SUPPORTING INFORMATION

Copper-mediated cross-coupling of phenylboronic acid and 2(1*H*)-Pyrazinones facilitated by Microwave Irradiation with Simultaneous Cooling

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General Remarks:

^1H NMR spectra were recorded on a Bruker Avance 300 MHz instrument, using CDCl_3 as solvent unless otherwise stated. The ^1H and ^{13}C chemical shifts are reported in ppm relative to tetramethylsilane, using the residual solvent signal as an internal reference. Mass spectra were recorded by using a Kratos MS50TC and a Kratos Mach III data system. The ion source temperature was 150-250°C as required. High resolution EI-mass spectra were performed with a resolution of 10000. The low resolution spectra were obtained with a HP5989A MS instrument. For thin layer chromatography, analytical TLC plates (Alugram SIL G/UV₂₅₄ and 70-230 mesh silicagel (E.M.Merck)) were used. All reagents purchased from commercial sources were used without further purification.

Microwave Irradiation Experiments:

All microwave irradiation experiments were carried out in a dedicated CEM-Discover-CoolmateTM monomode microwave apparatus (CEM Corporation P.O. Box 200 Matthews, NC 28106), operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300 W. The reactions were carried out in an open 10 mL double walled glass vial which was cooled to 0 °C using a microwave transparent cooling liquid. The temperature was measured with a fiber-optic device inserted into the reaction vessel.

General Procedure of Chan-Lam Coupling of Pyrazinone 1 with Boronic Acids 2a-f,i,j:

A) Chan-Lam Condition: To a suspension of pyrazinone **1** (0.05 g, 0.21 mmol) in CH_2Cl_2 (3 mL) were added boronic acid **2a-f,i,j** (0.42 mmol, 2 equiv), $\text{Cu}(\text{OAc})_2$ (0.076 g, 0.42 mmol, 2 equiv) and Et_3N (0.06 mL, 0.43 mmol, 2 equiv). The reaction mixture was stirred at r.t. for 12 h in ambient atmosphere. After completion of the reaction, the solvent was evaporated. The crude product was then absorbed on silica gel and the residue was purified by column chromatography over silica gel using n-Hexane/ CH_2Cl_2 (1:1) as the eluent, to give the N-arylated pyrazinones **3a-f,i,j**.

B) Upon microwave irradiation with simultaneous cooling at 0 °C : To a suspension of pyrazinone **1** (0.05 g, 0.21 mmol) in CH₂Cl₂ (3 mL) were added boronic acid **2a-f,i,j** (0.42 mmol, 2 equiv), Cu(OAc)₂ (0.076 g, 0.42 mmol, 2 equiv), Et₃N (0.021 g, 0.22 mmol, 1 equiv) and pyridine (0.033 g, 0.84 mmol, 2 equiv). The mixture was irradiated at 0°C for 1 h, continuously at the maximum power of 300 W. After completion of the reaction the solvent was evaporated. The crude product was then absorbed on silica gel and the residue was purified by column chromatography over silica gel using n-Hexane/ CH₂Cl₂ (1:1) as the eluent, to give the N-arylated pyrazinones **3a-f,i,j**.

5-Chloro-1-(3-trifluoromethyl)-3-(phenylthio)-2(1H)-pyrazinone (3a). It was obtained as a yellow solid m.p. 172.4-173.8 °C in 93 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.0 (s, 1H), 7.93-7.82 (m, 3H), 7.61-7.58 (m, 3H), 7.51-7.49 (m, 3H); ¹³C NMR (75 MHz, CDCl₃): 161.2, 153.2, 140.7, 136.4, 132.4, 132.0, 131.7, 130.9, 130.6, 129.2, 128.6, 127.1, 125.0, 124.9, 123.9, 123.3 and 119.7. HRMS (EI): calcd for C₁₇H₁₀ClF₃N₂OS: 382.0154, found: 382.0146.

5-Chloro-1-(3-chlorophenyl)-3-(phenylthio)-2(1H)-pyrazinone (3b). It was obtained as a yellow solid m.p. 162-163 °C in 97 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.58-7.55 (m, 2H), 7.44-7.3 (m, 7H), 7.01 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): 161.1, 151.8, 139.1, 135.2, 130.5, 129.6, 129.2, 127.3, 127.1, 126.1, 124.0 and 120.8. HRMS (EI): calcd for C₁₆H₁₀Cl₂N₂OS: 347.9890, found: 347.9888.

