A Facile Route to 1,3-Diazaheterocycle Fused [1,2-*b*]Isoquinolin-1(2*H*)-one Derivatives *via* Substitution-Cyclization Reactions

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Supporting Information

General Information

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 125 MHz, ^{19}F: 470 MHz), chemical shifts(δ) are expressed in ppm, and *J* values are given in Hz, and deuterated DMSO-d_6 was used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. HRMs were performed on a Agllent LC/Msd TOF instrument.

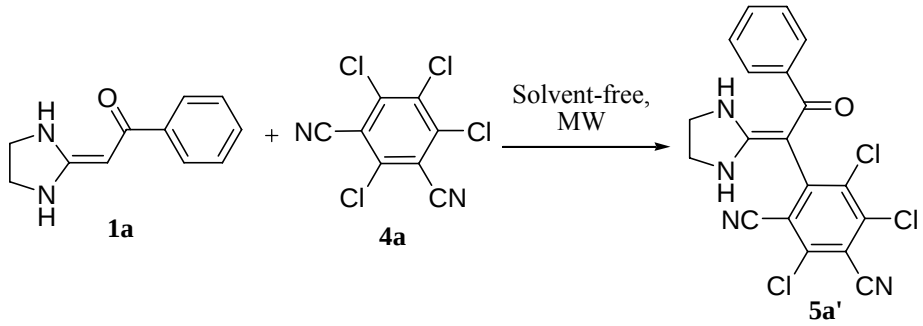
All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

The materials **1a–1d** and **2** were synthesized according to the literature.[1] Compounds **1e** and **3** were prepared according to the literature[2,3] respectively. **4a**–**4c** were purchased from Adrich Corporation Limited.

Screening Temperature and Maximum Power of Microwave Irradiation

To examine the practicality of the projected synthetic route, a set of experiments were carried out using 2-(imidazolidin-2-ylidene)-1-phenylethanone **1a** and 2,4,5,6-tetrachloroisophthalonitrile **4a** as model substrates under microwave irradiation (MW) in solvent-free conditions. All experiments were conducted in septum-sealed reaction vessels with a single-mode cavity to ensure optimal reproducibility of the chemical transformations. We investigated the reaction with a temperature-controlled program at 110 °C (power maximum 170 W) (Table S1, entry 1). After performing the reaction for 12 min, the final product **5a'** was obtained in at least 70% yield.

Table S1. Solvent-free, microwave assisted synthesis of **5a'**

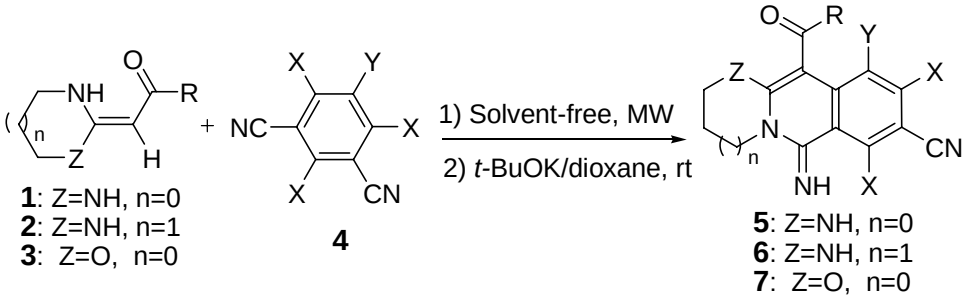


Entry	Power	T (°C)	Time (min)	**5a'** Yield (%)[a]
1	MW/170 W	110	12	70
2	MW/170 W	120	12	88
3	MW/170 W	130	12	86
4	MW/200 W	110	12	70
5	MW/200 W	120	12	89
6	MW/200 W	130	12	84
7	MW/230 W	110	12	71
8	MW/230 W	120	12	87
9	MW/230 W	130	12	80

[a] HKAs **1a** (1.0 mmol), polyhalo isophthalonitrile **4a** (1.1 mmol)

We then explored the effect of increasing the temperature to 120 °C under the same maximum power of 170 W (Table S1, entry 2), which increased the yield of **5a'** to 88%. Upon further increasing the temperature to 130 °C for 12 min, the reaction to form the product **5a'** was accompanied with production of unidentified compounds that led to a lower yield (Table S1, entry 3). At the same time, the impact of microwave power on reaction yield was examined (Table S1, entries 1-9). It was found that the optimum reaction conditions to form the product **5a'** were 120 °C for 12 min with a maximum power of 200 W (Table S1, entry 5).

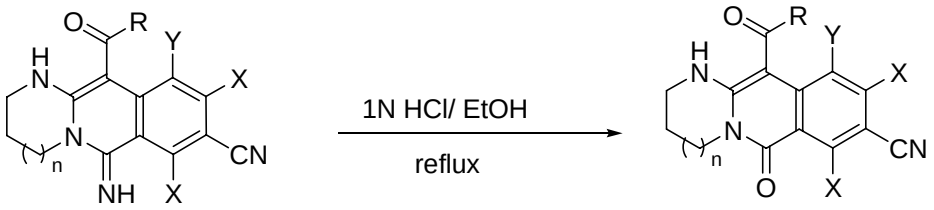
General Procedure for the Synthesis of Polyhalo 1,3-Diazaheterocyclie Fused [1,2-*b*]Isoquinolin-1(2*H*)-imine 5~7



A dry mortar was charged with HKAs **1-3** (1 mmol) and polyhalo isophthalonitrile **4** (1.1 mmol). The mixture was mixed at room temperature by vigorously grinding

with a pestle for a few minutes (*ca.*1–2 min). The mixture was placed in a microwave tube and irradiated in a microwave reactor (Discover), with control of power and temperature by infrared detection, at 120 °C for 12 min (maximum power 200 W). After cooling, the resulting mixture was transferred to a 50 mL flask, and dissolved in 25 mL 1,4-dioxane, before addition of *t*-BuOK (1.5 mmol). Stirring at room temperature, the reaction process was monitored by TLC. After completion, the reaction mixture was poured into 60 mL of water and filtered to obtain the crude products, which were purified by column chromatography (petrol:ethyl acetate = 1:3, v/v) on silica-gel to give the desired products **5-7**, i.e. 1,3-diazaheterocycle fused [1,2-*b*]isoquinolin-1(2*H*)-imine **5a** as a yellow solid (0.37g, 89%), Mp 216-219°C.

General Procedure for the Synthesis of Polyhalo 1,3-Diazaheterocyclie Fused [1,2-*b*]Isoquinolin-1(2*H*)-ones 8~9



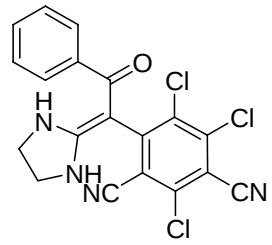
5: Z=NH, n=0
6: Z=NH, n=1

8: Z=NH, n=0
9: Z=NH, n=1

Polyhalo [1,2-*b*]isoquinolin-1(2*H*)-imines **5-6** (1 mmol) were suspended in 20 mL of ethyl alcohol, and 10 mL of 1N aqueous hydrochloric acid , and stirred at reflux for 24 h. The mixture was cooled to room temperature, neutralized with a saturated solution of Na_2CO_3 to a pH of 8-9, and then EtOAc (30 mL) was added. The organic phase was washed with water (10 mL ×3), dried over Na_2SO_4, concentrated and purified by flash column chromatography, to afford polyhalo [1,2-*b*]isoquinolin-1(2*H*)-ones **8-9** in 73-86% yield.

Spectroscopic Data of *C*-Arylation Product 5a'

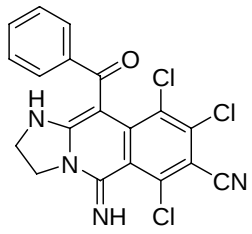
2,4,5-trichloro-6-(1-(imidazolidin-2-ylidene)-2-oxo-2-phenylethyl)isophthalo-nitrile (5a')



Yellow solid (0.372 g, 89%); Mp 263–265 °C; IR (KBr) (ν_{max}, cm^{-1}) 3425, 3248, 2236, 1598,1538, 1320, 649; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.66 (br, 1H, NH), 7.25–7.03 (m, 6H, PhH, NH), 3.75–3.72 (m, 2H, NCH_2), 3.54–3.48 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 184.7, 163.2, 149.8, 142.4, 140.4, 138.2, 137.1, 129.3, 128.0, 127.2, 118.8, 114.3, 113.7, 113.2, 88.1, 44.2, 42.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{11}Cl_3N_4NaO^+$ [$(M+Na)^+$], 438.9891;found, 438.9898.

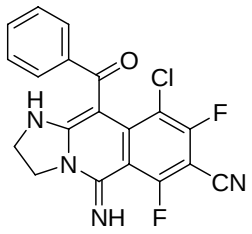
Spectroscopic Data of Tetrahydroimidazo[1,2-*b*]isoquinolinimine 5

5-imino-10-benzoyl-6,8,9-trichloro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5a)



Yellow solid (0.370 g, 89%); Mp 216–219°C; IR (KBr) (ν_{max}, cm^{-1}) 3378, 2224, 1598, 1248, 1078, 806, 636; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.35 (br. s, 1H, NH), 8.70 (br, 1H, NH), 7.50 (d, J = 7.3 Hz, 2H, PhH) , 7.46 (d, J = 7.3 Hz, 1H, PhH) , 7.32 (t, J = 7.3 Hz, 2H, PhH), 4.10–4.0 (m, 2H, NCH_2), 3.82 (t, J = 8.5 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.8, 157.0, 151.8, 143.3, 141.2, 137.4, 134.7, 132.0, 128.7, 128.0, 125.7, 117.9, 114.7, 108.3, 89.0, 45.3, 43.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{12}Cl_3N_4O^+$ [M^+], 417.0071; found, 417.0069.

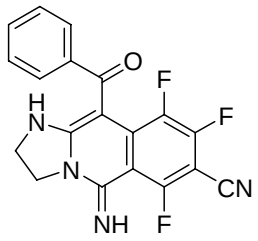
5-imino-10-benzoyl-9-chloro-6,8-difluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5b)



Yellow solid (0.346 g, 90%); Mp 260–262°C; IR (KBr) (ν_{max}, cm^{-1}) 3375, 2236, 1606, 1311, 1026, 854; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.64 (br. s, 2H, NH, =NH), 7.55 (d, J = 7.3 Hz, 2H, PhH), 7.50–7.47 (m, 1H, PhH), 7.36 (t, J = 7.3 Hz, 2H, PhH), 4.08–4.00 (m, 2H, NCH_2), 3.78 (t, J = 8.8 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.5, 162.8, 161.3 (d, J = 268.8 Hz), 156.2, 149.3, 143.6, 141.1, 132.3, 128.8, 128.2, 109.9, 109.5, 106.4, 88.9, 84.7, 44.9, 43.2;

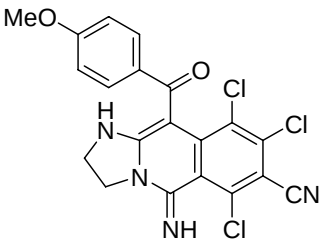
^{19}F NMR (470 MHz, DMSO-d_6) δ -101.8 (s, 1F), -111.5 (s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_{10}ClF_2N_4O^-$ [M$^-$], 383.0517; found, 383.0520.

5-imino-10-benzoyl-6,8,9-trifluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5c)



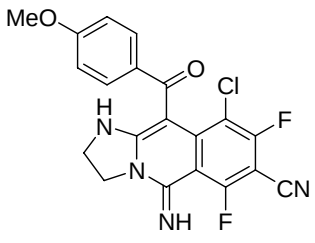
Yellow solid (0.345 g, 94%); Mp 257–259°C; IR (KBr) (ν_{max}, cm^{-1}) 3378, 2234, 1617, 1296, 1187, 1036, 840; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (br, 1H, NH), 8.59 (br. s, 1H, NH), 7.55 (d, J = 7.5 Hz, 2H, PhH), 7.50 (t, J = 7.5 Hz, 1H, PhH), 7.38 (t, J = 7.5 Hz, 2H, PhH), 4.05 (t, J = 8.7 Hz, 2H, NCH_2), 3.82 (t, J = 8.7 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.6, 158.7 (d, J = 258.8 Hz), 155.8, 150.3 (d, J = 265.0 Hz), 149.0, 140.7, 139.1 (d, J = 233.8 Hz), 134.7, 132.0, 128.8, 127.7, 109.8, 105.7, 85.9, 84.1 (d, J = 21.3 Hz), 44.9, 43.2; ^{19}F NMR (470 MHz, DMSO-d_6) δ -114.9 (s, 1F), -129.8 (s, 1F), -138.9 (s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_{10}F_3N_4O^-$ [M$^-$], 367.0812; found, 367.0814.

