Pd-catalysed *ortho*-C-H acylation/cross coupling of 2-arylbenzo[d]thiazoles with aldehydes using *tert*-butyl hydroperoxide as oxidant

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An efficient palladium-catalysed protocol for direct C–H bond acylation by cross coupling of 2-arylbenzo[d]thiazoles and aldehydes using *tert*-butyl hydroperoxide as the oxidant is reported. The process provides a useful method for the synthesis of aromatic ketones directly from aldehydes. In addition, the reaction can tolerate various functional groups in good yield with high regioselectivity.

Keywords: 2-arylbenzo[d]thiazole, C–H activation, acylation, cross-coupling

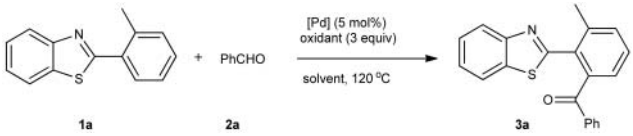
Diaryl and aryl alkyl ketones are important building blocks in the synthesis of natural products, pharmaceutical, functional materials and agrochemicals.[1–5] Friedel–Crafts acylation reactions are usually their classical method of synthesis.[6–8] The narrow scope of substrate, poor functional group compatibility, the requirement of a stoichiometric amount of Lewis acid and the untunable regioselectivity limit their applications. Thus it is highly desirable to develop efficient methods for access to elaborated ketones.

Recently, much progress has been made in transition-metal-catalysed direct conversion of aromatic C–H bonds into carbon–carbon and carbon–heteroatom bonds.[9–15] The transition-metal-catalysed *ortho* C–H acylation of arenes with aldehydes represents another direct and promising approach to the access to ketones.[16–25] For example, in 2009, Cheng and co-workers[16] pioneered the development of Pd-catalysed direct *ortho*-C–H acylation of 2-arylpyridines with aldehydes to give aromatic ketones using air as the terminal oxidant. In 2010, Li and co-workers[17] reported the same acylation reaction using *tert*-butyl hydroperoxide (TBHP) as the oxidant. In 2010, Yu and co-workers[18] developed the direct C–H bond acylation by cross coupling aromatic oximes and aldehydes in the presence of TBHP. In 2010, the groups of Yu,[19] Wang,[20] and Kwong[21] also developed the Pd-catalysed direct *ortho*-C–H bond activation of anilides by oxidative cross-coupling with aldehydes using TBHP as oxidant. During the course of our investigation, Wu and co-workers developed an efficient Pd-catalysed protocol for benzoxazole-directed *ortho*-acylation with aldehydes using TBHP as oxidant and PPh_3 as ligand in chlorobenzene.[22] In addition, there are also some reports using toluene derivatives[26,27] as useful carbonyl sources in the presence of a transition-metal catalyst and oxidant. Inspired by the recent studies of direct *ortho*-C–H bond activation of arenes and our interests in C–H functionalisation of 2-arylbenzothiazoles,[28,29] we have explored the possibility of *ortho*-acylation of 2-aryl-benzo[d]thiazoles with aldehydes through direct C–H bond activation. We have achieved this transformation. We now describe the Pd-catalysed *ortho*-acylation of 2-aryl-benzo[d]thiazoles with aldehydes using TBHP as oxidant under ligand-free conditions.

Based on previous work, we began by examining the reaction of 2-(*o*-tolyl)benzo[d]thiazole (**1a**, 0.2 mmol) and benzaldehyde (**2a**, 0.6 mmol) using TBHP (0.6 mmol) as oxidant, in the presence of $Pd(OAc)_2$ (5 mmol%) in toluene (2 mL) at 120 °C for 2 h. The expected acylated product was obtained in 65% yield. We also tested other solvents, such as xylene, dioxane, AcOH, DMF, and PhCl (Table 1, entries 2–10). The results revealed that AcOH (70% yield) and PhCl (67% yield) were the suitable solvents, and only inferior results were observed in other solvents. Subsequently, various Pd(II) salts or Pd(0) complexes were tested for this direct acylation in the presence of TBHP in AcOH. Poor yields were observed when other Pd(II) salts (such as $PdCl_2$, $Pd(PPh_3)_2Cl_2$, $Pd(CH_3CN)_2Cl_2$, $Pd(PhCN)_2Cl_2$) were used as catalysts; only $Pd(dba)_2$ (62%) exhibited significant activity (Table 1, entries 11–15). The desired product was obtained in 23% yield when oxygen was used as the sole oxidant (Table 1, entry 16). However, the use of other oxidants, such as oxone, benzoquinone (BQ) and $K_2S_2O_8$, were relatively ineffective for the direct acylation reaction (Table 1, entries 17–19). Further optimisation demonstrated that the yields could be reduced when the amount of **2a** was cut down (Table 1, entries 20 and 21). However, when the amount of TBHP was reduced to 2.0 equiv, the coupling yield (74%) could be further improved (Table 1, entry 22).

