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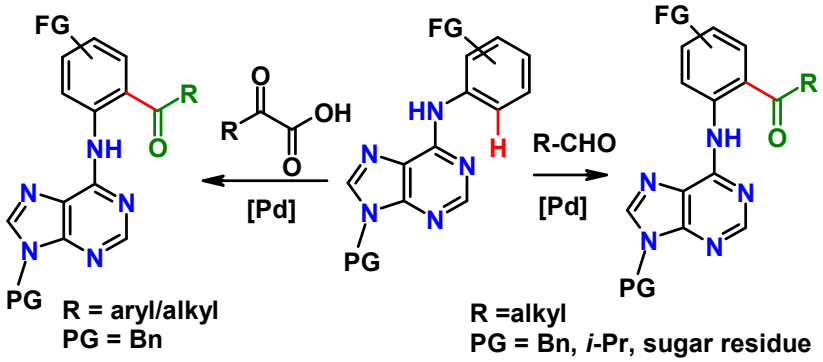
Purinyl N1-directed *ortho*-acylation of 6-anilinopurines was achieved in the presence of [Pd]-catalyst using aldehydes/α-oxocarboxylic acids as the acylating source.



Journal Name

ARTICLE

Palladium-catalysed *ortho*-acylation of 6-anilinopurines/purine nucleosides via C-H activation

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Purinyl N1 directed *ortho*-acylation of 6-anilinopurines was achieved *via* C(sp^2)-H bond activation in the presence of [Pd]-catalyst using aldehydes or α-oxocarboxylic acids as the acylating source. A wide variety of purine appended 2'-aminoacetophenones/benzophenones are isolated in good to excellent yields. These catalytic conditions are also successfully applied to 6-anilinopurine nucleosides.

Introduction

Aryl ketones are important building blocks in several biologically active natural products, pharmaceuticals and agrochemicals.[1] Thus, construction of these motifs always attracts considerable attention from synthetic chemists. Among the numerous methods developed for the synthesis of aryl ketones, Friedel-Crafts acylation is the most accepted synthetic procedure.[2] However, poor regioselectivity, limited functional group tolerance and using an over-stoichiometric amount of Lewis acid catalyst limits the scope of this reaction. Therefore, it is highly desirable to develop a mild and efficient method for the synthesis of aryl ketones.

Recently transition metal catalysed direct C-H bond acylation of arenes has been reported by several pioneering groups using aldehydes,[3] α-oxocarboxylic acids,[4] alcohols,[5] toluene derivatives,[6] benzylamines,[7] benzyl chlorides/bromides,[8] carboxylic acids,[9] diketones[10] or benzylic ethers[11] as acylating source with the aid of directing groups. This direct acylation reaction is more atom economic and environmentally friendly alternative to the Friedel–Crafts acylation, which is commonly used for the synthesis of aryl ketones. Purine could also be used as a directing group for the *ortho*-C-H functionalization of aryl moieties.[12] As our ongoing work on C-H activation[13] and modification of nucleoside derivatives,[14] we herein report the palladium-catalysed *ortho*-acylation of 6-anilinopurines with aldehydes/ α-oxocarboxylic acids *via* purinyl N1 directed C-H bond activation. More importantly, this study provides the purine appended 2'-aminoacetophenones/benzophenones, which may be used as active pharmaceutical ingredients.[15]

Results and Discussion

To achieve *ortho*-acylation, we have initiated our studies by performing the reaction of 6-anilinopurine **1a** with 1-heptanal in the presence of $Pd(OAc)_2$ (5 mol %) with TBHP (3 equiv) as an oxidant under neat conditions at 110 ^oC for 24 h. We were happy to find that *ortho*-acylated purine derivative **2a** was obtained in 38% isolated yield (Table 1, entry 1). Inspired by this result, we proceeded to maximise the yield of the product **2a** by varying the reaction parameters as depicted in Table 1. Among the solvents DMF, NMP, CH_3CN, DCE, dioxane, toluene, xylene and AcOH, only dioxane gave moderate yield (44%). In the remaining cases, product **2a** yield was poor or negligible (Table 1, entries 2-9). Among the palladium catalysts, only palladium acetate gave better conversion to the acylated product **2a** (Table 1, entries 10-12). Proper oxidant is also crucial for this reaction. Compared to TBHP, benzoyl peroxide or H_2O_2 or benzoquinone gave lower yields of the product **2a** (Table 1, entries 13-15). Gratifyingly, further optimisation revealed that reaction proceeds better in dioxane/AcOH/DMSO (7/2/1, v/v/v) solvent mixture to afford the *ortho*-acylated product in good yield of 62%. Increasing the amount of catalyst $Pd(OAc)_2$ from 5 mol % to 10 mol % improved the yield of the product **2a** to 74% after isolation (Table 1, entry 17). Thus, the optimised reaction conditions for the present reaction were: $Pd(OAc)_2$ (10 mol %), TBHP (3 equiv) and dioxane/AcOH/DMSO (7/2/1, v/v/v, 3 mL) at 110 °C (oil bath temperature) for 24 h.

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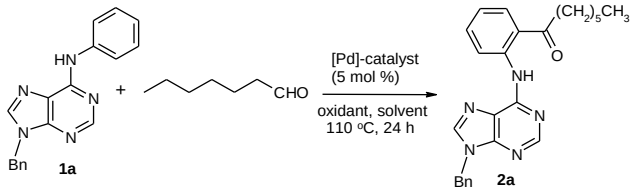
†Electronic Supplementary Information (ESI) available: ^1H and ^{13}C NMR spectra. CCDC reference number for compound **2m** is 1423000. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/x0xx00000x

Table 1. Optimisation study for the [Pd]-catalysed *ortho*-acylation of 6-anilinopurines with aldehydes[a]



