Mechanistic development of a mild palladium-catalyzed C-S/C-H cross-coupling of thioesters with azoles

Authors and affiliations

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1. Utilized chemicals

The following chemicals were purchased from commercial suppliers and used without further purification:

Supplementary Table 1: Overview of chemicals acquired from commercial suppliers.

Compound (purity, if provided by supplier)	Supplier	Supplier product nr.
1,3,5-Tri-*tert*-butylbenzene (> 98%)	TCI Europe	T1633
Tetradecane [standard material for GC] (> 99.5%)	TCI Europe	S0286
Pd(COD)DQ (> 95%)	Merck	938718
Pd_2dba_3	Merck	683345
$Pd(OAc)_2$ (> 99.9%)	Merck	520764
$[(cinnamyl)PdCl]_2$ (> 97%)	Merck	720526
n-butyl acetate (>99%, extra dry)	Thermo Fisher	429231000
N,N-dimethyl acetamide (99.5%, extra dry)	Fisher Scientific	10023743
Acetonitrile (> 99.9%, extra dry)	Fisher Scientific	10193051
1,4-Dioxane (> 99.5%, extra dry)	Thermo Fisher	364341000
2-MeTHF (> 99%, extra dry)	Thermo Fisher	396621000
Cyclopentyl methyl ether (> 99.5%, extra dry)	Thermo Fisher	397251000
Toluene (> 99.85%, extra dry)	Fischer Scientific	10354113
Methanol d4 (> 99.8%)	Merck	151947
Chloroform d (> 99.8%)	Merck	434876
Potassium carbonate (> 98%, - 325 mesh)	Merck	347825
Potassium phosphate tribasic (> 97%, Redi-Dri)	Merck	RDD019
Potassium phosphate dibasic (> 98%, Redi-Dri)	Merck	795496
Potassium hydrogen carbonate (> 99.7%)	Thermo Fisher	446301000
Lithium carbonate (> 99%)	Merck	62470
Sodium carbonate (> 99.5%)	VWR Chemicals	27767.295
Cesium carbonate (> 99.9%)	Merck	202126
Copper(I) bromide (> 98%)	TCI Europe	C2161
Copper(I) chloride (> 99.995%)	Merck	229628
Copper(I) bromide-dimethyl sulfide complex (> 99%)	Thermo Fisher	213180100
Copper(I) iodide (> 98%)	TCI Europe	C2163
Copper(I) 2-thiophenecarboxylate	TCI Europe	C2312
Copper(II) bromide (> 99%)	Merck	221775
Copper(II) trifluoromethanesulfonate	Merck	283673
Zinc bromide (> 98%)	TCI Europe	Z0013
Iron(II) bromide (> 98%)	Thermo Fisher	388720100
Silver(I) acetate (> 99%)	Strem Chemicals	93-4701
Triethyl phosphite (> 98%)	Merck	T61204
Triisopropyl phosphite (> 96%)	Thermo Fisher	372381000
Triphenyl phosphite (> 97%)	TCI Europe	T0510
Triphenylphosphine (> 99%)	Merck	T84409
Tri(2-furyl)phosphine (> 98%)	TCI Europe	T1643
1,1'-Bis(diphenylphosphino)ferrocene (> 96%)	TCI Europe	B2027
JohnPhos (> 97%)	Merck	638439
CyJohnPhos (> 97%)	Merck	638099
Xantphos (> 97%)	Merck	526460
Tris(2-methoxyphenyl)phosphine (> 97%)	TCI Europe	T3005
Tris(4-methoxyphenyl)phosphine (> 97%)	Ambeed	A354955
S-butyl thiobenzoate (> 97%)	TCI Europe	B1009
S-methyl thiobutyrate (> 98%)	TCI Europe	M1818
S-methyl-2-methyl propanethioate	ABCR	AB589418
S-propyl thioacetate (> 98%)	TCI Europe	P1716
S-methyl furan-2-carbothioate (> 95%)	BLDPharm	BD138381

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Supplementary Table 1: continued

Compound (purity, if provided by supplier)	Supplier	Supplier product nr.
Benzothiazole (> 96%)	TCI Europe	B0092
Benzoxazole (> 98%)	Merck	B11702
1-methylbenzimidazole (> 98%)	TCI Europe	M2173
1-methylimidazole (> 99%)	Fisher Scientific	11404284
1-phenylimidazole (> 98%)	TCI Europe	P2030
Imidazo[1,2-a]Pyridine (> 99%)	Thermo Fisher	439940050
Thiazole (> 99%)	Thermo Fisher	166130010
Oxazole (> 98%)	TCI Europe	00287
1-(4-Methylthiazol-5-yl)ethenone (> 95%)	BLDPharm	BD989911
6-bromo-1,3-benzothiazole (> 98%)	TCI Europe	B6336
5-bromo-1-methyl benzimidazole (> 95%)	BLDPharm	BD102559
4-Chlorotoluene (> 98%)	Alfa Aesar	11381657
4-bromotoluene (> 98%)	Alfa Aesar	11324769
4-iodotoluene (> 99%)	TCI Europe	I0218-25G
4,4,5,5-Tetramethyl-2-(p-tolyl)-1,3,2-dioxaborolane (> 98%)	TCI Europe	T2888-5G
4-methylphenylboronic acid	TCI Europe	M1126-5G
Ethyl acetate (> 99.5%)	Fisher Scientific	E/0900/15
Petroleum Ether	Thermo Fisher	180210010

S-ethyl-4-acetoxythiobenzoate and S-ethyl-4-(N,N-dipropylsulfamoyl)thiobenzoate were prepare via literature procedure.[1]

2. Reaction optimization

Supplementary Table 2: Complete reaction optimization data.

Pd-source (mol%)	Ligand (mol%)	Base (eq.)	Additive (eq.)	Solvent	Temperature (°C)	Yield (%)
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	62
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	70	24
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	90	53
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	100	54
Pd_2dba_3 (0.5)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	60
$Pd(OAc)_2$ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	68
$[(cinnamyl)PdCl]_2$ (0.5)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	63
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	DMA	80	32
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	Acetonitrile	80	28
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	1,4-dioxane	80	49
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	2-MeTHF	80	58
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	CPME	80	16
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	Toluene	80	21
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuCl (1.5)	*n*-butyl acetate	80	55
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuBr.dimethyl sulfide (1.5)	*n*-butyl acetate	80	50
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuI (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	CuTC (1.5)	*n*-butyl acetate	80	56
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	$CuBr_2$ (1.5)	*n*-butyl acetate	80	8
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	$Cu(OTf)_2$ (1.5)	*n*-butyl acetate	80	2
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	$ZnBr_2$ (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	$FeBr_2$ (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2CO_3 (1.5)	AgOAc (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_3PO_4 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	47
Pd(COD)DQ (1)	Triethyl phosphite (40)	K_2HPO_4 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	2
Pd(COD)DQ (1)	Triethyl phosphite (40)	$KHCO_3$ (1.5)	CuBr (1.5)	*n*-butyl acetate	80	13
Pd(COD)DQ (1)	Triethyl phosphite (40)	Li_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	Na_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	nd
Pd(COD)DQ (1)	Triethyl phosphite (40)	Cs_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	41

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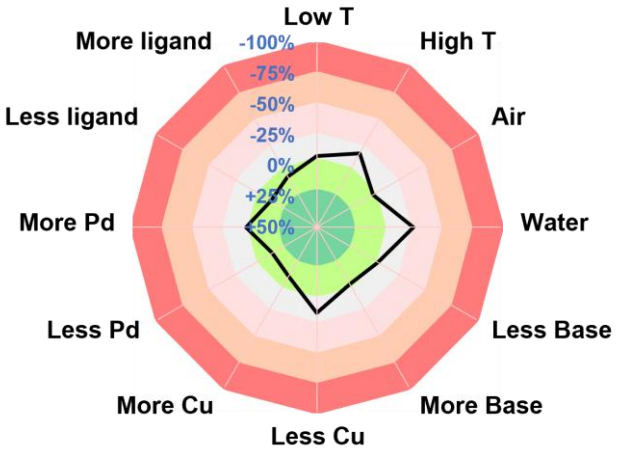
Supplementary Table 2: Continued

Pd-source (mol%)	Ligand (mol%)	Base (eq.)	Additive (eq.)	Solvent	Temperature (°C)	Yield (%)
Pd(COD)DQ (1)	Triethyl phosphite (10)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	17
Pd(COD)DQ (1)	Triethyl phosphite (20)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	32
Pd(COD)DQ (1)	Triethyl phosphite (30)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	48
Pd(COD)DQ (1)	Triethyl phosphite (50)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	62
Pd(COD)DQ (1)	Triphenylphosphine (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	7
Pd(COD)DQ (1)	Tri(2-furyl)phosphine (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	3
Pd(COD)DQ (1)	1,1'-Bis(diphenylphosphino)ferrocene (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	5
Pd(COD)DQ (1)	Triisopropyl phosphite(40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	73
Pd(COD)DQ (1)	Triphenyl phosphite (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	1
Pd(COD)DQ (1)	JohnPhos (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	4
Pd(COD)DQ (1)	CyJohnPhos (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	3
Pd(COD)DQ (1)	Xantphos (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	2
Pd(COD)DQ (1)	Tri(2-methoxyphenyl)-phosphine (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	1
Pd(COD)DQ (1)	Tri(4-methoxyphenyl)-phosphine (40)	K_2CO_3 (1.5)	CuBr (1.5)	*n*-butyl acetate	80	25
Pd(COD)DQ (1)	Triisopropyl phosphite(40)	K_2CO_3 (2)	CuBr (2)	*n*-butyl acetate	80	83 (86%)[a]
Pd(COD)DQ (1)	Triisopropyl phosphite(40)	K_2CO_3 (2)	CuBr (2)	*n*-butyl acetate	80	77[b]

[a]Determined using ^{1}H-NMR with 1,3,5-tri-*tert*-butylbenzene as internal standard. [b]1.1 eq. benzothiazole, 24 h.

3. Sensitivity assessment

The sensitivity of the reaction to variations in reaction conditions was assessed using the procedure described by Glorius (supplementary Figure 1, Supplementary Table 3).[2] Reactions were set up and analyzed according to the general procedure. These experiments revealed that the reaction generally has low sensitivity. The largest variations were observed when increasing the temperature, lowering the Cu salt loading or when adding water to the reaction mixture.



Supplementary Figure 1: Visual representation of the sensitivity to variations in reaction conditions. Made using template published by Glorius.[2]

Supplementary Table 3: Exact conditions and numerical data of sensitivity assessment experiments. Standard reaction conditions (except for varied parameter): S-butyl thiobenzoate (0.2 mmol), Benzothiazole (1.1 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%), K_2CO_3 (2 eq.), CuBr (2 eq.), *n*-butyl acetate (0.8 ml), 80 °C, argon atmosphere, 24 h.

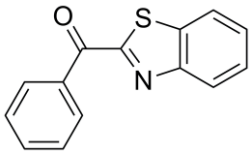
Condition	Exact variation	Yield (%)	% Deviation
Standard	NA	83	NA
Low T	70 °C	77	-8
High T	90 °C	67	-20
Air	No inert atmosphere	81	-3
Water	5 µl water added to reaction mixture	59	-29
Less Base	1.5 eq. K_2CO_3	77	-7
More Base	2.5 eq. K_2CO_3	80	-4
Less Cu	1.5 eq. Cu(I)Br	67	-20
More Cu	2.5 eq. Cu(I)Br	86	4
Less Pd	0.5 mol% Pd(COD)DQ	90	8
More Pd	2 mol% Pd(COD)DQ	77	-8
Less Ligand	30 mol% triisopropyl phosphite	89	7
More Ligand	50 mol% triisopropyl phosphite	85	3

4. General procedure for the cross-coupling of thioester with azoles

First, 1,3,5-tri-*tert*-butylbenzene (0.081 mmol, 20mg), K_2CO_3 (0.4 mmol, 55.3 mg), CuBr (0.4 mmol, 57.4 mg) and Pd(COD)DQ (0.002 mmol, 0.76 mg) were weighed with an analytic balance and added to a 1.5 ml vial. After adding a magnetic stirring bar the vial was closed off with a cap containing a PTFE septum. Subsequently, the vial was sparged with argon using a Schlenk line. Afterwards, 0.8 ml *n*-butyl acetate (extra dry) was added using a syringe and needle. Triisopropyl phosphite (0.08 mmol, 18.3 µl), S-butyl thiobenzoate (0.2 mmol, 37 µl) and benzothiazole (0.22 mmol, 23.8 µl) were added using Hamilton syringes. Finally, the cap with perforated septum was replaced under argon flow and the vial was put in a preheated heating block on a magnetic stirring plate. After reaction the vial was removed from the heating block and allowed to cool to ambient temperature. Subsequently, the crude mixture was diluted with 0.7 ml *n*-butyl acetate and centrifuged to sediment solids. Finally a sample was extracted for analysis.

Identification of products was performed using an Agilent 6890 gas chromatograph equipped with HP-1ms column, connected to an Agilent 5973 MSD utilizing electron ionization. In case of multiple feasible products with identical mass and for novel compounds, a ^{1}H-NMR and/or ^{13}C-NMR spectrum was measured of the crude reaction mixture using a Bruker Avance II+ 600 MHz spectrometer. Product quantification was performed using a Shimadzu GC-2014 gas chromatograph equipped with a CP-Sil-8 column, connected to a flame ionization detector, using the added internal standard and the ECN method.[3] For the optimized reaction conditions, the accuracy of the yield determined by GC-FID (83%) was confirmed by also measuring the yield of the same sample using ^{1}H-NMR with 1,3,5-tri-*tert*-butylbenzene as internal standard (86%).

3) 2-benzoyl benzothiazole

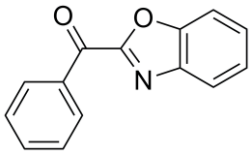


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), benzothiazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[4]

[M+] calculated for $C_{14}H_9NOS$: 239.04 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 239.1 (37), 212.1 (16), 211.1 (100), 210.1 (15),105.1 (94), 90.1 (11), 77.1 (83), 63.1 (10), 51.1 (32), 50.2 (14)

4) 2-benzoyl benzoxazole

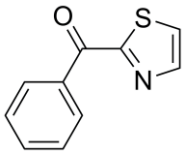


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), benzoxazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[4]

[M+] calculated for $C_{14}H_9NO_2$: 223.06 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 223.1 (17), 195.1 (35), 106.1 (7), 105.1 (100), 90.1 (8), 77.1 (66), 76.2 (6), 63.1 (14), 51.1 (24), 50.1 (10)

5) 2-benzoyl thiazole

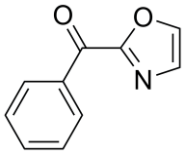


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), thiazole (1.1 eq), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[4]

[M+] calculated for $C_{10}H_7NOS$: 189.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 189.0 (26), 162.0 (11), 161.1 (97), 105.1 (80), 77.1 (100), 74.1 (10), 58.1 (27), 57.1 (29), 51.1 (50), 50.1 (24)

6) 2-benzoyl oxazole

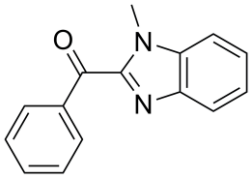


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), oxazole (1.1 eq), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[5]

[M+] calculated for $C_{10}H_7NO_2$: 173.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 173.1 (11), 145.1 (51), 106.1 (8) 105.1 (100), 77.1 (97), 76.1 (8), 74.1 (8), 51.1 (37), 50.2 (37), 40.1 (18)

7) 2-benzoyl-1-methyl benzimidazole

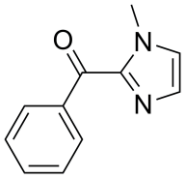


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), 1-methyl benzimidazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[6]

[M+] calculated for $C_{15}H_{12}N_2O$: 236.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 236.1 (35), 235.1 (81), 208.2 (17), 207.1 (100), 105.1 (18), 78.2 (6), 77.1 (67), 76.1 (9), 51.1 (22), 50.1 (8)

8) 2-benzoyl-1-methyl imidazole

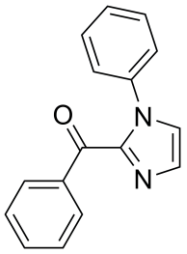


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), 1-methyl imidazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (100 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[7]

[M+] calculated for $C_{11}H_{10}N_2O$: 186.08 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 186.1 (28), 185.1 (100), 158.1 (14), 157.1 (95), 109.1 (7), 105.1 (26), 77.1 (61), 54.1 (7) 51.1 (28), 50.1 (12)

9) 2-benzoyl-1-phenyl imidazole

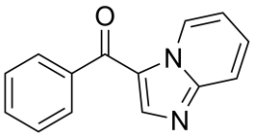


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), 1-phenyl imidazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (100 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[8]

[M+] calculated for $C_{16}H_{12}N_2O$: 248.1 **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 248.1 (46), 247.1 (89), 220.1 (22), 219.1 (76), 171.1 (16), 105.1 (39), 89.1 (11), 77.1 (100), 51.1 (37), 50.2 (12).

10) imidazo[1,2-a]pyridin-3-yl(phenyl)methanone



Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), imidazo[1,2-a]pyridine (3 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (100 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[9]

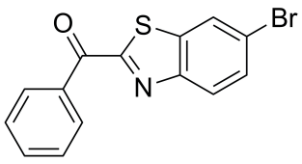
[M+] calculated for $C_{14}H_{10}N_2O$: 222.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 223.1 (16), 222.1 (100), 221.1 (70), 194.1 (13), 145.1 (53), 117.0 (13), 90.1 (28), 77.1 (35), 63.1 (15), 51.1 (28)

This compound is known in literature. Crude ^{1}H-NMR and ^{13}C-NMR were measured and matched literature report:[9]

^{1}H-NMR (600 MHz, $CDCl_3$): δ 9.70 (d, 1H), 8.28 (s, 1H), 7.86-7.80 (m, 3H), 7.53-7.43 (m, 4H), 7.11 (1H)

^{13}C{^{1}H}-NMR (150 MHz, $CDCl_3$): δ 184.8, 148.8, 145.5, 139.1, 132.1, 129.7, 128.8, 128.6, 128.5, 123.3, 117.6, 115.3.

11) 2-benzoyl-6-bromo benzothiazole

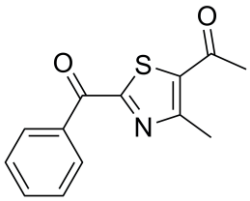


Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), 6-bromo benzothiazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[10]

[M+] calculated for $C_{14}H_8BrNOS$: 317.0 **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 319.0 (25), 317.0 (25), 291.0 (54), 290.0 (15), 289.0 (52), 133.0 (41), 105.1 (88), 77.1 (100), 51.1 (39), 50.1 (19).

12) 1-(2-benzoyl-4-methylthiazol-5-yl)ethenone



Prepared according to general procedure using S-butyl thiobenzoate (0.2 mmol), 1-(4-Methylthiazol-5-yl)ethanone (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours. Isolated yield was determined for reaction at 0.5 mmol scale. Compound was purified by silica gel column chromatography using petroleum ether:ethyl acetate (15:1) as mobile phase. The compound was obtained as a yellow solid (51.1 mg, 42% yield).

