Copper-Diamine Catalyzed *N*-Arylation of Pyrroles, Pyrazoles, Indazoles, Imidazoles, and Triazoles

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Supporting Information

Table of Contents

General Procedure for the <i>N</i> -Arylation of Nitrogen Heterocycles	S2
¹ H NMR spectrum of 1-(4'-Methylphenyl)-2-acetylpyrrole	S3
¹³ C NMR spectrum of 1-(4'-Methylphenyl)-2-acetylpyrrole	S4
¹ H NMR spectrum of 1-(3'-Pyridine)-ethyl-4-pyrazolecarboxylate	S5
¹³ C NMR spectrum of 1-(3'-Pyridine)-ethyl-4-pyrazolecarboxylate	S6
¹ H NMR spectrum of 3,5-Dimethyl-1-phenylpyrazole	S7
¹³ C NMR spectrum of 3,5-Dimethyl-1-phenylpyrazole	S8
¹ H NMR spectrum of 1-(3'-Aminomethylphenyl)-2,4-triazole	S9
¹³ C NMR spectrum of 1-(3'-Aminomethylphenyl)-2,4-triazole	S10
X-ray data for 1-Phenyl-3-(trifluoromethyl)-ethylpyrazole-4-carboxylate	S11
NOE difference spectra for 2,5-Diphenyl-3-amino-pyrazole	S16

A General Procedure for the *N*-Arylation of Nitrogen Heterocycles.

To a resealable Schlenk tube or alternatively, a screw-cap test tube, were added CuI, the heterocycle (1.00 equiv), base (2.10 mmol), and a stir bar. The reaction vessel was fitted with a rubber septum, was evacuated and back-filled with argon, and this sequence was repeated an additional time. The aryl halide (1.20 equiv), diamine (10-20 mol%) and solvent (1 mL) were then added successively under a stream of argon. The reaction tube was sealed (caution: build-up of pressure possible; use a safety shield) and immersed in a preheated oil bath at 110 °C for 24 h and the solution was stirred with the aid of a magnetic stirrer. The reaction mixture was removed from heating, allowed to attain ambient temperature, diluted with ethyl acetate (2-3 mL), filtered through a plug of silica gel or Celite, and eluted with additional ethyl acetate (10-20 mL). The filtrate was concentrated and the resulting residue was purified by silica gel column chromatography (2 X 25 cm of silica) to provide the desired product.

Current Date Parameters
NAME Nov02-2001-41s
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20011102
Time 10.20
INSTRUM spect
PROBHD 5mm BBO BB-1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 20125.629 Hz
FIDRES 0.36387 Hz
AQ 1.3042164 sec
RG 4096
DN 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00020000 sec

===== CHANNEL f1 =====
NUC1 13C
P1 15.25 usec
PL1 3.00 dB
SF01 100.6237959 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 107.50 usec
PL2 0.00 dB
PL12 24.00 dB
PL13 24.00 dB
SF02 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128008 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.00 cm
F1P 207.394 ppm
F1 20866.47 Hz
F2P -515.28 ppm
F2 -515.28 Hz
PRACH 10.62576 ppm/cm
HZCM 1069.08728 Hz/cm

3176

Current Data Parameters
 NAME Aug15-2001-4ja
 EXPNO 10
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20010815
 Time 15.26
 INSTRUM spect
 PROBHD 5mm BBO BB-1
 PULPROG zg30
 TD 65536
 SOLVENT CDCl3
 NS 16
 DS 2
 SWH 8278.146 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 40.3
 DW 60.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 7.90 usec
 PL1 0.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1299729 MHz
 WDW EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 20.00 cm
 F1P 10.102 ppm
 F1 4042.15 Hz
 F2P -0.219 ppm
 F2 -87.78 Hz
 PPMCM 0.51607 ppm/cm
 HZCM 206.49681 Hz/cm

3176

Current Data Parameters
NAME Aug15-2001-4ja
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20010815
Time 15.30
INSTRUM spect
PROBHD 5mm BBO BB-1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 3251
DM 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

----- CHANNEL f1 -----
NUC1 13C
P1 15.25 usec
PL1 3.00 dB
SF01 100.6237959 MHz

----- CHANNEL f2 -----
CPDPRG2 waltz16
NUC2 1H
PCPD2 107.50 usec
PL2 0.00 dB
PL12 24.00 dB
PL13 24.00 dB
SF02 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127840 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

10 NMR plot parameters
CX 20.00 cm
F1P 202.324 ppm
F1 20356.42 Hz
F2P -4.954 ppm
F2 -498.40 Hz
PPMCM 10.36390 ppm/cm
HZCM 1042.74133 Hz/cm

4232

TABLE 2 - Entry 12

Current Data Parameters
 NAME Jul19-2002-41a
 EXPNO 30
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020719
 Time 9.25
 INSTRUM spect
 PROBHD 5mm BBO BB-1
 PULPROG zg30
 TO 65636
 SOLVENT CDCl3
 NS 16
 DS 2
 SMH 8278.145 Hz
 FIDRES 0.126314 Hz
 AQ 3.9584243 sec
 RG 32
 DM 60.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

----- CHANNEL f1 -----
 NUC1 1H
 P1 7.90 usec
 PL1 0.00 dB
 SFO1 400.1324710 MHz

F2 - Processing parameters
 SI 32768
 SF 400.1300050 MHz
 NDM EM
 SSB 0
 LB 0.30 Hz
 GB 0
 PC 1.00

ID NMR plot parameters
 CX 20.00 cm
 F1P 10.387 ppm
 F1 4156.25 Hz
 F2P -0.277 ppm
 F2 -110.73 Hz
 PPMCM 0.53320 ppm/cm
 HZCM 213.34958 Hz/cm

