, 137.9, 129.0, 128.2, 127.6, 126.1, 125.2 (q, $J = 35.4$ Hz), 121.3 (q, $J = 277.7$ Hz), 111.8, 110.2, 110.1, 109.8, 63.9, 56.3, 56.2, 56.1, 13.9. IR (ATR): $\nu$ 2938, 2842, 1745, 1655, 1583, 1512, 1463, 1421, 1382, 1353, 1265, 1243, 1210, 1146, 1116, 1036, 1017, 995, 918, 863, 843, 815, 789, 766, 734, 702, 675, 643, 592, 537, 482, 450, 431 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{26}$H$_{24}$F$_3$N$_2$O$_8$ [M + H]$^+$: 549.1479; found: 549.1480.

ethyl 5,6-bis(2,5-dimethoxybenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3h)

Obtained as a yellow solid in 50% yield (41 mg). Mp: 171–173 °C. $R_f$ (petroleum ether : ethyl acetate = 3 : 1) = 0.41. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46 (s, 1H), 7.22 –
7.01 (m, 3H), 6.88 (t, $J = 9.9$ Hz, 2H), 4.58 (q, $J = 7.2$ Hz, 2H), 3.82 (s, 3H), 3.74 (s, 3H), 3.59 (s, 3H), 3.48 (s, 3H), 1.46 (t, $J = 7.2$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -56.9 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.2, 187.8, 163.6, 156.2, 154.3, 154.2, 153.9, 153.6, 151.3 (q, $J = 1.8$ Hz), 139.7 (q, $J = 2.3$ Hz), 126.0, 124.9, 124.3, 123.1 (q, $J = 35.5$ Hz), 122.4, 121.7 (q, $J = 276.5$ Hz), 114.1, 113.8, 113.6, 112.0, 63.6, 56.5, 55.9, 55.8, 13.9. IR (ATR): $\nu$ 2956, 2920, 2852, 2158, 2026, 1973, 1747, 1611, 1582, 1497, 1462, 1419, 1378, 1277, 1227, 1205, 1159, 1106, 1042, 1017, 913, 865, 819, 729, 668 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{26}$H$_{24}$F$_3$N$_2$O$_8$ [M + H]$^+$: 549.1479; found: 549.1480.

ethyl 5,6-bis(4-hydroxybenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3i)

Obtained as a yellow solid in 67% yield (49 mg). Mp: 152–154 °C. $R_f$ (petroleum ether : ethyl acetate = 3 : 1) = 0.35. $^1$H NMR (400 MHz, DMSO-$d_6$) $\delta$ 10.85 (br s, 2H), 7.78 (d, $J = 7.8$ Hz, 2H), 7.74 (d, $J = 7.9$ Hz, 2H), 6.88 (d, $J = 7.8$ Hz, 2H), 6.76 (d, $J = 7.5$ Hz, 2H), 4.56 (q, $J = 7.1$ Hz, 2H), 1.39 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, DMSO-$d_6$) $\delta$ -56.2 (s, 3F). $^{13}$C NMR (101 MHz, DMSO-$d_6$) $\delta$ 188.6, 188.2, 164.3, 164.2, 163.7, 157.7, 151.3 (q, $J = 2.0$ Hz), 137.6 (q, $J = 2.4$ Hz), 134.4, 132.9, 127.0, 126.3, 125.3 (q, $J = 35.4$ Hz), 121.8 (q, $J = 277.4$ Hz), 116.0, 115.4, 64.0, 14.2. IR (ATR): $\nu$ 3367, 2254, 2188, 1655, 1599, 1455, 1381, 1236, 1170, 1048, 1023, 995, 823, 761, 611, 579, 533, 514, 490, 448 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{15}$F$_3$N$_2$O$_8$Na [M + Na]$^+$: 483.0774; found: 483.0775.
ethyl 5,6-bis(4-cyanobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3j)

Obtained as a white solid in 80% yield (57 mg). Mp: 180–182 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.55. 1H NMR (400 MHz, CDCl3) δ 8.16 (d, J = 7.6 Hz, 2H), 7.97 – 7.76 (m, 6H), 4.64 (q, J = 7.1 Hz, 2H), 1.51 (t, J = 7.1 Hz, 3H). 19F NMR (376 MHz, CDCl3) δ -56.1 (s, 3F). 13C NMR (101 MHz, CDCl3) δ 188.8, 162.5, 155.8, 151.9, 138.3, 137.7, 137.1, 132.9, 132.4, 131.7, 129.3, 125.7 (q, J = 35.7 Hz), 120.9 (q, J = 277.9 Hz), 118.0, 117.9, 117.5, 117.4, 64.3, 13.9. IR (ATR): ν 2986, 2925, 2232, 1746, 1678, 1613, 1582, 1534, 1478, 1442, 1407, 1380, 1350, 1297, 1246, 1223, 1159, 1133, 1094, 1017, 989, 976, 905, 879, 858, 837, 817, 768, 736, 718, 696, 675, 650, 590, 545, 487, 432, 416, 404 cm⁻¹. HRMS (ESI) m/z: calcd. for C24H14O4N4F3 [M + H]^+: 479.0962; found: 479.0963.