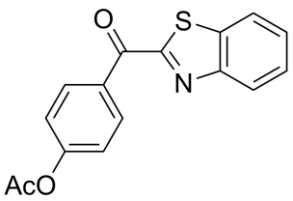
This compound is known in literature.[11]

[M+] calculated for $C_{13}H_{11}NO_2S$: 245.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 245.1 (25), 230.1 (9), 217.1 (54), 202.1 (56), 105.1 (100), 77.1 (88), 67.1 (9), 51.1 (30), 50.1 (10), 43.1 (23)

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.50 (d, 2H), 7.78 (t, 1H), 7.56 (t, 2H), 2.86 (s, 3H), 2.66 (s, 3H)

^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$): δ 190.8, 183.9, 167.0, 160.0, 135.5, 134.6, 134.1, 131.3, 128.5, 31.2, 18.6.

13) 2-(4-acetoxybenzoyl)benzothiazole



Prepared according to general procedure using S-ethyl-4-acetoxythiobenzoate (0.2 mmol), benzothiazole (2 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 6 hours.

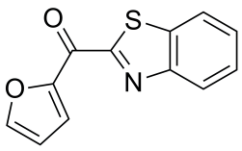
[M+] calculated for $C_{16}H_{11}NO_3S$: 297.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 297.1 (20), 255.1 (65), 227.1 (83), 226.1 (14), 121.1 (100), 93.1 (16), 92.1 (17), 65.1 (17), 63.1 (19), 43.1 (60)

Crude ^{1}H-NMR and ^{13}C-NMR were measured to complement GC-MS identification.

^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.67 (d, 2H), 8.23 (d, 1H), 8.01 (d, 1H), 7.59-7.53 (m, 2H), 7.31 (d, 2H), 2.35 (s, 3H).

^{13}C{^{1}H}-NMR (150 MHz, $CDCl_3$): δ 183.8, 168.6, 167.0, 155.1, 153.9, 137.0, 133.1, 127.7, 127.0, 125.7, 123.7, 122.2, 121.7, 21.2.

14) 2-furoyl benzothiazole

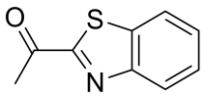


Prepared according to general procedure using S-Methyl furan-2-carbothioate (0.2 mmol), benzothiazole (2 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours.

This compound is known in literature.[12]

[M+] calculated for $C_{12}H_7NO_2S$: 229.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 229.1 (50), 202.1 (12), 201.1 (92), 173.1 (24), 134.1 (12), 95.1 (100), 90.1 (13), 63.1 (12), 39.2 (42), 38.2 (12)

15) 2-acetyl benzothiazole

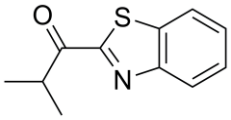


Prepared according to general procedure using S-propyl thioacetate (0.2 mmol), benzothiazole (2 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 6 hours.

This compound is known in literature.[13]

[M+] calculated for C_9H_7NOS: 177.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 177.1 (95), 149.1 (56), 135.1 (100), 134.1 (35), 108.1 (31), 90.1 (19), 82.1 (15), 69.1 (25), 63.1 (21), 43.1 (61)

16) 2-isobutyryl benzothiazole

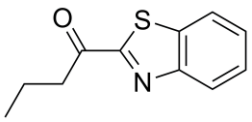


Prepared according to general procedure using S-methyl-2-methylpropanethioate (0.2 mmol), benzothiazole (2 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 6 hours.

This compound is known in literature.[13]

[M+] calculated for $C_{11}H_{11}NOS$: 205.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 205.1 (27), 177.1 (47), 162.1 (100), 135.1 (62), 134.1 (62), 90.1 (26), 43.2 (43), 41.2 (38), 39.2 (33), 27.2 (34)

17) 2-butyryl benzothiazole

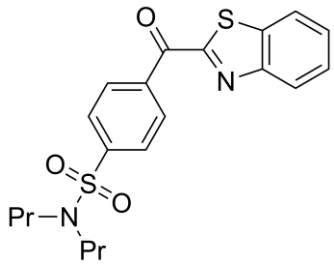


Prepared according to general procedure using S-methyl thiobutyrate (0.2 mmol), benzothiazole (2 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 6 hours.

This compound is known in literature.[13]

[M+] calculated for $C_{11}H_{11}NOS$: 205.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 205.1 (15), 177.1 (67), 162.1 (100), 149.1 (31), 135.1 (87), 134.1 (49), 108.1 (23), 90.1 (25), 43.2 (39), 41.2 (25), 27.2 (26)

18) 4-(benzo[d]thiazole-2-carbonyl)-N,N-dipropylbenzenesulfonamide



Prepared according to general procedure using S-ethyl-4-(N,N-dipropylsulfamoyl)thiobenzoate (0.2 mmol), benzothiazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (0.8 ml), at 80 °C for 24 hours. Isolated yield was determined for reaction at 0.5 mmol scale. Compound was purified by silica gel column chromatography using petroleum ether:ethyl acetate (7:1) as mobile phase. The compound was obtained as a white solid (69.6 mg, 35% yield).

[M+] calculated for $C_{20}H_{22}N_2O_3S_2$: 402.2 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 402.2 (1), 375.1 (12), 374.1 (22), 373.1 (100), 302.0 (17), 238.1 (47), 210.1 (46), 209.1 (10), 104.1 (10), 76.1 (10), 43.2 (14)

^{1}H-NMR (400 MHz, $CDCl_3$): δ 8.73 (d, 2H), 8.28 (d, 1H), 8.07 (d, 1H), 8.02 (d, 2H), 7.63 (m, 2H), 3.17 (t, 4H), 1.62 (sext, 4H), 0.92 (t, 6H).

^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$): δ 184.2, 166.3, 153.9, 144.7, 137.8, 137.2, 131.9, 128.1, 127.3, 127.0, 125.9, 122.3, 50.2, 22.1, 11.2.

5. H/D exchange experiments

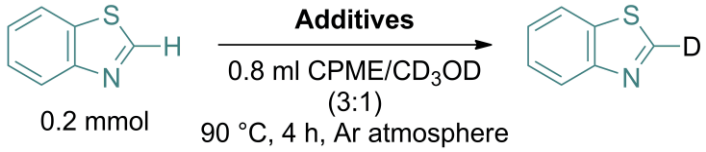
If required, K_2CO_3 (0.02 mmol, 2.8 mg or 0.4 mmol, 55.3 mg) and/or CuBr (0.02 mmol, 2.9 mg or 0.4 mmol, 57.4 mg) were were weighed with an analytic balance under ambient atmosphere and added to a 1.5 ml vial. After adding a magnetic stirring bar the vial was closed off with a cap containing a PTFE septum. Subsequently the vial was sparged with argon using a Schlenk line. Afterwards, 0.8 ml CD_3OD/CPME (v:v = 25:75) was added using a syringe and needle. Triethyl phosphite (0.04 mmol, 6.9 µl or 0.08 mmol, 14 µl), if required, and benzothiazole (0.2 mmol, 22 µl) were added using Hamilton syringes. Finally, the cap with perforated septum was replaced under argon flow and the vial was put in a preheated heating block on a magnetic stirring plate. After reaction the vial was removed from the heating block and allowed to cool to ambient temperature. Samples were analyzed using ^{1}H- and ^{2}H-NMR using a Bruker Avance II+ 600 MHz spectrometer.

The exchanged proton was identified qualitatively using ^{2}H-NMR. Afterwards, the degree of deuteration was calculated using ^{1}H-NMR. First, all peaks corresponding to the five protons of benzothiazole were integrated. Second, the average peak area was determined for the four non-exchanged protons. The degree of deuteration was then calculated by following formula:

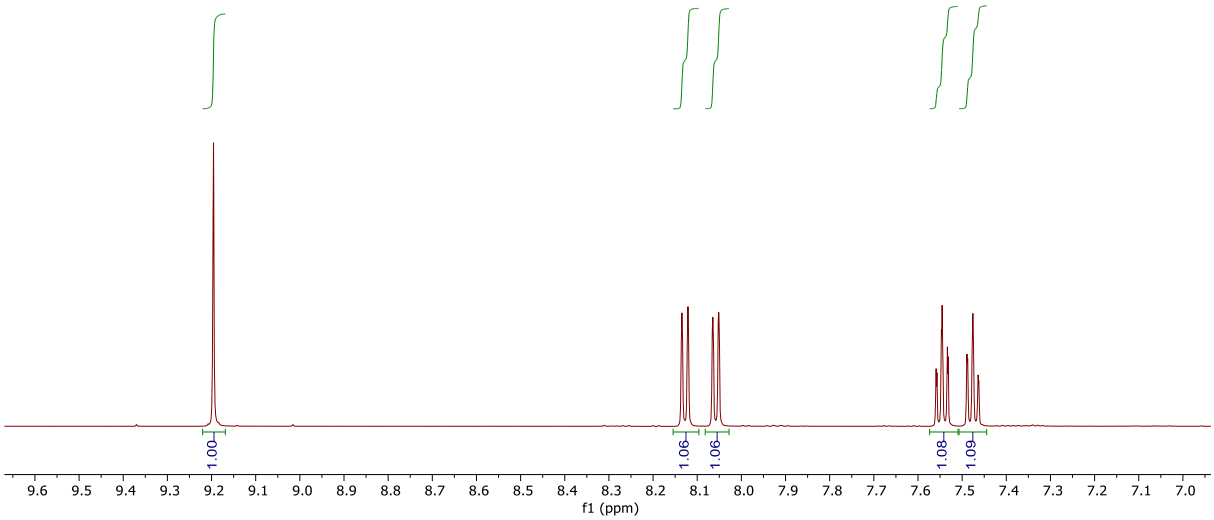
$$\%Deuteration = \left(1 - \frac{A_{ex}}{A_{av}}\right) * 100\%$$

With A_{ex} the peak area of the exchanged proton and A_{av} the average area of the four other protons of benzothiazole.

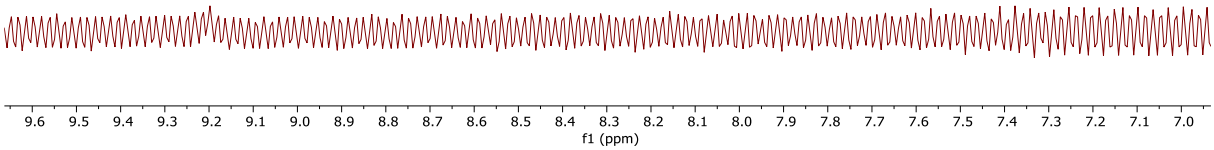
Supplementary Table 4: Quantitative data for H/D exchange experiments.



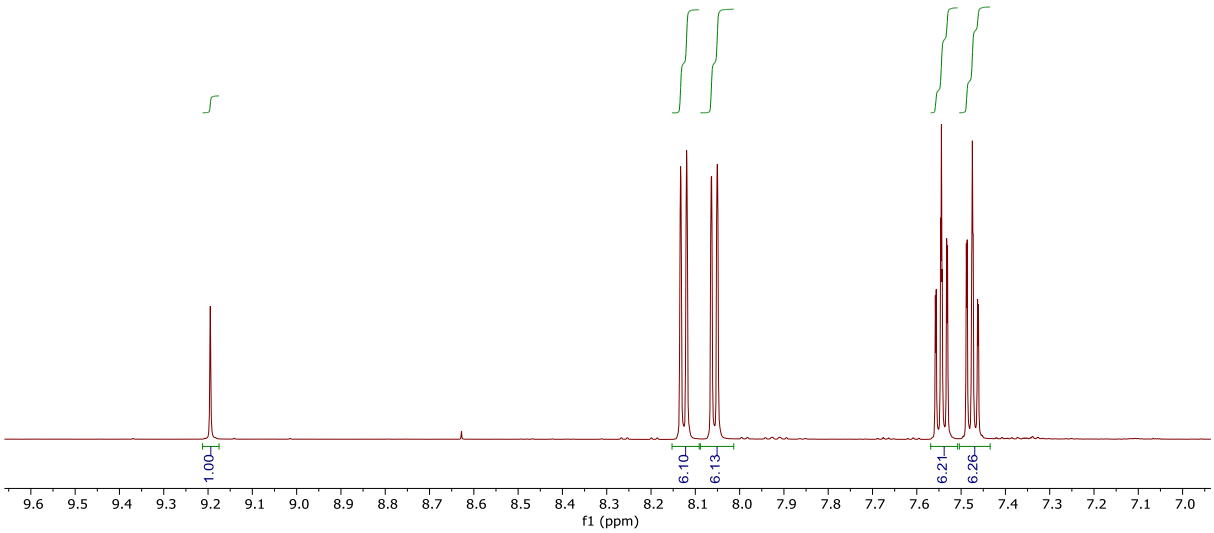
Additives (mol%)	A_{ex}	A_1	A_2	A_3	A_4	A_{av}	%Deuteration
None	1	1.06	1.06	1.08	1.09	1.0725	7
K_2CO_3 (10)	1	6.1	6.13	6.21	6.26	6.175	84
K_2CO_3 (10), CuBr (10)	1	1.135	1.135	1.14	1.14	1.1375	12
K_2CO_3 (10), CuBr (10), Triethyl phosphite (20)	1	1.66	1.61	1.65	1.64	1.64	39
K_2CO_3 (200), CuBr (200), Triethyl phosphite (40)	1	2.855	2.855	3.025	3.025	2,94	66



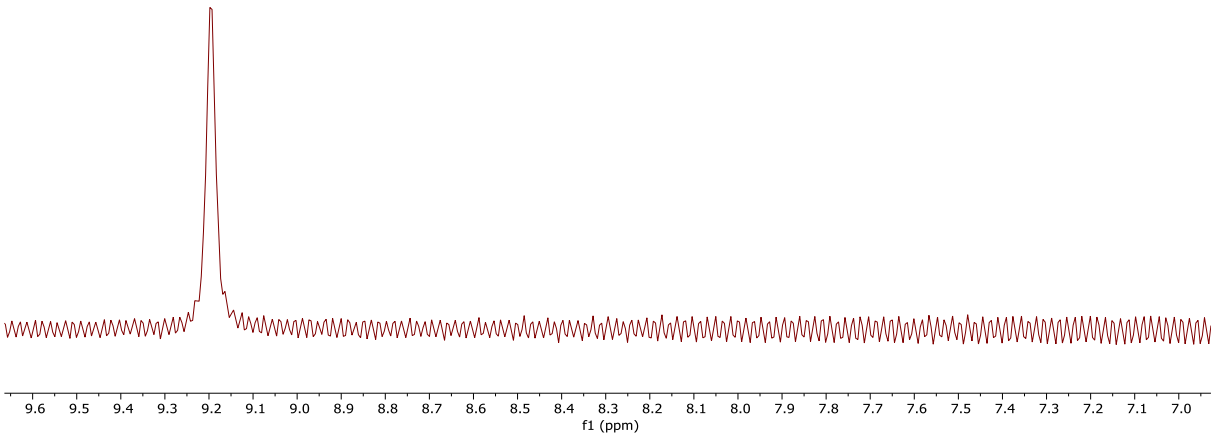
Supplementary Figure 2: 600 MHz ^{1}H-NMR spectrum after experiment without additive.



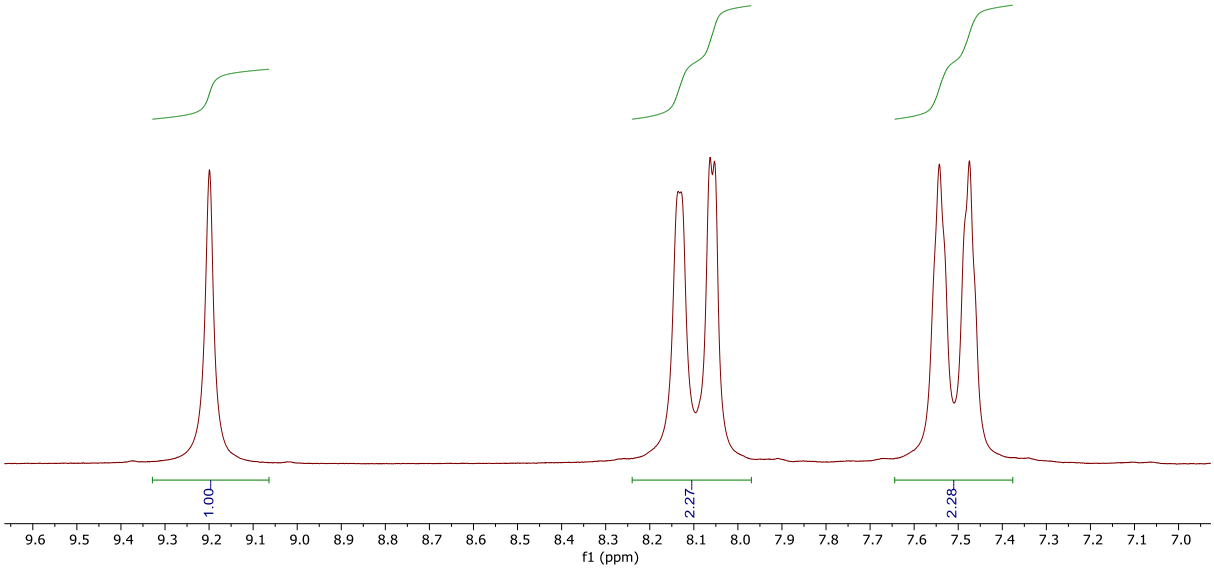
Supplementary Figure 3: 92.1 MHz ^{2}H-NMR spectrum after experiment without additive.



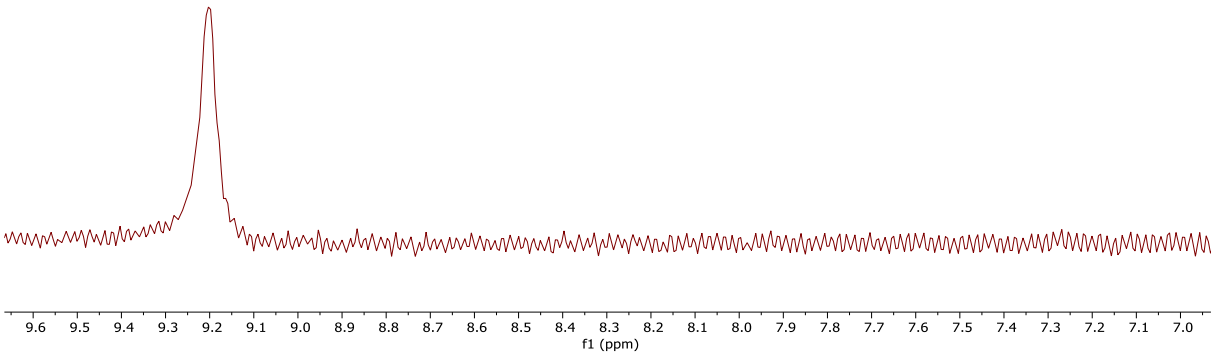
Supplementary Figure 4: 600 MHz ^{1}H-NMR spectrum after experiment with 10 mol% K_2CO_3.