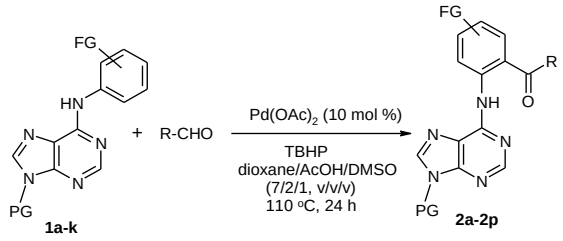
Entry	Catalyst (5 mol %)	Oxidant	Solvent	Yield (%)[b]
1	$Pd(OAc)_2$	TBHP	-	38
2	$Pd(OAc)_2$	TBHP	DMF	trace
3	$Pd(OAc)_2$	TBHP	NMP	21
4	$Pd(OAc)_2$	TBHP	CH_3CN (90 °C)	trace
5	$Pd(OAc)_2$	TBHP	DCE (90 °C)	23
6	$Pd(OAc)_2$	TBHP	dioxane	44
7	$Pd(OAc)_2$	TBHP	toluene	10
8	$Pd(OAc)_2$	TBHP	xylene	32
9	$Pd(OAc)_2$	TBHP	AcOH	trace
10	$PdCl_2$	TBHP	dioxane	18
11	$PdCl_2(CH_3CN)_2$	TBHP	dioxane	24
12	$PdCl_2(PPh_3)_2$	TBHP	dioxane	trace
13	$Pd(OAc)_2$	benzoyl peroxide	dioxane	ND
14	$Pd(OAc)_2$	H_2O_2	dioxane	31
15	$Pd(OAc)_2$	benzoquinone	dioxane	16
16	$Pd(OAc)_2$	TBHP	dioxane/AcOH/DMSO (7/2/1, v/v/v)	62
17	**$Pd(OAc)_2$ (10 mol %)**	**TBHP**	**dioxane/AcOH/DMSO (7/2/1, v/v/v)[c]**	**74**

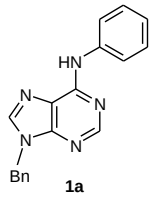
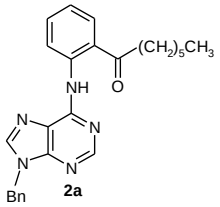
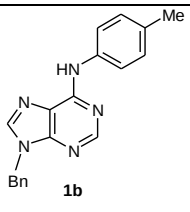
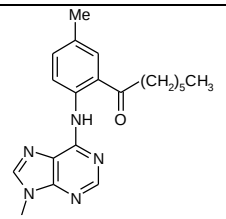
[a]Reaction conditions: **1a** (0.3 mmol), 1-heptanal (0.6 mmol), oxidant (3 equiv), solvent (3 mL), 110 °C (oil bath temperature). [b]Isolated yields. ND = not detected. [c] This solvent system was earlier used by Ge and coworkers.[4b]

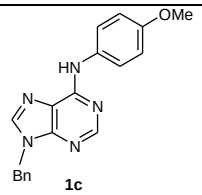
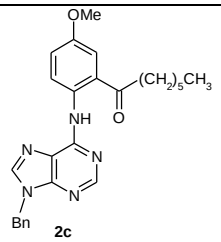
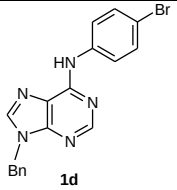
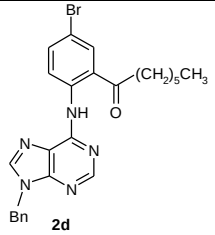
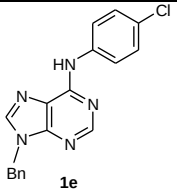
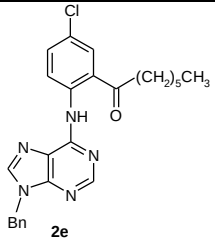
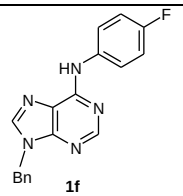
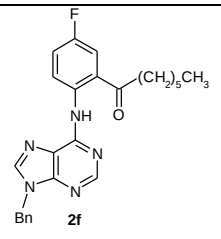
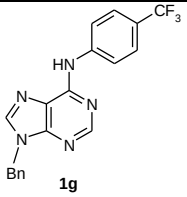
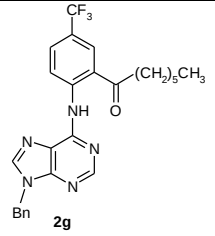
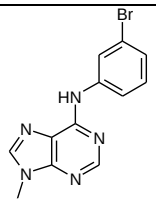
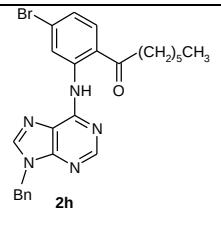
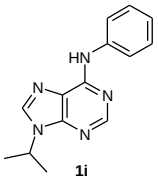
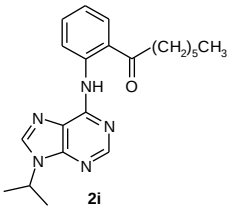
After having the optimised reaction conditions in hand, we examined the substrate scope by varying the 6-anilinopurine derivatives and aldehydes (Table 2). Anilines bearing electron-donating or withdrawing substituents underwent cross-dehydrogenative coupling (CDC) with heptanal smoothly and produced the corresponding acylated derivatives **2a-2h** in good to excellent yields (61-74%). Bromo and chloro functional groups were well tolerated and afforded *ortho*-acyl derivatives **2d** and **2e**. These products can pave way for further manipulation *via* cross-coupling reactions utilising the -Br/-Cl functionalities. The reaction is highly regioselective when performed with *meta*-substituted amines. In these cases, only one regioisomer was observed and the sterically less hindered C-H position was acylated. Under these catalytic conditions *ortho*-substituted 6-anilinopurines did not furnish the corresponding acyalted derivatives.[4a,5b] We have also examined the effect of purine N9-substituent on the course of the reaction. Thus, the reaction of (9-isopropyl-9H-purin-6-yl) phenyl-amine **1i** with heptanal afforded the *ortho*-acylated derivative **2i** in good yield (70%). The generality of the methodology was then extended to 6-anilinopurine nucleoside **1j** with 1-heptanal and 1-hexanal; in both the cases we have isolated the corresponding *ortho*-acylated nucleosides **2j** and **2k** respectively, in decent yields (54-56%). The reaction worked well in the case of simple 2-anilinopyrimidine, though.