ethyl 5,6-bis(4-nitrobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3k)

Obtained as a yellow solid in 78% yield (59 mg). Mp: 168–170 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.37. 1H NMR (400 MHz, CDCl3) δ 8.42 (d, J = 8.9 Hz, 2H), 8.38 (d, J = 8.9 Hz, 2H), 8.27 (d, J = 9.0 Hz, 2H), 7.97 (d, J = 8.8 Hz, 2H), 4.66 (q, J = 7.1 Hz, 2H), 1.52 (t, J = 7.1 Hz, 3H). 19F NMR (376 MHz, CDCl3) δ -56.1 (s, 3F). 13C NMR (101 MHz, CDCl3) δ 188.6, 188.4, 162.4, 155.7, 151.9 (q, J = 2.0 Hz), 151.1, 139.7 (q, J = 1.5 Hz), 138.5, 137.7 (q, J = 2.1 Hz), 132.5, 130.0, 125.7 (q, J = 35.7 Hz), 124.4, 123.7, 120.9 (q, J = 277.9 Hz), 64.4, 13.9. IR (ATR): ν 2987, 2926,
2233, 1746, 1678, 1613, 1533, 1478, 1442, 1408, 1380, 1349, 1293, 1245, 1222, 1158, 1133, 1094, 1018, 1001, 990, 975, 905, 879, 857, 816, 768, 735, 718, 696, 675, 650, 589, 545, 489, 437, 417 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for C\(_{22}\)H\(_{13}\)F\(_3\)N\(_4\)O\(_8\) Na [M + Na]\(^+\): 541.0578; found: 541.0582.

**ethyl 5,6-bis(3-nitrobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3l)**

Obtained as a yellow solid in 75% yield (58 mg). Mp: 165–167 °C. \(R_f\) (petroleum ether : ethyl acetate = 5 : 1) = 0.48. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.94 (s, 1H), 8.62 (s, 1H), 8.57 (d, \(J = 8.2\) Hz, 2H), 8.45 (d, \(J = 7.7\) Hz, 1H), 8.11 (d, \(J = 7.6\) Hz, 1H), 7.85 – 7.73 (m, 2H), 4.66 (q, \(J = 7.1\) Hz, 2H), 1.52 (t, \(J = 7.1\) Hz, 3H). \(^1\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -56.1 (s, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 188.0, 162.4, 155.8, 153.1, 152.0, 148.7, 148.3, 137.6 (q, \(J = 2.0\) Hz), 136.9 (q, \(J = 1.2\) Hz), 136.8, 135.2, 134.3, 130.5, 130.0, 129.0, 128.9, 126.2, 125.8 (q, \(J = 35.4\) Hz), 123.5, 121.0 (q, \(J = 278.0\) Hz), 64.4, 13.9. IR (ATR): ν 3068, 2966, 2906, 1748, 1676, 1582, 1556, 1516, 1492, 1466, 1383, 1272, 1259, 1238, 1217, 1162, 1137, 1121, 1095, 1082, 1032, 972, 894, 863, 846, 825, 787, 761, 731, 704, 677, 595, 564, 527, 486, 453, 435, 421, 411 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for C\(_{22}\)H\(_{14}\)F\(_3\)N\(_4\)O\(_8\) [M + H]\(^+\): 519.0758; found: 519.0759.
**ethyl**

**4-(trifluoromethyl)-5,6-bis(4-(trifluoromethyl)benzoyl)pyridazine-3-carboxylate (3m)**

Obtained as a white solid in 73% yield (62 mg). Mp: 162–162 °C. $R_f$ (petroleum ether : ethyl acetate = 8 : 1) = 0.55. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.13 (d, $J = 8.0$ Hz, 2H), 7.83 (d, $J = 8.1$ Hz, 2H), 7.38 – 7.30 (m, 4H), 4.63 (q, $J = 7.1$ Hz, 2H), 1.50 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -56.3 (s, 3F), -57.5 (s, 3F), -57.6 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.6, 188.3, 162.8, 156.7, 153.9 (q, $J = 1.6$ Hz), 153.7 (q, $J = 1.6$ Hz), 151.6 (q, $J = 1.9$ Hz), 137.8 (q, $J = 1.9$ Hz), 133.7, 133.6, 132.2, 131.3, 125.5 (q, $J = 35.5$ Hz), 120.8 (q, $J = 278.3$ Hz), 120.5, 120.2, 120.2 (q, $J = 258.3$ Hz), 120.1 (q, $J = 258.3$ Hz), 64.1, 13.9. IR (ATR): ν 2988, 1747, 1676, 1602, 1506, 1468, 1414, 1382, 1361, 1303, 1246, 1208, 1155, 1124, 1016, 985, 959, 927, 879, 860, 766, 747, 702, 661, 588, 509, 481, 432 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{24}$H$_{14}$F$_9$N$_2$O$_4$ [M + H]$^+$: 567.0961; found: 567.0958.