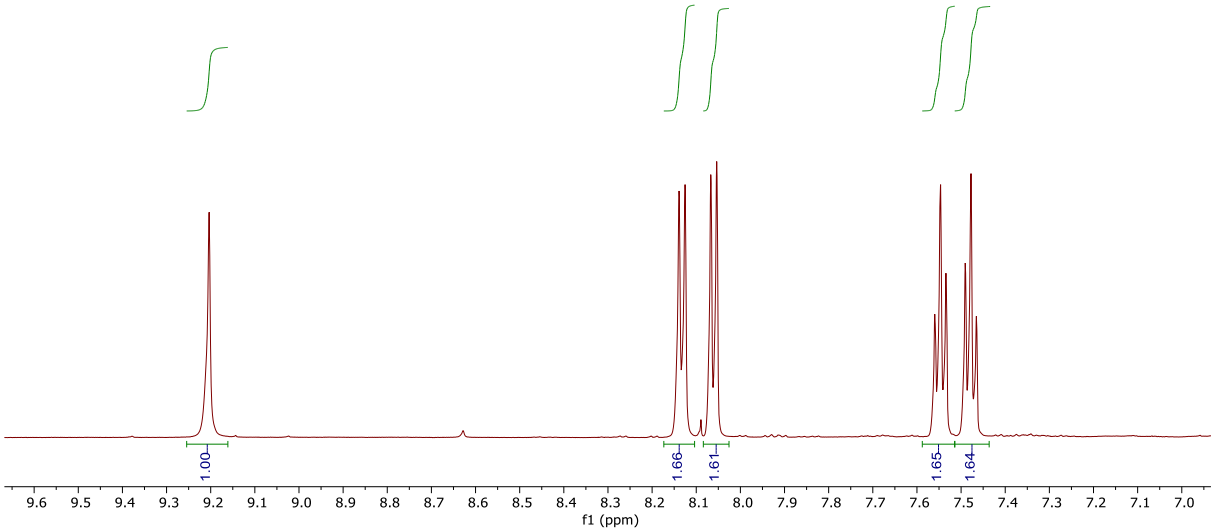
Supplementary Figure 5: 92.1 MHz ^{2}H-NMR spectrum after experiment with 10 mol% K_2CO_3.



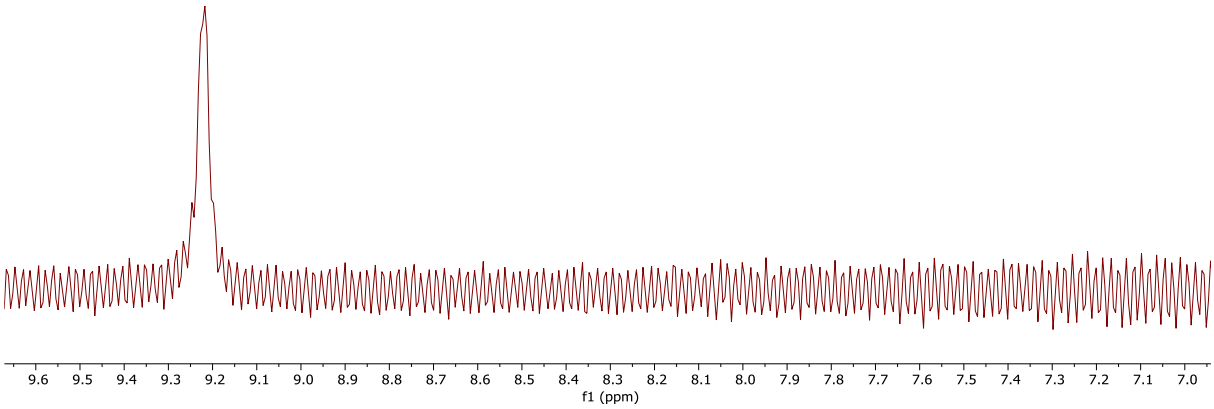
Supplementary Figure 6: 600 MHz ^{1}H-NMR spectrum after experiment with 10 mol% K_2CO_3 and 10 mol% CuBr.



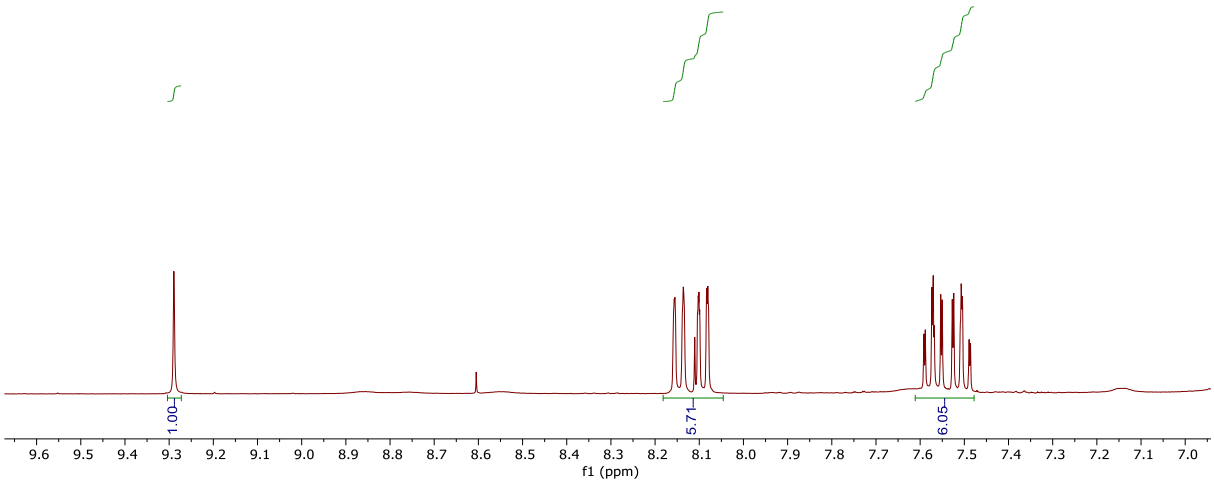
Supplementary Figure 7: 92.1 MHz ^{2}H-NMR spectrum after experiment with 10 mol% K_2CO_3 and 10 mol% CuBr.



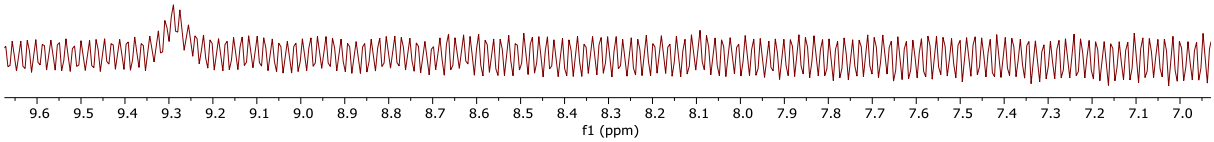
Supplementary Figure 8: 600 MHz ^{1}H-NMR spectrum after experiment with 10 mol% K_2CO_3, 10 mol% CuBr and 20 mol% Triethyl phosphite.



Supplementary Figure 9: 92.1 MHz ^{2}H-NMR spectrum after experiment with 10 mol% K_2CO_3, 10 mol% CuBr and 20 mol% Triethyl phosphite.



Supplementary Figure 10: 400 MHz ^{1}H-NMR spectrum after experiment with 200 mol% K_2CO_3, 200 mol% CuBr and 40 mol% Triethyl phosphite.



Supplementary Figure 11: 61.4 MHz ^{2}H-NMR spectrum after experiment with 200 mol% K_2CO_3, 200 mol% CuBr and 40 mol% Triethyl phosphite.

6. Additive experiments

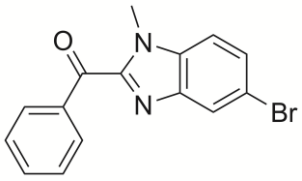
Reactions were set up according to the general procedure. 0.2 mmol of additive (solid or liquid) was added analogously to the other reagents. Product yield and additive recovery were determined by GC-FID with 1,3,5-tri-*tert*-butylbenzene as internal standard.

7. Orthogonal cross-coupling sequence

The first reaction was set up according to the general procedure performed at 0.5 mmol scale. After reaction, the mixture was cooled down, centrifuged and the liquid phase was obtained. The follow-up Suzuki-Miyaura coupling was performed using this liquid phase without any further purification.

The reaction setup was identical to the general procedure. K_2CO_3 (0.75 mmol, 103.7 mg), 4-methylphenyl boronic acid (0.75 mmol, 102.0 mg), $[(cinnamyl)PdCl]_2$ (0.0125 mmol, 6.5 mg) and 1,1'-Bis(diphenylphosphino)-ferrocene (0.05 mmol, 27.7 mg) were dissolved in the liquid phase of the previous reaction, put in a preheated reaction block at 80 °C and stirred for 24 hours. Product yields were determined via GC-FID using 1,3,5-tri-*tert*-butylbenzene as internal standard.

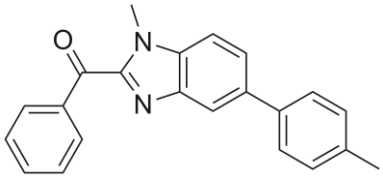
19) 2-benzoyl-5-bromo-1-methyl benzimidazole



Prepared according to general procedure using S-butyl thiobenzoate (0.5 mmol), 5-bromo-1-methyl benzimidazole (1.1 eq.), CuBr (2 eq.), K_2CO_3 (2 eq.), Pd(COD)DQ (1 mol%), triisopropyl phosphite (40 mol%) and *n*-butyl acetate (2 ml), at 80 °C for 24 hours.

[M+] calculated for $C_{15}H_{11}BrN_2O$: 314.0 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 316.1 (46), 315.1 (95), 314.1 (49), 313.1 (90), 287.0 (100), 285.0 (100), 206.1 (20), 105.1, (38), 77.1 (76), 51.1 (21).

20) 2-benzoyl-5-(*p*-tolyl)-1-methyl benzimidazole

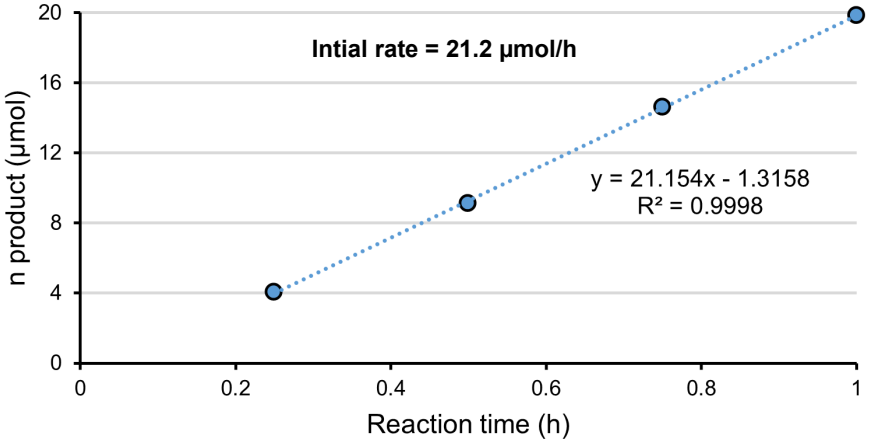


Prepared using 4-methylphenyl boronic acid (0.75 mmol), K_2CO_3 (0.75 mmol), $[(cinnamyl)PdCl]_2$ (0.0125 mmol) and 1,1'-Bis(diphenylphosphino)-ferrocene (0.05 mmol) at 80 °C for 24 hours.

[M+] calculated for $C_{22}H_{18}N_2O$: 326.1 g/mol. **GC-MS (EI, 70 eV)**: m/z (rel. Int%): 327.2 (17), 326.2 (76), 325.2 (66), 298.2 (24), 297.2 (100), 221.1 (6), 165.1 (7), 152.1 (8), 105.1 (16), 77.1 (31).

8. Initial rate experiments

Reactions were set up analogously to the general procedure. After startup 10 µl of reaction mixture was extracted through the septum using a Hamilton syringe every 15 minutes. This was done a total of four times resulting in a total reaction time of one hour. Each sample was diluted with 90 µl *n*-butyl acetate and the amount of product formed in µmol was determined by GC-FID with 1,3,5-tri-*tert*-butylbenzdene as internal standard. Subsequently, a linear fit of the amount of product formation over time was calculated using Microsoft Excel, of which the slope is equal to the initial rate in µmol/h.



[a]*Conditions: S-butyl thiobenzoate (0.2 mmol), Benzothiazole (3 eq.), Pd(COD)DQ (2.5 mol%), triethyl phosphite (20 mol%), K2CO3 (1.5 eq.), CuBr (1.5 eq.), n-butyl acetate (0.8 ml), 80 °C, Argon atmosphere*

Supplementary Figure 12: Example of the determination of the initial rate by linear fitting.

8.1 Parallel kinetic isotope effect

Benzothiazole-D was obtained by stirring K_2CO_3 (1 mmol, 138.2 mg), and benzothiazole (9.17 mmol, 1 ml), in 4 ml CD_3OD at 80 °C under Ar atmosphere for 24 hours. The crude mixture was diluted with toluene. Afterwards, solids were removed by centrifugation and solvent was evaporated under vacuum.

The initial rate was determined for two identical reactions performed in different vials, one using benzothiazole and the other using benzothiazole-D. The parallel kinetic isotope effect is equal to the ratio of these initial rates.[14]

Supplementary Table 5: Quantitative data for KIE experiments.

Reaction time (min)	Product amount H (µmol)	Product amount D (µmol)
15	8.8	2.7
30	23.3	9.6
45	35.5	16.1
60	47.9	22.6
Initial rate (µmol/h)	**51.8**	**26.5**

8.2 Arrhenius Plot

Supplementary Table 6: Quantitative data for Arrhenius plot experiments.

T (°C)	T (K)	1/T (E-03 1/K)	Initial rate (µmol/h)	ln(initial rate)
70	343.15	2.914	7.8	2.1
80	353.15	2.832	21.2	3.1
90	363.15	2.754	41.6	3.7
100	373.15	2.68	106.4	4.7

Taking the natural logarithm of the Arrhenius equation gives the following:

$$\ln(k) = \frac{-E_{app}}{R} * \frac{1}{T} + \ln(A)$$

With E_{app} the apparent activation energy in J/mol, R the universal gas constant in J/(mol*K), T the temperature in K and A the pre-exponential factor. For a classical Arrhenius plot (ln(rate) ~ 1/T) this means that:

$$slope = \frac{-E_{app}}{R}$$

The slope was determined to be equal to -10885 K. As such the apparent activation energy is:

$$E_{app} = 10885\ K * 8.314\ \frac{J}{K * mol} = 90497\ \frac{J}{mol} = 21.6\ \frac{kcal}{mol}$$

8.3 Reaction order determination

Supplementary Table 7: Quantitative data for reaction order determination.

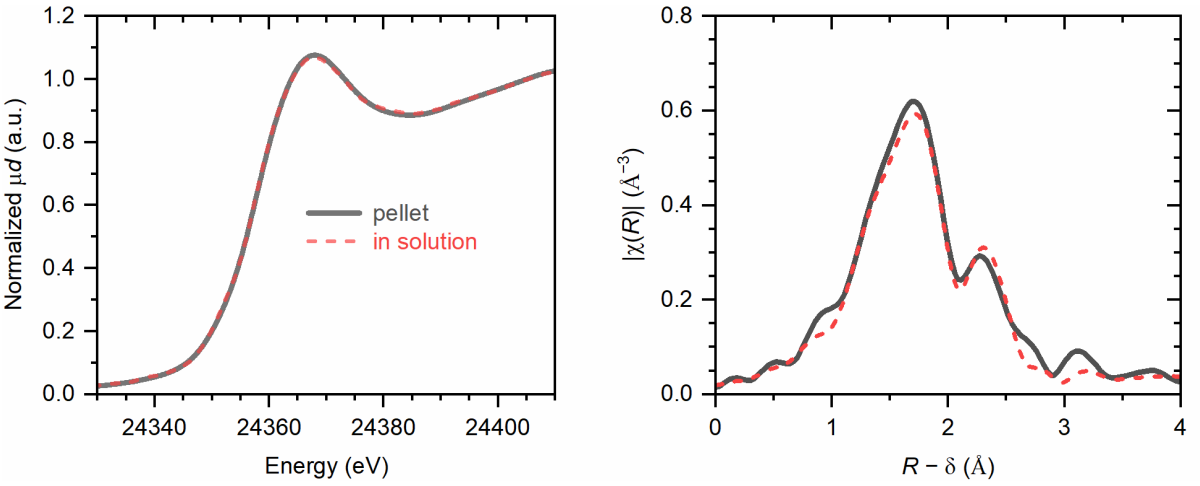
mol% Pd	Initial rate (µmol/h)	mmol $P(OEt)_3$	Initial rate (µmol/h)	mmol Benzothiazole	Initial rate (µmol/h)
0	0	0.02	5.2	0.1	5.5
0.05	24.6	0.03	13.1	0.15	9.1
0.125	25.4	0.04	21.2	0.2	11.9
0.25	25.0	0.05	28.7	0.3	16.3
0.5	23.3	0.06	39.7	0.4	20.5
1	24.2	0.07	43.5	0.5	20.0
1.75	22.1	0.08	54.8	0.6	21.2
mmol CuBr	**Initial rate (µmol/h)**	**mmol thioester**	**Initial rate (µmol/h)**	**mmol K_2CO_3**	**Initial rate (µmol/h)**
0.1	17.9	0.1	21.8	0.1	0
0.2	16.7	0.15	21.7	0.2	15.1
0.3	21.2	0.2	21.3	0.3	21.2
0.4	18.7	0.3	24.0	0.4	19.0
0.5	19.9	0.4	25.5	0.5	19.6

9. *In operando* X-ray absorption spectroscopy

Pd *K*-edge X-ray absorption spectroscopy (XAS) data were collected at SuperXAS beamline of SLS 2.0 synchrotron (Villigen, Switzerland).[15] The energy was scanned by Si(311) channel-cut quick-EXAFS monochromator oscillating at 1 Hz, resulting in 2 spectra per second. Then, only the spectra collected upon increasing energy were selected and averaged to desired statistics. In a typical procedure 1 min average data were used to check for the evolution of the system and 10 to 30 min averaged data were used for analysis. The rejection of higher harmonics was done by Pt-coated collimating mirror. The beam was focused down to 1.0x0.2 mm2 size using a Pt-coated refocusing mirror. The measurements were performed in transmission mode using ionization chambers with identical filling of 1.4 bar N2 and 0.6 bar Ar. Palladium foil has been installed between the second and third ionization chambers and was measured simultaneously with the samples. Ex situ samples were measured as pellets of optimal thickness.

In situ samples were prepared according to general procedure and measured directly in glass vials while heating at 80 °C for one hour. All samples used a Pd concentration of 12.5 µmol/ml in *n*-butyl acetate as solvent. Data analysis was performed in Demeter package.[16] First-shell fitting was performed in R-space for the data Fourier-transformed in 2.5 - 12 Å−1 k-range. For some data, the higher k-boundary had to be reduced to 11 Å−1. The fit used simultaneously k1, k2, and k3 weightings. The R-ranges was from 1.0 to 2.5 or 3.2 depending on the data. The phases and amplitudes of Pd-X paths (X = C, P, Br, Cu) were calculated in FEFF6.[17] Coordination numbers were typically fixed to represent must plausible models, while the Debye-Waller parameters and interatomic distances were fitted for each path. ΔE0 parameter was shared between all paths. S02 parameter was fixed to 0.8 determined by fitting the Pd foil.