5-imino-6,8,9-trichloro-10-(4-methoxybenzoyl)-1,2,3,5-tetrahydroimidazo[1,2-*b*] isoquinoline-7-carbonitrile (5d)



Yellow solid (0.354 g, 79%); Mp 223–225°C; IR (KBr) (ν_{max}, cm^{-1}) 3380, 2226, 1629, 1252, 1165, 1027, 839, 604 ; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.33 (br. s, 1H, NH), 8.57 (br, 1H, NH), 7.47 (d, J = 8.3 Hz, 2H, ArH), 6.86 (d, J = 8.3 Hz, 2H, ArH), 4.05–4.00 (m, 2H, NCH_2), 3.80–3.75 (m, 5H, NCH_2, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.1, 162.4, 156.6, 151.8, 143.4, 137.4, 134.7, 133.9, 130.1, 125.5, 117.7, 114.8, 114.0, 107.9, 89.0, 55.7, 45.4, 43.4; HRMS (TOF ES$^-$): *m/z* calcd for $C_{20}H_{12}Cl_3N_4O_2^-$ [M$^-$], 445.0031; found, 445.0033.

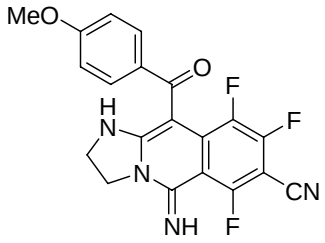
5-imino-9-chloro-6,8-difluoro-10-(4-methoxybenzoyl)-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5e)



Yellow solid (0.348 g, 84%); Mp 212–213°C; IR (KBr) (ν_{max}, cm^{-1}) 3383, 2235, 1605, 1260, 1026, 853; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.43 (br. s, 1H, NH), 8.41 (br, 1H, NH), 7.51 (d, J = 8.3 Hz, 2H, ArH), 6.86 (d, J = 8.3 Hz, 2H, ArH), 4.05–4.00 (m, 2H, NCH_2), 3.79–3.74 (m, 5H,

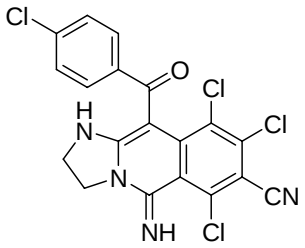
NCH_2, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.7, 162.6, 161.6 (d, J = 263.8 Hz), 159.7, 155.7 (d, J = 258.8 Hz), 149.4, 143.5, 133.7, 130.3, 114.0, 109.9, 109.1 (d, J = 16.3 Hz), 105.9, 89.0, 84.2 (d, J = 22.5 Hz), 55.7, 45.0, 43.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.8 (s, 1F), -111.6 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{12}ClF_2N_4O_2^-$ [M^-], 413.0622; found, 413.0628.

5-imino-6,8,9-trifluoro-10-(4-methoxybenzoyl)-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5f)



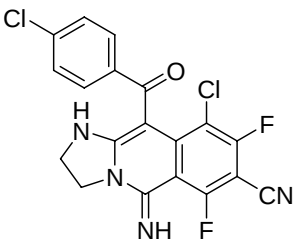
Yellow solid (0.354 g, 89%); Mp 202–204°C; IR (KBr) (ν_{max}, cm^{-1}) 3990, 2234, 1607, 1298, 1263, 1032, 837; ^1H NMR (500 MHz, DMSO-d_6) δ 8.60 (br, H, NH), 8.50 (br. s, H, NH), 7.55 (d, J = 6.9 Hz, 2H, ArH), 6.91 (d, J = 6.9 Hz, 2H, ArH), 4.06–4.00 (m, 2H, NCH_2), 3.83–3.78 (m, 5H, NCH_2, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.8, 162.5, 158.9 (d, J = 258.8 Hz), 155.4, 151.3, 149.1, 139.0 (d, J = 241.3 Hz), 134.8, 133.1 (d, J = 6.3 Hz), 129.9, 114.0, 109.9, 105.4, 85.9, 83.5, 55.7, 44.9, 43.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.0 (s, 1F), -130.0 (s, 1F), -139.4 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{12}F_3N_4O_2^-$ [M^-], 397.0918; found, 397.0920.

5-imino-6,8,9-trichloro-10-(4-chlorobenzoyl)-1,2,3,5-tetrahydroimidazo[1,2-*b*] isoquinoline-7-carbonitrile (5g)



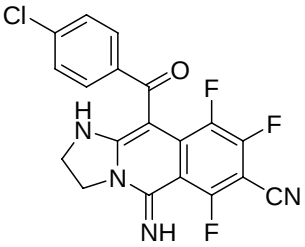
Yellow solid (0.361 g, 80%); Mp 235–236°C; IR (KBr) (ν_{max}, cm^{-1}) 3423, 3300, 2227, 1600, 1300, 1166, 1085, 834, 644; ^1H NMR (500 MHz, DMSO-d_6) δ 9.41 (br, 1H, NH), 8.78 (br, 1H, NH), 7.50 (d, J = 7.6 Hz, 2H, ArH), 7.38 (d, J = 7.6 Hz, 2H, ArH), 4.10–4.00 (m, 2H, NCH_2), 3.82 (t, J = 8.1 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.3, 157.2, 152.0, 143.1, 140.0, 137.6, 136.7, 134.7, 129.8, 128.8, 125.6, 118.0, 114.7, 108.6, 88.8, 45.4, 43.6; HRMS (TOF ES^-): *m/z* calcd for $C_{19}H_9Cl_4N_4O^-$ [M^-], 448.9536; found, 448.9541.

5-imino-9-chloro-10-(4-chlorobenzoyl)-6,8-difluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5h)



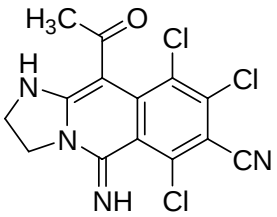
Yellow solid (0.352 g, 84%); Mp 244–245°C; IR (KBr) (ν_{max}, cm^{-1}) 3400, 2233, 1602, 1306, 1091, 815, 593; ^1H NMR (500 MHz, DMSO-d_6) δ 8.68 (br, 2H, NH, =NH), 7.54 (d, J = 6.6 Hz, 2H, ArH), 7.39 (d, J = 6.6 Hz, 2H, ArH), 4.08–4.03 (m, 2H, NCH_2), 3.84–3.79 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.0, 161.2 (d, J = 262.5 Hz), 157.1 (d, J = 195.0 Hz), 156.3, 149.2, 143.3, 139.9, 136.9, 130.0, 128.9, 109.8, 109.4 (d, J = 16.3 Hz), 106.5, 88.8, 85.0, 44.9, 43.3; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.3 (s, 1F), -111.5 (s, 1F); HRMS (TOF ES^-): m/z calcd for $C_{19}H_9Cl_2F_2N_4O^-$ [M^-], 417.0127; found, 417.0123.

5-imino-10-(4-chlorobenzoyl)-6,8,9-trifluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5i)



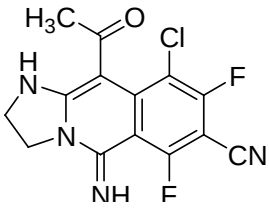
Yellow solid (0.366 g, 91%); Mp 243–244°C; IR (KBr) (ν_{max}, cm^{-1}) 3392, 2235, 1606, 1293, 1040, 824, 671; ^1H NMR (500 MHz, DMSO-d_6) δ 8.88 (br, 1H, NH), 8.64 (br. s, 1H, NH), 7.57 (d, J = 8.2 Hz, 2H, ArH), 7.44 (d, J = 8.2 Hz, 2H, ArH), 4.04 (t, J = 8.9 Hz, 2H, CH_2), 3.81 (t, J = 8.9 Hz, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.2, 158.7 (d, J = 258.8 Hz), 156.0, 150.6 (d, J = 276.3 Hz), 148.9, 139.5, 139.0 (d, J = 251.3 Hz), 136.6, 134.4, 129.5, 128.9, 109.7, 105.9, 85.8, 84.3-84.1, 44.8, 43.3; ^{19}F NMR (470 MHz, DMSO-d_6) δ -114.9 (s, 1F), -129.3 (s, 1F), -139.2 (s, 1F); HRMS (TOF ES^+): m/z calcd for $C_{19}H_{11}ClF_3N_4O^+$ [M^+], 403.0568; found, 403.0567.

10-acetyl-5-imino-6,8,9-trichloro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5j)



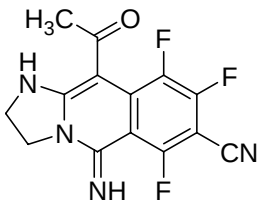
Yellow solid (0.288 g, 81%). Mp 197–199°C; IR (KBr) (ν_{max}, cm^{-1}) 3399, 2227, 1645, 1359, 1175, 1023, 817, 567; ^1H NMR (500 MHz, DMSO-d_6) δ 9.32 (br. s, 1H, NH), 8.73 (br, 1H, NH), 4.05–3.97 (m, 2H, NCH_2), 3.79–3.75 (m, 2H, NCH_2), 2.07 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.3, 155.7, 151.9, 142.9, 138.0, 134.4, 125.6, 118.8, 114.7, 108.7, 92.6, 45.1, 43.5, 30.4; HRMS (TOF ES^+): m/z calcd for $C_{14}H_{10}Cl_3N_4O^+$ [M^+], 354.9915; found, 354.9916.

10-acetyl-5-imino-9-chloro-6,8-difluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (5k)



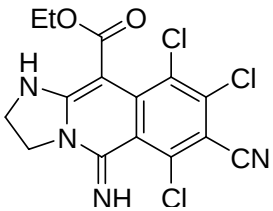
Yellow solid (0.268 g, 83%). Mp 198–200°C; IR (KBr) (ν_{max}, cm^{-1}) 3370, 3280, 2229, 1602, 1300, 1225, 827, 582; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.69 (br, 1H, NH), 8.62 (br. s, 1H, NH), 3.97 (t, J = 8.6 Hz, 2H, NCH_2), 3.77 (t, J = 8.6 Hz, 2H, NCH_2), 2.10 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.9, 161.0 (d, J = 262.5 Hz), 159.4 (d, J = 255.0 Hz), 155.1, 149.2, 143.2, 109.9, 109.5, 107.1, 92.4, 85.3 (d, J = 20.0 Hz), 44.6, 43.3, 30.7; ^{19}F NMR (470 MHz, DMSO-d_6) δ -100.2 (s, 1F), -111.9 (s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{14}H_8ClF_2N_4O^-$ [M^-], 321.0360; found, 321.0361.