![Diagram of the molecular structure of the compound](image)

**ethyl 5,6-bis(4-fluorobenzoyl)-4-(trifluoromethyl)pyrazine-3-carboxylate (3n)**

Obtained as a yellow solid in 64% yield (45 mg). Mp: 165–167 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.66. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.10 (t, $J = 6.7$ Hz, 2H), 7.80 (t, $J = 6.7$ Hz, 2H), 7.27 – 7.14 (m, 4H), 4.63 (q, $J = 7.1$ Hz, 2H), 1.50 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -56.3 (s, 3F), -100.9 – -101.0 (m, 1F), -101.0 – -101.1 (m, 1F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.5, 188.2, 166.8 (d, $J = 259.3$ Hz), 166.6 (d, $J = 258.4$ Hz), 162.9, 157.0, 151.5 (q, $J = 2.1$ Hz), 137.9 (q, $J = 2.1$ Hz), 134.4 (d, $J = 10.0$ Hz), 132.2, 132.0 (d, $J = 10.0$ Hz), 130.7 (d, $J = 2.9$ Hz), 125.5 (q, $J = 35.6$ Hz), 121.2 (q, $J = 277.2$ Hz), 116.4 (d, $J = 22.3$ Hz), 116.1 (d, $J =$ 258.3 Hz).

![Ethyl 5,6-bis(4-chlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3o)](image1)

**ethyl 5,6-bis(4-chlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3o)**

Obtained as a yellow solid in 81% yield (60 mg). Mp: 170–172 °C. Rₜ (petroleum ether : ethyl acetate = 5 : 1) = 0.64. ¹H NMR (400 MHz, CDCl₃) δ 7.99 (d, J = 7.8 Hz, 2H), 7.71 (d, J = 7.9 Hz, 2H), 7.55 – 7.45 (m, 4H), 4.63 (q, J = 7.1 Hz, 2H), 1.50 (t, J = 7.1 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 188.9, 188.6, 162.8, 156.8, 151.6, 141.8, 141.6, 137.8 (q, J = 2.2 Hz), 134.0 (q, J = 1.4 Hz), 132.7, 132.5, 130.5, 129.5, 129.1, 125.4 (q, J = 35.2 Hz), 121.1 (q, J = 277.7 Hz), 64.1, 13.9. IR (ATR): ν 2985, 1746, 1670, 1586, 1520, 1488, 1466, 1403, 1380, 1359, 1248, 1223, 1157, 1123, 1091, 1013, 985, 958, 844, 800, 758, 737, 716, 703, 691, 656, 625, 586, 556, 526, 496, 476, 404 cm⁻¹. HRMS (ESI) m/z: calcd. for C₂₂H₁₄Cl₂F₅N₂O₄ [M + H]⁺: 497.0277; found: 497.0276.

![Ethyl 5,6-bis(3-chlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3p)](image2)

**ethyl 5,6-bis(3-chlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3p)**

Obtained as a yellow solid in 82% yield (60 mg). Mp: 170–172 °C. Rₜ (petroleum ether : ethyl acetate = 5 : 1) = 0.64. ¹H NMR (400 MHz, CDCl₃) δ 8.02 (s, 1H), 7.93
(d, J = 7.8 Hz, 1H), 7.81 (s, 1H), 7.69 – 7.60 (m, 2H), 7.57 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.8 Hz, 2H), 4.64 (q, J = 7.0 Hz, 2H), 1.50 (t, J = 7.1 Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -56.2 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 188.7, 188.6, 162.8, 156.5, 151.7, 137.7 (q, J = 2.2 Hz), 137.0 (q, J = 2.2 Hz), 135.7, 135.6, 135.0, 134.8, 131.0, 130.3, 130.0, 129.6, 128.7, 127.5, 125.7 (q, J = 35.6 Hz), 121.1 (q, J = 277.8 Hz), 64.1, 13.9. IR (ATR): $\nu$ 2986, 1746, 1674, 1591, 1571, 1519, 1470, 1428, 1381, 1359, 1280, 1243, 1219, 1159, 1129, 1095, 1076, 1016, 997, 969, 891, 862, 802, 778, 751, 734, 718, 700, 674, 656, 633, 591, 542, 505, 470, 448, 419 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$Cl$_2$F$_3$N$_2$O$_4$ [M + H]$^+$: 497.0277; found: 497.0276.