1-(3-Bromophenyl)-5-chloro-3-(phenylthio)-2(1H)-pyrazinone (3c). It was obtained as a yellow solid m.p. 160 °C (decom) in 88 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.6-7.55 (m, 4H), 7.46-7.37 (m, 5H), 7.01 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): 165.1, 156.3, 143.5, 139.3, 137.0, 135.2, 134.0, 133.6, 133.3, 131.8, 131.5, 128.9, 127.1 and 125.5. HRMS (EI): calcd for C₁₆H₁₀BrClN₂OS: 391.9385, found: 391.9388.

5-Chloro-1-(3-ethoxyphenyl)-3-(phenylthio)-2(1H)-pyrazinone (3d). It was obtained as a yellow solid m.p. 155-156 °C in 64 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.59-7.56 (m, 2H), 7.45-7.35 (m, 4H), 7.0 (s, 1H), 6.98-6.93 (m, 3H), 4.07-4.0 (q, *J* = 7.3 Hz, 2H), 1.4-1.4 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): 160.8, 159.6, 152.0, 139.3, 135.0, 130.3, 129.5, 129.2, 127.6, 126.8, 121.6, 117.4, 115.8, 111.9, 63.8, and 14.6. HRMS (EI): calcd for C₁₈H₁₅ClN₂O₂S: 358.0542, found: 358.0537.

5-Chloro-1-(4-methoxyphenyl)-3-(phenylthio)-2(1H)-pyrazinone (3e). It was obtained as a yellow solid m.p. 202-204 °C (decom) in 69 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.58-7.56 (m, 2H), 7.45-7.44 (m, 3H), 7.34-7.31 (d, *J* = 9.13 Hz, 2H), 7.03-7.0 (d, *J* = 8.2 Hz, 2H), 6.97 (s, 1H), 3.84 (s, 3H); ¹³C NMR (75 MHz, CDCl₃): 160.5, 159.9, 152.3, 135.0, 131.1, 129.4,

127.7, 127.5, 126.8, 121.9, 114.6 and 55.5. HRMS (EI): calcd for $C_{17}H_{13}ClN_2O_2S$: 344.0386, found: 344.0379.

5-Chloro-1-phenyl-3-(phenylthio)-2(1H)-pyrazinone (3f). It was obtained as a yellow solid m.p. 194-196 °C in 94 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.57-7.4 (m, 10H), 7.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): 161.6, 152.1, 138.2, 135.0, 129.58, 129.36, 129.1, 128.9, 127.38, 127.05, 125.5 and 121.56. HRMS (EI): calcd for $C_{16}H_{11}ClN_2OS$: 314.0286, found: 314.0281.

5-Chloro-1-(4-phenoxyphenyl)-3-(phenylthio)-2(1H)-pyrazinone (3i). It was obtained as a yellow solid m.p. 162.6-164 °C in 53 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.56-7.44 (m, 2H), 7.41-7.36 (m, 7H), 7.19-7.04 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): 160.7, 158.3, 155.8, 152.2, 135.0, 132.8, 130.0, 129.5, 129.2, 127.6, 127.1, 126.9, 124.3, 121.6, 119.7, and 118.7. HRMS (EI): calcd for $C_{22}H_{15}ClN_2O_2S$: 406.0542, found: 406.0543.

5-Chloro-1-(2-naphthyl)-3-(phenylthio)-2(1*H*)-pyrazinone (3j). It was obtained as a yellow solid m.p. 169.8-171.2 °C in 91 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.97-7.85 (m, 5H), 7.62-7.44 (m, 7H), 7.16 (s, 1H); ¹³C NMR (75 MHz, CDCl₃): 161.1, 153.4, 137.8, 136.4, 134.5, 134.3, 130.8, 130.6, 130.3, 129.5, 129.4, 129.1, 128.5, 128.2, 127.0, 126.3, 125.2, and 124.5 HRMS (EI): calcd for C₂₀H₁₃ClN₂OS: 364.0437, found: 364.0438.