10-acetyl-5-imino-6,8,9-trifluoro-1,2,3,5-tetrahydro[1,2-*b*]isoquinoline-7-carbonitrile (5l)



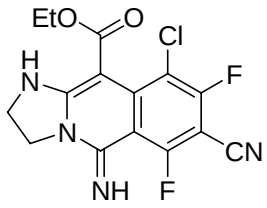
Yellow solid (0.275 g, 90%). Mp 220–222°C; IR (KBr) (ν_{max}, cm^{-1}) 3396, 3285, 2233, 1603, 1297, 1189, 1033, 843; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.93 (br, 1H, NH), 8.60 (br. s, 1H, NH), 3.98 (t, J = 8.5 Hz, 2H, NCH_2), 3.78 (t, J = 8.5 Hz, 2H, NCH_2), 2.09 (s, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.4, 158.5 (d, J = 261.3 Hz), 155.0, 151.2 (d, J = 260 Hz), 148.8, 139.3 (d, J = 232.5 Hz), 133.9, 109.8, 106.4,88.9, 84.6, 44.6, 43.3, 29.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.1 (s, 1F), -128.1 (s, 1F), -140.7 (s, 1F); HRMS (TOF ES$^+$): *m/z* calcd for $C_{14}H_{10}F_3N_4O^+$ [M^+], 307.0801; found, 307.0797.

ethyl 5-imino-6,8,9-trichloro-7-cyano-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-10-carboxylate (5m)



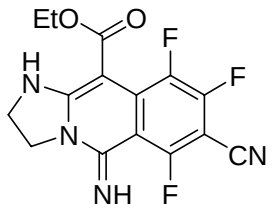
Yellow solid (0.351 g, 91%); Mp 234–236°C; IR (KBr) (ν_{max}, cm^{-1}) 3360, 2223, 1670, 1304, 1158, 1037, 803, 641; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.30 (br, 1H, NH), 8.30 (br, 1H, NH), 4.16 (q, J = 7.1 Hz, 2H, OCH_2), 3.99 (t, J = 8.8 Hz, 2H, NCH_2), 3.76 (t, J = 8.8 Hz, 2H, NCH_2), 1.21 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.2, 156.3, 151.6, 141.9, 137.1, 133.8, 125.8, 117.8, 114.3, 107.5, 80.5, 59.7, 45.2, 43.8, 14.1; HRMS (TOF ES$^-$): *m/z* calcd for $C_{15}H_{10}Cl_3N_4O_2^-$ [M^-], 382.9875; found, 382.9876.

ethyl 5-imino-9-chloro-7-cyano-6,8-difluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-10-carboxylate (5n)



Yellow solid (0.331 g, 94%); Mp 226-227°C; IR (KBr) (ν_{max}, cm^{-1}) 3357, 2232, 1681, 1303, 1152, 1035, 814, 617; ^1H NMR (500 MHz, DMSO-d_6) δ 8.50 (br, 1H, NH), 8.24 (br. s, 1H, NH), 4.17 (q, J = 7.2 Hz, 2H, OCH_2), 3.98 (t, J = 8.7 Hz, 2H, NCH_2), 3.77 (t, J = 8.7 Hz, 2H, NCH_2), 1.21 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.6, 162.1, 160.0, 158.9 (d, J = 260 Hz), 149.3, 142.6, 109.9, 106.6, 84.4, 81.0, 60.3, 45.1, 43.0, 14.5; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.3 (s, 1F), -112.2 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{15}H_{10}ClF_2N_4O_2^-$ [M^-], 351.0466; found, 351.0467.

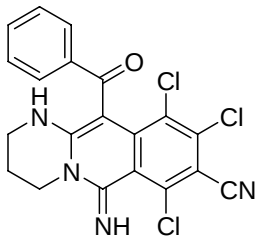
ethyl 5-imino-7-cyano-6,8,9-trifluoro-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-10-carboxylate (5o)



Yellow solid (0.309 g, 92%); Mp 218–219°C; IR (KBr) (ν_{max}, cm^{-1}) 3344, 2230, 1668, 1308, 1036, 783; ^1H NMR (500 MHz, DMSO-d_6) δ 8.45 (br. s, 1H, NH), 8.31 (br, 1H, NH), 4.19 (q, J = 7.2 Hz, 2H, OCH_2), 3.97 (t, J = 8.7 Hz, 2H, NCH_2), 3.77 (t, J = 8.7 Hz, 2H, NCH_2), 1.23 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.2, 158.5 (d, J = 257.5 Hz), 155.5, 150.7 (d, J = 268.8 Hz), 149.0, 139.7 (d, J = 261.3 Hz), 133.4, 109.8, 105.9, 84.0, 77.2, 60.3, 45.1, 43.0, 14.5; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.6 (s, 1F), -129.1 (d, J = Hz, 18.8Hz, 1F), -137.7 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{15}H_{10}F_3N_4O_2^-$ [M^-], 335.0761; found, 335.0764.

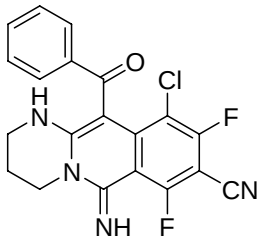
Spectroscopic Data of Tetrahydropyrimido[1,2-*b*]isoquinolinimine 6

6-imino-11-benzoyl-7,9,10-trichloro-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6a)



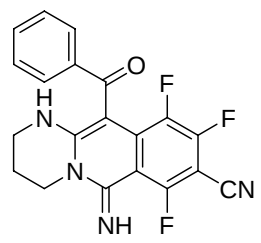
Yellow solid (0.354 g, 82%); Mp 194–197°C; IR (KBr) (ν_{max}, cm^{-1}) 3436, 2227, 1597, 1328, 1184, 1084, 734; ^1H NMR (500 MHz, DMSO-d_6) δ 10.24 (br, 1H, NH), 9.90 (br, 1H, NH), 7.43–7.41 (m, 3H, PhH), 7.31–7.29 (m, 2H, PhH), 3.91–3.87 (m, 2H, NCH_2), 3.48–3.44 (m, 2H, NCH_2), 2.11–2.08 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.4, 154.7, 153.8, 142.1, 137.1, 133.5, 131.7, 130.7, 128.6, 128.5, 126.1, 119.0, 114.7, 108.0, 89.2, 42.9, 38.0, 19.8; HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{12}Cl_3N_4O^-$ [M^-], 429.0082; found, 429.0081.

6-imino-11-benzoyl-10-chloro-7,9-difluoro-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6b)



Yellow solid (0.339 g, 85%); Mp 245–246°C; IR (KBr) (ν_{max}, cm^{-1}) 3386, 2233, 1596, 1334, 1144, 1088, 851, 739; ^1H NMR (500 MHz, DMSO-d_6) δ 10.20 (br, 1H, NH), 9.34 (br, 1H, NH), 7.48–7.42 (m, 3H, PhH), 7.30 (t, J = 7.5 Hz, 2H, PhH), 3.94–3.90 (m, 2H, NCH_2), 3.48-3.44 (m, 2H, NCH_2), 2.10–2.05 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.1, 159.9 (d, J = 261.3 Hz), 158.6 (d, J = 253.8 Hz), 153.4, 151.7, 142.7, 141.9, 131.8, 131.6, 128.7, 128.5, 109.9, 106.7, 89.1, 84.7 (t, J = 22.5 Hz), 42.5, 38.1, 19.7; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.9 (s, 1F), -111.8 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{12}ClF_2N_4O^-$ [M^-], 397.0673; found, 397.0676.

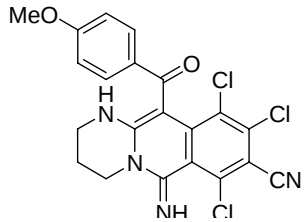
6-imino-11-benzoyl-7,9,10-trifluoro-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6c)



Yellow solid (0.351 g, 92%); Mp 229–231°C; IR (KBr) (ν_{max}, cm^{-1}) 3387, 2232, 1596, 1342, 1148, 946, 806; ^1H NMR (500 MHz, DMSO-d_6) δ 10.20 (br, 1H, NH_2), 9.34 (br, 1H, NH_2), 7.48–7.42 (m, 3H, PhH), 7.30 (t, J = 7.5 Hz, 2H, PhH),

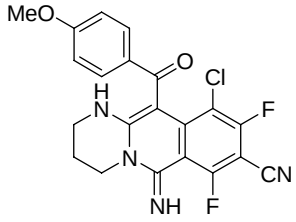
3.94–3.90 (m, 2H, NCH_2), 3.48–3.44 (m, 2H, NCH_2), 2.10–2.05 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.7, 157.5 (d, J = 257.5 Hz), 153.4, 151.3, 149.1, 141.4, 138.8 (d, J = 235.0 Hz), 133.8, 131.6, 128.6, 128.0, 109.8, 105.8, 86.0, 83.9, 42.4, 38.1, 19.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.1 (s, 1F), -130.1 (br, 1F), -139.7(s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{12}F_3N_4O^-$ [M^-], 381.0969; found, 381.0970.

6-imino-7,9,10-trichloro-11-(4-methoxybenzoyl)-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6d)



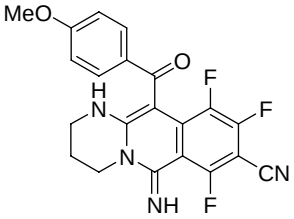
Yellow solid (0.383 g, 83%); Mp 204–206°C; IR (KBr) (ν_{max}, cm^{-1}) 3436, 2226, 1596, 1261, 1162, 1029, 842, 604; ^1H NMR (500 MHz, DMSO-d_6) δ 10.14 (br, 1H, NH), 9.85 (br, 1H, NH), 7.41 (d, J = 7.4 Hz, 2H, ArH), 6.83 (d, J = 7.4 Hz, 2H, ArH), 3.90–3.85 (m, 2H, NCH_2), 3.79 (s, 3H, OCH_3), 3.47–3.43 (m, 2H, NCH_2), 2.10–2.05 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.7, 162.1, 154.7, 153.5, 142.2, 137.0, 134.7, 133.5, 130.5, 125.9, 118.7, 114.8, 113.8, 107.5, 89.1, 55.7, 42.9, 38.0, 19.9; HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}Cl_3N_4O_2^-$ [M^-], 459.0188; found, 459.0185.

6-imino-10-chloro-7,9-difluoro-11-(4-methoxybenzoyl)-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6e)



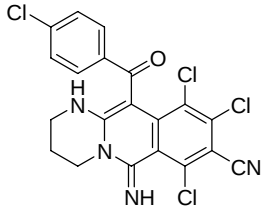
Yellow solid (0.364 g, 85%). Mp 242–244°C; IR (KBr) (ν_{max}, cm^{-1}) 3401, 2233, 1597, 1265, 1159, 847, 608; ^1H NMR (500 MHz, DMSO-d_6) δ 10.03 (br, 1H, NH), 9.26 (br. s, 1H, NH), 7.43 (br s, 2H, ArH), 6.81 (br s, 2H, ArH), 3.93–3.89 (m, 2H, NCH_2), 3.76 (s, 3H, OCH_3), 3.46–3.40 (m, 2H, NCH_2), 2.09–2.04 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.5, 162.2, 160.0 (d, J = 265.0 Hz), 158.5 (d, J = 256.3 Hz), 153.1, 151.7, 142.7, 134.5, 130.7, 113.8, 110.0, 109.6 (d, J = 15.0 Hz), 106.4, 89.1, 84.2, 55.7, 42.5, 38.0, 19.7; ^{19}F NMR (470 MHz, DMSO-d_6) δ -102.0 (s, 1F), -111.8 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}ClF_2N_4O_2^-$ [M^-], 427.0779; found, 427.0779.

6-imino-7,9,10-trifluoro-11-(4-methoxybenzoyl)-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6f)



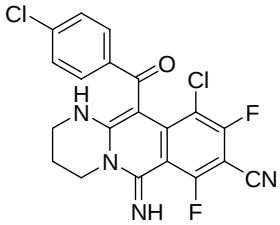
Yellow solid (0.379 g, 92%); Mp 235–238°C; IR (KBr) (ν_{max}, cm^{-1}) 3413, 2231, 1606, 1340, 1164, 1026, 814; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.30 (br, 1H, NH), 9.18 (br, 1H, NH), 7.48 (d, J = 8.1 Hz, 2H, ArH), 6.90 (d, J = 8.1 Hz, 2H, ArH), 3.96–3.92 (m, 2H, NCH_2), 3.79 (s, 3H, OCH_3), 3.47–3.43 (m, 2H, NCH_2), 2.09–2.04 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.0, 162.2, 157.7 (d, J = 257.5 Hz), 153.0, 151.4, 150.1 (d, J = 271.3 Hz), 138.7 (d, J = 243.8 Hz), 134.0, 133.9, 130.1, 113.9, 109.9, 105.4, 85.9, 83.4, 55.7, 42.4, 38.0, 19.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.1 (s, 1F), -130.2 (d, J = 18.8 Hz, 1F), -140.2 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}F_3N_4O_2^-$ [M^-], 411.1074; found, 411.1076.

7,9,10-trichloro-11-(4-chlorobenzoyl)-6-imino-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6g)



Yellow solid (0.382 g, 82%); Mp 162–164°C; IR (KBr) (ν_{max}, cm^{-1}) 3434, 2226, 1596, 1543, 1325, 1147, 1091, 840; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.24 (s, 1H, NH), 9.92 (s, 1H, NH), 7.44–7.36 (m, 4H, ArH), 3.90–3.84 (m, 2H, NCH_2), 3.61–3.60 (m, 2H, NCH_2), 2.10–2.09 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 187.8, 153.7, 141.9, 140.8, 137.3, 136.3, 133.6, 130.4, 129.1, 128.6, 125.9, 119.1, 114.7, 108.4, 89.2, 43.0, 38.0, 19.7; HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{11}Cl_4N_4O_2^-$ [M^-], 462.9692; found, 462.9686.