Additional data



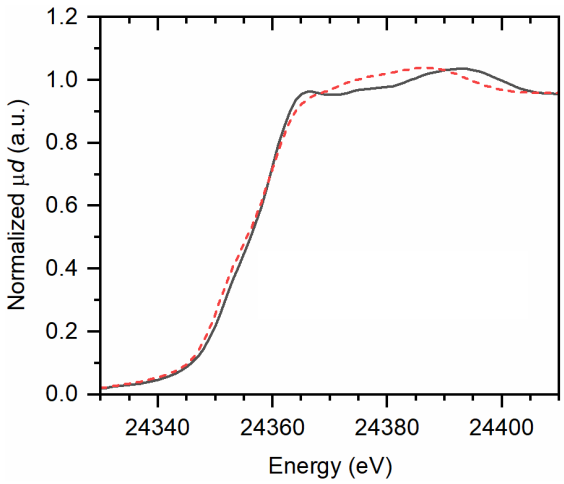
Supplementary Figure 13: XANES (left) and EXAFS (right) data of Pd(COD)DQ pellet (grey line) and 12.5 µmol/ml Pd(COD)DQ in *n*-butyl acetate (red dashed line).

Supplementary Table 8: Structural parameters obtained from fitting EXAFS data of 12.5 µmol/ml Pd(COD)DQ with 4 eq. $P(OEt)_3$.

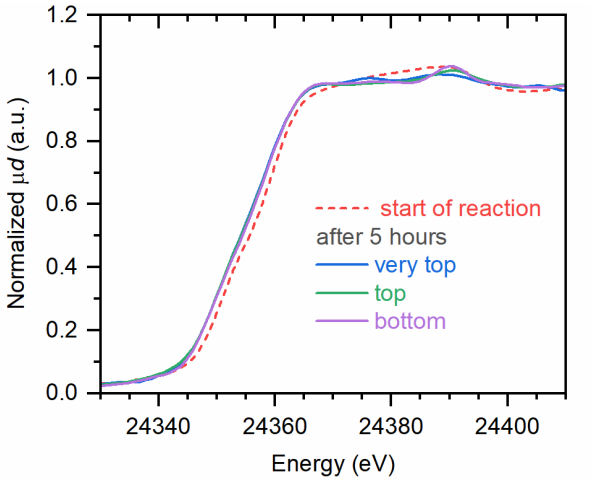
Path	R (Å)	Coordination number
Pd-C	2.15(2)	2
Pd-P	2.37(1)	2

Supplementary Table 9: Structural parameters obtained from fitting EXAFS data of 12.5 µmol/ml Pd(COD)DQ with 4 eq. $P(OEt)_3$, 30 eq. Cu(I)Br and 20 eq. S-butyl thiobenzoate.

Path	R (Å)	Coordination number
Pd-P/S	2.26(2)	3
Pd-Br	2.46(4)	1
Pd-Cu	3.03(7)	1



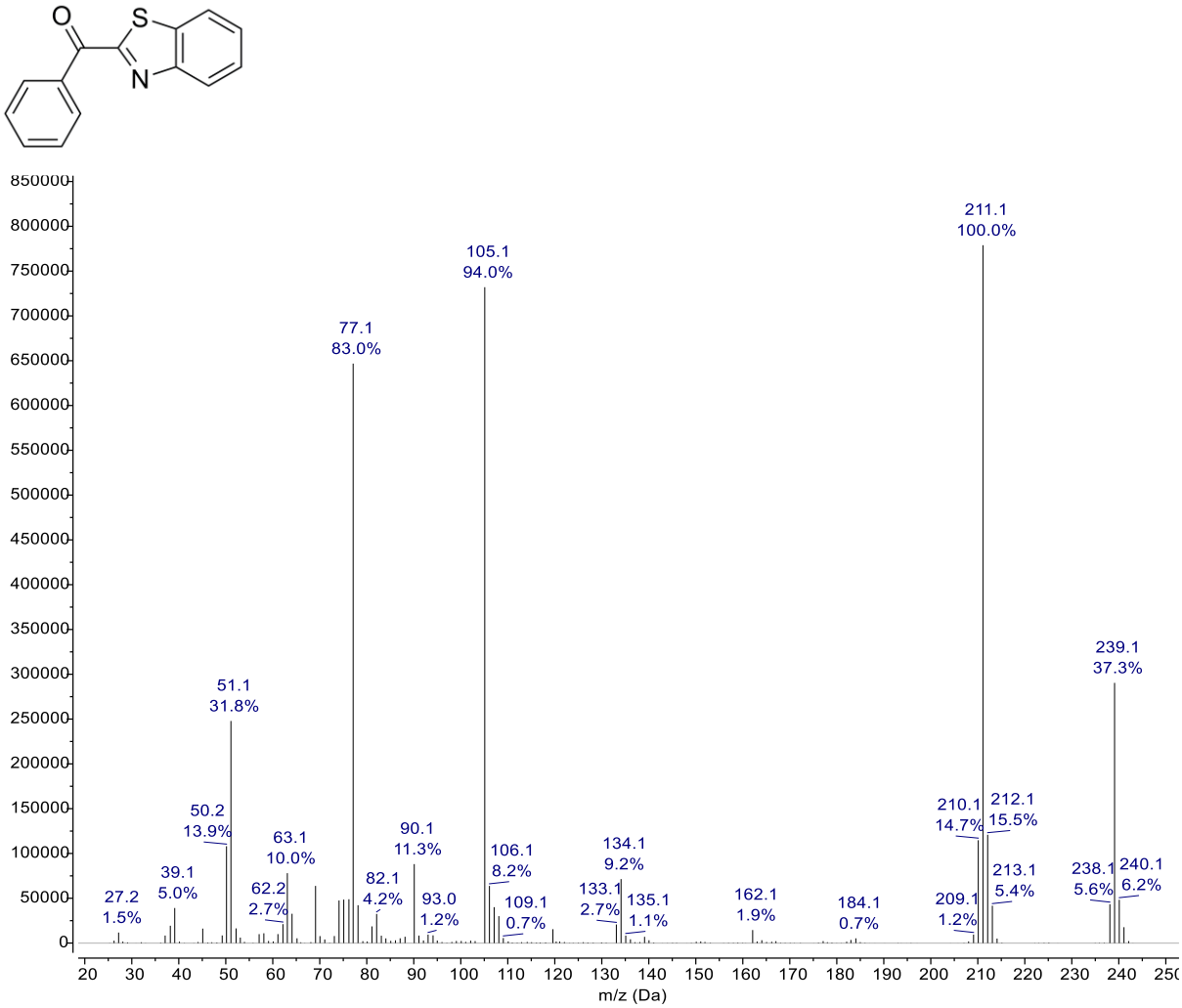
Supplementary Figure 14: XANES measured of sample containing 12.5 µmol/ml Pd(COD)DQ with 4 eq. $P(OEt)_3$ and 30 eq. Cu(I)Br (black line) and of sample containing 12.5 µmol Pd(COD)DQ with 4 eq. $P(OEt)_3$, 30 eq. Cu(I)Br and 20 eq. S-butyl thiobenzoate (red dashed line).



Supplementary Figure 15: XANES measured during full reaction conditions at start of reaction and after 5 hours, at various heights in the vial.

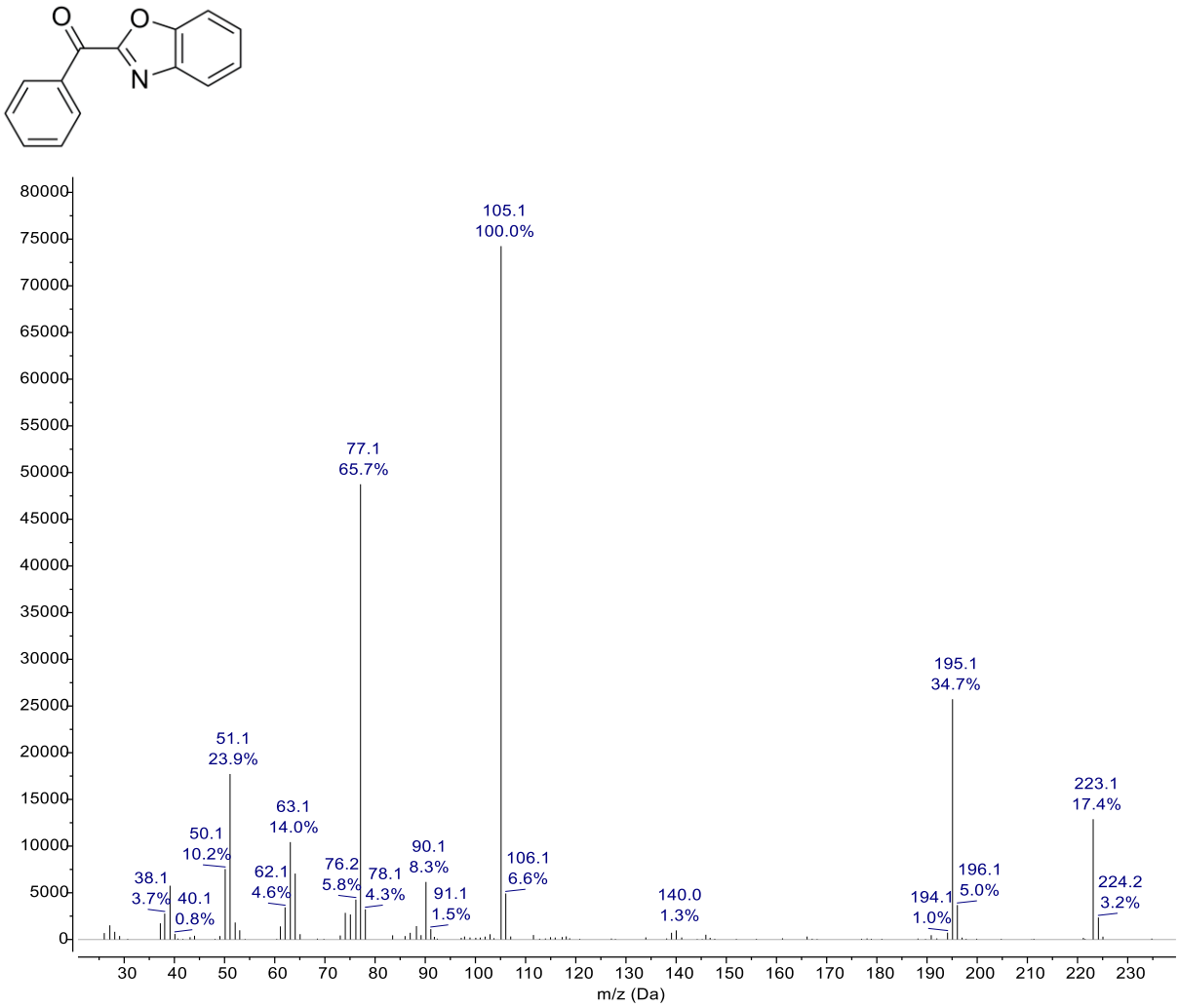
10. Characterization data of products

3) 2-benzoyl benzothiazole



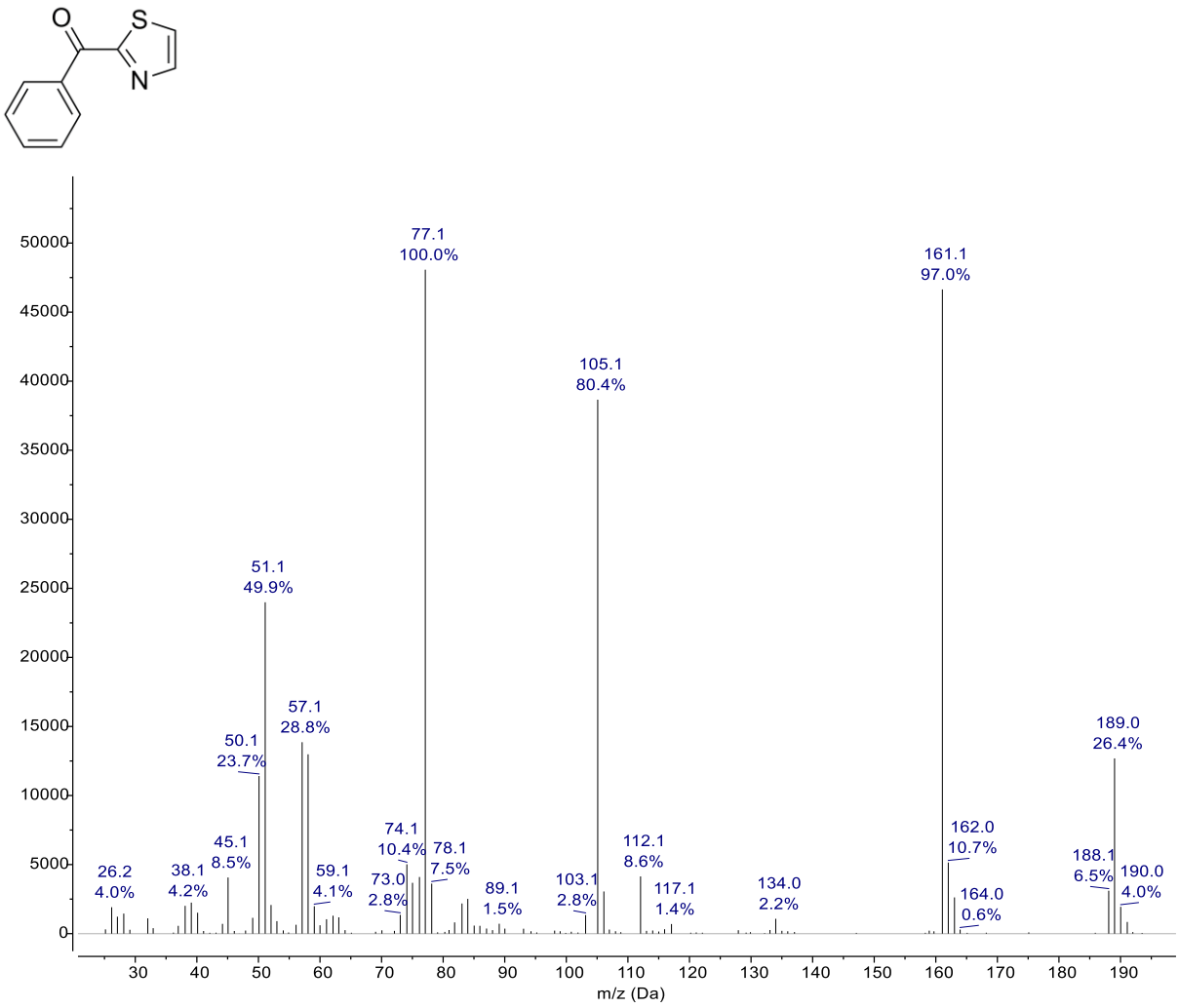
Supplementary Figure 16: Mass spectrum (EI, 70 eV) of 2-benzoyl benzothiazole.

4) 2-benzoyl benzoxazole



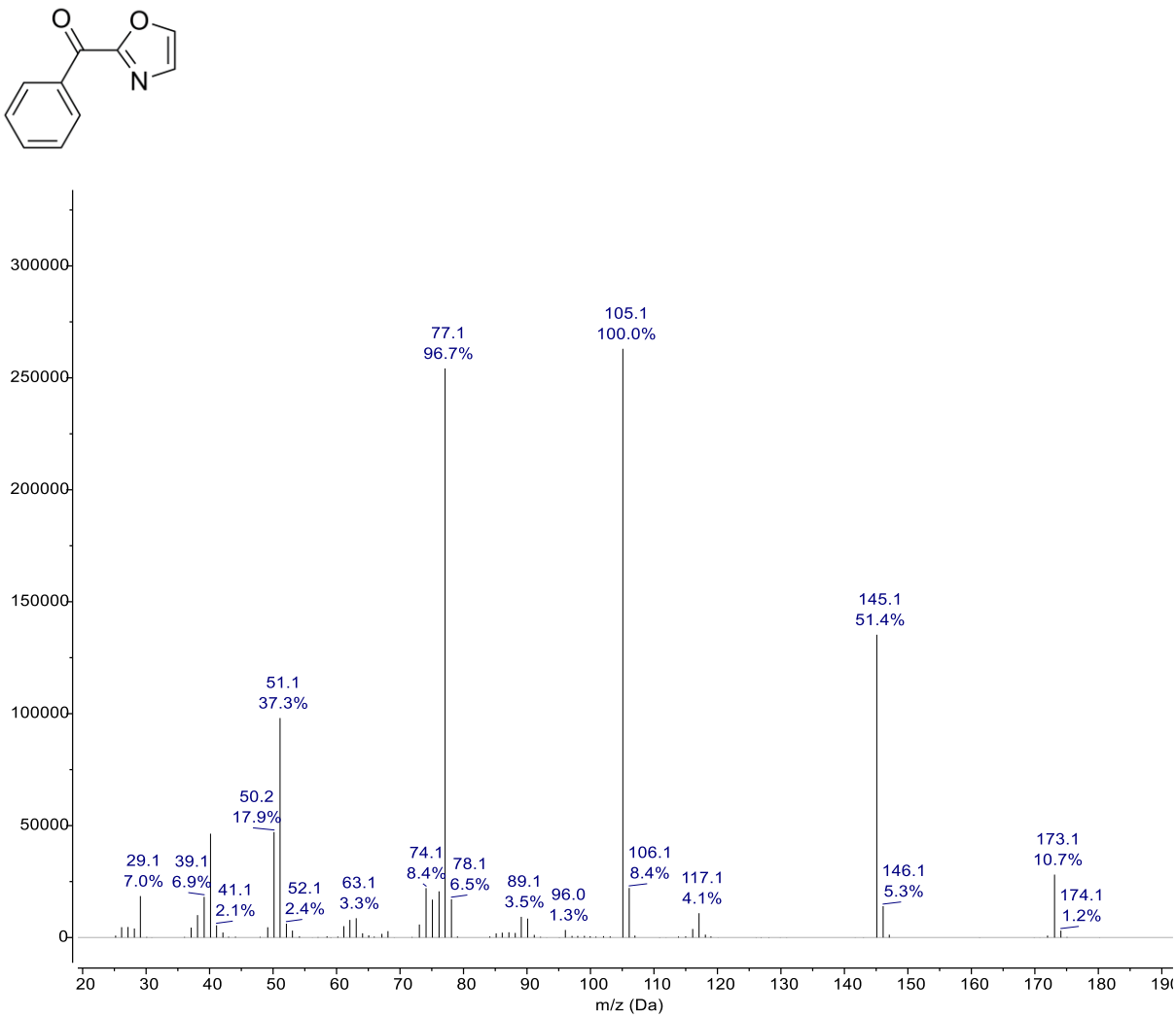
Supplementary Figure 17: Mass spectrum (EI, 70 eV) of 2-benzoyl benzoxazole.