Under the optimised reaction conditions [$Pd(OAc)_2$ (5 mol%), ratio of **1/2** = 1/3, TBHP (2.0 equiv.), 120 °C], the reactivity of different 2-arylbenzo[d]thiazoles was investigated (Table 2).

Table 1 Optimisation of the reaction conditions[a]



Entry	[Pd]	Oxidant	Solvent	Yield/%[b]
1	$Pd(OAc)_2$	TBHP	Toluene	65
2	$Pd(OAc)_2$	TBHP	Xylene	46
3	$Pd(OAc)_2$	TBHP	Dioxane	Trace
4	$Pd(OAc)_2$	TBHP	DMAc	Trace
5	$Pd(OAc)_2$	TBHP	AcOH	70
6	$Pd(OAc)_2$	TBHP	DMF	Trace
7	$Pd(OAc)_2$	TBHP	PhCl	67
8	$Pd(OAc)_2$	TBHP	HCOOH	16
9	$Pd(OAc)_2$	TBHP	Ac2O	30
10	$Pd(OAc)_2$	TBHP	TfOH	–
11	$PdCl_2$	TBHP	AcOH	16
12	$Pd(PPh)_3Cl_2$	TBHP	AcOH	16
13	$Pd(CH_3CN)_2Cl_2$	TBHP	AcOH	10
14	$Pd(PhCN)_2Cl_2$	TBHP	AcOH	18
15	$Pd(dba)_2$	TBHP	AcOH	62
16	$Pd(OAc)_2$	O_2	AcOH	23
17	$Pd(OAc)_2$	Oxone	AcOH	–
18	$Pd(OAc)_2$	BQ	AcOH	Trace
19	$Pd(OAc)_2$	$K_2S_2O_8$	AcOH	–
20[c]	$Pd(OAc)_2$	TBHP	AcOH	60
21[d]	$Pd(OAc)_2$	TBHP	AcOH	55
22[e]	$Pd(OAc)_2$	TBHP	AcOH	74

[a]Conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), [Pd] catalyst (5 mol %), oxidant (3.0 equiv.), 120 °C, 2 h. [b]Isolated yield. [c]2.5 equiv. of **2a** were used. [d]2.0 equiv. of **2a** were used. [e]2.0 equiv. of TBHP were used.

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The coupling of 2-arylbenzo[d]thiazoles **1b–i** with electron-withdrawing groups (Cl, F) at the *ortho*-position of the 2-phenyl ring smoothly underwent the acylation reaction to afford the corresponding products **3b–i** in good yields. For example, the reaction of 2-(2-chlorophenyl)benzo[d]thiazole **1b** under the standard conditions gave **3b** in 87% yield. A relatively lower yield was obtained when 2-(2-fluorophenyl) benzo[d]thiazole **1f** was used, and the desired product **3f** was achieved in 67% yield. However, a moderate electron-donating group (CH_3) at the *ortho*-position of 2-arylbenzo[d]thiazoles gave a lower yield of oxidative cross-coupling product **3j**. 6-Chloro-2-(o-tolyl)benzo[d]thiazole **1l** and 6-fluoro-2-(o-tolyl)benzo[d]thiazole **1m** (with electron-withdrawing group Cl and F, respectively, on the phenyl ring of the benzo[d]thiazole) were found to be good substrates for this transformation, affording the corresponding products **3l** and **3m** in good yields. Then, the regioselective *ortho* acylation of *meta*-substituted 2-arylbenzo[d]thiazoles was also investigated. The acylation reaction of 2-arylbenzo[d]thiazoles **1n–q** occurred exclusively at the less sterically hindered position, and gave moderate to good yields with high regioselectivity.

To examine the substrate scope and limitations, a broad range of aldehydes was screened in coupling with 6-chloro-2-(2-chlorophenyl)benzo[d]thiazole **1d** under optimal reaction conditions (Table 3). In general, electron-donating (Me, OMe) and -withdrawing (F, Cl, Br and CN) groups are tolerated. In contrast, electron-rich aldehydes were less reactive under the standard reaction conditions. The reaction yield decreased dramatically when the aliphatic aldehyde butyraldehyde **2h** was used as the substrate, and only a 19% yield of product **3y** was achieved.