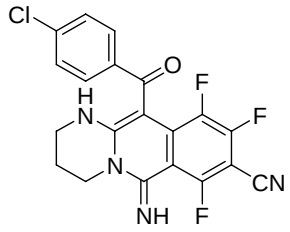
10-chloro-11-(4-chlorobenzoyl)-7,9-difluoro-6-imino-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6h)



Yellow solid (0.376 g, 87%); Mp 257–258°C; IR (KBr) (ν_{max}, cm^{-1}) 3386, 2231, 1595, 1328, 1185, 1090, 843, 786; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.21 (s, 1H, NH), 9.40 (s, 1H, NH), 7.47–7.36 (m, 4H, ArH), 3.93–3.89 (m, 2H, NCH_2), 3.48–3.44 (m, 2H, NCH_2), 2.09–2.04 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 188.5, 159.9 (d, J = 260.0 Hz), 159.7, 157.7, 153.6, 151.7, 142.4, 140.7, 136.4, 130.5, 128.7, 109.9, 106.9, 89.0, 85.1, 42.5, 38.1, 19.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.6 (s, 1F), -112.0 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for

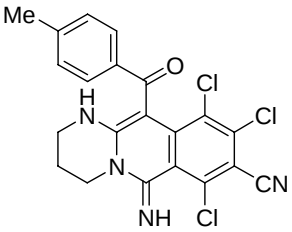
$C_{20}H_{12}Cl_2F_2N_4O^-$ [M^-], 431.0283; found, 431.0281.

11-(4-chlorobenzoyl)-7,9,10-trifluoro-6-imino-2,3,4,6-tetrahydro-1*H*-pyrimido[1, 2-*b*]isoquinoline-8-carbonitrile (6i)



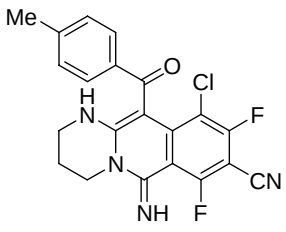
Yellow solid (0.362 g, 87%); Mp 145–147°C; IR (KBr) (v_{max}, cm^{-1}) 3396, 2233, 1596, 1341, 1139, 1088, 938; ^1H NMR (500 MHz, DMSO-d_6) δ 10.54 (br, 1H, NH), 9.31 (br, 1H, NH), 7.51 (d, J = 7.9 Hz, 2H, ArH), 7.40 (d, J = 7.9 Hz, 2H, ArH), 3.96–3.92 (m, 2H, NCH_2), 3.49–3.45 (m, 2H, NCH_2), 2.09–2.04 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.0, 157.5 (d, J = 260.0 Hz), 153.5, 151.2, 149.4, 140.2, 138.8 (d, J = 233.8 Hz), 136.2, 133.5, 129.8, 128.8, 109.7, 105.9, 85.9, 84.3 (d, J = 17.5 Hz), 42.4, 38.1, 19.5; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.3 (d, J = 9.4 Hz, 1F), -129.7 (d, J = 23.5, 1F), -140.3–-140.4 (m, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{11}ClF_3N_4O^-$ [M^-], 415.0579; found, 415.0574.

7,9,10-trichloro-6-imino-11-(4-methylbenzoyl)-2,3,4,6-tetrahydro-1*H*-pyrimido[1, 2-*b*]isoquinoline-8-carbonitrile (6j)



Yellow solid (0.374 g, 84%); Mp 160–162°C; IR (KBr) (v_{max}, cm^{-1}) 3359, 3202, 2227, 1594, 1537, 1320, 1180, 835, 600; ^1H NMR (500 MHz, DMSO-d_6) δ 9.35 (br, 1H, NH), 7.73–7.10 (m, 5H, ArH, NH), 3.99–3.91 (m, 2H, NCH_2), 3.30–3.20 (m, 2H, NCH_2), 2.19 (s, 3H, CH_3), 2.02–1.99 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.4, 156.1, 148.4, 143.8, 141.5, 138.7, 137.5, 136.4, 129.5, 129.2, 114.2, 109.8, 109.4, 94.5, 88.5, 47.0, 38.4, 21.2, 18.8; HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}Cl_3N_4O^-$ [M^-], 443.0239; found, 443.0243.

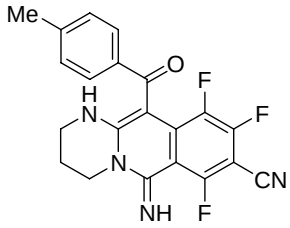
10-chloro-7,9-difluoro-6-imino-11-(4-methylbenzoyl)-2,3,4,6-tetrahydro-1*H*-pyri mido[1,2-*b*]isoquinoline-8-carbonitrile (6k)



Yellow solid (0.343 g, 83%); Mp 243–244°C; IR (KBr) (v_{max}, cm^{-1}) 3392, 2229, 1596, 1330, 1276, 1153, 836, 758, 607; ^1H NMR (500 MHz, DMSO-d_6) δ 10.12 (br, 1H, NH), 9.34 (br, 1H, NH), 7.37 (d, J = 7.5 Hz, 2H, ArH), 7.11 (d, J = 7.5 Hz, 2H, ArH), 3.93–3.89 (m, 2H, NCH_2), 3.46–3.42 (m, 2H,

NCH_2), 2.30 (s, 3H, CH_3), 2.08–2.02 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.7, 162.3 (d, J = 267.5 Hz), 1590 (d, J = 252.5 Hz), 153.7, 148.5, 144.3, 140.3, 137.2, 129.6, 129.4, 108.5, 108.4, 99.3, 95.6, 85.6, 47.0, 39.1, 21.4, 18.9; ^{19}F NMR (470 MHz, DMSO-d_6) δ -101.9 (s, 1F), -111.7 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}ClF_2N_4O^-$ [M^-], 411.0830; found, 411.0827.

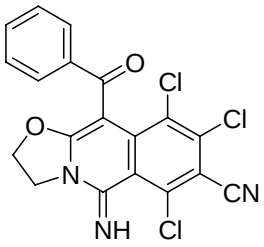
7,9,10-trifluoro-6-imino-11-(4-methylbenzoyl)-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (6l)



Yellow solid (0.356 g, 90%); Mp 215–218°C; IR (KBr) (ν_{max}, cm^{-1}) 3368, 2231, 1594, 1341, 1149, 937, 852; ^1H NMR (500 MHz, DMSO-d_6) δ 10.46 (br, 1H, NH), 9.24 (br, 1H, NH), 7.39 (d, J = 7.6 Hz, 2H, ArH), 7.15 (d, J = 7.6 Hz, 2H, ArH), 3.95–3.89 (m, 2H, NCH_2), 3.48–3.44 (m, 2H, NCH_2), 2.32 (s, 3H, CH_3), 2.09–2.06 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.5, 157.5 (d, J = 258.8 Hz), 153.2, 151.4, 149.0, 141.7, 138.8 (d, J = 252.5 Hz), 138.7, 133.9, 129.2, 128.1, 109.8, 105.6, 86.0, 83.7, 42.4, 38.0, 21.4, 19.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ -115.0 (s, 1F), -130.1 (d, J = 23.5 Hz, 1F), -139.9 (d, J = 14.1 Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{14}F_3N_4O^-$ [M^-], 395.1125; found, 395.1120.

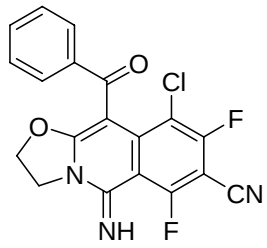
Spectroscopic Data of Dihydroxazolo[3,2-*b*]isoquinolinimine 7

10-benzoyl-6,8,9-trichloro-5-imino-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7a)



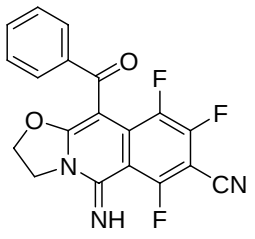
Yellow solid (0.352 g, 84%); Mp 244–246 °C; IR (KBr) (ν_{max}, cm^{-1}) 3422, 3270, 2239, 1624, 1435, 1357, 1065, 963, 750; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (br, 1H, NH), 7.32 (d, J = 7.1 Hz, 1H, PhH), 7.25 (t, J = 7.1 Hz, 2H, PhH), 7.13 (d, J = 7.1 Hz, 2H, PhH), 4.56 (t, J = 8.2 Hz, 2H, OCH_2), 3.94–3.88 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 187.7, 167.7, 148.6, 141.5, 140.8, 138.7, 136.4, 130.8, 128.7, 128.1, 118.0, 114.9, 114.9, 113.6, 88.1, 69.4, 44.6; HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_9Cl_3N_3O_2^-$ [M$^-$], 415.9766; found, 415.9765.

10-benzoyl-9-chloro-6,8-difluoro-5-imino-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7b)



Yellow solid (0.339 g, 88%); Mp 238–240°C; IR (KBr) (ν_{max}, cm^{-1}) 3421, 3265, 2244, 1600, 1438, 1358, 1113, 973, 709; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.48 (br, 1H, NH), 7.37–7.21 (m, 5H, PhH), 4.61 (q, J = 8.9 Hz, 2H, OCH_2), 3.94 (q, J = 8.9 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 187.9, 167.4, 159.8 (d, J = 265.0 Hz), 153.1(d, J = 265.0 Hz), 145.7, 140.5, 138.7-138.6, 130.4, 128.3, 127.9, 111.6, 108.2, 101.5 (d, J = 12.5 Hz), 92.1 (d, J = 17.5 Hz), 80.9, 69.0, 44.2; ^{19}F NMR (470 MHz, DMSO-d_6) δ -112.3 (br, 1F), -112.6 (br s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_9ClF_2N_3O_2^-$ [M$^-$], 384.0357; found, 384.0359.

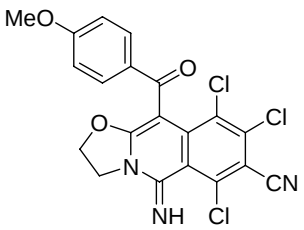
10-benzoyl-6,8,9-trifluoro-5-imino-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7c)



Yellow solid (0.347 g, 94%); Mp 187–189°C; IR (KBr) (ν_{max}, cm^{-1}) 3416, 3251, 2243, 1611, 1476, 1345, 1115, 962; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.48 (br, 1H, NH), 7.37–7.21 (m, 5H, PhH), 4.64–4.57 (m, 2H, OCH_2), 4.04–3.91 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 187.8, 167.4, 159.8 (d, J = 263.8 Hz), 153.2 (d, J = 261.3 Hz), 144.7 (d, J = 240.0 Hz), 140.5, 138.7-138.4, 130.4, 128.3, 127.9, 111.6, 108.2, 101.4 (d, J = 13.8 Hz), 92.0 (t, J = 18.8 Hz), 80.9,

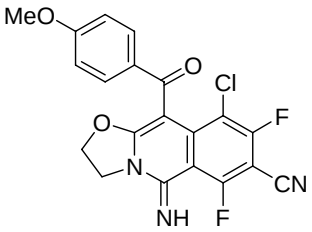
69.0, 44.2; ^{19}F NMR (470 MHz, DMSO-d_6) δ -104.5 (d, J = 14.1 Hz, 1F), -120.3 (d, J = 23.5 Hz, 1F), -134.7 (dd, J = 23.5 Hz, 14.1 Hz, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_9F_3N_3O_2^-$[M$^-$], 368.0652; found, 368.0656.