![Chemical Structure](image)

**ethyl 5,6-bis(2-chlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3q)**

Obtained as a yellow solid in 79% yield (59 mg). Mp: 166–168 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.63. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.12 (s, 1H), 7.62 – 7.50 (m, 4H), 7.46 (d, J = 7.8 Hz, 2H), 7.41 (t, J = 7.5 Hz, 1H), 4.60 (q, J = 7.1 Hz, 2H), 1.48 (t, J = 7.1 Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -56.6 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.8, 187.9, 162.9, 154.8, 152.0 (q, J = 25.1 Hz), 135.6, 135.1, 134.3, 133.3, 132.3, 131.5, 131.1, 130.4, 127.4, 126.9, 124.6 (q, J = 35.8 Hz), 121.3 (q, J = 277.8 Hz), 63.9, 13.9. IR (ATR): $\nu$ 2984, 2964, 1673, 1584, 1556, 1522, 1466, 1436, 1382, 1358, 1259, 1237, 1216, 1158, 1128, 1095, 1060, 1031, 1015, 972, 962, 893, 880, 861, 818, 802, 779, 736, 703, 677, 650, 637, 593, 564, 547, 520, 474, 452, 435 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$Cl$_2$F$_3$N$_2$O$_4$ [M + H]$^+$: 497.0277; found: 497.0278.
ethyl 5,6-bis(3,4-dichlorobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3r)

Obtained as a yellow solid in 61% yield (51 mg). Mp: 174–176 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.60. ¹H NMR (400 MHz, CDCl₃) δ 8.19 (s, 1H), 7.95 – 7.86 (m, 2H), 7.62 (dt, J = 8.4, 2.1 Hz, 2H), 7.52 (d, J = 8.2 Hz, 1H), 4.64 (q, J = 7.1 Hz, 2H), 1.51 (t, J = 7.1 Hz, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -56.2 (s, 3F). ¹³C NMR (101 MHz, CDCl₃) δ 187.8, 187.6, 162.6, 156.2, 151.8 (q, J = 1.8 Hz), 140.0, 139.8, 137.5 (q, J = 2.0 Hz), 135.1, 134.2, 133.6, 133.5, 133.1, 131.3, 130.9, 130.5, 130.4, 128.0, 125.7 (q, J = 35.6 Hz), 121.0 (q, J = 277.7 Hz), 64.2, 13.9. IR (ATR): ν 2966, 2158, 2029, 1748, 1676, 1582, 1556, 1516, 1492, 1466, 1383, 1272, 1258, 1238, 1162, 1137, 1121, 1095, 1082, 1031, 972, 894, 863, 846, 825, 786, 761, 731, 704, 676, 595, 578, 564, 526, 486, 474, 453, 435, 421, 411, 403 cm⁻¹. HRMS (ESI) m/z: calcd. for C₂₂H₁₂Cl₂F₃N₂O₄ [M + H]⁺: 564.9498; found: 564.9500.

ethyl 5,6-bis(4-bromobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3s)

Obtained as a yellow solid in 93% yield (78 mg). Mp: 155–157 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.55. ¹H NMR (400 MHz, CDCl₃) δ 7.91 (d, J = 7.7 Hz, 2H), 7.72 – 7.64 (m, 4H), 7.62 (d, J = 8.1 Hz, 2H), 4.62 (q, J = 7.1 Hz, 2H), 1.49 (t, J = 7.1 Hz, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -56.2 (s, 3F). ¹³C NMR (101 MHz, CDCl₃) δ 189.1, 188.8, 162.8, 156.7, 151.6 (q, J = 2.1 Hz), 137.8 (q, J = 2.1 Hz),
134.4 (q, $J = 1.2$ Hz), 132.9, 132.7, 132.5, 132.1, 130.7, 130.5, 130.4, 125.5 (q, $J = 35.7$ Hz), 121.0 (q, $J = 276.8$ Hz), 64.1, 13.9. IR (ATR): ν 2985, 1745, 1670, 1584, 1519, 1484, 1446, 1399, 1383, 1359, 1295, 1247, 1221, 1155, 1123, 1069, 1011, 984, 957, 977, 841, 796, 756, 737, 703, 683, 654, 634, 623, 587, 545, 495, 475, 456 cm$^{-1}$.

HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$Br$_2$F$_3$N$_2$O$_4$ [M + H]$^+$: 584.9267; found: 584.9271.