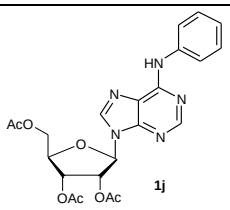
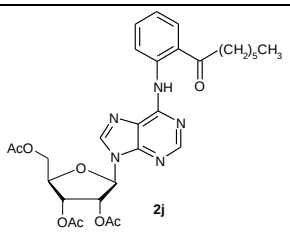
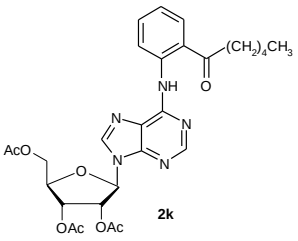
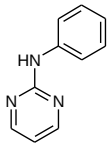
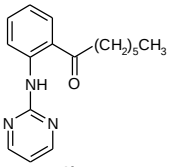
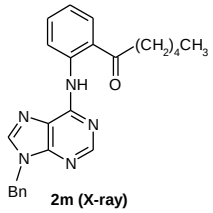
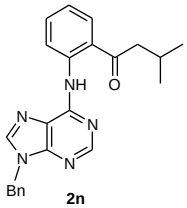
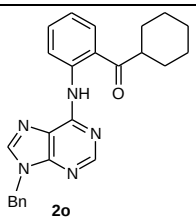
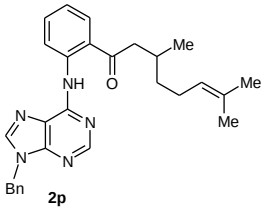
We then investigated the effect of a wide range of alkyl aldehydes. The reaction worked well with isovaleraldehyde (a branched aldehyde) and produced the acylated derivative **2n** in good yield (68%). Cyclohexane carboxaldehyde also participated in this coupling and gave the corresponding ketone **2o** in 60% yield. It is noteworthy that citronellal, a monoterpenoid could also provide the acylated derivative **2p** in moderate yield (54%). Rather surprisingly, aryl aldehydes underwent oxidation to the corresponding carboxylic acids under these conditions. Thus, we observed the reactivity difference between the other directing group assisted cross-dehyodrogenative coupling (CDC) reaction of aryl aldehydes with the purine directed CDC reactions.[3] The structure of one of the acylated derivatives (**2m**) was further confirmed by using X-ray crystallography (Figure 1).

Table 2. Scope of the *ortho*-acylation reaction with 6-anilinopurines and aldehydes[a]



Entry No.	Substrate	Product	Yield (%)
1	 1a	 2a	74
2	 1b	 2b	71

3	 **1c**	 **2c**	72
4	 **1d**	 **2d**	66
5	 **1e**	 **2e**	62
6	 **1f**	 **2f**	68
7	 **1g**	 **2g**	61
8	 **1h**	 **2h**	63
9	 **1i**	 **2i**	70

10	 **1j**	 **2j**	56
11	**1j**	 **2k**	54
12	 **1k**	 **2l**	68
13	**1a**	 **2m (X-ray)**	71
14	**1a**	 **2n**	68
15	**1a**	 **2o**	60
16	**1a**	 **2p**	54

[a]Reaction conditions: amine **1** (0.3 mmol), aldehyde (0.6 mmol), $Pd(OAc)_2$ (10 mol %), TBHP (3 equiv) and dioxane/AcOH/DMSO (7/2/1, v/v/v, 3 mL) at 110 °C (oil bath temperature) for 24 h. [b]Isolated yield.

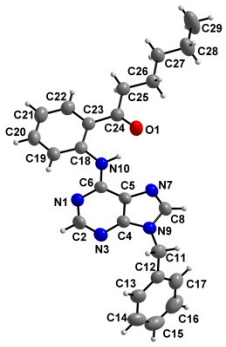
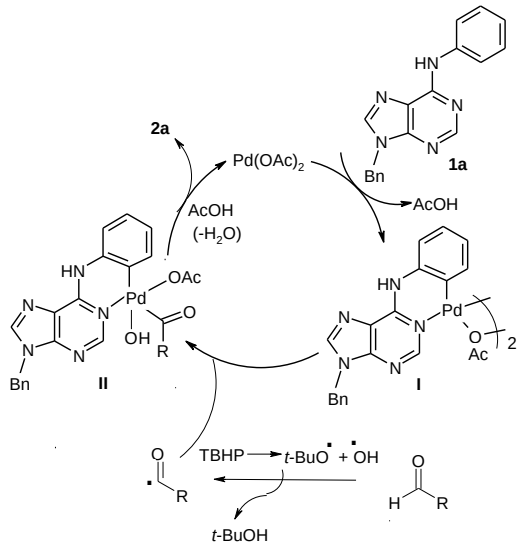


Figure 1. Molecular structure of compound **2m**. Selected bond lengths [Å] with esd's in parentheses: C(24)-O(1) 1.2263(17), C(24)-C(23) 1.490(2), N(10)-C(18) 1.3964(19), N(10)-C(6) 1.3621(18), N(9)-C(11) 1.4604(18).

Plausible mechanistic pathway for the *ortho*-acylation using aldehydes

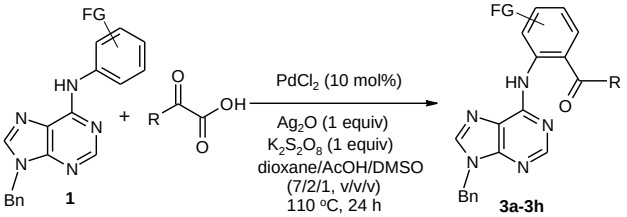
Based on previous reports,[3] a plausible pathway is outlined for Pd-catalysed *ortho*-acylation in Scheme 1. Initially, through the chelate-directed C-H activation of purine N1 atom, the six-membered cyclopalladated intermediate **I** is formed. The reaction of aldehyde with TBHP generates reactive acyl and OH radicals which react with intermediate **I** to produce the Pd(IV) intermediate **II**.[3] Finally, species **II** undergoes reductive elimination leading to the formation of acylated derivative **2a** (or **2b-2p**). The active Pd(II) is regenerated for next catalytic cycle.



Scheme 1 Plausible reaction pathway for the formation of *ortho*-acylated derivatives from 6-anilinopurines with aldehydes

Palladium-catalysed C(sp^2)-H bond acylation of 6-anilinopurines with α-oxocarboxylic acids

The above $Pd(OAc)_2$/TBHP catalytic system was applicable to alkyl aldehydes only; aryl aldehydes under those catalytic conditions were oxidized to corresponding carboxylic acids. We overcame this drawback by choosing α-oxocarboxylic acid as the acylating source. Ag_2O and $K_2S_2O_8$ were used as oxidant and co-oxidant respectively (Scheme 2), under conditions similar to that available in the literature.[4b] Thus, the reaction of 6-anilinopurine **1a** with phenylglyoxylic acid in the presence of $PdCl_2$ (10 mol %) afforded the corresponding acylated derivative **3a** in good yield (64%). Although $Pd(OAc)_2$ also worked, the yield was lower (50%). Under these catalytic conditions, we have examined the substrate scope with respect to 4-Cl and 3-OMe substituted anilinopurines (**1e** and **1j**) also. In both the cases, the corresponding *ortho*-aroyl derivative was isolated in good yield. Arylglyoxylic acids containing Me, F or Br functional groups are well tolerated under these conditions and afford the *ortho*-aroyl derivatives **3d-3g** in good yields. It is noteworthy that the reaction also proceeded smoothly with 2-ketobutyric acid (an alkyl α-oxocarboxylic acid) by furnishing the *ortho*-acyl derivative **3h** in 63% yield. Thus, our protocol is applicable for both aryl and alkyl α-oxocarboxylic acids.