Based on the previous reports, the proposed reaction pathway of the palladium-catalysed *ortho*-acylation of 2-arylbenzo[d]thiazole with aldehyde through direct C–H bond activation is suggested in Scheme 1. First, Pd-catalysed sp^2 C–H bond activation of 2-arylbenzo[d]thiazole occurs to form a five-membered palladacycle intermediate **A**. Second, the palladacycle **A** reacted with the acyl radical which was produced from aldehyde in the presence of TBHP to form either a reactive Pd^{III} or Pd^{IV} intermediate **B**. Finally, intermediate **B** underwent reductive elimination to form the coupling product **3** and regenerate Pd^{II} for the next catalytic cycle.

In summary, an efficient approach for the direct acylation of the aromatic sp^2 C–H bond has been developed. The process provided a very useful method for the synthesis of aromatic ketones directly from aldehydes. In addition, the reaction can tolerate various functional groups in good yields with high regioselectivity.

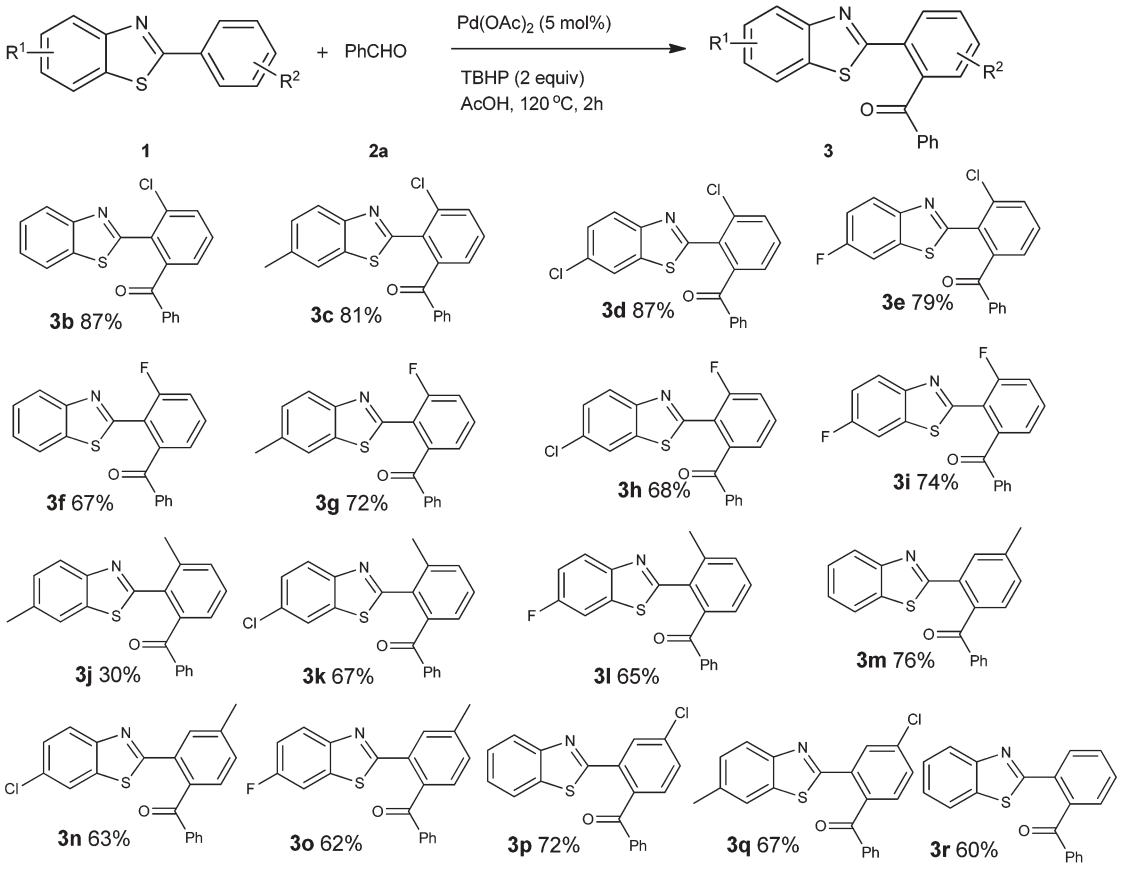
Experimental

C–H bond activation/acylation of 2-arylbenzothiazoles **1** *with aldehydes* **2**; *general procedure*

In a 20-mL reaction tube, a mixture of 2-arylbenzothiazole **1** (0.3 mmol, 1.0 equiv.), aldehyde **2** (0.9 mmol, 3.0 equiv.), TBHP (2.0 equiv, 65% aqueous) and $Pd(OAc)_2$ (3.5 mg, 5 mol %) in AcOH (2.0 mL) was stirred at 120 °C for 2 h. After completion of the reaction, as indicated by TLC, the mixture was cooled to room temperature, the resulting mixture was extracted with ethyl acetate (3 × 20 mL). The organic layer was evaporated under vacuum, and then the residue was purified by flash column chromatography on silica gel to provide the corresponding pure coupling product **3**.