6,8,9-trichloro-5-imino-10-(4-methoxybenzoyl)-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7d)



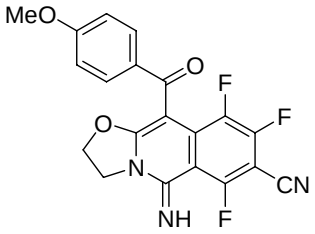
Yellow solid (0.386 g, 86%); Mp 287–289°C; IR (KBr) (ν_{max}, cm^{-1}) 3428, 3261, 2237, 1618, 1440, 1251, 974, 780; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.29 (br, 1H, NH), 7.10 (d, J = 8.3 Hz, 2H, ArH), 6.79 (d, J = 8.3 Hz, 2H, ArH), 4.55 (t, J = 8.5 Hz, 2H, OCH_2), 3.89 (t, J = 8.5 Hz, 2H, NCH_2), 3.73 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 186.8, 167.7, 161.4, 148.9, 140.8, 138.7, 136.3, 133.8, 130.1, 117.9, 114.8, 114.7, 114.1, 113.7, 87.9, 69.3, 56.0, 44.6; HRMS (TOF ES$^-$): *m/z* calcd for $C_{20}H_{11}C_{l3}N_3O_3^-$ [M$^-$], 445.9871; found, 445.9870.

9-chloro-6,8-difluoro-5-imino-10-(4-methoxybenzoyl)-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7e)



Yellow solid (0.382 g, 92%); Mp 220–222°C; IR (KBr) (ν_{max}, cm^{-1}) 3425, 3268, 2245, 1597, 1438, 1253, 972, 840; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.35 (br, 1H, NH), 7.13 (d, J = 8.4 Hz, 2H, ArH), 6.78 (d, J = 8.4 Hz, 2H, ArH), 4.56 (t, J = 8.5 Hz, 2H, OCH_2), 3.90(t, J = 8.5 Hz, 2H, NCH_2), 3.73 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 187.1, 167.6, 162.7 (d, J = 267.5 Hz), 161.8 (d, J = 263.8 Hz), 161.4, 150.0, 133.7, 130.3, 121.3 (d, J = 12.5 Hz), 114.0, 112.3, 108.9, 103.5 (d, J = 11.3 Hz), 92.8 (d, J = 20.0 Hz), 85.9, 69.3, 55.9, 44.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ -94.7 (s, 1F), -101.9 (s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{20}H_{11}ClF_2N_3O_3^-$ [M$^-$], 414.0462; found, 414.0463.

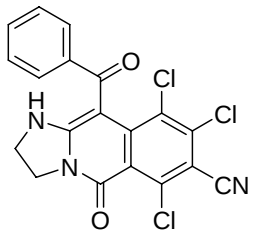
6,8,9-trifluoro-5-imino-10-(4-methoxybenzoyl)-3,5-dihydro-2*H*-oxazolo[3,2-*b*]isoquinoline-7-carbonitrile (7f)



Yellow solid (0.383 g, 96%); Mp 190–192°C; IR (KBr) (ν_{max}, cm^{-1}) 3270, 2244, 1608, 1473, 1255, 983; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.36 (br, 1H, NH), 7.16 (d, J = 8.4 Hz, 2H, ArH), 6.79 (d, J = 8.5 Hz, 2H, ArH), 4.61–4.54 (m, 2H, OCH_2), 3.89 (q, J = 8.0 Hz, 2H, NCH_2), 3.74 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 186.9, 167.3, 161.0, 158.8, 153.2 (d, J = 273.8 Hz), 144.6 (d, J = 238.8 Hz), 139.0 (d, J = 15.0 Hz), 132.9, 129.9, 113.6, 111.7, 108.4, 101.3, 91.8 (d, J = 18.8 Hz), 80.6, 68.9, 55.5, 44.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -104.7 (d, J = 14.1 Hz, 1F), -120.3 (d, J = 23.5 Hz, 1F), -135.0 (dd, J = 23.5 Hz, 14.1Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{11}F_3N_3O_3^-$ [M^-], 398.0758; found, 398.0762.

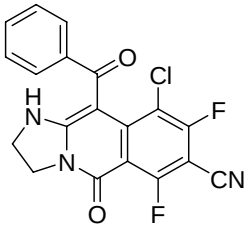
Spectroscopic Data of Tetrahydroimidazo[1,2-*b*]isoquinolinone 8

10-benzoyl-6,8,9-trichloro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8a)



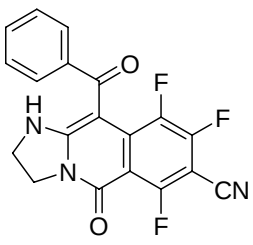
Yellow solid (0.305 g, 73%); Mp >300°C; IR (KBr) (ν_{max}, cm^{-1}) 3371, 2228, 1630, 1301, 1180, 1004, 735; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.55 (s, 1H, NH), 7.57–7.37 (m, 5H, PhH), 4.19–4.09 (m, 2H, NCH_2), 3.81–3.71 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.7, 162.7, 157.0, 154.1, 144.3, 140.5, 138.0, 132.7, 128.9, 128.4, 124.8, 116.1, 114.8, 108.3, 90.3, 44.5, 43.0; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{10}Cl_3N_3O_2$ [M], 416.9839; found, 416.9845.

10-benzoyl-9-chloro-6,8-difluoro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8b)



Yellow solid (0.297 g, 77%); Mp 280–281°C; IR (KBr) (ν_{max}, cm^{-1}) 3376, 2236, 1598, 1308, 1016, 789, 697; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.51 (br, 1H, NH), 7.65 (d, J = 7.3 Hz, 2H, PhH), 7.53 (t, J = 7.3 Hz, 1H, PhH), 7.40 (t, J = 7.3 Hz, 2H, PhH), 4.15 (t, J = 8.9 Hz, 2H, NCH_2), 3.79–3.73 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.0, 163.1 (d, J = 271.3 Hz), 159.2 (d, J = 253.8 Hz), 155.8, 154.4, 144.2, 140.4, 132.9, 129.0, 128.6, 110.0, 108.5 (d, J = 16.3 Hz), 106.4, 90.5, 84.9 (d, J = 20.0 Hz), 44.1, 43.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -100.5 (s, 1F), -104.2 (d, J = 4.7 Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{19}H_9ClF_2N_3O_2^-$ [M^-], 384.0357; found, 384.0352.

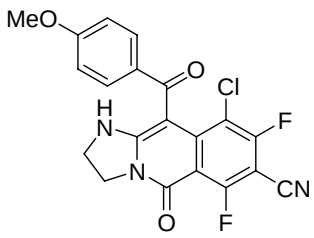
10-benzoyl-6,8,9-trifluoro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8c)



Yellow solid (0.303 g, 82%); Mp 263–264°C; IR (KBr) (ν_{max}, cm^{-1}) 3384, 2236, 1615, 1307, 1183, 1032, 800; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.74 (s, 1H, NH), 7.65 (d, J = 7.6 Hz, 2H, PhH), 7.56 (t, J = 7.6 Hz, 1H, PhH), 7.43 (t, J = 7.6 Hz, 2H, PhH), 4.15 (t, J = 8.7 Hz, 2H), 3.79 (t, J = 8.7 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 191.9, 160.2 (d, J = 270.0 Hz), 155.5, 154.3, 150.7 (dd, J = 252.5 Hz, 10.0 Hz), 140.1, 139.8–137.8 (m), 135.8, 132.7, 128.9,

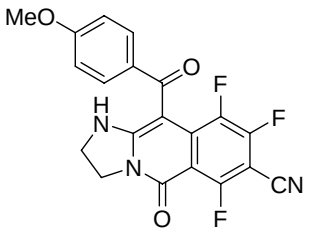
128.1, 109.8, 105.8, 87.6, 84.2 (t, J = 16.3 Hz), 44.0, 43.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -108.0 (d, J = 9.4 Hz, 1F), -128.8 (d, J = 18.8 Hz, 1F), -140.1–-140.2 (m, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_9F_3N_3O_2^-$ [M$^-$], 368.0652; found, 368.0644.

9-chloro-6,8-difluoro-10-(4-methoxybenzoyl)-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8d)



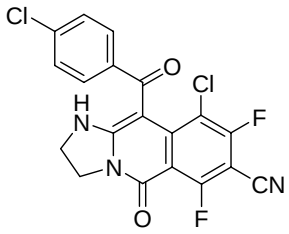
Yellow solid (0.324 g, 78%); Mp 261–262°C; IR (KBr) (ν_{max}, cm^{-1}) 3412, 2234, 1597, 1256, 1020, 857, 601; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.34 (s, H, NH), 7.64 (d, J = 8.4 Hz, 2H, ArH), 6.93 (d, J = 8.4 Hz, 2H, ArH), 4.13 (t, J = 9.0 Hz, 2H, NCH_2), 3.81 (s, 3H, OCH_3), 3.76–3.68 (m, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.9, 163.2 (d, J = 272.5 Hz), 163.2, 159.1 (d, J = 253.8 Hz), 155.7, 153.9, 144.0, 133.1, 131.0, 114.3, 110.1, 108.2 (d, J = 17.5 Hz), 106.1, 90.8, 84.4 (d, J = 21.3 Hz), 55.8, 44.1, 43.0; ^{19}F NMR (470 MHz, DMSO-d_6) δ -100.7 (d, J = 9.4 Hz, 1F), -104.1 (d, J = 9.4 Hz, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{20}H_{11}ClF_2N_3O_3^-$[M$^-$], 414.0462; found, 414.0462.

6,8,9-trifluoro-10-(4-methoxybenzoyl)-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8e)



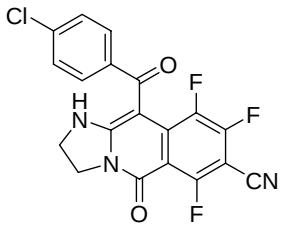
Yellow solid (0.323 g, 81%); Mp 276–278°C; IR (KBr) (ν_{max}, cm^{-1}) 3414, 2234, 1626, 1308, 1261, 1031, 844; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.53 (br, H, NH), 7.66 (d, J = 8.1 Hz, 2H, ArH), 6.95 (d, J = 8.1 Hz, 2H, ArH), 4.13 (t, J = 8.7 Hz, 2H, NCH_2), 3.75 (t, J = 8.7 Hz, 2H, NCH_2), 3.82 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.7, 163.1, 160.4 (d, J = 271.3 Hz), 155.5. 153.7, 150.6 (dd, J = 256.3 Hz, 16.3 Hz), 139.7–137.7 (m), 135.8, 132.3, 130.7, 114.2, 110.0, 105.6, 87.7, 83.7 (d, J = 18.8 Hz), 55.8, 44.0, 43.0; ^{19}F NMR (470 MHz, DMSO-d_6) δ -108.0 (d, J = 9.4 Hz, 1F), -129.0–-129.1 (m, 1F), -141.0–-140.1 (m, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{20}H_{11}F_3N_3O_3^-$ [M$^-$], 398.0758; found, 398.0751.

9-chloro-10-(4-chlorobenzoyl)-6,8-difluoro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8f)



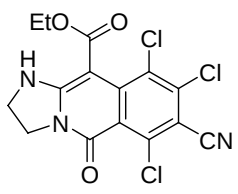
Yellow solid (0.311 g, 74%); Mp 295–297°C; IR (KBr) (ν_{max}, cm^{-1}) 3408, 2237, 1591, 1305, 1097, 787; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.58 (s, 1H, NH), 7.65 (d, J = 8.1 Hz, 2H, ArH), 7.45 (d, J = 8.1 Hz, 2H, ArH), 4.14 (t, J = 8.9 Hz, 2H, NCH_2), 3.80–3.72 (m, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.6, 163.0 (d, J = 267.5 Hz), 159.5 (d, J = 256.3 Hz), 155.8, 154.5, 144.1, 139.2, 137.6, 130.4, 129.1, 109.9, 108.5 (d, J = 16.3 Hz), 106.6, 90.3, 85.1 (t, J = 20.0 Hz), 44.1, 43.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -100.0 (d, J = 4.7 Hz, 1F), -104.2 (s, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_8Cl_2F_2N_3O_2^-$ [M^-], 417.9967; found, 417.9965.

10-(4-chlorobenzoyl)-6,8,9-trifluoro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-7-carbonitrile (8g)



Yellow solid (0.343 g, 85%); Mp 281–283°C; IR (KBr) (ν_{max}, cm^{-1}) 3379, 2236, 1619, 1486, 1304, 1039, 825; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.81 (s, 1H, NH), 7.66 (d, J = 8.2 Hz, 2H, ArH), 7.49 (d, J = 8.2 Hz, 2H, ArH), 4.14 (t, J = 8.7 Hz, 2H, NCH_2), 3.80 (t, J = 8.7 Hz, 2H, NCH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.5, 160.2 (d, J = 270.0 Hz), 155.5, 154.5, 149.8, 139.7–137.7 (m), 138.8, 137.4, 135.7, 130.0, 129.1, 109.8, 106.0, 87.4, 84.5 (d, J = 17.5 Hz), 44.0, 43.2; ^{19}F NMR (470 MHz, DMSO-d_6) δ -108.1 (s, 1F), -128.2 (d, J = 23.5 Hz, 1F), -140.2–-140.3 (m, 1F); HRMS (TOF ES$^-$): *m/z* calcd for $C_{19}H_8ClF_3N_3O_2^-$ [M^-], 402.0263; found, 402.0263.