FG = H, Cl, OMe

FG = H, R = C_6H_5	**3a** (64%)
FG = 4-Cl, R = C_6H_5	**3b** (55%)
FG = 3-OMe, R = 2,4,6-Me-C_6H_2	**3c** (63%)
FG = H, R = 2,4,6-Me-C_6H_2	**3d** (60%)
FG = H, R = 4-Me-C_6H_4	**3e** (61%)
FG = H, R = 4-F-C_6H_4	**3f** (66%)
FG = H, R = 4-Br-C_6H_4	**3g** (58%)
FG = H, R = *n*-Pr	**3h** (63%)

Scheme 2 Synthesis of *ortho*-aroyl 6-anilinopurines using α-oxocarboxylic acids as acylating source

Conclusions

In summary, we have developed an efficient method for the Pd-catalysed oxidative *orho*-acylation of 6-anilinopurines with alkyl aldehydes *via* C-H bond activation. A broad range of functional groups and a variety of alkyl aldehydes were well tolerated under these catalytic conditions. This protocol was also successfully applied on 6-anilinopurine nucleoside. 2'-Aminobenzophenones are synthesized by using α–oxocarboxylic acids as the acylating source. Further studies on mechanistic investigation are currently going on in our laboratory.

Experimental Section

General Comments. Solvents were dried according to known methods as appropriate.[16] ^1H, ^{13}C spectra (^1H, 400 MHz; ^{13}C, 100 MHz) were recorded using a 400 MHz spectrometer in $CDCl_3$ with shifts referenced to $SiMe_4$ (δ = 0). IR spectra were recorded on an FTIR spectrophotometer. Melting points were determined by using a local hot-stage melting point apparatus and are uncorrected. Elemental analyses were carried out on a

CHN analyser. Mass spectra were recorded using LC-MS and HRMS (ESI-TOF analyser) equipment.

General procedure for the *ortho*-acylation of 6-anilinopurine derivatives with aldehydes: Synthesis of compounds 2a-2p

A mixture of 6-anilinopurine (0.3 mmol) and $Pd(OAc)_2$ (10 mol %) was taken in a Schlenk tube under N_2. To this, dioxane/AcOH/DMSO (7/2/1, v/v/v, 3 mL) solvent mixture was added and stirring was continued at rt for 10 min. To this mixture, aldehyde (0.6 mmol) and TBHP (0.9 mmol) were added. The contents were heated with stirring at 110 ^oC (oil bath temperature) for 24 h. After cooling to rt, the reaction mixture was extracted with EtOAc (3x30 mL) and water. The combined organic phase was washed with brine solution (30 mL), dried over anh. Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by column chromatography on silica gel using *n*-hexane-EtOAc (4:1) mixture as the eluent.

Compound 2a. Yield 0.092 g (74%); white solid; mp = 164-168 ^oC; IR υ_{max} (KBr): 3284, 3059, 1615, 1576, 1480, 1449, 1256, 1151, 1024, 891, 725, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.66 (s, 1H), 9.27 (d, *J* = 8.4 Hz, 1H), 8.63 (s, 1H), 7.99-7.97 (m, 1H), 7.93 (s, 1H), 7.63-7.58 (m, 1H), 7.37-7.29 (m, 5H), 7.07 (t, *J* ~ 7.4 Hz, 1H), 5.42 (s, 2H), 3.06 (t, *J* ~ 7.4 Hz, 2H), 1.81-1.76 (m, 2H), 1.40-1.26 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.8, 152.7, 152.2, 150.1, 142.4, 141.5, 135.7, 134.5, 131.2, 129.1, 128.4, 127.7, 121.8, 121.6, 120.9, 120.8, 47.3, 40.0, 31.7, 29.1, 24.8, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{25}H_{28}N_5O$ $[M^+$+H]: *m/z* 414.2295. Found: 414.2302.

Compound 2b. Yield 0.091g (71%); white solid; mp = 154-158 ^oC; IR υ_{max} (KBr): 3079, 2915, 1611, 1567, 1534, 1463, 1299, 1178, 784, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.49 (s, 1H), 9.12 (d, *J* = 8.8 Hz, 1H), 8.61 (s, 1H), 7.90 (s, 1H), 7.77 (s, 1H), 7.43 (d, *J* = 8.8 Hz, 1H), 7.37-7.27 (m, 5H), 5.42 (s, 2H), 3.05 (t, *J* ~ 7.4 Hz, 2H), 2.40 (s, 3H), 1.81-1.78 (m, 2H), 1.43-1.31 (m, 6H), 0.91-0.88 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.7, 152.7, 152.2, 149.9, 141.2, 139.9, 135.7, 135.2, 131.2, 130.3, 129.1, 128.4, 127.6, 121.8, 121.6, 120.8, 47.2, 39.9, 31.7, 29.1, 24.7, 22.6, 20.9, 14.1; HRMS (ESI): Calcd. for $C_{26}H_{30}N_5O$ $[M^+$+H]: *m/z* 428.2451. Found: 428.2450.

Compound 2c. Yield 0.096 g (72%); white solid; mp = 132-136 ^oC; IR υ_{max} (KBr): 3441, 3083, 2952, 1608, 1586, 1478, 1350, 1248, 1175, 1047, 979, 840, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.20 (s, 1H), 9.15 (d, *J* = 9.6 Hz, 1H), 8.59 (s, 1H), 7.89 (s, 1H), 7.47 (d, *J* = 3.2 Hz, 1H), 7.35-7.29 (m, 5H), 7.21 (dd, *J* ~ 9.4 Hz, ~ 3.0 Hz, 1H), 5.42 (s, 2H), 3.87 (s, 3H), 3.03 (t, *J* = 7.6 Hz, 2H), 1.81-1.77 (m, 2H), 1.40-1.30 (m, 6H), 0.89 (t, *J* ~ 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.4, 153.6, 152.8, 152.2, 149.9, 141.1, 135.9, 135.8, 129.1, 128.4, 127.7, 123.0, 122.5, 121.5, 120.1, 116.0, 55.9, 47.3, 40.1, 31.7, 29.1, 24.7, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{26}H_{30}N_5O_2$ $[M^+$+H]: *m/z* 444.2400. Found: 444.2399.