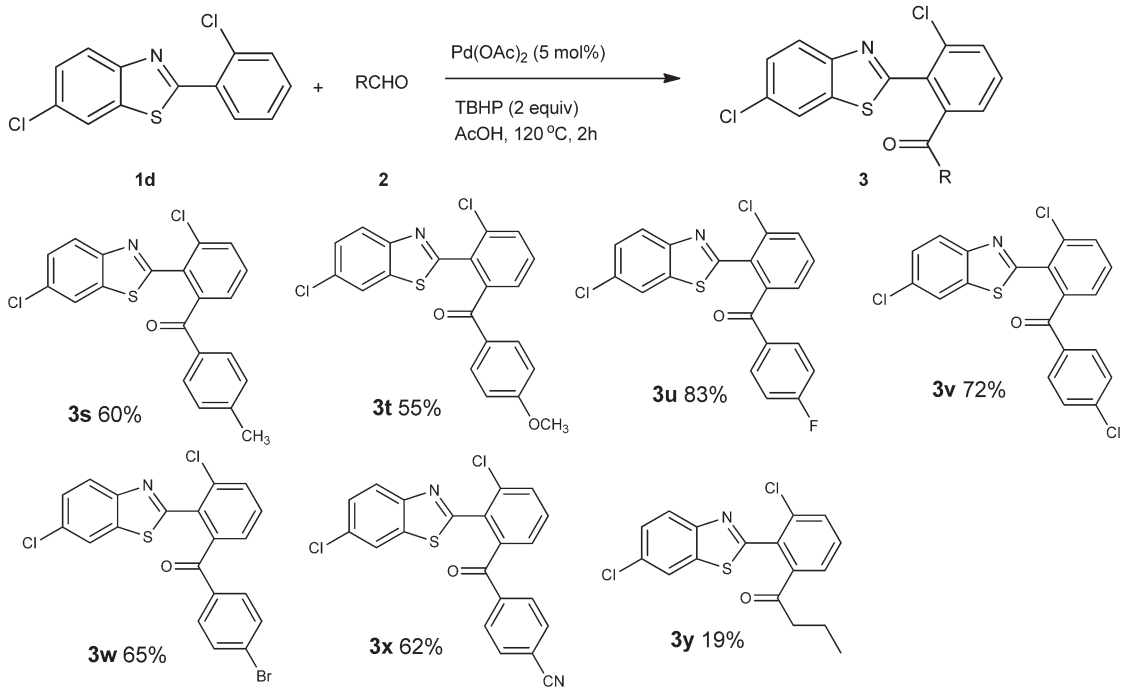
(*2-(Benzo[d]thiazol-2-yl)-3-methylphenyl)(phenyl)methanone* (**3a**): Yellow solid;74% yield, m.p. 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.27 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.37–7.42 (m, 3H), 7.46–7.48 (m, 2H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.93 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 121.3, 123.4, 125.2, 126.0, 126.6, 128.0, 129.3, 129.9,

Table 2 Reaction of benzaldehyde with 2-arylbenzo[d]thiazole[a]

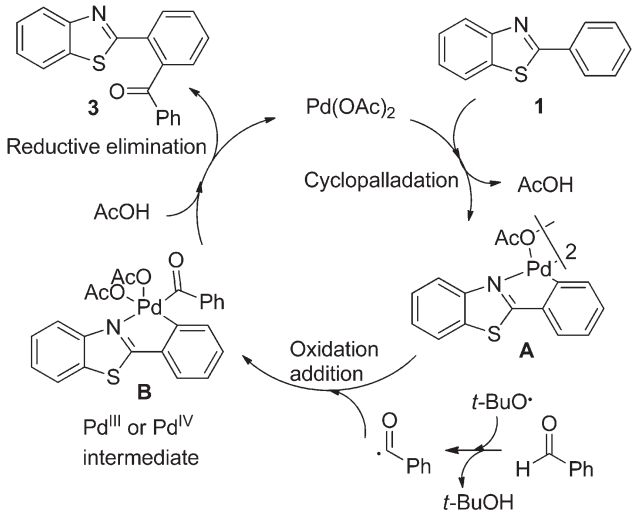


[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.9 mmol), $Pd(OAc)_2$ (5 mol%), TBHP (2 equiv.), 120 °C, 2 h in air. [b] Isolated yields based on **1**.