**ethyl 5,6-bis(3-bromobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3t)**

Obtained as a yellow solid in 89% yield (78 mg). Mp: 154–156 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.64. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.18 (s, 1H), 8.01 – 7.91 (m, 2H), 7.81 (t, $J = 6.9$ Hz, 2H), 7.61 (d, $J = 7.6$ Hz, 1H), 7.41 (t, $J = 7.9$ Hz, 2H), 4.64 (q, $J = 7.1$ Hz, 2H), 1.52 (t, $J = 7.1$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -56.2 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 188.6, 188.5, 162.8, 156.4, 151.7 (q, $J = 2.1$ Hz), 137.7 (q, $J = 2.1$ Hz), 137.2 (q, $J = 2.1$ Hz), 135.9, 133.9, 131.6, 130.6, 130.2, 130.0, 127.9, 125.6 (q, $J = 35.4$ Hz), 123.5, 122.9, 121.0 (q, $J = 277.2$ Hz), 64.1, 13.9. IR (ATR): ν 2984, 1746, 1671, 1589, 1566, 1519, 1470, 1446, 1424, 1380, 1360, 1279, 1241, 1215, 1155, 1127, 1095, 1068, 1014, 998, 966, 886, 861, 842, 799, 772, 732, 696, 672, 646, 632, 590, 541, 486, 463, 428 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$Br$_2$F$_3$N$_2$O$_4$ [M + H]$^+$: 584.9267; found: 584.9268.
ethyl 5,6-bis(2-bromobenzoyl)-4-(trifluoromethyl)pyridazine-3-carboxylate (3u)

Obtained as a yellow solid in 95% yield (81 mg). Mp: 151–153 °C. R_f (petroleum ether : ethyl acetate = 5 : 1) = 0.66. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.97 (br s, 1H), 7.72 (d, \(J = 8.2\) Hz, 1H), 7.65 – 7.63 (m, 1H), 7.55 – 7.46 (m, 3H), 7.46 – 7.37 (m, 2H), 4.59 (q, \(J = 7.1\) Hz, 2H), 1.46 (t, \(J = 7.1\) Hz, 3H). \(^1^9\)F NMR (376 MHz, CDCl\(_3\)) \(\delta\) -56.5 (s, 3F). \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \(\delta\) 192.3, 188.5, 162.9, 154.8, 151.8 (q, \(J = 1.8\) Hz), 138.8, 137.5, 135.3, 135.0, 134.6, 133.5, 133.2, 133.1, 131.2, 127.8, 127.4, 124.9 (q, \(J = 35.5\) Hz), 122.8, 121.3 (q, \(J = 277.7\) Hz), 121.1, 63.9, 13.9. IR (ATR): \(\nu\) 2984, 1746, 1671, 1589, 1566, 1519, 1470, 1446, 1424, 1380, 1360, 1279, 1241, 1215, 1155, 1127, 1095, 1068, 1014, 998, 966, 886, 861, 842, 799, 772, 732, 696, 672, 646, 632, 590, 541, 486, 463, 428 cm\(^{-1}\). HRMS (ESI) m/z: calcd. for C\(_{22}\)H\(_{14}\)Br\(_2\)F\(_3\)N\(_2\)O\(_4\) [M + H]\(^+\): 584.9267; found: 584.9265.
-2-(2-(1,4-di([1,1'-biphenyl]-4-yl)-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-4,4,4-trifluoro-3-oxobutanoate (4)

Obtained as a yellow solid in 52% yield (93.0 mg). Mp: 140–142 °C. Rf (petroleum ether : ethyl acetate = 5 : 1) = 0.32. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 15.46 (s, 1H), 8.16 (d, $J$ = 8.4 Hz, 2H), 8.07 (d, $J$ = 8.4, Hz, 2H), 7.75 (dd, $J$ = 8.5, 2.0 Hz, 4H), 7.67 (d, $J$ = 7.6 Hz, 4H), 7.56 – 7.47 (m, 4H), 7.46 – 7.40 (m, 2H), 6.70 (s, 1H), 4.55 (q, $J$ = 7.1 Hz, 2H), 1.47 (t, $J$ = 7.1 Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -72.2 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 190.7, 189.2, 174.9 (q, $J$ = 34.7 Hz), 160.4, 153.4, 147.3, 146.3, 139.6, 139.5, 136.2, 133.5, 130.2, 129.1, 129.0, 128.7, 128.5, 127.5, 127.5, 127.4, 127.3, 127.0, 115.7 (q, $J$ = 292.6 Hz), 101.5, 62.9, 14.1. IR (ATR): $\nu$ 3062, 2988, 2256, 1842, 1725, 1679, 1634, 1600, 1559, 1509, 1452, 1372, 1285, 1253, 1191, 1148, 1044, 1008, 970, 909, 880, 823, 726, 695, 648, 587, 561, 472 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{34}$H$_{26}$O$_5$N$_2$F$_3$ [M + H]$^+$: 599.1788; found: 599.1785.
-2-(2-(1,4-di([1,1'-biphenyl]-4-yl)-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-3-oxo
butanoate (4')

Obtained as a yellow solid in 40% yield (66.0 mg). Mp: 179–181 °C.  

\[ \text{C}_{34}\text{H}_{29}\text{N}_{2}\text{O}_5 [\text{M} + \text{H}]^+ : 545.2074; \text{found: } 545.2074. \]

\[ \text{C}_{34}\text{H}_{29}\text{N}_{2}\text{O}_5 [\text{M} + \text{H}]^+ : 545.2071; \text{found: } 545.2074. \]