5) 2-benzoyl thiazole



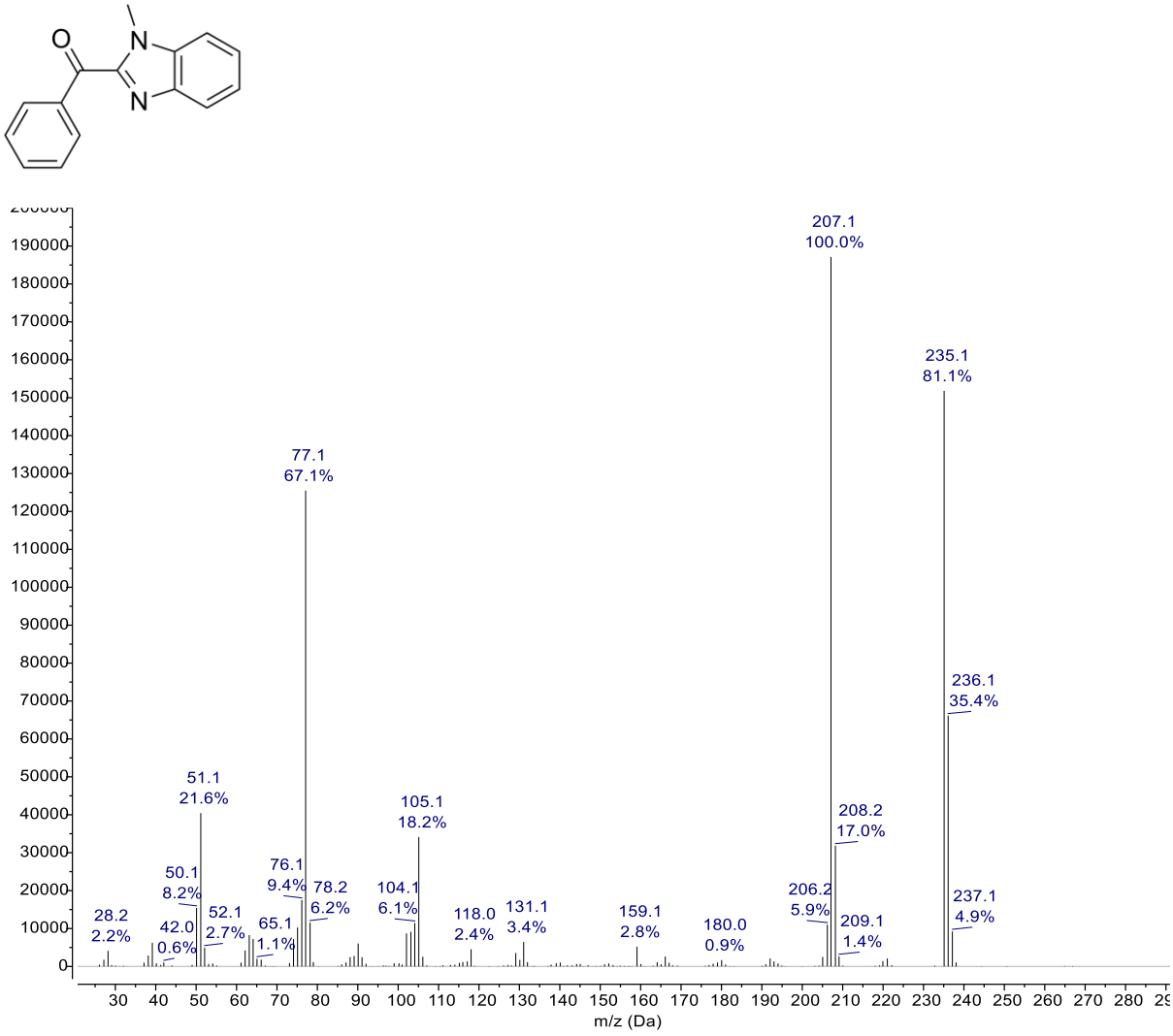
Supplementary Figure 18: Mass spectrum (EI, 70 eV) of 2-benzoyl thiazole.

6) 2-benzoyl oxazole



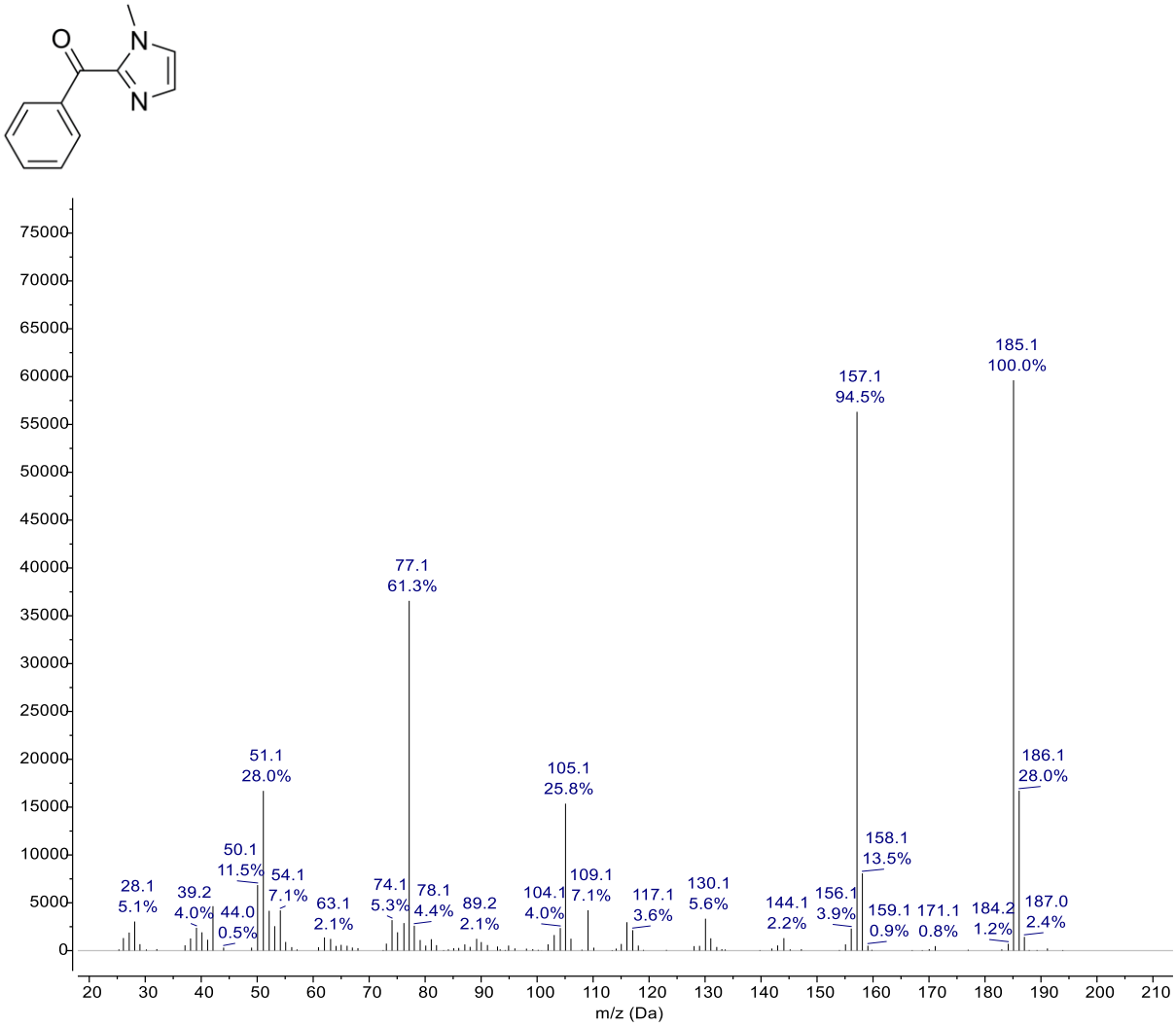
Supplementary Figure 19: Mass spectrum (EI, 70 eV) of 2-benzoyl oxazole.

7) 2-Benzoyl-1-methyl benzimidazole



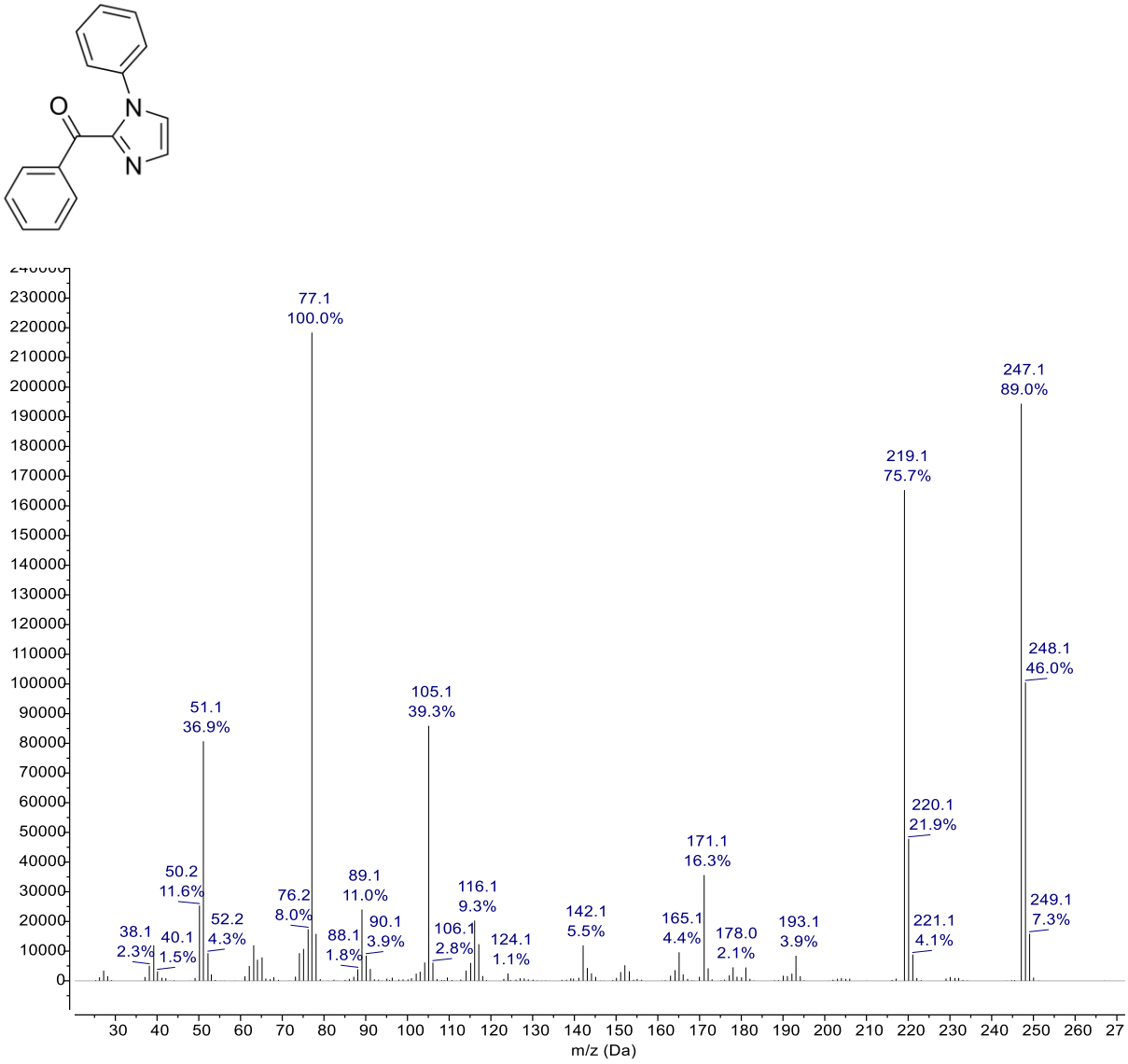
Supplementary Figure 20: Mass spectrum (EI, 70 eV) of 2-Benzoyl-1-methyl benzimidazole.

8) 2-benzoyl-1-methyl imidazole



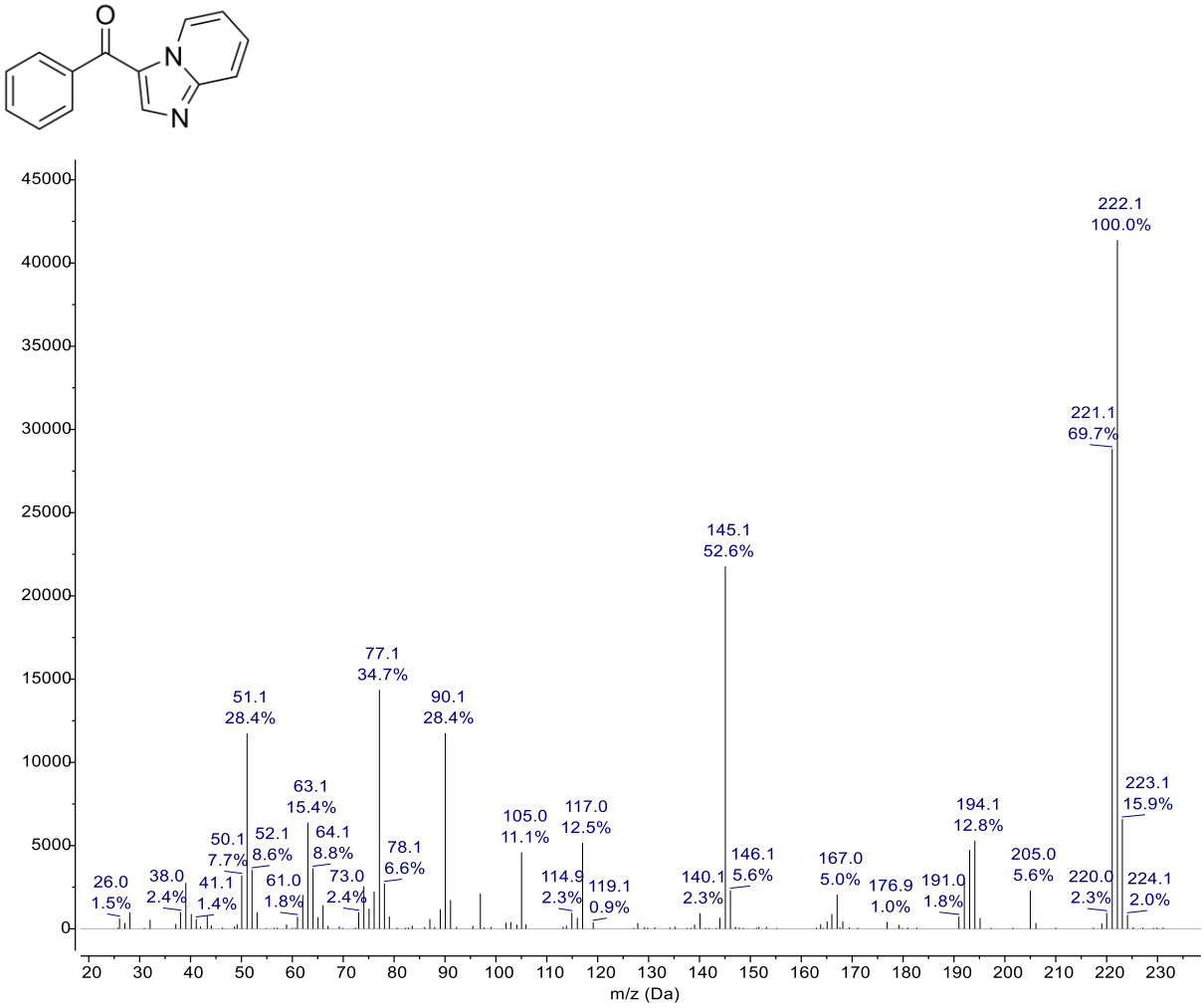
Supplementary Figure 21: Mass spectrum (EI, 70 eV) of 2-benzoyl-1-methyl imidazole.

9) 2-benzoyl-1-phenyl imidazole

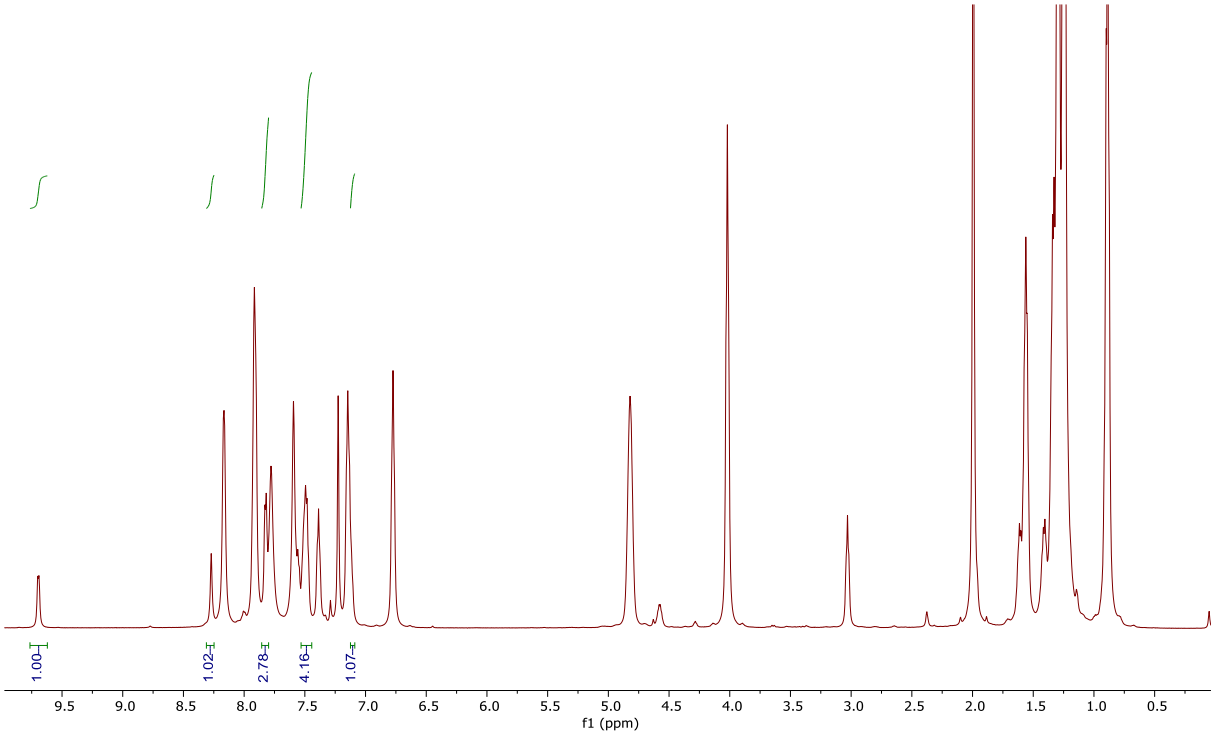


Supplementary Figure 22: Mass spectrum (EI, 70 eV) of 2-benzoyl-1-phenyl imidazole.