Table 3 Scope of aldehydes[a]



[a] Reaction conditions: **1d** (0.3 mmol), **2** (0.9 mmol), $Pd(OAc)_2$ (5 mol%), TBHP (2 equiv.), 120 °C, 2 h in air. [b] Isolated yields based on **1d**.



Scheme 1 Proposed mechanism for the Pd-catalysed *ortho*-acylation reaction.

132.5, 132.7, 132.8, 136.2, 137.4, 138.2, 140.7, 152.9, 165.2, 197.3; IR (KBr) ν/cm^{-1}: 2923, 1735, 1458, 1087, 775; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{16}NOS$: 330.0953; found: 330.0950.

(2-(Benzo[d]thiazol-2-yl)-3-chlorophenyl)(phenyl)methanone (**3b**): Yellow solid; 87% yield; m.p. 178–179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.6 Hz, 2H), 7.31–7.41 (m, 3H), 7.49–7.56 (m, 2H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.3, 123.6, 125.6, 126.1, 127.5, 128.1, 129.4, 130.6, 131.8, 132.0, 132.9, 134.2, 136.3, 137.0, 142.9, 152.2, 162.1, 195.8; IR (KBr) ν/cm^{-1}: 1669, 1317, 758; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{13}ClNOS$: 350.0406, found: 350.0400.

(3-Chloro-2-(6-methylbenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3c**): Yellow solid; 81% yield; m.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.19 (d, *J* = 8.4 Hz, 1H), 7.25 (t, *J* = 7.2 Hz, 2H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.47–7.52 (m, 2H), 7.57 (s, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 120.9, 123.0, 127.4, 127.7, 128.1, 129.4, 130.5, 131.8, 131.9, 132.8, 134.1, 135.8, 136.5, 137.0, 142.9, 150.4, 160.9, 195.8; IR (KBr) ν/cm^{-1}: 2922, 1670, 1276, 707; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}ClNOS$: 364.0563, found: 363.0568.

(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3d**): Yellow solid; 87% yield; m.p. 147–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.76 (t, *J* = 4.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 120.9, 124.3, 127.0, 127.6, 128.2, 129.4, 130.9, 131.3, 131.6, 132.1, 133.0, 134.1, 136.9, 137.5, 142.9, 150.7, 162.7, 195.6; IR (KBr) ν/cm^{-1}: 1672, 1303, 826; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{12}Cl_2NOS$: 384.0017, found: 384.0021.

(3-Chloro-2-(6-fluorobenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3e**): Yellow solid; 79% yield; m.p. 152–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, *J* = 8.8 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.46–7.51 (m, 2H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 1H), 7.81 (dd, *J* = 4.8, 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 107.4 (d, $^2J_{C\text{-}F}$ = 27.0 Hz), 114.9 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 124.6 (d, $^3J_{C\text{-}F}$ = 10.0 Hz), 127.6, 128.2, 129.4, 130.8, 131.4, 132.0, 132.9, 134.1, 136.9, 137.3 (d, $^3J_{C\text{-}F}$ = 11.0 Hz), 142.9, 148.8, 160.6 (d, $^1J_{C\text{-}F}$ = 245.0 Hz), 195.7; IR (KBr) ν/cm^{-1}: 1667, 1321, 750; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{12}ClFNOS$: 368.0312, found: 368.0310.

(2-(Benzo[d]thiazol-2-yl)-3-fluorophenyl)(phenyl)methanone (**3f**): Yellow solid; 67% yield; m.p. 108–109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.40 (m, 8H), 7.53–7.59 (m, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.87 (dd, *J* = 4.0, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.6 (d, $^2J_{C\text{-}F}$ = 23.0 Hz), 120.4 (d, $^3J_{C\text{-}F}$ = 13.0 Hz), 121.3, 123.4, 124.7, 125.5, 126.1, 128.2, 129.0, 131.7 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 132.6, 135.8, 137.6, 142.4, 152.0, 158.3, 160.1 (d, $^1J_{C\text{-}F}$ = 252.0 Hz), 196.0; IR (KBr) ν/cm^{-1}: 1668, 1299, 1273, 757; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{13}FNOS$: 334.0702, found: 334.0700.

(3-Fluoro-2-(6-methylbenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3g**): Yellow solid; 72% yield; m.p. 131–132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 6.8 Hz, 2H), 7.37 (t, *J* = 9.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.57 (s, 1H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 117.6 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 120.5 (d, $^2J_{C\text{-}F}$ = 14.0 Hz), 120.9, 122.9, 124.7, 127.8, 128.2,

128.9, 131.5 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 132.6, 135.8, 136.0, 137.6, 142.3, 150.2, 157.1, 160.0 (d, $^1J_{C\text{-}F}$ = 253.0 Hz), 196.1; IR (KBr) ν/cm^{-1}: 2923, 1671, 1299, 745; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}FNOS$: 348.0858, found: 348.0859.