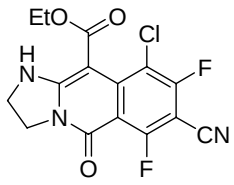
ethyl 6,8,9-trichloro-7-cyano-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-10-carboxylate (8h)



Yellow solid (0.290 g, 74%); Mp 285–287°C; IR (KBr) (ν_{max}, cm^{-1}) 3373, 2224, 1660, 1302, 1179, 1083, 790; ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.31 (br, 1H, NH), 4.24 (q, J = 6.6 Hz, 2H, OCH_2), 4.12 (t, J = 8.5 Hz, 2H, NCH_2), 3.78 (t, J = 8.5 Hz,

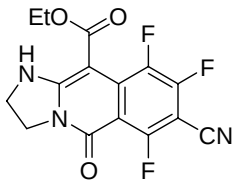
NCH_2), 1.24 (t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.8, 156.7, 154.0, 143.5, 138.1, 137.6, 125.4, 116.6, 114.7, 108.3, 83.3, 60.8, 44.6, 43.0, 14.4; HRMS (TOF ES^-): *m/z* calcd for $C_{15}H_9Cl_3N_3O_3^-$ [M^-], 383.9715; found, 383.9716.

ethyl 9-chloro-7-cyano-6,8-difluoro-5-oxo-1,2,3,5-tetrahydro-imidazo[1,2-*b*]isoquinoline-10-carboxylate (8i)



Yellow solid (0.279 g, 79%); Mp 253–255°C; IR (KBr) (ν_{max}, cm^{-1}) 3370, 2235, 1667, 1306, 1145, 1031, 789; ^1H NMR (500 MHz, DMSO-d_6) δ 8.36 (br, 1H, NH), 4.23 (q, J = 6.6 Hz, 2H, OCH_2), 4.10 (t, J = 8.4 Hz, 2H, NCH_2), 3.77 (t, J = 8.4 Hz, 2H, NCH_2), 1.23(t, J = 6.6 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.6, 162.8 (dd, J =272.5 Hz, 5.0 Hz), 159.4 (d, J = 255.0 Hz), 155.5, 154.4, 143.3, 109.9, 109.2 (d, J = 16.3 Hz), 106.7, 84.9 (d, J = 21.3 Hz), 83.6, 60.9, 44.1, 43.1, 14.3; ^{19}F NMR (470MHz, DMSO-d_6) δ -99.7 (s, 1F), -104.6 (s, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{15}H_9ClF_2N_3O_3^-$ [M^-], 352.0306; found, 352.0303.

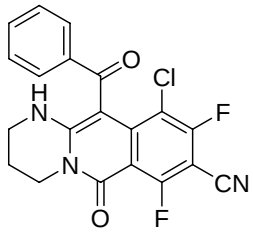
ethyl 7-cyano-6,8,9-trifluoro-5-oxo-1,2,3,5-tetrahydroimidazo[1,2-*b*]isoquinoline-10-carboxylate (8j)



Yellow solid (0.290 g, 86%); Mp 217–218°C; IR (KBr) (ν_{max}, cm^{-1}) 3367, 22420, 1677, 1305, 1032, 788; ^1H NMR (500 MHz, DMSO-d_6) δ 8.36 (br, 1H, NH), 4.25 (q, J = 6.8 Hz, 2H, OCH_2), 4.11 (t, J = 9.0 Hz, 2H, NCH_2), 3.80 (q, J = 9.0 Hz, 2H, NCH_2), 1.27 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.1, 160.0 (d, J = 267.5 Hz), 155.3, 153.9, 152.2 (dd, J = 256.3 Hz, 16.3 Hz), 139.4 (d, J = 247.5 Hz), 134.6, 109.7, 106.2, 84.6 (t, J = 17.5 Hz), 79.9, 60.9, 44.1, 43.1, 14.4; ^{19}F NMR (470 MHz, DMSO-d_6) δ -108.2 (d, J = 14.1 Hz, 1F), -127.8 (d, J = 18.8 Hz, 1F), -139.1 (dd, J = 18.8 Hz, 14.1 Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{15}H_9F_3N_3O_3^-$ [M^-], 336.0601; found, 336.0601.

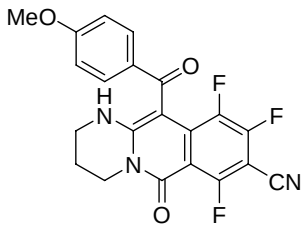
Spectroscopic Data of Tetrahydropyrimido[1,2-*b*]isoquinolinone 9

11-benzoyl-10-chloro-7,9-difluoro-6-oxo-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*] isoquinoline-8-carbonitrile (9a)



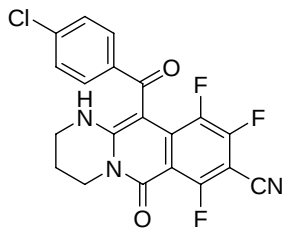
Yellow solid (0.316 g, 79%); Mp 271–273°C; IR (KBr) (ν_{max}, cm^{-1}) 3437, 2233, 1594, 1285, 1112, 927, 852, 784; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.23 (br, 1H, NH), 7.50 (d, J = 7.3 Hz, 2H, PhH), 7.59 (t, J = 7.3 Hz, 1H, PhH), 7.36 (t, J = 7.3 Hz, 2H, PhH), 4.00–3.96 (m, 2H, NCH_2), 3.45–3.41 (m, 2H, NCH_2), 2.06–2.00 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.7, 163.1 (d, J = 275.0 Hz), 159.0 (d, J = 251.3 Hz), 157.0, 151.8, 143.3, 141.1, 132.6, 129.0, 128.8, 110.0, 108.4 (d, J = 16.3 Hz), 104.9, 91.0, 84.6, 40.7, 38.1, 19.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -100.4 (d, J = 4.7 Hz, 1F), -103.6 (d, J = 4.7 Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{11}ClF_2N_3O_2^-$ [M^-], 398.0513; found, 398.0511.

11-benzoyl-7,9,10-trifluoro-6-oxo-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquino line-8-carbonitrile (9b)



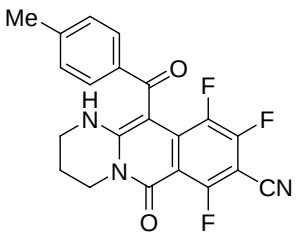
Yellow solid (0.343 g, 83%); Mp 257–258°C; IR (KBr) (ν_{max}, cm^{-1}) 3432, 2233, 1597, 1267, 1169, 789; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (br, 1H, NH), 7.64 (d, J = 8.0 Hz, 2H, ArH), 6.92 (d, J = 8.0 Hz, 2H, ArH), 4.01–3.97 (m, 2H, NCH_2), 3.82 (s, 3H, OCH_3), 3.42–3.38 (m, 2H, NCH_2), 2.05–2.01 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.0, 163.1, 160.7 (d, J = 270.0 Hz), 156.6, 151.1, 149.2 (d, J = 17.5 Hz), 138.2 (dd, J = 243.8.0 Hz, 10.0 Hz), 134.7, 132.9, 130.9, 114.2, 110.0, 103.6, 88.5, 83.0 (t, J = 18.8 Hz), 55.8, 40.6, 39.1, 19.1; ^{19}F NMR (470 MHz, DMSO-d_6) δ -107.7 (d, J = 14.1 Hz, 1F), -129.6 (d, J =18.8 Hz, 1F), -141.7–-141.8 (m, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{13}F_3N_3O_3^-$ [M^-], 412.0914; found, 412.0912.

11-(4-chlorobenzoyl)-7,9,10-trifluoro-6-oxo-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (9c)



Yellow solid (0.334 g, 80%); Mp 274–275°C; IR (KBr) (ν_{max}, cm^{-1}) 3447, 2231, 1599, 1492, 1281, 1093, 802; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.60 (br, 1H, NH), 7.63 (d, J = 7.8 Hz, 2H, ArH), 7.45 (d, J = 7.8 Hz, 2H, ArH), 3.98–3.94 (m, 2H, NCH_2), 3.44–3.40 (m, 2H, NCH_2), 2.04–2.00 (br s, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.4, 161.4, 159.3, 156.7, 151.9, 139.3, 139.2, 134.7, 130.3, 129.0, 129.0, 109.9, 104.3, 87.8, 84.1 (d, J = 21.3 Hz), 40.6, 38.5, 18.9; ^{19}F NMR (470 MHz, DMSO-d_6) δ -107.6 (d, J = 14.1 Hz, 1F), -128.5 (d, J = 18.8 Hz, 1F), -141.1–-141.2 (m, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{20}H_{10}ClF_3N_3O_2^-$ [M^-], 416.0419; found, 416.0405.

7,9,10-trifluoro-11-(4-methylbenzoyl)-6-oxo-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*b*]isoquinoline-8-carbonitrile (9d)



Yellow solid (0.342 g, 86%); Mp 283–285°C; IR (KBr) (ν_{max}, cm^{-1}) 3435, 2230, 1595, 1280, 1178, 1058, 778; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.31 (br, 1H, NH), 7.54 (d, J = 7.6 Hz, 2H, ArH), 7.20 (d, J = 7.6 Hz, 2H, ArH), 3.99–3.95 (m, 2H, NCH_2), 3.42–3.38 (m, 2H, NCH_2), 2.34 (s, 3H, CH_3), 2.05–2.00 (m, 2H, CH_2); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.8, 160.5 (d, J = 270.0 Hz), 156.7, 151.5, 151.2 (d, J = 266.3 Hz), 142.9， 139.2–137.3 (m), 137.8，134.8, 129.5, 128.6, 110.0, 103.8, 88.3, 83.3 (t, J = 18.8 Hz), 40.6, 39.0, 21.5, 19.0; ^{19}F NMR (470 MHz, DMSO-d_6) δ -107.4 (d, J = 14.1 Hz, 1F), -129.3 (d, J = 23.5 Hz, 1F), -141.2 (dd, J = 23.5 Hz, 14.1 Hz, 1F); HRMS (TOF ES^-): *m/z* calcd for $C_{21}H_{13}F_3N_3O_2^-$ [M^-], 396.0965; found, 396.0964.

Anti-cancer activities of compounds 5-7[4]

The cytotoxic potential of the newly synthesized 1,3-diazahetero-cycle fused [1,2-*b*] isoquinolin-1(2*H*)-imines **5-7** were evaluated in vitro against a series of human tumor cell lines according to the procedure described in the literature.[4] The tumor cell lines including myeloid leukaemia (HL-60 and K562), epidermoid carcinoma (A431), ovarian carcinoma (Skov-3), laryngeal carcinoma (Hep-2). Cisplatin (DDP) was servered as the reference drug. (IC_{50} value, defined as the concentrations corresponding to 50% growth inhibition). The tested compounds showed moderate to excellent cellular cytotoxicity in the in vitro antitumor screening expressed by the IC_{50} values.