2-(2-(1,4-bis(4-bromophenyl)-1,4-dioxobut-2-en-2-yl)hydrazineylidene)-3-oxo-3-p
henylpropanoate (4'')

Obtained as a brown solid in 81% yield (244.0 mg). Mp: 148–150 °C.  

\[ \text{C}_{34}\text{H}_{29}\text{N}_{2}\text{O}_5 [\text{M} + \text{H}]^+ : 545.2074; \text{found: } 545.2074. \]
2H), 6.30 (s, 1H), 4.47 (q, $J = 7.1$ Hz, 2H), 1.36 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 189.9, 189.6, 188.1, 161.0, 154.7, 136.6, 135.2, 134.2, 133.9, 133.2, 132.2, 132.0, 130.5, 129.8, 129.7, 129.6, 128.3, 128.1, 96.9, 62.7, 14.0. IR (ATR): ν 3083, 2845, 2181, 1597, 1557, 1519, 1492, 1441, 1402, 1371, 1348, 1292, 1269, 1243, 1188, 1141, 1073, 1047, 1009, 894, 856, 756, 724, 684, 617, 606, 596, 586, 552, 542, 535, 521, 483, 424, 402 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{27}$H$_{21}$Br$_2$N$_2$O$_5$ [M + H]$^+$: 610.9817; found: 610.9814.

![5,6-dibenzoyl-4-(trifluoromethyl)pyridazine-3-carboxamide (5a)](image)

Obtained as a white solid in 94% yield (37.0 mg). Mp: 192–194 °C. $R_f$ (petroleum ether : ethyl acetate = 1 : 1) = 0.23. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 8.67 (d, $J = 7.3$ Hz, 2H), 8.46 (s, 1H), 8.19 (s, 1H), 7.71 – 7.65 (m, 3H), 7.35 – 7.32 (m, 3H), 7.31 – 7.27 (m, 2H). $^{19}$F NMR (376 MHz, DMSO-$d_6$) δ -56.5 (s, 3F). $^{13}$C NMR (101 MHz, DMSO-$d_6$) δ 166.3, 163.3, 161.2, 152.3, 149.5, 137.6, 132.9, 131.3, 129.8, 129.4, 128.8, 128.6, 125.7, 121.9 (q, $J = 276.5$ Hz), 121.2 (q, $J = 36.1$ Hz), 101.1. IR (ATR): ν 3462, 3181, 2924, 2855, 1692, 1593, 1562, 1492, 1451, 1346, 1269, 1184, 1154, 1069, 1022, 976, 952, 920, 860, 770, 729, 693, 656, 624, 543, 483, 454, 420 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{20}$H$_{13}$O$_3$N$_3$F$_3$ [M + H]$^+$: 400.0903; found: 400.0904.
**5,8-di([1,1'-biphenyl]-4-yl)-4-(trifluoromethyl)pyridazino[4,5-c]pyridazine-3-carboxylate (6c)**

Obtained as a yellow solid in 72% yield (41.0 mg). Mp: 220–222 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.40. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.46 (d, $J$ = 8.1 Hz, 2H), 7.89 (d, $J$ = 8.1 Hz, 2H), 7.86 – 7.70 (m, 7H), 7.56 – 7.50 (m, 4H), 7.49 – 7.42 (m, 3H), 4.66 (q, $J$ = 7.1 Hz, 2H), 1.52 (t, $J$ = 7.1 Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -51.9 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.5, 156.0, 155.8, 150.3, 147.9, 143.9, 143.4, 142.5, 140.2, 140.0, 136.5, 132.8, 131.7, 130.3, 129.9, 129.0, 128.1, 127.4, 127.3, 127.2, 127.1, 121.3 (q, $J$ = 277.4 Hz), 120.8 (q, $J$ = 35.4 Hz), 113.7, 64.0, 14.0. IR (ATR): ν 3031, 2926, 1745, 1606, 1487, 1447, 1401, 1370, 1306, 1255, 1196, 1167, 1145, 1007, 878, 768, 736, 697, 672, 616, 566, 502, 486, 457, 446, 435, 414 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{34}$H$_{24}$F$_3$N$_4$O$_2$ [M + H]$^+$: 577.1846; found: 577.1844.

**5,8-bis(4-cyanophenyl)-4-(trifluoromethyl)pyridazino[4,5-c]pyridazine-3-carboxylate (6j)**

Obtained as a yellow solid in 50% yield (24.0 mg). Mp: 215–217 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.38. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.46 (d, $J$ = 8.0 Hz,
2H), 7.96 (d, J = 8.0 Hz, 2H), 7.90 (d, J = 8.0 Hz, 2H), 7.82 (d, J = 8.0 Hz, 2H), 4.66 (q, J = 7.2 Hz, 2H), 1.51 (t, J = 7.2 Hz, 3H). $^1^H$ NMR (376 MHz, CDCl$_3$) δ -52.0 (s, 3F). $^{1^3}$C NMR (101 MHz, CDCl$_3$) δ 163.0, 155.7, 155.6, 150.6, 141.8, 141.0, 132.8, 132.4, 132.2, 130.2, 121.1 (q, J = 276.8 Hz), 119.9 (q, J = 36.5 Hz), 118.2, 117.9, 116.1, 115.0, 114.7, 113.7, 64.4, 13.9.