(2-(6-Chlorobenzo[d]thiazol-2-yl)-3-fluorophenyl)(phenyl)methanone (**3h**): Yellow solid; 68% yield; m.p. 170–171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.42 (m, 6H), 7.57–7.62 (m, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 7.6 Hz, 2H), 7.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 117.7 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 120.0 (d, $^2J_{C\text{-}F}$ = 13.0 Hz), 120.8, 124.1, 124.8, 127.0, 128.3, 128.9, 131.5, 132.0 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 132.7, 136.9 (d, $^3J_{C\text{-}F}$ = 6.0 Hz), 137.5, 142.3, 150.5, 158.8, 160.1 (d, $^1J_{C\text{-}F}$ = 253.0 Hz), 195.8; IR (KBr) ν/cm^{-1}: 2956, 1671, 1309, 722; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{12}ClFNOS$: 368.0312, found: 368.0315.

(3-Fluoro-2-(6-fluorobenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3i**): Colourless solid; 74% yield; m.p. 124–125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (t, *J* = 8.8 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.34–7.41 (m, 3H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.56–7.61 (m, 1H), 7.67–7.73 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 107.3 (d, $^2J_{C\text{-}F}$ = 27.0 Hz), 114.9 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 117.6 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 120.1 (d, $^3J_{C\text{-}F}$ = 13.0 Hz), 124.4 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 124.8, 128.3, 128.9, 131.8 (d, $^3J_{C\text{-}F}$ = 9.0 Hz), 132.7, 136.9, 137.5, 142.3, 148.6, 158.1, 160.0 (d, $^1J_{C\text{-}F}$ = 252.0 Hz), 160.6 (d, $^1J_{C\text{-}F}$ = 245.0 Hz), 195.9; IR (KBr) ν/cm^{-1}: 2919, 1665, 1279, 7788; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{12}F_2NOS$: 352.0608, found: 352.0612.

(3-Methyl-2-(6-methylbenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3j**): Brown solid; 30% yield; m.p. 70–71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 2.45 (s, 3H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.38–7.44 (m, 2H), 7.46–7.49 (m, 2H), 7.57 (s, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 21.5, 121.0, 122.8, 126.5, 127.6, 128.0, 129.2, 129.9, 132.6, 132.7, 132.8, 135.3, 136.4, 137.4, 138.2, 140.7, 151.1, 164.0, 197.4; IR (KBr) ν/cm^{-1}: 2919, 1668, 1275, 774; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{22}H_{18}NOS$: 344.1109, found: 344.1111.

(2-(6-Chlorobenzo[d]thiazol-2-yl)-3-methylphenyl)(phenyl)methanone (**3k**): White solid (67% yield; m.p. 122–123 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.37 (d, *J* = 8.8 Hz,1H), 7.39–7.44 (m, 2H), 7.49 (d, *J* = 3.6 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.76 (s, 1H), 7.83 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 120.9, 124.1, 126.8, 126.9, 128.1, 129.5, 129.9, 131.2, 132.1, 132.8, 132.9, 137.3, 137.4, 138.2, 140.6, 151.4, 165.8, 197.2; IR (KBr) ν/cm^{-1}: 2920, 1668, 1279, 719; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}ClNOS$: 364.0563, found: 364.0568.

(2-(6-Fluorobenzo[d]thiazol-2-yl)-3-methylphenyl)(phenyl)methanone (**3l**): Yellow solid; 65% yield; m.p. 132–133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 7.38–7.48 (m, 5H), 6.68 (d, *J* = 7.6 Hz, 2H), 7.85 (dd, *J* = 4.8, 8.4 Hz,1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 107.5 (d, $^2J_{C\text{-}F}$ = 26.0 Hz), 114.7 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 124.3 (d, $^3J_{C\text{-}F}$ = 10.0 Hz), 126.7, 128.1, 129.4, 129.9, 132.2, 132.8, 132.9, 137.2 (d, $^3J_{C\text{-}F}$ = 11.0 Hz), 137.4, 138.2, 140.6, 149.5, 160.4 (d, $^1J_{C\text{-}F}$ = 245.0 Hz), 165.0, 197.2; IR (KBr) ν/cm^{-1}: 2962, 1668, 1282, 849; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}FNOS$: 348.0858, found: 348.0862.