3a ¹H NMR

3a ¹³C NMR

13C (zgpg30)

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*** Current Data Parameters ***
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EXPNO     : 2
PROCNO    : 1
*** Acquisition Parameters ***
AQ_mod    : qsm
BF2       : 300.1300000 MHz
BF3       : 300.1300000 MHz
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DATE_d    : Jan 09 2006
DECNUC    : off
DS         : 2
LOCNUC    : 2H
NS         : 1065
NUC1      : 13C
NUC2      : 1H
PARMODE   : 1D
PULPROG   : zgpg30
SFO1      : 75.4760204 MHz
SFO2      : 300.1312005 MHz
SFO3      : 300.1300000 MHz
SOLVENT   : DMSO
SW        : 249.5149 ppm
TE        : 300.0 K
*** Processing Parameters ***
LB        : 1.00 Hz
*** 1D NMR Plot Parameters ***
SOLVENT   : ?

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3b ^1H NMR

3b ^{13}C NMR

*** Current Data Parameters ***

NAME : bks-2

EXPNO : 2

PROCNO : 1

*** Acquisition Parameters ***

AQ_mod : qsin

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BF3 : 300.1300000 MHz

DATE_1 : 11:41:57

DATE_d : Nov 25 2005

DECNUC : off

DS : 2

LOCNUC : ^2H

NS : 3584

NUC1 : ^{13}C

NUC2 : ^1H

PARAMODE : 1D

PULPROG : zgpg30

SFO1 : 75.4760204 MHz

SFO2 : 300.1312005 MHz

SFO3 : 300.1300000 MHz

SOLVENT : CDCl₃

SW : 249.5149 ppm

TE : 300.0 K

*** Processing Parameters ***

LB : 1.00 Hz

*** ID NMR Plot Parameters ***

SOLVENT : ?

3c ^1H NMR*1D proton, long sweepwith*

3c ^{13}C NMR

*** Current Data Parameters ***

NAME	:	bkw
EXPNO	:	6
PROCNO	:	1

*** Acquisition Parameters ***

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BF2	:	300.130000 MHz
BF3	:	300.130000 MHz
DATE_1	:	18-31-21
DATE_d	:	Jan 02 2006
DECNUC	:	off
DS	:	2
LOCNUC	:	2H
NS	:	4608
NUC1	:	^{13}C
NUC2	:	^1H
PARAMODE	:	1D
PULPROG	:	zgpg30
SFO1	:	75.4760204 MHz
SFO2	:	300.1312005 MHz
SFO3	:	300.1300000 MHz
SOLVENT	:	CDCl3
SW	:	249.5149 ppm
TE	:	300.0 K

*** Processing Parameters ***

LB	:	1.00 Hz
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*** 1D NMR Plot Parameters ***

SOLVENT	:	?
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3d ¹H NMR **3d ¹³C NMR**

*** Current Data Parameters ***

NAME :	bks-7
EXPNO :	2
PROCNO :	1

*** Acquisition Parameters ***

AQ_mod :	gsim
BF2 :	300.1300000 MHz
BF3 :	300.1300000 MHz
DATE_1 :	16-21-51
DATE_d :	Nov 28 2005
DECNUC :	off
DS :	2
LOCNUC :	2H
NS :	6144
NUC1 :	¹³ C
NUC2 :	¹ H
PARAMODE :	1D
PULPROG :	zgpg30
SFO1 :	75.4760204 MHz
SFO2 :	300.1312005 MHz
SFO3 :	300.1300000 MHz
SOLVENT :	CDCl ₃
SW :	249.5149 ppm
TE :	300.0 K

*** Processing Parameters ***

LB :	1.00 Hz
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*** 1D NMR Plot Parameters ***

SOLVENT :	?
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3e ¹H NMR

3e ^{13}C NMR

*** Current Data Parameters ***

NAME	:	bks-6
EXPNO	:	2
PROCNO	:	1

*** Acquisition Parameters ***

AQ_mod	:	qsm
BF2	:	300.1300000 MHz
BF3	:	300.1300000 MHz
DATE_1	:	12-06-38
DATE_d	:	Nov 28 2005
DECNUC	:	qff
DS	:	2
LOCNUC	:	2H
NS	:	5120
NUC1	:	13C
NUC2	:	1H
PARMODE	:	1D
PULPROG	:	zgpg30
SFO1	:	75.4760204 MHz
SFO2	:	300.1312005 MHz
SFO3	:	300.1300000 MHz
SOLVENT	:	CDCl3
SW	:	249.5149 ppm
TE	:	300.0 K