Compound 2d. Yield 0.098 g (66%); white solid; mp = 170-174 ^oC; IR υ_{max} (KBr): 3429, 3079, 2952, 1612, 1581, 1525, 1486, 1381, 1300, 1184, 1023, 837, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.53 (s, 1H), 9.25 (d, *J* = 9.2 Hz, 1H), 8.63 (s, 1H), 8.06 (br, 1H), 7.93 (s, 1H), 7.67 (dd, *J* ~ 9.0 Hz, ~ 2.2 Hz, 1H), 7.38-7.28 (m, 5H), 5.43 (s, 2H), 3.03 (t, *J* ~ 7.4 Hz, 2H), 1.83-1.76 (m, 2H), 1.42-1.26 (m, 6H), 0.90 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 152.6, 151.9, 150.3, 141.7, 141.4, 137.1, 135.6, 133.5, 129.2, 128.5, 127.7, 123.1, 122.7, 121.9, 113.0, 47.4, 40.0, 31.7, 29.0, 24.5, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{25}H_{27}BrN_5O$ $[M^+$+H]: *m/z* 492.1400. Found: 492.1399.

Compound 2e. Yield 0.083 g (62%); white solid; mp = 184-188 ^oC; IR υ_{max} (KBr): 3449, 3106, 2928, 1614, 1583, 1525, 1466, 1405, 1351, 1327, 1298, 1139, 1018, 837, 725 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.53 (s, 1H), 9.30 (d, *J* = 9.2 Hz, 1H), 8.62 (s, 1H), 7.93 (s, 1H), 7.92 (d, *J* = 2.4 Hz, 1H), 7.54 (dd, *J* = 9.2 Hz, = 2.4 Hz, 1H), 7.37-7.29 (m, 5H), 5.43 (s, 2H), 3.03 (t, *J* ~ 7.4 Hz, 2H), 1.83-1.75 (m, 2H), 1.42-1.32 (m, 6H), 0.91-0.89 (m, 3H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 152.6, 151.9, 150.2, 141.7, 141.0, 135.6, 134.3, 130.6, 129.1, 128.5, 127.7, 125.7, 122.6, 122.3, 121.8, 47.3, 40.0, 31.7, 29.0, 24.5, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{25}H_{27}ClN_5O$ $[M^+$+H]: *m/z* 448.1905. Found: 448.1903.

Compound 2f. Yield 0.088 g (68%); white solid; mp = 132-13[illegible] ^oC; IR υ_{max} (KBr): 3453, 3100, 2930, 1620, 1588, 1472, 1328, 1259, 1175, 1023, 833, 726 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.40 (s, 1H), 9.29 (dd, *J* = 9.2 Hz, 5.2 Hz, 1H), 8.61 (s, 1H), 7.92 (s, 1H), 7.64 (dd, *J* ~ 9.4 Hz, ~ 3.0 Hz, 1H), 7.37-7.28 (m, 6H), 5.43 (s, 2H), 3.02 (t, *J* = 7.6 Hz, 2H), 1.81-1.75 (m, 2H), 1.42-1.26 (m, 6H), 0.89 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 156.5 (d, $J_{(C-F)}$ = 240.5 Hz), 152.6, 152.0, 150.1, 141.5, 138.7, 135.7, 129.2, 128.5, 127.7, 122.8, 122.7, 122.5, 121.7, 121.6, 121.5, 116.9, 116.6, 47.3, 40.1, 31.7, 29.1, 24.6, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{25}H_{27}FN_5O$ $[M^+$+H]: *m/z* 432.2200. Found: 432.2200.

Compound 2g. Yield 0.088 g (61%); white solid; mp = 160-164 ^oC; IR υ_{max} (KBr): 3463, 2931, 2849, 1731, 1616, 1589, 1468, 1233, 1123, 1025, 729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.81 (s, 1H), 9.49 (d, *J* = 8.8 Hz, 1H), 8.67 (s, 1H), 8.21 (s, 1H), 7.96 (s, 1H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.38-7.29 (m, 5H), 5.44 (s, 2H), 3.10 (t, *J* ~ 7.4 Hz, 2H), 1.85-1.78 (m, 2H), 1.44-1.33 (m, 6H), 0.92-0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0, 152.5, 151.7, 150.5, 145.2, 142.0, 135.5, 130.9, 129.2, 128.6, 128.2, 127.8, 122.1, 121.0, 120.8, 47.4, 40.0, 31.7, 29.0, 24.5, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{26}H_{27}F_3N_5O$ $[M^+$+H]: *m/z* 482.2168. Found: 482.2167.

Compound 2h. Yield 0.093 g (63%); white solid; mp = 152-156 ^oC; IR υ_{max} (KBr): 2937, 2849, 1644, 1605, 1567, 1463, 1408, 1025, 882 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.72 (s, 1H), 9.63 (s, 1H), 8.67 (s, 1H), 7.93 (s, 1H), 7.82 (d, *J* = 8.8 Hz, 1H), 7.38-7.27 (m, 5H), 7.19 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 5.43 (s, 2H), 3.02 (t, *J* ~ 7.4 Hz, 2H), 1.82-1.75 (m, 2H), 1.41-1.31 (m, 6H), 0.89 (t, *J* ~ 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.2, 152.7, 151.8, 150.3, 143.4, 141.8, 135.6, 132.2, 129.4, 129.2, 128.5, 127.7, 123.9, 123.5, 121.9, 120.0, 47.3, 40.1, 31.7, 29.1, 24.7, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{25}H_{27}BrN_5O$ $[M^+$+H]: *m/z* 492.1400. Found: 492.1399.

Compound 2i. Yield 0.077 g (70%); white solid; mp = 88-92 ^oC; IR υ_{max} (KBr): 3096, 2948, 1616, 1584, 1534, 1447, 1238, 9[illegible]5 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.62 (s, 1H), 9.26 (d, *J* = 8.8 Hz, 1H), 8.60 (s, 1H), 8.00 (s, 1H), 7.98 (s, 1H), 7.63-7.59 (m, 1H), 7.09-7.05 (m, 1H), 4.94-4.84 (m, 1H), 3.06 (t, *J* = 7.6 Hz, 2H), 1.88-1.78 (m, 2H), 1.64 (d, *J* = 6.8 Hz, 6H), 1.42-1.31 (m,

6H), 0.89 (t, *J* ~ 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.8, 152.2, 152.1, 149.6, 142.5, 139.1, 134.5, 131.2, 122.3, 121.7, 120.9, 120.8, 47.2, 40.1, 31.8, 29.2, 24.8, 22.8, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{21}H_{28}N_5O$ [M^++H]: *m/z* 366.2295. Found: 366.2293.