(2-(Benzo[d]thiazol-2-yl)-4-methylphenyl)(phenyl)methanone (**3m**): White solid; 76% yield; m.p. 129–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 7.25–7.30 (m, 3H), 7.32–7.39 (m, 2H), 7.41 (s, 7.41), 7.45 (d, *J* = 7.6 Hz, 1H), 7.73–7.81 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 121.4, 123.4, 125.2, 126.1, 128.2, 129.1, 129.3, 130.3, 131.0, 132.3, 132.6, 135.4, 137.0, 138.0, 140.6, 153.5, 165.6, 197.7; IR (KBr) ν/cm^{-1}: 3022, 1663, 1281, 732; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{16}NOS$: 330.0953, found: 330.0949.

(2-(6-Chlorobenzo[d]thiazol-2-yl)-4-methylphenyl)(phenyl)methanone (**3n**): Yellow solid; 63%), m.p. 125–126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 3H), 7.25–7.32 (m, 3H), 7.35–7.46 (m, 3H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.69 (s, 1H), 7.71–7.76 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 121.0, 124.1, 127.0, 128.2, 129.2, 130.2, 131.1, 131.2 131.9, 132.7, 136.5, 137.0, 137.9, 140.8, 152.0, 166.1, 197.5; IR (KBr) ν/cm^{-1}: 1683, 1292, 814; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}ClNOS$: 364.0563, found: 364.0567.

(2-(6-Fluorobenzo[d]thiazol-2-yl)-4-methylphenyl)(phenyl)methanone (**3o**): Yellow solid; 62% yield; m.p. 138–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.51 (s, 3H), 7.08 (t, *J* = 8.8 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 2H), 7.35–7.46 (m, 4H), 7.68 (s, 1H), 7.70–7.75 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 107.6 (d, $^2J_{C\text{-}F}$ = 27.0 Hz), 114.8 (d, $^2J_{C\text{-}F}$ = 24.0 Hz), 124.3 (d, $^3J_{C\text{-}F}$ = 10.0 Hz), 128.2, 129.2, 129.3, 130.2, 131.0, 132.0, 132.6, 136.3 (d, $^3J_{C\text{-}F}$ = 12.0 Hz), 136.9, 137.9, 140.7, 150.1, 160.5 (d, $^1J_{C\text{-}F}$ = 244.0 Hz), 165.4, 197.6; IR (KBr) ν/cm^{-1}: 2926, 1663, 1280, 929, 733; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}FNOS$: 348.0858, found: 348.0861.

(2-(Benzo[d]thiazol-2-yl)-4-chlorophenyl)(phenyl)methanone (**3p**): White solid (72% yield; m.p. 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25–7.34 (m, 3H), 7.35–7.41 (m, 2H), 7.48 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 7.6 Hz, 2H), 7.79 (t, *J* = 6.8 Hz, 2H), 7.93 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.5, 123.6, 125.7, 126.4, 128.3, 129.2, 129.5, 130.2, 130.3, 132.9, 133.9, 135.4, 136.2, 137.5, 138.0, 153.3, 163.7, 196.5; IR (KBr) ν/cm^{-1}: 2960, 1665, 1277, 778; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{13}ClNOS$: 350.0406, found: 350.0411.

(4-Chloro-2-(6-methylbenzo[d]thiazol-2-yl)phenyl)(phenyl)methanone (**3q**): Yellow solid; 67% yield; m.p. 87–88 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.56 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.73 (d, *J* = 7.6 Hz, 2H), 7.90 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 121.2, 123.1, 128.0, 128.3, 129.2, 129.3, 130.1, 130.3, 132.9, 134.0, 135.6, 136.0, 136.2, 137.5, 137.9, 151.5, 162.5, 196.6; IR (KBr) ν/cm^{-1}: 2961, 1666, 1273, 738; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{15}ClNOS$: 364.0563, found: 364.0559.

(2-(Benzo[d]thiazol-2-yl)-4-methylphenyl)(phenyl)methanone (**3r**): Yellow solid; 76% yield; m.p. 109–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, *J* = 7.6 Hz, 3H), 7.34–7.38 (m, 2H), 7.54 (d, *J* = 6.8 Hz, 1H), 7.60–7.64 (m, 2H), 7.77 (t, *J* = 7.6 Hz, 4H), 7.93 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.4, 123.4, 125.3, 126.2, 128.2, 128.9, 129.3, 129.6, 130.2, 130.3, 132.1, 132.7, 135.3, 137.8, 139.7, 153.5, 165.3, 197.7; IR (KBr) ν/cm^{-1}: 2924, 1666, 1256, 799; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{14}NOS$: 316.0796, found: 316.0791.