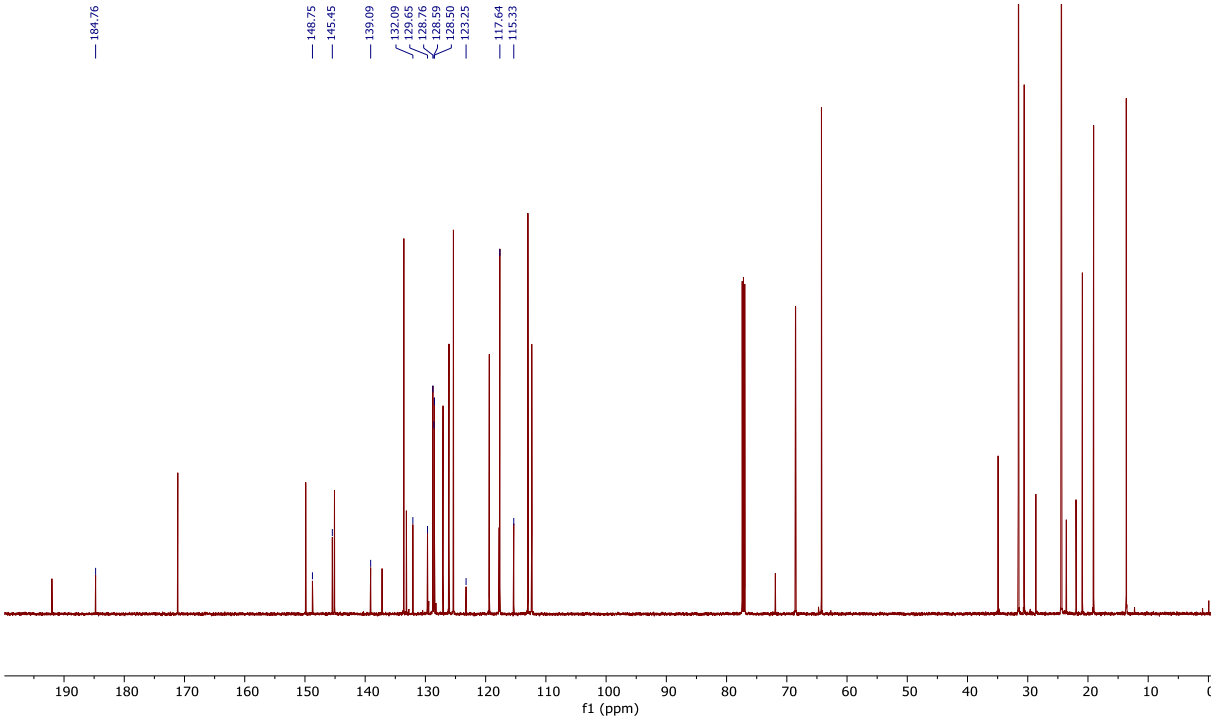
10) imidazo[1,2-a]pyridin-3-yl(phenyl)methanone



Supplementary Figure 23: Mass spectrum (EI, 70 eV) of imidazo[1,2-a]pyridine-3-yl(phenyl)methanone.

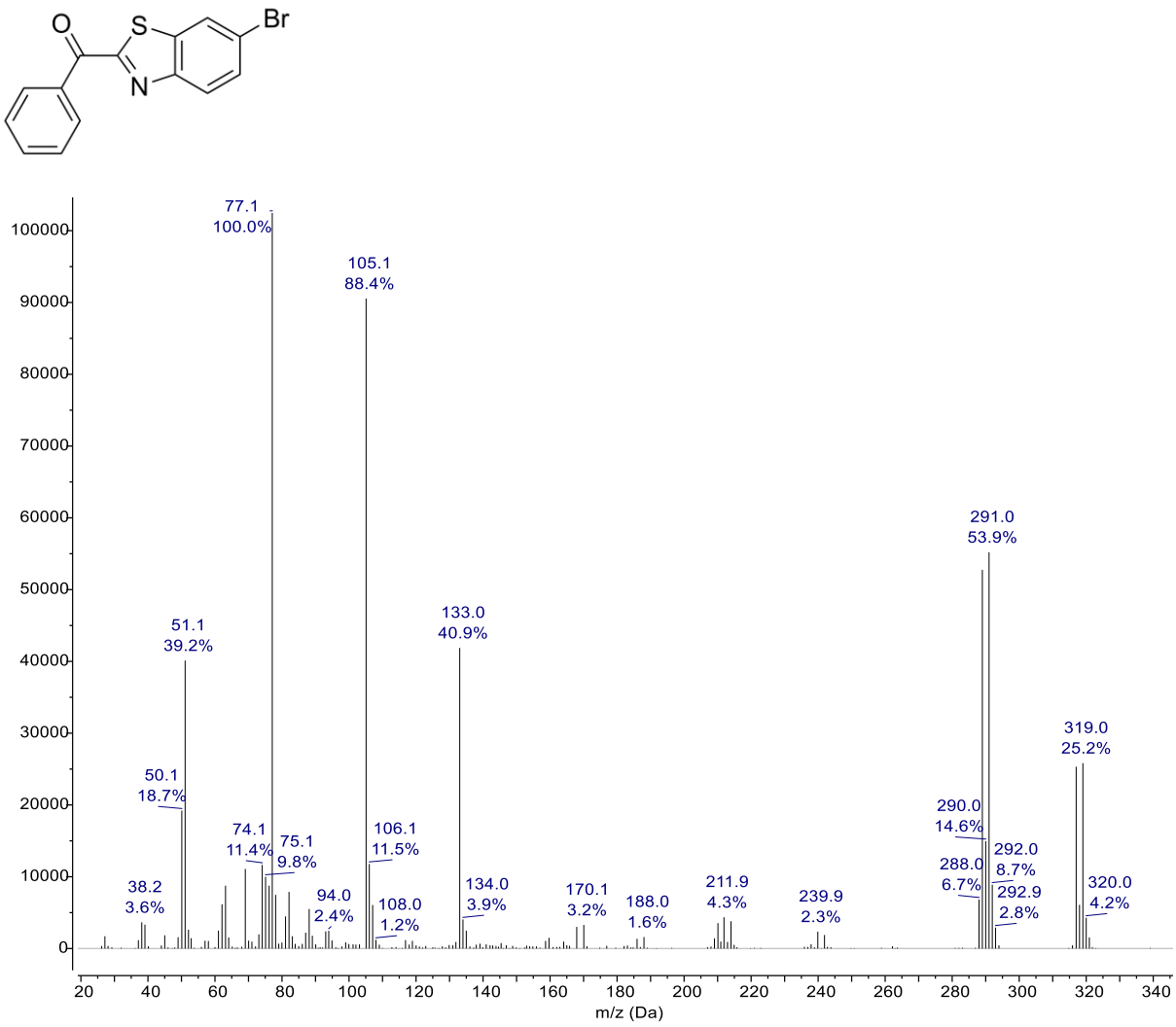


Supplementary Figure 24: ^{1}H-NMR spectrum (600 MHz, $CDCl_3$) of crude reaction mixture of the cross-coupling of S-butyl thiobenzoate and imidazo[1,2-a]pyridine.



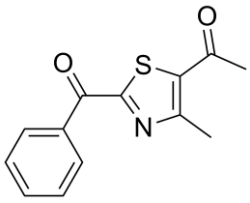
Supplementary Figure 25: $^{13}C\{^{1}H\}$-NMR spectrum (150 MHz, $CDCl_3$) of crude reaction mixture of the cross-coupling of S-butyl thiobenzoate and imidazo[1,2-a]pyridine.

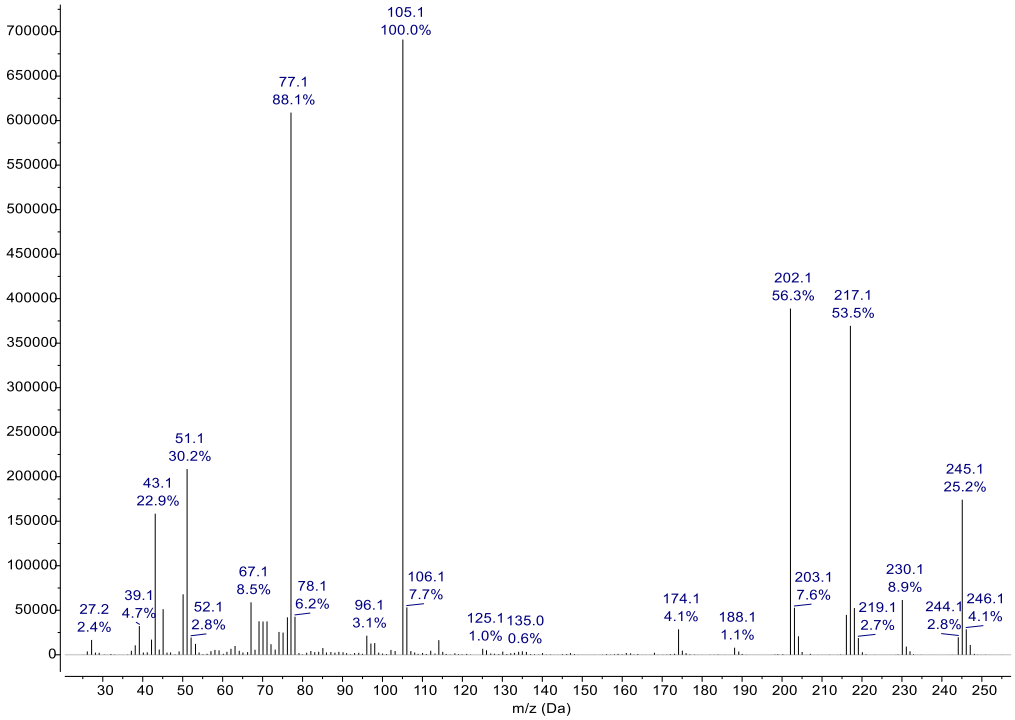
11) 2-benzoyl-6-bromo benzothiazole



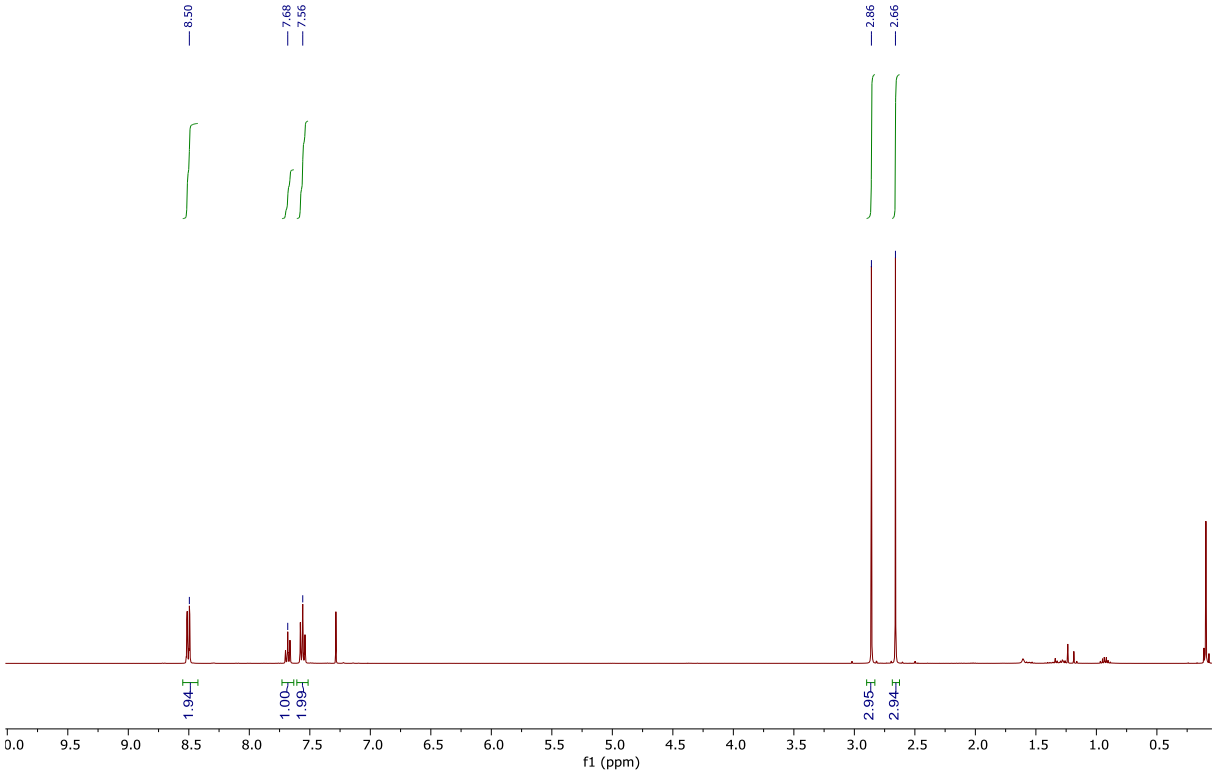
Supplementary Figure 26: Mass spectrum (EI, 70 eV) of 2-benzoyl-6-bromo benzothiazole.

12) 1-(2-benzoyl-4-methylthiazol-5-yl)ethenone

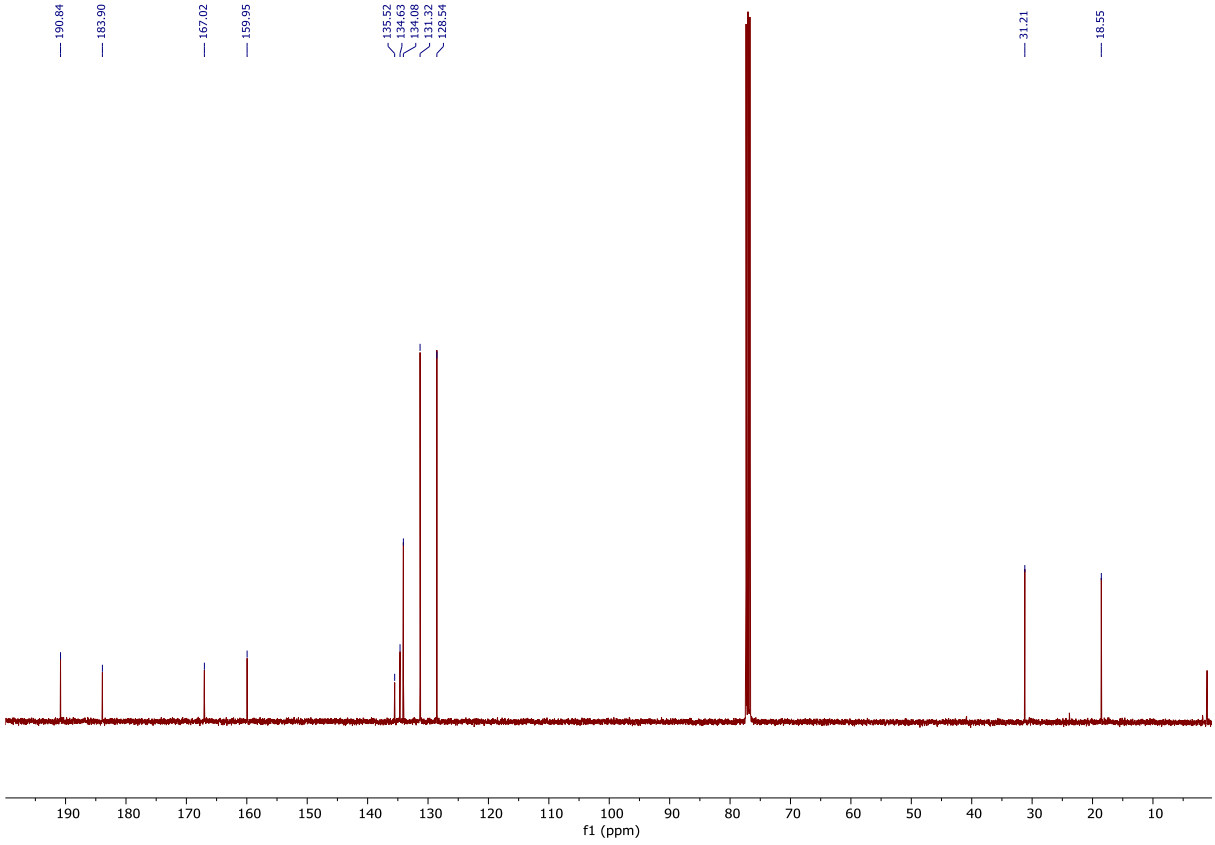




Supplementary Figure 27: Mass spectrum (EI, 70 eV) of 1-(2-benzoyl-4-methylthiazol-5-yl)ethenone.

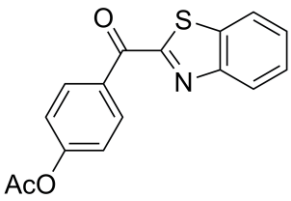


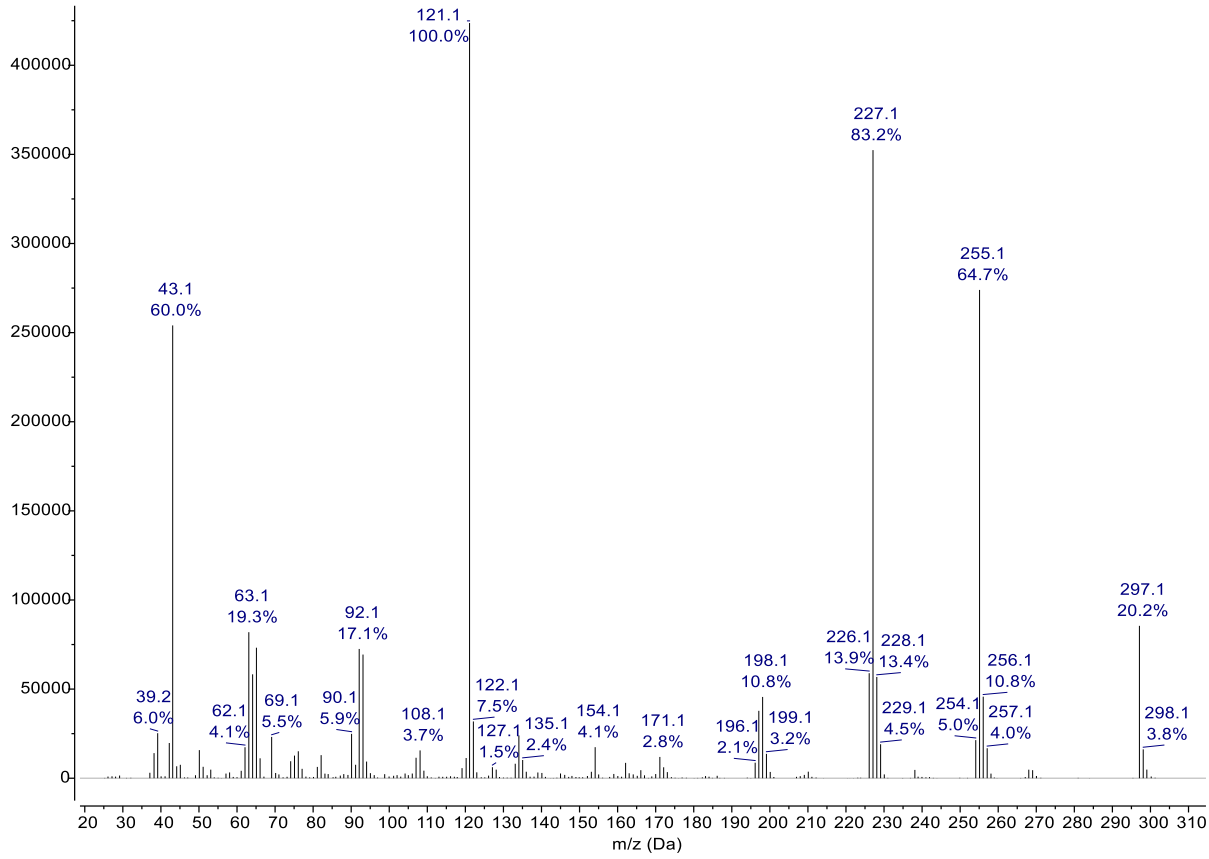
Supplementary Figure 28: ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of 1-(2-benzoyl-4-methylthiazol-5-yl)ethenone.