IR (ATR): ν 3097, 2986, 2359, 2230, 1743, 1609, 1467, 1445, 1401, 1371, 1339, 1306, 1256, 1238, 1194, 1168, 1143, 1112, 1033, 1016, 947, 913, 847, 780, 730, 706, 660, 647, 614, 598, 571, 549, 509, 463, 434, 413, 404 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{24}$H$_{14}$F$_3$N$_6$O$_2$ [M + H]$^+$: 475.1125; found: 475.1124.

**ethyl 5,8-bis(4-fluorophenyl)-4-(trifluoromethyl)pyridazo[4,5-c]pyridazine-3-carboxylate (6n)**

Obtained as a yellow solid in 56% yield (26.0 mg). Mp: 191–193 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.42. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.41 – 8.36 (m, 2H), 7.73 – 7.63 (m, 2H), 7.37 – 7.32 (m, 2H), 7.30 – 7.26 (m, 2H), 4.66 (q, J = 7.1 Hz, 2H), 1.51 (t, J = 7.1 Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -52.1 (s, 3F), -108.5 – -108.4 (m, 1F), -109.3 – -109.2 (m, 1F). $^{1^3}$C NMR (101 MHz, CDCl$_3$) δ 165.0 (d, J = 253.0 Hz), 164.2 (d, J = 252.0 Hz), 163.4, 155.4 (d, J = 8.8 Hz), 150.3 (d, J = 2.6 Hz), 142.2, 134.5 (d, J = 8.8 Hz), 133.6, 131.6 (d, J = 8.6 Hz), 128.9 (d, J = 3.4 Hz), 122.5, 121.1 (q, J = 278.6 Hz), 120.5 (q, J = 36.0 Hz), 116.0, 115.8, 113.7, 64.1, 13.9.

IR (ATR): ν 3078, 2986, 1743, 1603, 1514, 1473, 1402, 1371, 1337, 1302, 1255, 1238, 1194, 1160, 1143, 1097, 1032, 1014, 947, 914, 843, 817, 782, 732, 707, 647, 612, 570.
525, 500, 457, 415 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$F$_3$N$_4$O$_2$ [M + H]$^+$: 461.1031; found: 461.1031.

![Chemical Structure](attachment:image.png)

**5,8-bis(4-chlorophenyl)-4-(trifluoromethyl)pyridazino[4,5-c]pyridazine-3-carboxylate (6o)**

Obtained as a yellow solid in 68% yield (33.0 mg). Mp: 196–198 °C. $R_f$ (petroleum ether : ethyl acetate = 5 : 1) = 0.51. $^1$H NMR (400 MHz, CDCl$_3$) δ 8.30 (d, $J = 8.5$ Hz, 2H), 7.67 – 7.59 (m, 4H), 7.56 (d, $J = 8.3$ Hz, 2H), 4.65 (q, $J = 7.2$ Hz, 2H), 1.50 (t, $J = 7.2$ Hz, 3H). $^{19}$F NMR (376 MHz, CDCl$_3$) δ -52.0 (s, 3F). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.3, 155.5, 155.4, 150.4, 142.1, 138.0, 137.2, 135.8, 133.5, 131.1, 130.8, 129.0, 128.9, 121.1 (q, $J = 277.8$ Hz), 120.4 (q, $J = 36.2$ Hz), 113.6, 64.2, 13.9. IR (ATR): ν 2986, 2359, 2342, 1744, 1684, 1595, 1559, 1540, 1493, 1446, 1400, 1370, 1337, 1303, 1255, 1239, 1195, 1168, 1143, 1093, 1012, 946, 912, 862, 834, 799, 751, 727, 698, 668, 653, 629, 576, 562, 554, 517, 504, 491, 479, 460, 447, 441, 433, 421, 401 cm$^{-1}$. HRMS (ESI) m/z: calcd. for C$_{22}$H$_{14}$Cl$_2$F$_3$N$_4$O$_2$ [M + H]$^+$: 493.0440; found: 493.0442.
Crystal structure analyses

The crystal samples of 3a, 4, and 6j were prepared by slow volatilization in a CH2Cl2/CDCl3 (3:1) solvent mixture. The suitable crystals of 3a (CCDC 2102384), 4 (CCDC 2133310), and 6j (CCDC 2155007) were mounted on quartz fibers and X-ray data collected on a Bruker AXS APEX diffractometer, equipped with a CCD detector at -50 °C, using MoKα radiation (\( \lambda = 0.71073 \) Å). The data was corrected for Lorentz and polarisation effect with the SMART suite of programs and for absorption effects with SADABS. Structure solution and refinement were carried out with the SHELXTL suite of programs. The structure was solved by direct methods to locate the heavy atoms, followed by difference maps for the light non-hydrogen atoms.
ORTEP diagram of compound 3a. Thermal ellipsoids are drawn at 40% probability.
ORTEP diagram of compound 4. Thermal ellipsoids are drawn at 40% probability
ORTEP diagram of compound 6j. Thermal ellipsoids are drawn at 40% probability.
References