(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)(p-tolyl)-methanone (**3s**): Yellow solid; 60% yield; m.p. 115–116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.31 (s, 3H), 7.10 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.77 (s, 1H), 7.79 (d, *J* = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 120.9, 124.4, 126.9, 127.4, 129.0 129.8, 130.7, 131.3, 131.5, 131.8, 134.2, 134.3, 137.5, 143.1, 144.1, 150.8, 162.8, 195.2; IR (KBr) ν/cm^{-1}: 2922, 1664, 1276, 752; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{14}Cl_2NOS$: 398.0173, found: 398.0168.

(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)(4-methoxyphenyl)methanone (**3t**): Yellow oil; 55% yield;; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (s, 3H), 6.79 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.4Hz, 1H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.52 (t, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 3H), 7.79 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.5, 113.6, 120.9, 124.3, 126.9, 127.1, 129.7, 130.7, 131.1, 131.5, 131.6, 132.1, 134.3, 137.5, 143.1, 150.9, 162.9, 163.6, 194.1; IR (KBr) ν/cm^{-1}: 2938, 1659, 1256, 765; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{14}Cl_2NO_2S$: 414.0122, found: 414.0116.

(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)(4-fluorophenyl)methanone (**3u**): White solid; 83% yield; m.p. 116–117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 (t, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.8 Hz, 1H), 7.47 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.65–7.71 (m, 3H), 7.76 (t, *J* = 8.8 Hz, 1H), 7.79 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.5 (d, $^2J_{C\text{-}F}$ = 22.0 Hz), 120.9, 124.2, 127.2 (d, $^2J_{C\text{-}F}$ = 24.0 Hz), 130.9, 131.1, 131.7, 131.9 (d, $^3J_{C\text{-}F}$ = 10.0 Hz), 132.1, 133.4, 134.1, 137.4, 142.6, 150.6, 162.5, 165.5 (d, $^1J_{C\text{-}F}$ = 254.0 Hz), 194.1; IR (KBr) ν/cm^{-1}: 3064, 1670, 1597, 756; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{11}Cl_2FNO_2S$: 401.9922, found: 401.9916.

(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)(4-chlorophenyl)methanone (**3v**): Yellow solid; 72% yield; m.p. 136–137 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.80 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.0, 124.2, 127.1, 127.4, 128.6, 130.7, 130.9, 131.2, 131.8, 132.2, 134.1, 135.3, 137.4, 139.4, 142.5, 150.6, 162.4, 194.4; IR (KBr) ν/cm^{-1}: 3086, 1667, 1275, 809; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{11}Cl_3NO_2S$: 417.9627, found: 417.9618.

(4-Bromophenyl)(3-chloro-2-(6-chlorobenzo[d]thiazol-2-yl)-phenyl)methanone (**3w**): Yellow solid; 65% yield; m.p. 133–134 °C;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.46 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.52 (d, *J* = 8.8Hz, 2H), 7.55 (t, *J* = 8.0 Hz, 1H), 7.70 (dd, *J* = 1.2, 8.0 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H),7.80 (d, *J* = 1.6 Hz,1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 121.0, 124.3, 127.1, 127.4, 128.2, 130.8, 130.9, 131.2, 131.6, 131.8, 132.3, 134.1, 135.7, 137.4, 142.4, 150.5, 162.4, 194.6; IR (KBr) ν/cm^{-1}: 3084, 1671, 781; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{11}BrCl_2NOS$: 461.9122, found: 461.9118.

4-(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)benzoyl)benzonitrile (**3x**): Yellow solid; 62% yield; m.p. 142–143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.8 Hz, 1H), 7.48–7.55 (m, 3H), 7.59 (t, *J* = 8.0 Hz, 1H), 7.65–7.79 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.7, 117.8, 121.0, 124.0, 127.3, 127.7, 128.8, 129.1, 130.9, 131.2, 132.0, 132.8, 133.9, 137.3, 140.4, 141.9, 150.1, 162.0, 167.8, 194.1; IR (KBr) ν/cm^{-1}: 3084, 1671, 781; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{11}Cl_2N_2OS$: 408.9969, found: 408.9976.

1-(3-Chloro-2-(6-chlorobenzo[d]thiazol-2-yl)phenyl)butan-1-one (**3y**): Brown oil (19% yield;; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.6 Hz, 3H), 1.56–1.61 (m, 2H), 2.60 (t, *J* = 7.2 Hz, 2H), 7.48 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.93 (d, *J* = 2.0 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 17.6, 43.9, 121.2, 124.4, 126.3, 127.2, 130.6, 131.1, 131.7, 132.3, 134.8, 137.7, 143.5, 151.1, 157.4, 203.0; IR (KBr) ν/cm^{-1}: 3064, 2930, 1696, 764; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{17}H_{14}Cl_2NOS$: 350.0173, found: 350.0169.

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