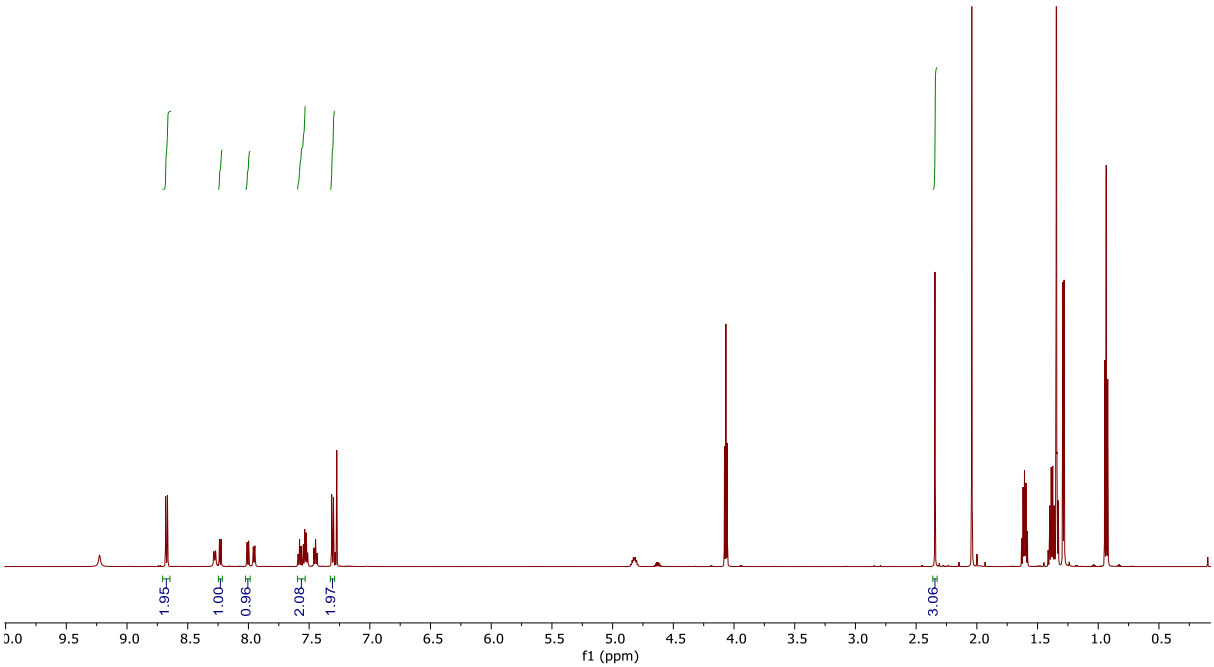
Supplementary Figure 29: $^{13}C\{^{1}H\}$-NMR spectrum (100 MHz, $CDCl_3$) of 1-(2-benzoyl-4-methylthiazol-5-yl)ethenone

13) 2-(4-acetoxybenzoyl)benzothiazole

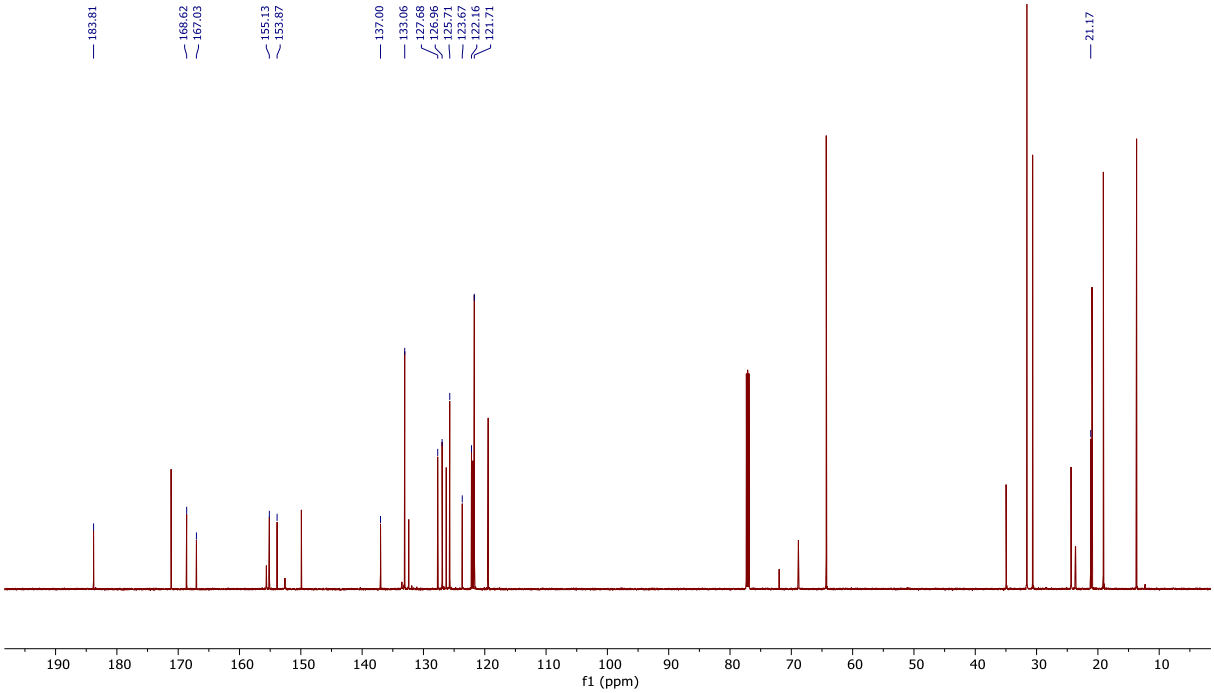




Supplementary Figure 30: Mass spectrum (EI, 70 eV) of 2-(4-acetoxybenzoyl)benzothiazole.

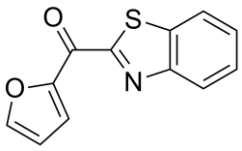


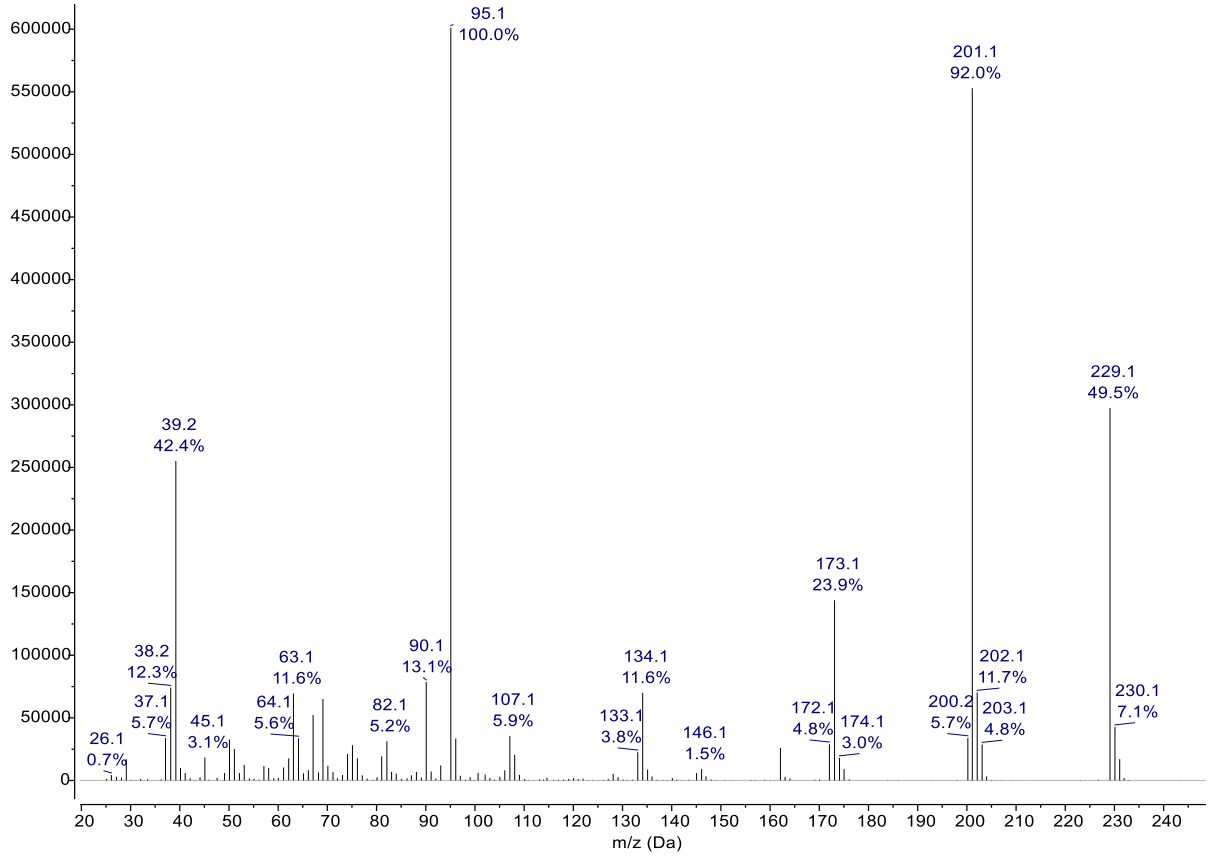
Supplementary Figure 31: ^{1}H-NMR spectrum (600 MHz, $CDCl_3$) of crude reaction mixture of the cross-coupling of S-ethyl-4-acetoxythiobenzoate and benzothiazole.



Supplementary Figure 32: ^{13}C-NMR spectrum (150 MHz, $CDCl_3$) of crude reaction mixture of the cross-coupling of S-ethyl-4-acetoxythiobenzoate and benzothiazole.

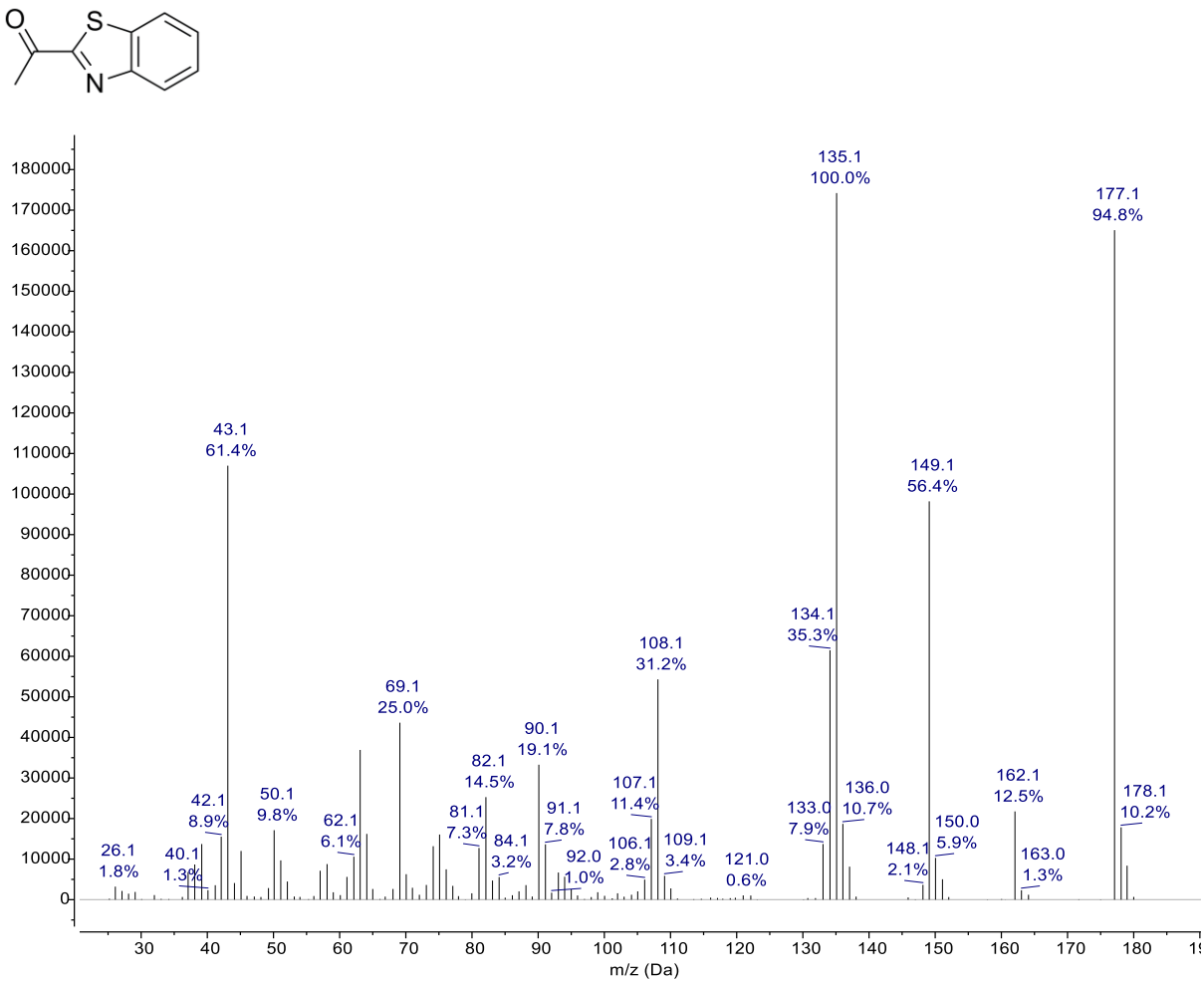
14) 2-furoyl benzothiazole





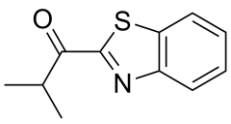
Supplementary Figure 33: Mass spectrum (EI, 70 eV) of 2-furoyl benzothiazole.

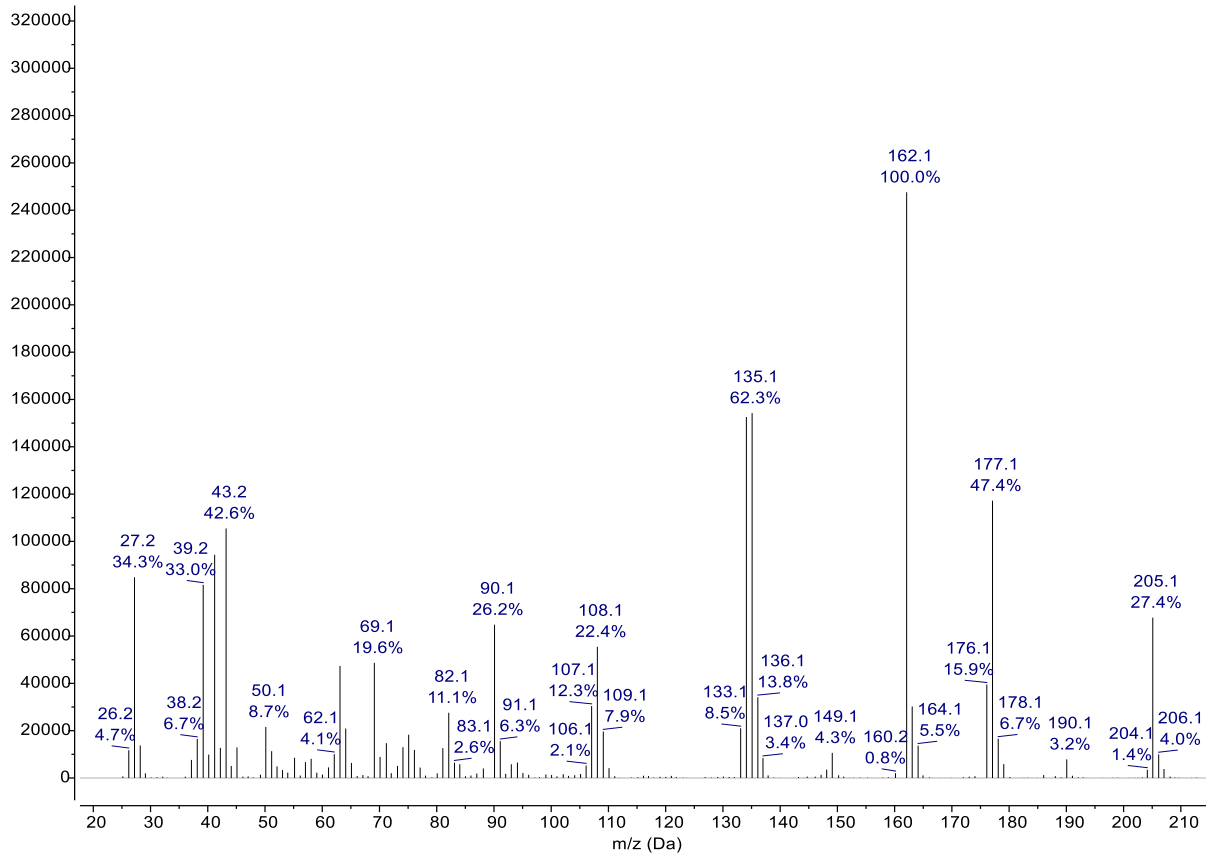
15) 2-acetyl benzothiazole



Supplementary Figure 34: Mass spectrum (EI, 70 eV) of 2-acetyl benzothiazole.

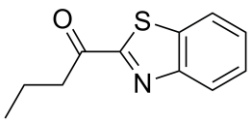
16) 2-isobutyryl benzothiazole

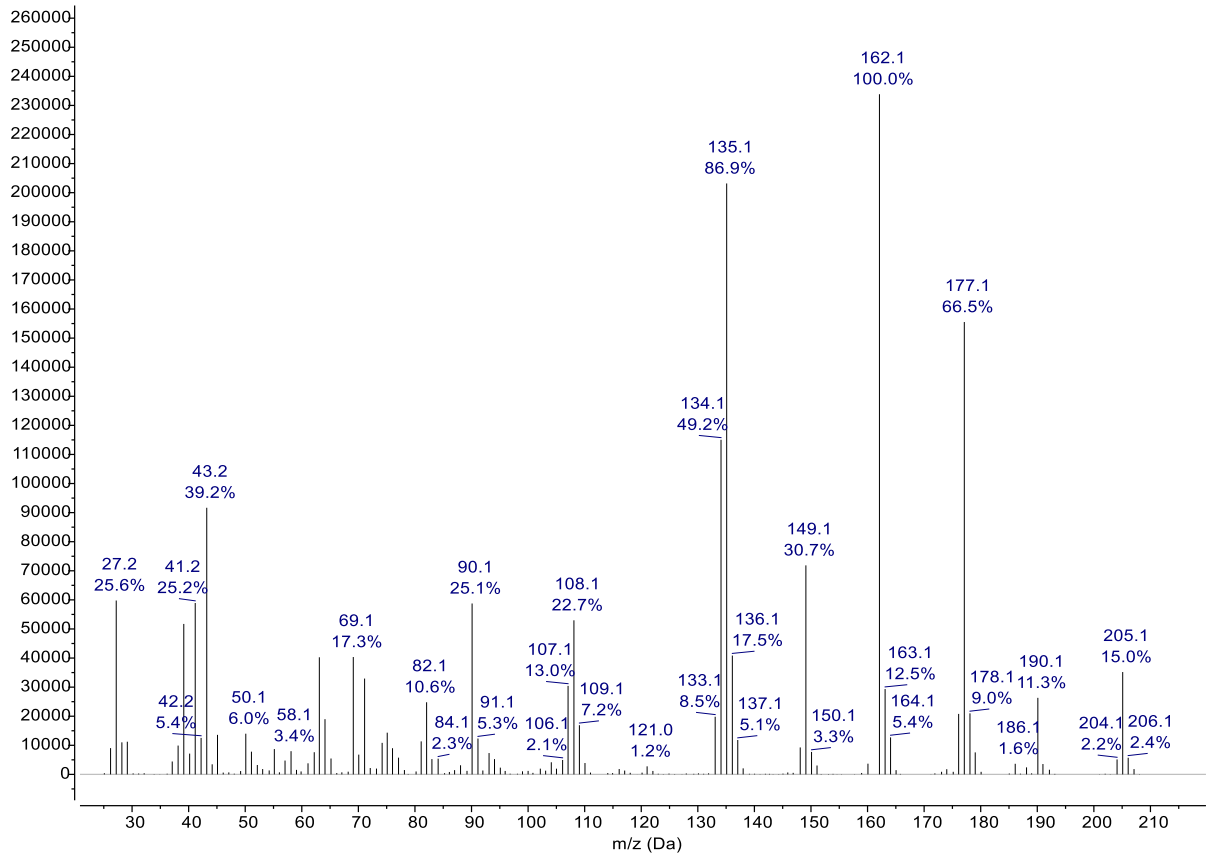




Supplementary Figure 35: Mass spectrum (EI, 70 eV) of 2-isobutyryl benzothiazole.