Compound 2j. Yield 0.065 g (56%); gummy liquid; IR υ_{max} (neat): 2948, 2860, 1753, 1560, 1447, 1353, 1227, 1096 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.69 (s, 1H), 9.26 (d, *J* = 8.4 Hz, 1H), 8.62 (s, 1H), 8.11 (s, 1H), 8.02 (d, *J* = 8.0 Hz, 1H), 7.64 (t, *J* ~ 7.6 Hz, 1H), 7.12 (t, *J* ~ 7.6 Hz, 1H), 6.25 (d, *J* = 5.2 Hz, 1H), 6.02 (t, *J* = 5.6 Hz, 1H), 5.73-5.71 (m, 1H), 4.50-4.39 (m, 3H), 3.09 (t, *J* ~ 7.4 Hz, 2H), 2.18-2.17 (m, 6H), 2.10 (s, 3H), 1.86-1.79 (m, 2H), 1.43-1.29 (m, 6H), 0.93-0.91 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.9, 170.5, 169.7, 169.4, 152.9, 152.3, 149.6, 142.2, 139.9, 134.6, 131.2, 122.5, 121.8, 121.2, 120.9, 86.3, 80.5, 73.1, 70.9, 63.2, 40.1, 31.7, 29.1, 24.8, 22.6, 20.9, 20.6, 20.5, 14.1; HRMS (ESI): Calcd. for $C_{29}H_{36}N_5O_8$ [M^++H]: *m/z* 582.2565. Found: 582.2568.

Compound 2k. Yield 0.061 g (54%); gummy liquid; IR υ_{max} (neat): 2953, 2931, 1753, 1605, 1447, 1227, 1096, 1047, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.67 (s, 1H), 9.24 (d, *J* = 8.4 Hz, 1H), 8.60 (s, 1H), 8.11 (s, 1H), 8.00 (d, *J* = 8.0 Hz, 1H), 7.62 (t, *J* ~ 7.8 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.24 (d, *J* = 5.6 Hz, 1H), 6.01 (t, *J* = 5.6 Hz, 1H), 5.71 (t, *J* ~ 4.8 Hz, 1H), 4.50-4.38 (m, 3H), 3.07 (t, *J* = 7.6 Hz, 2H), 2.16 (s, 3H), 2.15 (s, 3H), 2.08 (s, 3H), 1.83-1.80 (m, 2H), 1.41-1.37 (m, 4H), 0.94-0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.9, 170.4, 169.6, 169.4, 152.8, 152.3, 149.6, 142.1, 139.9, 134.5, 131.1, 122.4, 121.7, 121.1, 120.8, 86.2, 80.4, 73.1, 70.8, 63.2, 40.0, 31.6, 24.5, 22.6, 20.8, 20.6, 20.4, 14.0; HRMS (ESI): Calcd. for $C_{28}H_{34}N_5O_8$ [M^++H]: *m/z* 568.2408. Found: 568.2404.

Compound 2l. Yield 0.058 g (68%); white solid; mp = 80-84 °C; IR υ_{max} (KBr): 3216, 2931, 2849, 1655, 1573, 1562, 1523, 1441, 1304, 1162, 975, 800, 745 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.89 (s, 1H), 8.90 (d, *J* = 8.4 Hz, 1H), 8.60 (s, 1H), 8.52-8.50 (m, 1H), 7.95 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.58-7.54 (m, 1H), 7.04-7.00 (m, 1H), 6.81-6.78 (m, 1H), 3.05 (t, *J* ~ 7.4 Hz, 2H), 1.80-1.73 (m, 2H), 1.45-1.32 (m, 6H), 0.93-0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.3, 160.2, 157.9, 142.7, 134.3, 131.1, 121.3, 120.1, 119.5, 113.4, 40.0, 31.8, 29.1, 24.8, 22.6, 14.1; HRMS (ESI): Calcd. for $C_{17}H_{22}N_3O$ [M^++H]: *m/z* 284.1764. Found: 284.1763.

Compound 2m. Yield 0.085 g (71%); white solid; mp = 132-136 °C; IR υ_{max} (KBr): 3447, 3083, 2952, 1603, 1583, 1531, 1448, 1349, 1303, 1250, 1192, 1022, 972, 727 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 9.29 (d, *J* = 8.4 Hz, 1H), 8.65 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.94 (s, 1H), 7.62 (t, *J* ~ 7.8 Hz, 1H), 7.38-7.30 (m, 5H), 7.08 (t, *J* = 7.6 Hz, 1H), 5.44 (s, 2H), 3.07 (t, *J* ~ 7.4 Hz, 2H), 1.84-1.80 (m, 2H), 1.41-1.38 (m, 4H), 0.92 (t, *J* ~ 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.8, 152.6, 152.1, 150.0, 142.4, 141.4, 135.7, 134.5, 131.1, 129.1, 128.4, 127.6, 121.8, 121.6, 120.9, 120.7, 47.2, 39.9, 31.6, 24.5, 22.6, 14.0; HRMS (ESI): Calcd. for $C_{24}H_{26}N_5O$ [M^++H]: *m/z* 400.2138. Found: 400.2130. X-ray structure was determined for this compound.

Compound 2n. Yield 0.079 g (68%); white solid; mp = 134-138 °C; IR υ_{max} (KBr): 3079, 2959, 1611, 1584, 1523, 1457, 1304, 1200, 1025 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 9.30-9.28 (m, 1H), 8.65 (s, 1H), 8.00-7.97 (m, 1H), 7.95 (s, 1H), 7.64-7.60 (m, 1H), 7.38-7.30 (m, 5H), 7.11-7.06 (m, 1H), 5.44 (s, 2H), 2.94 (d, *J* = 6.8 Hz, 2H), 2.46-2.36 (m, 1H), 1.03 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.5, 152.6, 152.1, 150.0, 142.4, 141.4, 135.6, 134.5, 131.3, 129.1, 128.9, 128.4, 127.6, 121.9, 121.8, 120.9, 120.7, 48.8, 47.2, 25.5, 22.9; HRMS (ESI): Calcd. for $C_{23}H_{24}N_5O$ [M^++H]: *m/z* 386.1982. Found: 386.1978.