Table S2. Cytotoxic activities of polyhalo 1,3-diazahetero-cycle fused [1,2-*b*] isoquinolin-1(2*H*)-imines **5-7** in vitro[a] (IC_{50}, μg/ml[b])

Compd.	A431	HL60	HepG2	K562	Skov-3
DDP	1.1	0.5	0.06	1.0	3.9
5a	3.4	0.8	4.4	0.7	19.7
5b	4.8	0.1	0.3	0.4	5.8
5c	0.8	0.001	1.2	0.08	0.2
5d	2.1	0.3	11.3	0.7	9.2
5e	1.9	0.2	1.2	0.3	4.8
5f	7.5	0.5	0.9	0.4	2.4
5g	20.3	2.6	37.6	2.4	31.4
5h	5.0	0.3	12.4	0.4	34.9
5i	4.9	0.5	17.7	1.0	34.5
5j	308	4.7	503	3.6	78.4
5k	20.4	0.9	6.4	0.4	6.2
5l	4.4	0.02	3.1	0.1	0.02
5m	40.6	1.7	38.2	1.6	50.1
5n	2.2	0.003	1.5	0.0008	0.05
5o	3.4	0.02	0.4	0.0005	0.04

6a	10.1	10.7	9.3	1.2	51.2
6b	0.5	0.01	0.3	0.03	1.2
6c	2.4	0.3	1.1	0.02	16.4
6d	56.9	4.4	400	1.4	67.2
6e	2	0.5	0.8	0.07	26.8
6f	1.1	0.02	0.8	0.01	2.6
6g	8	4.4	30	1.2	52.2
6h	2.8	0.2	2.1	0.3	17.1
6i	4.3	4.7	8.4	0.5	15.1
6j	>1000	58.2	277	9.3	826
6k	27.5	14.6	24.6	2.3	76.4
6l	2.1	4.7	2.4	0.7	33.9
7a	14.5	6	10.3	2.2	17.4
7b	2.3	1.5	3.6	1.7	29.2
7c	0.3	0.008	0.1	0.0002	0.2
7d	11	24.2	2.7	0.8	32.2
7e	2.1	1	2	0.5	23.8
7f	1.5	0.1	0.5	1.8	0.2

[a] Cytotoxicity as IC_{50} for each cell line, is the concentration of compound which reduced by 50% the optical density of treated cells with respect to untreated cells using the MTT assay.
[b] Data represent the mean values of three independent determinations.

X-ray structure and data[5] of 5o

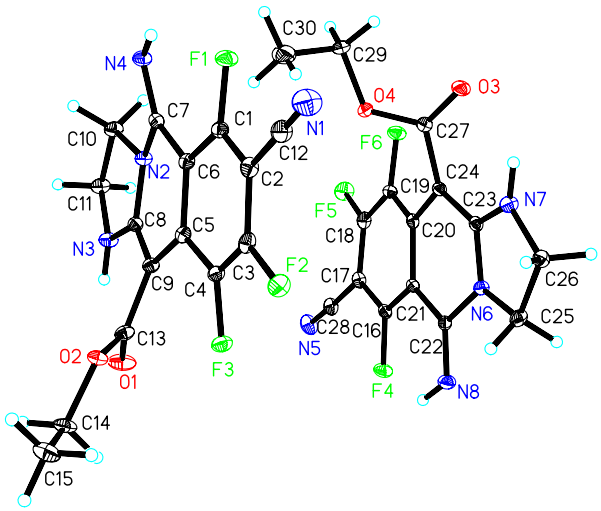


Fig. S1. X-Ray crystal structure of **5o**

Table S3 Crystal data and structure refinement for r08113a

Identification code	r08113a	
Empirical formula	$C_{15}H_{11}F_3N_4O_2$	
Formula weight	336.28	
Temperature	113(2) K	
Wavelength	0.71073 Å	
Crystal system, space group	Triclinic, P2-1	
Unit cell dimensions	a = 10.132(2) A	alpha = 71.25(3) deg.
	b = 11.359(2) A	beta = 80.58(3) deg.
	c = 14.539(3) A	gamma = 64.15(3) deg.
Volume	1425.4(5) A^3	
Z, Calculated density	4, 1.567 Mg/m^3	
Absorption coefficient	0.134 mm^-1	
F(000)	688	
Crystal size	0.34 x 0.32 x 0.28 mm	
Theta range for data collection	2.1 to 27.9 deg.	
Limiting indices	-13<=h<=13, -14<=k<=14, -19<=l<=19	
Reflection collected/unique	17780/6739[R(int) = 0.0431]	
Completeness to theta = 27.9	99.0%	
Absorption correction	MUTI-SCAN	

Max. and min. transmission	0.9635 and 0.9559
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	6739/ 0/ 451
Goodness-of-fit on F^2	1.014
Final R indices [I>2sigma(I)]	R1 = 0.0469, wR2 = 0.1182
R indices (all data)	R1 = 0.0661, wR2 = 0.1245
Absolute structure parameter	0.0(10)

Table S4. Bond lengths [A] and angles [deg] for r08113a.

N(1)-C(12)	1.1455 (0.0023)
N(2)-C(8)	1.3687 (0.0021)
N(2)-C(7)	1.3989 (0.0021)
N(2)-C(10)	1.4788 (0.0022)
N(3)-C(8)	1.3375 (0.0021)
N(3)-C(11)	1.4600 (0.0023)
N(3)-H(3)	0.8830 (0.0220)
N(4)-C(7)	1.2761 (0.0021)
N(4)-H(4)	0.8663 (0.0195)
N(5)-C(28)	1.1434 (0.0022)
N(6)-C(23)	1.3681 (0.0021)
N(6)-C(22)	1.3987 (0.0021)
N(6)-C(25)	1.4730 (0.0021)
N(7)-C(23)	1.3317 (0.0021)
N(7)-C(26)	1.4614 (0.0023)
N(7)-H(7)	0.8913 (0.0239)
N(8)-C(22)	1.2789 (0.0022)
N(8)-H(8)	0.8816 (0.0190)
O(1)-C(13)	1.2209 (0.0020)
O(2)-C(13)	1.3384 (0.0021)
O(2)-C(14)	1.4595 (0.0021)
O(3)-C(27)	1.2206 (0.0019)
O(4)-C(27)	1.3415 (0.0020)
O(4)-C(29)	1.4621 (0.0020)
F(1)-C(1)	1.3482 (0.0019)
F(2)-C(3)	1.3446 (0.0019)
F(3)-C(4)	1.3509 (0.0018)
F(4)-C(16)	1.3529 (0.0019)
F(5)-C(18)	1.3473 (0.0020)
F(6)-C(19)	1.3518 (0.0019)
C(1)-C(2)	1.3854 (0.0025)
C(1)-C(6)	1.3916 (0.0023)
C(2)-C(3)	1.3961 (0.0024)
C(2)-C(12)	1.4369 (0.0025)
C(3)-C(4)	1.3613 (0.0024)
C(4)-C(5)	1.4060 (0.0024)
C(5)-C(6)	1.4314 (0.0023)
C(5)-C(9)	1.4385 (0.0023)

C(6)-C(7)	1.4911 (0.0024)
C(8)-C(9)	1.3962 (0.0024)
C(9)-C(13)	1.4606 (0.0024)
C(10)-C(11)	1.5307 (0.0024)
C(10)-H(10A)	0.9900
C(10)-H(10B)	0.9900
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900
C(14)-C(15)	1.4896 (0.0027)
C(14)-H(14A)	0.9900
C(14)-H(14B)	0.9900
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(21)	1.3885 (0.0023)
C(16)-C(17)	1.3907 (0.0025)
C(17)-C(18)	1.3947 (0.0024)
C(17)-C(28)	1.4393 (0.0024)
C(18)-C(19)	1.3542 (0.0024)
C(19)-C(20)	1.4058 (0.0024)
C(20)-C(24)	1.4340 (0.0023)
C(20)-C(21)	1.4341 (0.0022)
C(21)-C(22)	1.4857 (0.0024)
C(23)-C(24)	1.3955 (0.0024)
C(24)-C(27)	1.4657 (0.0023)
C(25)-C(26)	1.5372 (0.0024)
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-H(26A)	0.9900
C(29)-C(30)	1.4743 (0.0029)
C(29)-H(29A)	0.9900
C(29)-H(29B)	0.9900
C(30)-H(30A)	0.9800
C(30)-H(30B)	0.9800
C(30)-H(30C)	0.9800
C(7)-N(2)-C(8)	124.20 (0.14)
C(7)-N(2)-C(10)	120.90 (0.14)
C(8)-N(2)-C(10)	110.87 (0.13)
C(8)-N(3)-C(11)	112.15 (0.14)
C(8)-N(3)-H(3)	121.42 (1.38)
C(11)-N(3)-C(3)	125.53 (1.38)
C(7)-N(4)-H(4)	112.63 (1.36)
C(22)-N(6)-C(23)	125.09 (0.14)
C(22)-N(6)-C(25)	121.57 (0.14)
C(23)-N(6)-C(25)	111.26 (0.13)
C(23)-N(7)-C(26)	112.80 (0.15)
C(23)-N(7)-H(7)	124.98 (1.44)
C(26)-N(7)-H(7)	122.19 (1.45)
C(22)-N(8)-H(8)	111.43 (1.32)

C(13)-O(2)-C(14)	116.69 (0.13)
C(27)-O(4)-C(29)	119.08 (0.13)
C(27)-O(4)-C(29)	119.08 (0.13)
C(2)-C(1)-F(1)	116.12 (0.14)
C(6)-C(1)-F(1)	120.33 (0.15)
C(6)-C(1)-C(2)	123.55 (0.16)
C(1)-C(2)-C(3)	116.86 (0.15)
C(1)-C(2)-C(12)	122.39 (0.16)
C(3)-C(2)-C(12)	120.74 (0.16)
C(2)-C(3)-F(2)	118.89 (0.15)
C(4)-C(3)-F(2)	119.55 (0.15)
C(4)-C(3)-C(2)	121.55 (0.15)
C(3)-C(4)-F(3)	116.96 (0.14)
C(5)-C(4)-F(3)	120.81 (0.15)
C(5)-C(4)-C(3)	122.20 (0.15)
C(6)-C(5)-C(4)	117.06 (0.15)
C(9)-C(5)-C(4)	122.72 (0.15)
C(9)-C(5)-C(6)	120.16 (0.15)
C(5)-C(6)-C(1)	118.48 (0.15)
C(7)-C(6)-C(1)	121.49 (0.15)
C(7)-C(6)-C(5)	120.02 (0.14)
N(2)-C(7)-N(4)	116.47 (0.15)
C(6)-C(7)-N(4)	130.48 (0.15)
C(6)-C(7)-N(2)	113.05 (0.14)
N(2)-C(8)-N(3)	109.38 (0.15)
C(9)-C(8)-N(3)	128.74 (0.16)
C(9)-C(8)-N(2)	121.74 (0.14)
C(5)-C(9)-C(8)	117.15 (0.15)
C(13)-C(9)-C(8)	115.95 (0.14)
C(13)-C(9)-C(5)	126.13 (0.15)
C(11)-C(10)-N(2)	102.32 (0.13)
H(10A)-C(10)-N(2)	111.30
H(10A)-C(10)-C(11)	111.30
H(10B)-C(10)-N(2)	111.30
H(10B)-C(10)-C(11)	111.30
H(10B)-C(10)-H(10A)	109.19
C(10)-C(11)-N(3)	103.36 (0.13)
H(11A)-C(11)-N(3)	111.09
H(11A)-C(11)-C(10)	111.09
H(10B)-C(11)-N(3)	111.09
H(10B)-C(11)-C(10)	111.09
H(10B)-C(11)-H(11A)	109.05
O(2)-C(12)-N(1)	177.07 (0.21)
O(2)-C(13)-O(1)	122.81 (0.16)
C(9)-C(13)-O(1)	123.86 (0.16)
C(9)-C(13)-O(2)	113.12 (0.14)
C(15)-C(14)-O(2)	107.27 (0.14)
H(14A)-C(14)-O(2)	110.26
H(14A)-C(14)-O(2)	110.26