7. SHELXTL version 5.03; Bruker Analytical X-ray Systems, Madison, WI. 1997.
Copies of $^1$H NMR, $^{19}$F NMR and $^{13}$C NMR spectra

400 MHz $^1$H NMR spectrum of 3a in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3a in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3a in CDCl$_3$

![376 MHz $^{19}$F NMR spectrum of 3a in CDCl$_3$](image)

400 MHz $^1$H NMR spectrum of 3b in CDCl$_3$

![400 MHz $^1$H NMR spectrum of 3b in CDCl$_3$](image)
101 MHz $^{13}$C NMR spectrum of 3b in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3b in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3c in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3c in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3e in CDCl$_3$

![376 MHz $^{19}$F NMR spectrum of 3e in CDCl$_3$](image)

400 MHz $^1$H NMR spectrum of 3d in CDCl$_3$

![400 MHz $^1$H NMR spectrum of 3d in CDCl$_3$](image)
101 MHz $^{13}$C NMR spectrum of 3d in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3d in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3e in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3e in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3e in CDCl$_3$

400 MHz $^1$H NMR spectrum of 3f in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3f in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3f in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3g in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3g in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3g in CDCl$_3$

400 MHz $^1$H NMR spectrum of 3h in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3h in CDCl$_3$

![C NMR spectrum of 3h in CDCl$_3$](image)

376 MHz $^{19}$F NMR spectrum of 3h in CDCl$_3$

![F NMR spectrum of 3h in CDCl$_3$](image)
400 MHz $^1$H NMR spectrum of 3i in DMSO-$d_6$

101 MHz $^{13}$C NMR spectrum of 3i in DMSO-$d_6$
376 MHz $^{19}$F NMR spectrum of 3i in DMSO-$d_6$

400 MHz $^1$H NMR spectrum of 3j in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3j in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3j in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3k in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3k in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3k in CDCl$_3$

400 MHz $^1$H NMR spectrum of 3l in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3l in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3l in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3m in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3m in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of $3m$ in CDCl$_3$

400 MHz $^1$H NMR spectrum of $3n$ in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3n in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3n in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3o in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3o in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3o in CDCl$_3$

400 MHz $^1$H NMR spectrum of 3p in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3p in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3p in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3q in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3q in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3q in CDCl$_3$

![F NMR spectrum of 3q in CDCl$_3$](image)

400 MHz $^1$H NMR spectrum of 3r in CDCl$_3$

![H NMR spectrum of 3r in CDCl$_3$](image)
101 MHz $^{13}$C NMR spectrum of 3r in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3r in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3s in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 3s in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3s in CDCl$_3$

400 MHz $^1$H NMR spectrum of 3t in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 3t in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 3t in CDCl$_3$
400 MHz $^1$H NMR spectrum of 3u in CDCl$_3$

$^{13}$C NMR spectrum of 3u in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 3u in CDCl$_3$

400 MHz $^1$H NMR spectrum of 4 in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 4 in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 4 in CDCl$_3$
400 MHz $^1$H NMR spectrum of 4' in CDCl$_3$

![400 MHz $^1$H NMR spectrum of 4' in CDCl$_3$](image)

101 MHz $^{13}$C NMR spectrum of 4' in CDCl$_3$

![101 MHz $^{13}$C NMR spectrum of 4' in CDCl$_3$](image)
400 MHz $^1$H NMR spectrum of 4'' in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 4'' in CDCl$_3$
400 MHz $^1$H NMR spectrum of 5a in DMSO-$d_6$

101 MHz $^{13}$C NMR spectrum of 5a in DMSO-$d_6$
376 MHz $^{19}$F NMR spectrum of 5a in DMSO-$d_6$

400 MHz $^1$H NMR spectrum of 6c in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 6c in CDCl₃

376 MHz $^{19}$F NMR spectrum of 6c in CDCl₃
400 MHz $^1$H NMR spectrum of $6j$ in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of $6j$ in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 6j in CDCl$_3$

400 MHz $^1$H NMR spectrum of 6n in CDCl$_3$
101 MHz $^{13}$C NMR spectrum of 6n in CDCl$_3$

376 MHz $^{19}$F NMR spectrum of 6n in CDCl$_3$
400 MHz $^1$H NMR spectrum of 6o in CDCl$_3$

101 MHz $^{13}$C NMR spectrum of 6o in CDCl$_3$
376 MHz $^{19}$F NMR spectrum of 60 in CDCl$_3$