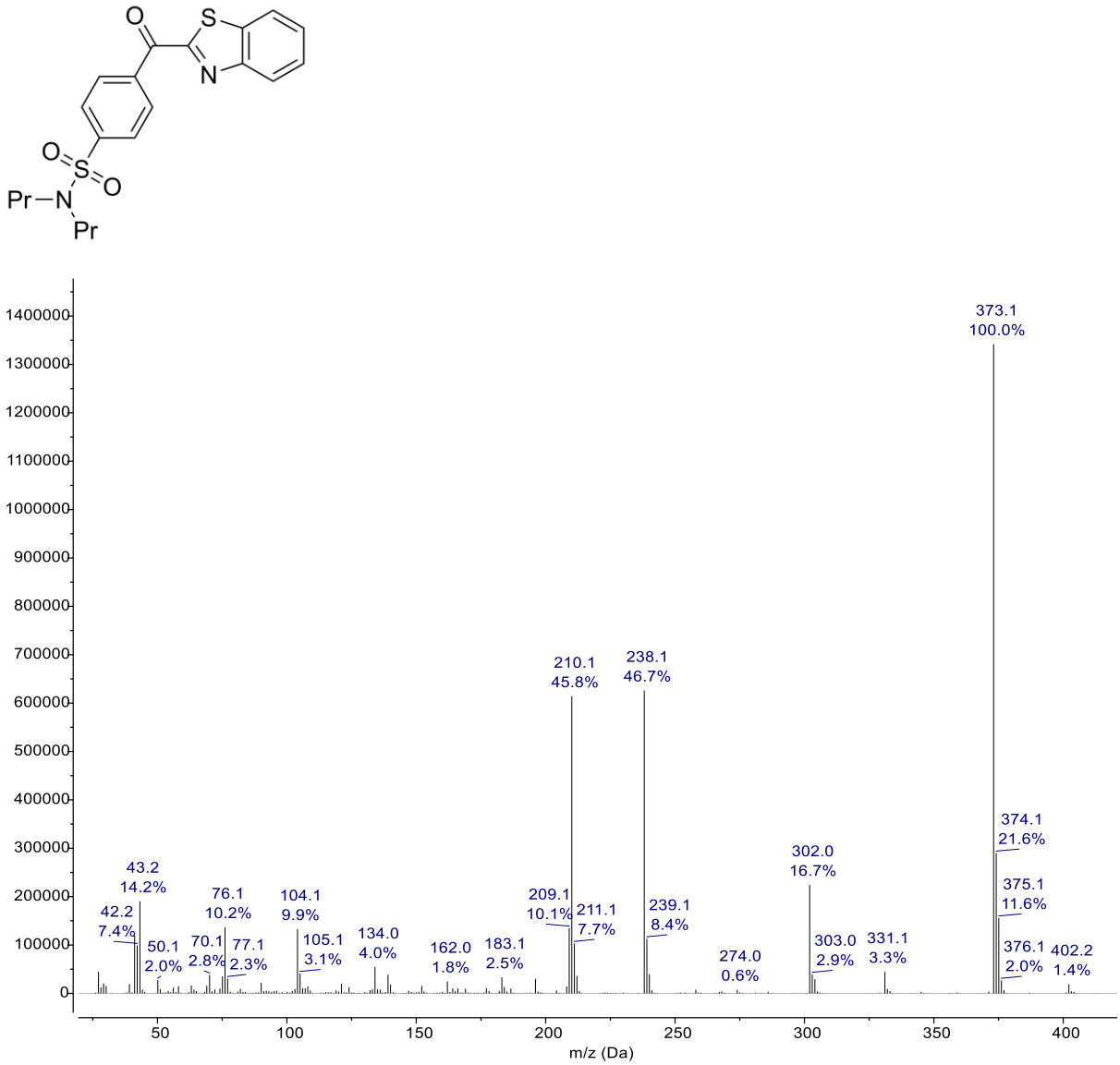
17) 2-butyryl benzothiazole



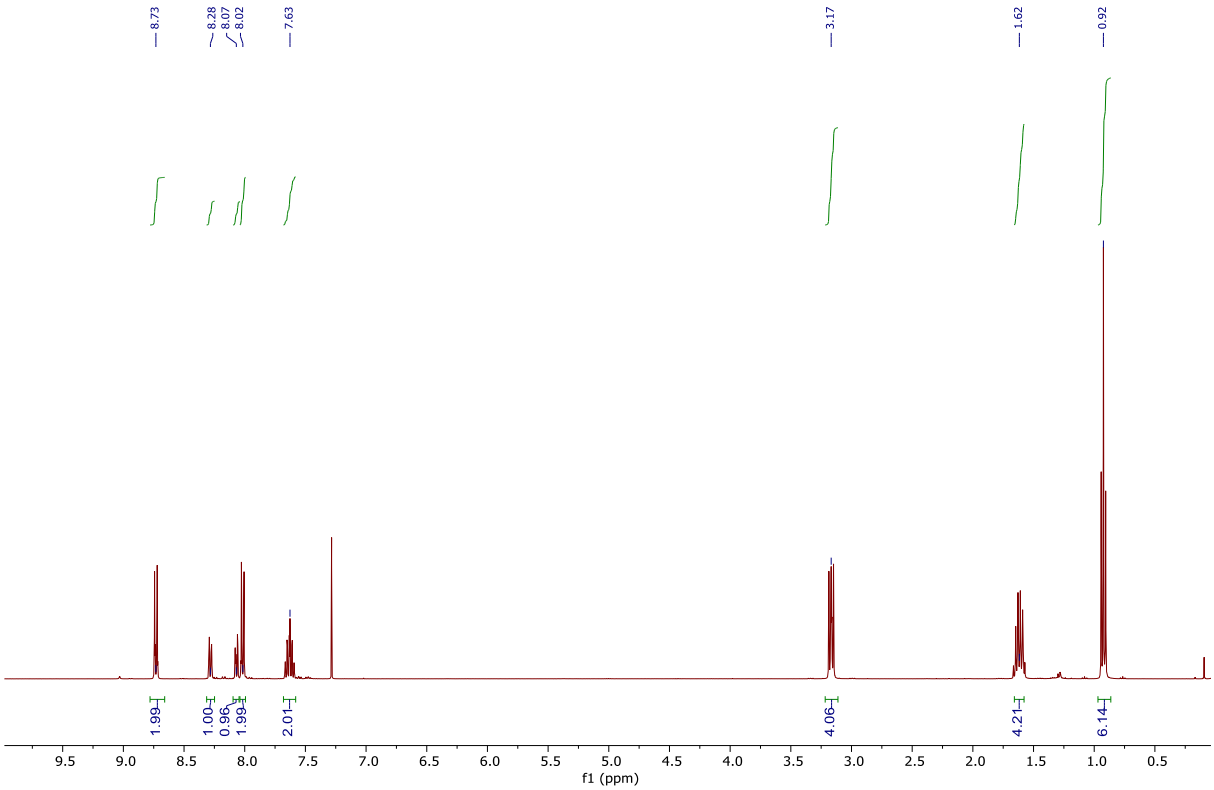


Supplementary Figure 36: Mass spectrum (EI, 70 eV) of 2-butyryl benzothiazole.

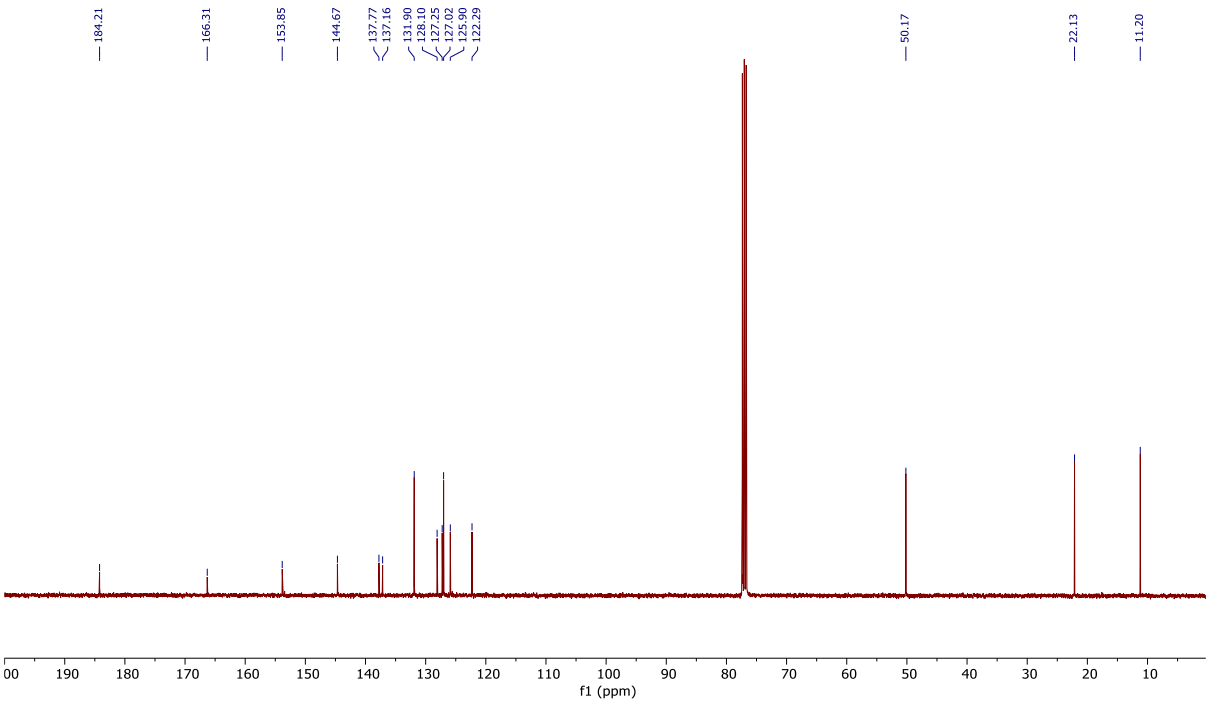
18) 4-(benzo[d]thiazole-2-carbonyl)-N,N-dipropylbenzenesulfonamide



Supplementary Figure 37: Mass spectrum (EI, 70 eV) of 4-(benzo[d]thiazole-2-carbonyl)-N,N-dipropylbenzenesulfonamide.

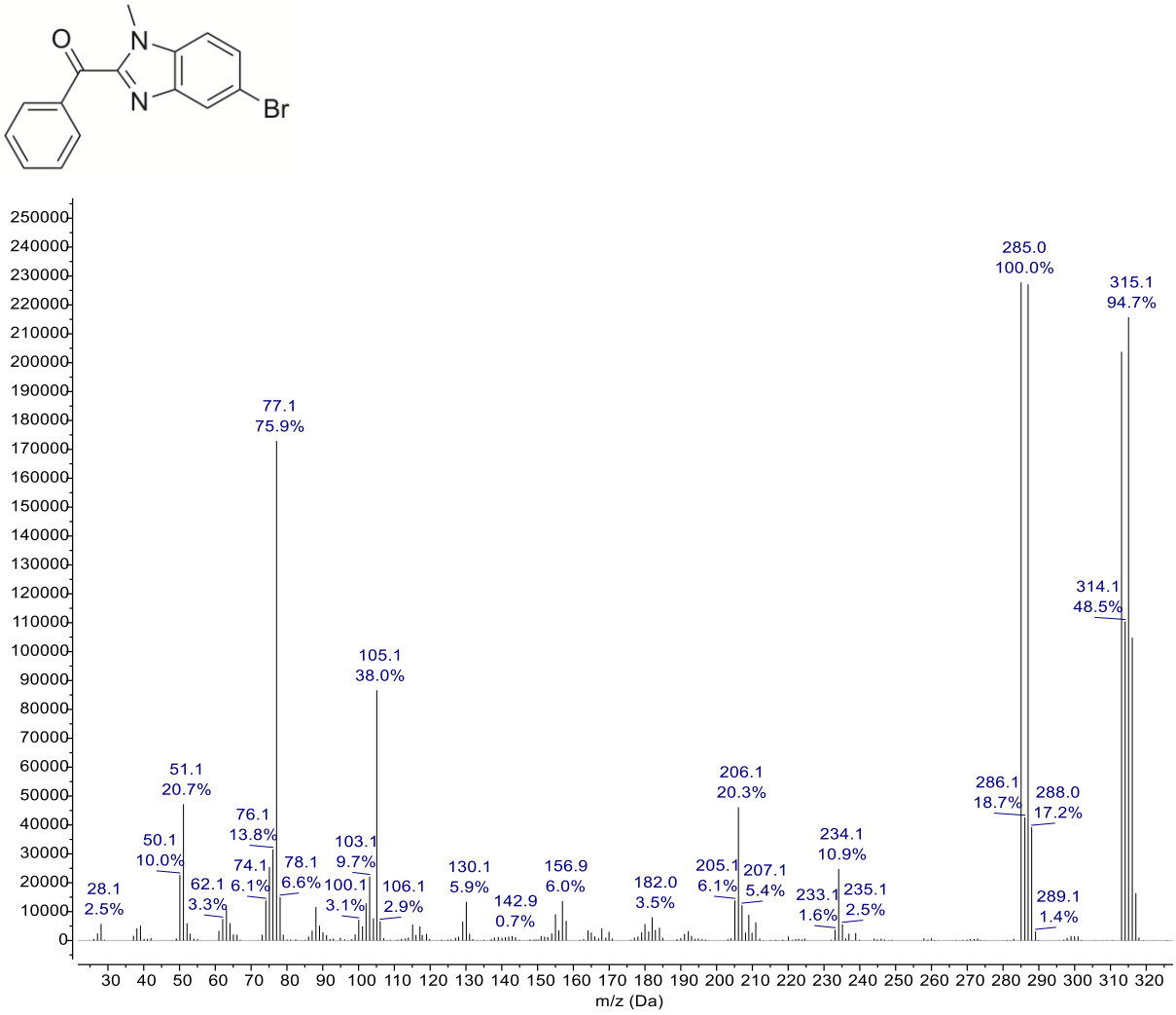


Supplementary Figure 38: ^{1}H-NMR spectrum (400 MHz, $CDCl_3$) of 4-(benzo[d]thiazole-2-carbonyl)-N,N-dipropylbenzenesulfonamide.



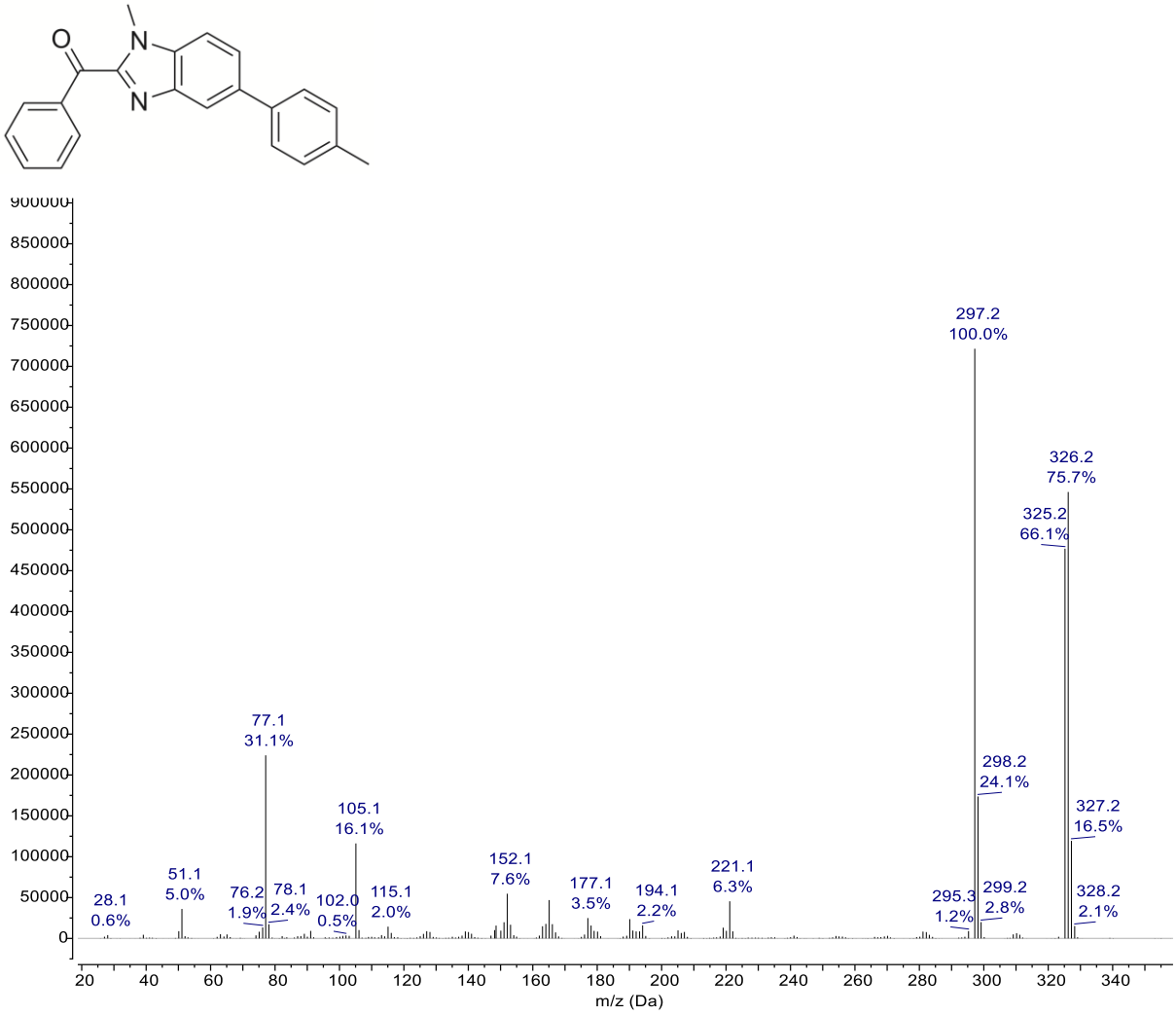
Supplementary Figure 39: $^{13}C\{^{1}H\}$-NMR spectrum (100 MHz, $CDCl_3$) of 4-(benzo[d]thiazole-2-carbonyl)-N,N-dipropylbenzenesulfonamide.

19) 2-benzoyl-5-bromo-1-methyl benzimidazole



Supplementary Figure 40: Mass spectrum (EI, 70 eV) of 2-benzoyl-5-bromo-1-methyl benzimidazole.

20) 2-benzoyl-5-(*p*-tolyl)-1-methyl benzimidazole



Supplementary Figure 41: Mass spectrum (EI, 70 eV) of 2-benzoyl-5-(p-tolyl)-1-methyl benzimidazole.

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