H(14B)-C(14)-C(15)	110.26
H(14B)-C(14)-C(15)	110.26
H(14B)-C(14)-H(14A)	108.53
H(15A)-C(15)-C(14)	109.47
H(15B)-C(15)-C(14)	109.47
H(15B)-C(15)-C(14)	109.47
H(15C)-C(15)-H(15A)	109.47
H(15C)-C(15)-H(15A)	109.47
H(15C)-C(15)-H(15B)	109.47
C(21)-C(16)-F(4)	120.57 (0.15)
C(17)-C(16)-F(14)	115.82 (0.14)
C(17)-C(16)-C(21)	123.61 (0.16)
C(18)-C(17)-C(16)	116.57 (0.15)
C(28)-C(17)-C(16)	122.50 (0.16)
C(28)-C(17)-C(18)	120.91 (0.16)
C(19)-C(18)-F(15)	119.79 (0.16)
C(17)-C(18)-F(5)	118.35 (0.15)
C(17)-C(18)-C(19)	121.85 (0.16)
C(18)-C(19)-F(6)	117.45 (0.15)
C(20)-C(19)-F(6)	120.35 (0.14)
C(20)-C(19)-C(18)	122.14 (0.16)
C(24)-C(20)-C(19)	122.32 (0.15)
C(21)-C(20)-C(19)	117.09 (0.15)
C(21)-C(20)-C(24)	120.52 (0.15)
C(20)-C(21)-C(16)	118.22 (0.15)
C(22)-C(21)-C(16)	121.74 (0.15)
C(22)-C(21)-C(20)	120.02 (0.14)
N(6)-C(22)-N(8)	115.79 (0.15)
C(21)-C(22)-N(8)	130.66 (0.15)
C(21)-C(22)-N(6)	113.53 (0.14)
N(6)-C(23)-N(7)	109.53 (0.14)
C(24)-C(23)-N(7)	128.92 (0.16)
C(24)-C(23)-N(6)	128.92 (0.16)
C(20)-C(24)-C(23)	117.17 (0.15)
C(27)-C(24)-C(23)	116.50 (0.14)
C(27)-C(24)-C(20)	125.48 (0.15)
C(26)-C(25)-N(6)	103.01 (0.14)
H(25A)-C(25)-N(6)	111.16
H(25A)-C(25)-N(6)	111.16
H(25B)-C(25)-C(26)	111.16
H(25B)-C(25)-C(26)	111.16
H(25B)-C(25)-H(25A)	109.10
C(25)-C(26)-N(7)	103.25 (0.13)
H(26A)-C(26)-N(7)	111.11
H(26A)-C(26)-N(7)	111.11
H(26B)-C(26)-C(25)	111.11
H(26B)-C(26)-C(25)	111.11
H(26B)-C(26)-H(26A)	109.07
O(4)-C(27)-O(3)	123.26 (0.15)
C(24)-C(27)-O(3)	124.25 (0.16)

C(24)-C(27)-O(4)	112.30 (0.14)
C(17)-C(28)-N(5)	176.93 (0.20)
C(30)-C(29)-O(4)	107.66 (0.16)
H(29A)-C(29)-O(4)	110.18
H(29B)-C(29)-O(4)	110.18
H(29A)-C(29)-C(30)	110.18
H(29B)-C(29)-C(30)	110.18
H(29B)-C(29)-H(29A)	108.47
H(30A)-C(30)-C(29)	109.47
H(30B)-C(30)-C(29)	109.47
H(30C)-C(30)-C(29)	109.47
H(30B)-C(30)-H(30)	109.47
H(30C)-C(30)-C(30)	109.47
H(30C)-C(30)-H(29A)	109.47

Symmetry transformations used to generate equivalent atoms:

Table S5 Selected torsion angles [deg.] for r08113a

F(1)-C(1)-C(2)-C(3)	-175.93(0.15)
C(6)-C(1)-C(2)-C(3)	4.19(0.27)
F(1)-C(1)-C(2)-C(12)	5.41(0.27)
C(6)-C(1)-C(2)-C(12)	-174.47(0.17)
C(1)-C(2)-C(3)-F(2)	177.53(0.16)
C(12)-C(2)-C(3)-F(2)	-3.79(0.26)
C(1)-C(2)-C(3)-C(4)	-1.46(0.27)
C(12)-C(2)-C(3)-C(4)	177.22(0.17)
F(2)-C(3)-C(4)–F(3)	-4.26(0.24)
C(2)-C(3)-C(4)–F(3)	174.71(0.16)
F(2)-C(3)-C(4)-C(5)	177.46(0.16)
C(2)-C(3)-C(4)-C(5)	-3.56(0.28)
F(3)-C(4)-C(5)-C(6)	-172.46(0.14)
C(3)-C(4)-C(5)-C(6)	5.76(0.26)
F(3)-C(4)-C(5)-C(9)	4.82(0.27)
C(3)-C(4)-C(5)-C(9)	-176.97(0.16)
F(1)-C(1)-C(6)-C(5)	178.23(0.15)
C(2)-C(1)-C(6)-C(5)	-1.91(0.26)
F(1)-C(1)-C(6)-C(7)	-2.76(0.25)
C(2)-C(1)-C(6)-C(7)	177.11(0.17)
C(4)-C(5)-C(6)-C(1)	-3.03(0.24)
C(9)-C(5)-C(6)-C(1)	179.63(0.16)
C(4)-C(5)-C(6)-C(7)	177.94(0.15)
C(9)-C(5)-C(6)-C(7)	0.60(0.25)
C(8)-N(2)-C(7)-N(4)	-158.43(0.16)
C(10)-N(2)-C(7)-N(4)	-3.12(0.24)
C(8)-N(2)-C(7)-C(6)	22.11(0.23)
C(10)-N(2)-C(7)-C(6)	177.41(0.15)
C(1)-C(6)-C(7)-N(4)	-14.17(0.29)
C(5)-C(6)-C(7)-N(4)	164.83(0.17)
C(1)-C(6)-C(7)-N(2)	165.20(0.15)

C(5)-C(6)-C(7)-N(2)	-15.80(0.23)
C(11)-N(3)-C(8)-N(2)	3.31(0.20)
C(11)-N(3)-C(8)-C(9)	179.00(0.18)
C(7)-N(2)-C(8)-N(3)	163.70(0.15)
C(10)-N(2)-C(8)-N(3)	6.26(0.20)
C(7)-N(2)-C(8)-C(9)	-12.35(0.26)
C(10)-N(2)-C(8)-C(9)	-169.79(0.16)
N(3)-C(8)-C(9)-C(5)	179.71(0.17)
N(2)-C(8)-C(9)-C(5)	-5.07(0.25)
N(3)-C(8)-C(9)-C(13)	-9.71(0.28)
N(2)-C(8)-C(9)-C(13)	165.51(0.16)
C(4)-C(5)-C(9)-C(8)	-167.00(0.17)
C(6)-C(5)-C(9)-C(8)	10.19(0.24)
C(4)-C(5)-C(9)-C(13)	23.49(0.28)
C(6)-C(5)-C(9)-C(13)	-159.32(0.17)
C(8)-N(2)-C(10)-C(11)	-12.38(0.19)
C(7)-N(2)-C(10)-C(11)	-170.67(0.15)
C(8)-N(3)-C(11)-C(10)	-10.84(0.20)
N(2)-C(10)-C(11)-N(3)	13.21(0.18)
C(1)-C(2)-C(12)-N(1)	124.56(3.95)
C(3)-C(2)-C(12)-N(1)	-54.05(4.05)
C(14)-O(2)-C(13)-O(1)	1.03(0.25)
C(14)-O(2)-C(13)-C(9)	175.86(0.15)
C(8)-C(9)-C(13)-O(1)	38.04(0.26)
C(5)-C(9)-C(13)-O(1)	-152.34(0.18)
C(8)-C(9)-C(13)-O(2)	-136.73(0.16)
C(5)-C(9)-C(13)-O(2)	32.89(0.25)
C(13)-O(2)-C(14)-C(15)	170.68(0.16)
F(4)-C(16)-C(17)-C(18)	-175.72(0.14)
C(21)-C(16)-C(17)-C(18)	4.80(0.26)
F(4)-C(16)-C(17)-C(28)	2.63(0.25)
C(21)-C(16)-C(17)-C(28)	-176.85(0.16)
C(16)-C(17)-C(18)-F(5)	174.84(0.16)
C(28)-C(17)-C(18)-F(5)	-3.53(0.25)
C(16)-C(17)-C(18)-C(19)	-4.07(0.26)
C(28)-C(17)-C(18)-C(19)	177.56(0.17)
F(5)-C(18)-C(19)-F(6)	-3.70(0.25)
C(17)-C(18)-C(19)-F(6)	175.20(0.16)
F(5)-C(18)-C(19)-C(20)	179.10(0.16)
C(17)-C(18)-C(19)-C(20)	-2.00(0.28)
F(6)-C(19)-C(20)-C(24)	7.02(0.26)
C(18)-C(19)-C(20)-C(24)	-175.86(0.16)
F(6)-C(19)-C(20)-C(21)	-169.85(0.14)
C(18)-C(19)-C(20)-C(21)	7.27(0.26)
F(4)-C(16)-C(21)-C(20)	-179.00(0.14)
C(17)-C(16)-C(21)-C(20)	0.46(0.26)
F(4)-C(16)-C(21)-C(22)	2.67(0.25)
C(17)-C(16)-C(21)-C(22)	-177.87(0.16)
C(19)-C(20)-C(21)-C(16)	-6.37(0.23)
C(24)-C(20)-C(21)-C(16)	176.70(0.16)

C(19)-C(20)-C(21)-C(22)	171.99(0.15)
C(24)-C(20)-C(21)-C(22)	-4.94(0.24)
C(23)-N(6)-C(22)-N(8)	-165.47(0.16)
C(25)-N(6)-C(22)-N(8)	-3.34(0.24)
C(23)-N(6)-C(22)-C(21)	15.96(0.23)
C(25)-N(6)-C(22)-C(21)	178.09(0.15)
C(16)-C(21)-C(22)-N(8)	-8.04(0.30)
C(20)-C(21)-C(22)-N(8)	173.66(0.17)
C(16)-C(21)-C(22)-N(6)	170.26(0.15)
C(20)-C(21)-C(22)-N(6)	-8.04(0.23)
C(26)-N(7)-C(23)-N(6)	-0.49(0.21)
C(26)-N(7)-C(23)-C(24)	176.05(0.17)
C(22)-N(6)-C(23)-N(7)	166.61(0.16)
C(25)-N(6)-C(23)-N(7)	2.89(0.20)
C(22)-N(6)-C(23)-C(24)	-10.24(0.26)
C(25)-N(6)-C(23)-C(24)	-173.95(0.16)
N(7)-C(23)-C(24)-C(20)	179.51(0.17)
N(6)-C(23)-C(24)-C(20)	-4.31(0.25)
N(7)-C(23)-C(24)-C(27)	-10.49(0.28)
N(6)-C(23)-C(24)-C(27)	165.69(0.15)
C(19)-C(20)-C(24)-C(23)	-165.46(0.16)
C(21)-C(20)-C(24)-C(23)	11.30(0.24)
C(19)-C(20)-C(24)-C(27)	25.54(0.27)
C(21)-C(20)-C(24)-C(27)	-157.70(0.16)
C(23)-N(6)-C(25)-C(26)	-3.89(0.19)
C(22)-N(6)-C(25)-C(26)	-168.26(0.15)
C(23)-N(7)-C(26)-C(25)	-1.92(0.20)
N(6)-C(25)-C(26)-N(7)	3.31(0.18)
C(29)-O(4)-C(27)-O(3)	1.45(0.25)
C(29)-O(4)-C(27)-C(24)	176.59(0.15)
C(23)-C(24)-C(27)-O(3)	36.93(0.25)
C(20)-C(24)-C(27)-O(3)	-154.00(0.17)
C(23)-C(24)-C(27)-O(4)	-138.15(0.16)
C(20)-C(24)-C(27)-O(4)	30.91(0.24)
C(16)-C(17)-C(28)-N(5)	-179.93(99.99)
C(18)-C(17)-C(28)-N(5)	-1.66(3.88)
C(27)-O(4)-C(29)-C(30)	-120.89(0.19)

Symmetry transformations used to generate equivalent atoms:

Table S6 Hydrogen bonds for r08113a [A and deg.].

D—H···A	d(D—H)	d(H···A)	d(D···A)	<(DHA)
N(4)—H(4)···F	0.866 (19)	2.19 (2)	2.820 (2)	129.3 (18)
N(4)—H(4)···O(2)^{i}	0.866 (19)	2.49 (2)	3.280 (2)	151.5 (18)
N(3)—H(3)···O(3)^{ii}	0.88 (2)	2.17 (2)	2.977 (2)	152.0 (19)
N(3)—H(3)···O(1)	0.88 (2)	2.22 (2)	2.787 (2)	121.8 (17)
N(8)—H(8)···F(4)	0.882 (19)	2.126 (19)	2.807 (2)	133.5 (18)
N(7)—H(7)···O(1)^{iii}	0.89 (2)	2.06 (2)	2.885 (2)	153 (2)
N(7)—H(7)···O(3)	0.89 (2)	2.28 (2)	2.808 (2)	118.0 (18)

Symmetry codes: (i) −*x*+1, −*y*, −*z*+1; (ii) *x*−1, *y*, *z*; (iii) *x*+1, *y*, *z*.

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5. CCDC 736001 contain the supplementary crystallographic data for compound **5o**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.