Compound 2o. Yield 0.074 g (60%); white solid; mp = 268-272 °C; IR υ_{max} (KBr): 3085, 2932, 2860, 1605, 1584, 1452, 1310, 1162, 981, 723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.75 (s, 1H), 9.29 (d, *J* = 7.6 Hz, 1H), 8.65 (s, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.95 (s, 1H), 7.65-7.61 (m, 1H), 7.39-7.29 (m, 5H), 7.11 (t, *J* = 7.6 Hz, 1H), 5.45 (s, 2H), 3.44-3.39 (m, 1H), 1.99-1.86 (m, 4H), 1.69-1.60 (m, 2H), 1.47-1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0, 152.6, 152.1, 150.0, 142.8, 141.4, 135.6, 134.5, 130.9, 129.0, 128.3, 127.6, 121.7, 120.9, 120.5, 47.2, 46.6, 29.8, 25.9; HRMS (ESI): Calcd. for $C_{25}H_{26}N_5O$ [M^++H]: *m/z* 412.2138. Found: 412.2141.

Compound 2p. Yield 0.073 g (54%); white solid; mp = 82-86 °C; IR υ_{max} (KBr): 2964, 2926, 1720, 1605, 1529, 1447, 1304, 1238, 1025 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 9.29 (d, *J* = 8.4 Hz, 1H), 8.67 (s, 1H), 7.99 (d, *J* = 8.0 Hz, 1H), 7.95 (s, 1H), 7.65-7.62 (m, 1H), 7.39-7.27 (m, 5H), 7.12-7.08 (m, 1H), 5.45 (s, 2H), 5.13-5.10 (m, 1H), 3.08 (dd, *J* = 15.4 Hz and *J* = 5.2 Hz, 1H), 2.85 (dd, *J* = 15.4 Hz and *J* = 8.4 Hz, 1H), 2.35-2.27 (m, 1H), 2.10-2.00 (m, 2H), 1.69 (s, 3H), 1.62 (s, 3H), 1.49-1.42 (m, 1H), 1.38-1.29 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.7, 152.7, 152.2, 150.1, 142.4, 141.5, 135.7, 134.6, 131.6, 131.3, 129.2, 128.5, 127.7, 124.5, 122.1, 121.9, 121.0, 120.8, 47.3, 37.4, 30.0, 25.8, 25.6, 20.2, 17.8; HRMS (ESI): Calcd. for $C_{28}H_{32}N_5O$ [M^++H]: *m/z* 454.2608. Found: 454.2610.

General procedure for the *ortho*-acylation of 6-anilinopurine derivatives with α–oxocarboxylic acids: Synthesis of compounds 3a-3h

A mixture of 6-anilinopurine (0.3 mmol), $PdCl_2$ (10 mol %), Ag_2O (0.3 mmol), $K_2S_2O_8$ (0.3 mmol) and α–oxocarboxylic acid (0.6 mmol) was taken in a Schlenk tube under N_2 atmosphere. To this, dioxane/AcOH/DMSO (7/2/1, v/v/v, 3 mL) mixture was added and the contents stirred at 110 °C (oil bath temperature) for 24 h. After cooling to rt, the reaction mixture was extracted with EtOAc (3x30 mL) and washed with water (30 mL). The combined organic phase was washed with brine solution (30 mL), dried over anh. Na_2SO_4 and concentrated *in vacuo.* The crude product was purified by column chromatography on silica gel using *n*-hexane-EtOAc (3:2) mixture as the eluent.

Compound 3a. Yield: 0.077 g (64%); white solid; mp = 190-194 °C; IR υ_{max} (KBr): 3299, 3058, 1622, 1573, 1474, 1321, 1249, 1156, 1025, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.76 (s, 1H), 9.14 (d, *J* = 8.8 Hz, 1H), 8.66 (br, 1H), 8.02 (d, *J* = 8.4 Hz, 1H), 7.93 (br, 1H), 7.79 (d, *J* = 7.6 Hz, 2H), 7 69-7.65 (m, 2H), 7.61-7.58 (m, 1H), 7.51-7.48 (m, 2H), 7.40-7.29 (m, 4H), 7.09 (t, *J* = 7.6 Hz, 1H), 5.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.4

152.7, 152.0, 150.1, 141.8, 141.3, 138.9, 135.6, 134.1, 134.0, 132.2, 130.1, 129.1, 128.4, 128.1, 127.7, 123.1, 121.5, 121.2, 120.9, 47.2; HRMS (ESI): Calcd. for $C_{25}H_{20}N_5O$ $[M^+ + H]$: *m/z* 406.1669. Found: 406.1667.

Compound 3b. Yield: 0.072 g (55%); white solid; mp = 202-206 °C; IR υ_{max} (KBr): 3423, 2920, 1615, 1521, 1479, 1323, 1249, 1026, 823, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 10.68 (s, 1H), 8.43 (s, 1H), 8.29 (d, *J* = 7.2 Hz, 1H), 8.15 (s, 1H), 7.72 (dd, *J* = 7.2 Hz and 2.0 Hz, 1H), 7.69 (s, 1H), 7.67 (s, 1H), 7.58-7.55 (m, 1H), 7.46-7.43 (m, 3H), 7.36-7.33 (m, 2H), 7.30-7.27 (m, 3H), 5.41 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 195.7, 151.9, 151.5, 150.3, 143.1, 138.2, 137.5, 137.2, 133.0, 132.8, 130.9, 129.9, 129.2, 128.7, 128.3, 128.1, 128.0, 126.9, 125.5, 122.6, 120.4, 46.8; HRMS (ESI): Calcd. for $C_{25}H_{19}ClN_5O$ $[M^+ + H]$: *m/z* 440.1279. Found: 440.1279.

Compound 3c. Yield 0.09 g (63%); white solid; mp = 232-236 °C; IR υ_{max} (KBr): 3443, 2920, 1602, 1585, 1467, 1338, 1264, 1240, 1098, 1027, 906, 722 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 13.13 (s, 1H), 9.08 (d, *J* = 2.4 Hz, 1H), 8.70 (s, 1H), 7.97 (s, 1H), 7.37-7.30 (m, 6H), 6.90 (s, 2H), 6.46 (dd, *J* ~ 9.0 Hz and ~ 2.6 Hz, 1H), 5.46 (s, 2H), 3.98 (s, 3H), 2.35 (s, 3H), 2.14 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.8, 165.1, 152.6, 152.3, 150.2, 145.5, 141.7, 138.2, 137.6, 136.3, 135.6, 134.1, 129.2, 128.5, 127.7, 122.0, 116.1, 108.1, 104.4, 55.7, 47.3, 21.2, 19.4; HRMS (ESI): Calcd. for $C_{29}H_{28}N_5O_2$ $[M^+ + H]$: *m/z* 478.2244. Found: 478.2240.