*** Processing Parameters ***

LB	:	1.00 Hz
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*** ID NMR Plot Parameters ***

SOLVENT	:	?
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3f ¹H NMR

3f ^{13}C NMR

*** Current Data Parameters ***

NAME : bkr
 EXPNO : 8
 PROCNO : 1

*** Acquisition Parameters ***

AQ_mod : qsin
 BF2 : 300.1300000 MHz
 BF3 : 300.1300000 MHz

DATE_1 : 21:44:38
 DATE_2 : Jan 02 2006

DECNUC : off
 DS : 2

LOCNUC : 2H
 NS : 4608

NUC1 : ^{13}C
 NUC2 : ^1H

PARAMODE : 1D
 PULPROG : zgpg30

SFO1 : 75.4760204 MHz
 SFO2 : 300.1312005 MHz

SFO3 : 300.1300000 MHz
 SOLVENT : CDCl3

SW : 249.5149 ppm
 TE : 300.0 K

*** Processing Parameters ***

LB : 1.00 Hz
 *** 1D NMR Plot Parameters ***

SOLVENT : ?

3i ¹H NMR

1D proton, long sweep with

*** Current Data Parameters ***

NAME :	bks-8
EXPNO :	1
PROCNO :	1

*** Acquisition Parameters ***

AQ_mod :	qsim
BF2 :	300.1300000 MHz
BF3 :	300.1300000 MHz
DATE_1 :	08:23:06
DATE_d :	Nov 28 2005
DECNUC :	off
DS :	0
LOCNUC :	2H
NS :	16
NUC1 :	1H
NUC2 :	off
PARAMODE :	1D
PULPROG :	zg30
SFO1 :	300.1313730 MHz
SFO2 :	300.1300000 MHz
SFO3 :	300.1318534 MHz
SOLVENT :	DMSO
SW :	24.9392 ppm
TE :	300.0 K

*** Processing Parameters ***

LB :	0.30 Hz
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*** 1D NMR Plot Parameters ***

SOLVENT :	?
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3i ¹³C NMR

3j ^1H NMR

*** Current Data Parameters ***

NAME : bk-11

EXPNO : 2

PROCNO : 1

*** Acquisition Parameters ***

AQ_mod : qsm

BF2 : 300.1300000 MHz

BF3 : 300.1300000 MHz

DATE_1 : 03-23-25

DATE_d : Jan 10 2006

DECNUC : off

DS : 0

LOCNUC : 2H

NS : 16

NUC1 : 1H

NUC2 : off

PARMODE : 1D

PULPROG : zg30

SFO1 : 300.1313730 MHz

SFO2 : 300.1300000 MHz

SFO3 : 300.1318534 MHz

SOLVENT : CDCl3

SW : 24.9392 ppm

TE : 300.0 K

*** Processing Parameters ***

LB : 0.30 Hz

*** 1D NMR Plot Parameters ***

SOLVENT : ?

3j ^{13}C NMR

*** Current Data Parameters ***

NAME	:	bky
EXPNO	:	4
PROCNO	:	1

*** Acquisition Parameters ***

AQ_mod	:	qsim
BF2	:	300.130000 MHz
BF3	:	300.130000 MHz
DATE_1	:	15:17:01
DATE_2	:	Jan 02 2006
DECNUC	:	off
DS	:	2
LOCNUC	:	2H
NS	:	4608
NUC1	:	^{13}C
NUC2	:	^1H
PARMODE	:	1D
PULPROG	:	zgpg30
SFO1	:	75.4760204 MHz
SFO2	:	300.1312005 MHz
SFO3	:	300.1300000 MHz

SOLVENT : Acetone

SW	:	249.5149 ppm
TE	:	300.0 K

*** Processing Parameters ***

LB	:	1.00 Hz
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*** 1D NMR Plot Parameters ***

SOLVENT	:	?
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