Compound 3d. Yield 0.08 g (60%); white solid; mp = 220-224 °C; IR υ_{max} (KBr): 2926, 1748, 1605, 1584, 1452, 1249, 1151, 1019, 915 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.82 (s, 1H), 9.37 (d, *J* = 8.4 Hz, 1H), 8.71 (s, 1H), 8.00 (s, 1H), 7.67-7.63 (m, 1H), 7.44 (d, *J* = 8.4 Hz, 2H), 7 37-7.29 (m, 5H), 6.98-6.92 (m, 2H), 5.47 (s, 2H), 2.36 (s, 3H), 2.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.8, 152.6, 152.2, 150.2, 143.0, 141.6, 138.5, 137.3, 135.6, 135.4, 134.1$_3$, 134.0$_9$, 129.1, 128.4, 128.3, 127.7, 122.1, 121.9, 121.2, 120.4, 47.3, 21.2, 19.5; HRMS (ESI): Calcd. for $C_{28}H_{26}N_5O$ $[M^+ + H]$: *m/z* 448.2138 Found: 448.2134.

Compound 3e. Yield 0.077 g (61%); white solid; mp = 204-208 °C; IR υ_{max} (KBr): 3298, 3052, 1632, 1583, 1501, 1462, 1358, 1254, 1029, 925, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 11.62 (s, 1H), 9.06 (d, *J* = 8.0 Hz, 1H), 8.63 (s, 1H), 7.92 (s, 1H), 7.71-7.62 (m, 4H), 7.36-7.26 (m, 7H), 7.11-7.07 (m, 1H), 5.44 (s, 2H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.9, 152.8, 152.0, 150.0, 143.1, 141.4, 141.3, 136.1, 135.6, 133.7$_4$, 133.6$_9$, 130.5, 130.2, 129.2, 129.1, 128.9, 128.5, 127.7, 123.9, 121.4, 121.0, 47.3, 21.7; LC-MS: *m/z* = 420 $[M+1]^+$; anal. calcd. for $C_{26}H_{21}N_5O$: C, 74.44; H, 5.05; N, 16.70; found: C, 74.53; H, 5.12; N, 16.75.

Compound 3f. Yield 0.084 g (66%); white solid; mp = 222-226 °C; IR υ_{max} (KBr): 3128, 2975, 1616, 1578, 1528, 1495, 1353, 1260, 1150, 1090, 931, 843 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 11.53 (s, 1H), 9.07 (dd, *J* = 8.5 Hz and 2.0 Hz, 1H), 8.64 (s, 1H), 7.92 (s, 1H), 7.84-7.81 (m, 2H), 7.68-7.62 (m, 2H), 7.38-7.28 (m, 5H), 7.18-7.14 (m, 2H), 7.12-7.09 (m, 1H), 5.44 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 197.7, 165.3 (d, $J_{(C-F)}$ = 252.6 Hz), 152.8, 152.0, 150.1, 141.6, 141.4, 135.6, 135.0$_1$, 134.9$_8$, 134.1, 133.5, 132.8$_3$, 132.7$_6$, 129.2, 128.5, 127.7, 123.4, 121.5$_2$, 121.4$_5$, 121.1, 115.6, 115.5, 115.3, 47.3; LC-MS: *m/z* = 424 $[M+1]^+$; anal. calcd. for $C_{25}H_{18}FN_5O$: C, 70.91; H, 4.28; N, 16.54; found: C, 70.82; H, 4.23; N, 16.45.

Compound 3g. Yield 0.084 g (58%); white solid; mp = 234-238 °C; IR υ_{max} (KBr): 3156, 2991, 1676, 1616, 1588, 1495, 1446, 1353, 1265, 1183, 1073, 936, 750 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 11.58 (s, 1H), 9.07 (dd, *J* = 8.5 Hz, 1H), 8.64 (s, 1H), 7.96-7.94 (m, 1H), 7.67-7.61 (m, 6H), 7.39-7.30 (m, 5H), 7.12-7.09 (m, 1H), 5.45 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 198.1, 152.8, 152.0, 150.1, 141.7, 141.5, 137.6, 135.5, 134.3, 133.6, 131.9, 131.7, 131.5, 129.2, 128.5, 127.8, 127.3, 123.2, 121.6, 121.4, 121.2, 47.4; LC-MS: *m/z* = 486 $[M+2]^+$; anal. calcd. for $C_{25}H_{18}BrN_5O$: C, 61.99; H, 3.75; N, 14.46; found: C, 61.85; H, 3.81; N, 14.38.

Compound 3h. Yield 0.067 g (63%); white solid; mp = 140-144 °C; IR υ_{max} (KBr): 3156, 2991, 1660, 1583, 1490, 1451, 1380, 1298, 1205, 1134, 1079, 953 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 12.68 (s, 1H), 9.29 (d, *J* = 8.0 Hz, 1H), 8.65 (s, 1H), 8.01 (dd, *J* = 8.0 Hz and 1.6 Hz, 1H), 7.94 (s, 1H), 7.65-7.60 (m, 1H), 7.3[illegible] 7.29 (m, 5H), 7.11-7.07 (m, 1H), 5.44 (s, 2H), 3.14 (qrt, *J* = 7.2 Hz, s), 1.29 (t, *J* = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.0, 152.7, 152.2, 150.1, 142.4, 141.5, 135.7, 134.6, 131.0, 129.1, 128.5, 127.7, 121.8, 121.5, 121.0, 120.8, 47.3, 33.2, 8.7; LC-MS: *m/z* = 358 $[M+1]^+$; anal. calcd. for $C_{21}H_{19}N_5O$: C, 70.57; H, 5.36; N, 19.59; found: C, 70.45; H, 5.41; N, 19.48.

X-ray Data

X-ray data for compounds **2m** was collected using Mo K_α (λ = 0.71073 Å) radiation. The structure was solved and refined by standard methods.[17]

Compound 2m. $C_{24}H_{25}N_5O$, *M* = 399.49, triclinic, Space group P_1, *a* = 8.249(3), *b* = 9.685(3), *c* = 14.060(5) Å, α = 94.073(6), β = 91.653(6), γ= 107.489(6), *V* = 1067.2(6) $Å^3$, *Z* = 2, μ = 0.079 mm^{-1}, data/restraints/parameters: 3797/0/276, R indices ($I > 2\sigma(I)$): R1 = 0.0443, *w*R2 (all data) = 0.1258. CCDC No. 1423000.

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