TABLE 2-Entry 12

Current Data Parameters
NAME Jul19-2002-4ja
EXPNO 31
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020719
Time 9.28
INSTRUM spect
PROBHD 5mm BBO BB-1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 25125.629 Hz
FIDRES 0.363387 Hz
AQ 1.3042164 sec
RG 4096
DM 19.900 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

----- CHANNEL f1 -----
NUC1 13C
P1 15.25 usec
PL1 3.00 dB
SFO1 100.6237959 MHz

----- CHANNEL f2 -----
CPDPRG2 waltz16
NUC2 1H
PCPD2 107.50 usec
PL2 0.00 dB
PL12 24.00 dB
PL13 24.00 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127909 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

ID NMR plot parameters
CX 20.00 cm
F1P 206.942 ppm
F1 20820.97 Hz
F2P -144.78 Hz
F2 10.41903 ppm/cm
PRMCM 1046.26784 Hz/cm
HZCM

TABLE 5-Entry 4

JB-I-112
exp2 std13c
SAMPLE DEC. & VT
date Apr 10 2002 dfreq 300.100
solvent CDCl3 dn H1
file exp dpwr 38
ACQUISITION dof 0
tn 75.482 dm 999
at 2.561 dmf 11000
np 113148 PROCESSING
sw 22824.4 lb 0.50
fb 12400 wtf11e
ds 16 proc rt
tpwr 55 fn 282144
pu 7.0
d1 0 werr
tof -26.0 wexp
nt 128 wbs
ct 128 wnt
elock n
deln not used
FLAGS
il n
in n
dp y
DISPLAY
sp 816.2
vp 12137.9
vs 162
sc 0
wc 250
hzmm 48.55
ls 500.40
rf1 8816.4
rfp 8810.4
th 12
ins 100.000
na no ph

TABLE 5-Entry 4

X-ray crystallography data for 1-Phenyl-3-(trifluoromethyl)-ethylpyrazole-4-carboxylate (Entry 10, Table 2):

ORTEP diagram of 1-Phenyl-3-(trifluoromethyl)-ethylpyrazole-4-carboxylate. Thermal ellipsoids are at 30% probability. Hydrogen atoms are omitted for clarity.

Table 1. Crystal data and structure refinement for 1-Phenyl-3-(trifluoromethyl)-ethylpyrazole-4-carboxylate.

Identification code	Entry 10, Table 2	
Empirical formula	C ₁₃ H ₁₁ F ₃ N ₂ O ₂	
Formula weight	284.24	
Temperature	194(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 7.6108(6) Å	α = 78.0200(10)°
	b = 8.2366(7) Å	β = 82.745(2)°
	c = 11.3879(10) Å	γ = 66.9750(10)°
Volume	641.89(9) Å ³	
Z	2	
Density (calculated)	1.471 Mg/m ³	
Absorption coefficient	0.129 mm ⁻¹	

F(000)	292
Crystal size	0.47 x 0.18 x 0.08 mm ³
Theta range for data collection	1.83 to 23.31°.
Index ranges	-8<= <i>h</i> <=8, -9<= <i>k</i> <=9, -8<= <i>l</i> <=12
Reflections collected	2903
Independent reflections	1833 [R(int) = 0.0115]
Completeness to theta = 23.31°	98.5 %
Absorption correction	SADABS
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	1833 / 0 / 182
Goodness-of-fit on F ²	1.055
Final R indices [I>2sigma(I)]	R1 = 0.0411, wR2 = 0.1142
R indices (all data)	R1 = 0.0440, wR2 = 0.1176
Largest diff. peak and hole	0.312 and -0.239 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$). U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(2)	3779(2)	-1001(2)	1975(1)	46(1)
N(2)	-1028(2)	2747(2)	3595(1)	41(1)
N(1)	-76(2)	2454(2)	4600(1)	37(1)
F(1)	652(2)	2436(2)	806(1)	85(1)
F(2)	-245(2)	274(2)	1423(1)	77(1)
O(1)	5258(2)	-1111(2)	3584(1)	61(1)
F(3)	-2186(2)	2931(2)	1512(1)	92(1)
C(2)	1992(2)	710(2)	3427(2)	37(1)
C(4)	-1012(3)	3437(2)	5550(2)	38(1)
C(1)	220(3)	1694(2)	2889(2)	39(1)
C(3)	1722(3)	1251(2)	4519(2)	39(1)
C(9)	-114(3)	3059(3)	6610(2)	50(1)
C(11)	3829(3)	-544(2)	3020(2)	41(1)
C(6)	-3701(3)	5727(3)	6305(2)	52(1)
C(5)	-2792(3)	4781(3)	5385(2)	47(1)

C(10)	-391(3)	1816(3)	1666(2)	49(1)
C(12)	5547(3)	-2282(3)	1540(2)	50(1)
C(7)	-2832(3)	5346(3)	7372(2)	51(1)
C(13)	5148(4)	-2647(3)	387(2)	59(1)
C(8)	-1036(3)	4025(3)	7515(2)	56(1)

Table 3. Bond lengths [$\text{\AA}$] and angles [$^\circ$]

O(2)-C(11)	1.330(2)
O(2)-C(12)	1.452(2)
N(2)-C(1)	1.324(2)
N(2)-N(1)	1.361(2)
N(1)-C(3)	1.345(2)
N(1)-C(4)	1.433(2)
F(1)-C(10)	1.329(3)
F(2)-C(10)	1.315(2)
O(1)-C(11)	1.212(2)
F(3)-C(10)	1.323(2)
C(2)-C(3)	1.372(2)
C(2)-C(1)	1.414(3)
C(2)-C(11)	1.463(3)
C(4)-C(5)	1.378(3)
C(4)-C(9)	1.381(3)
C(1)-C(10)	1.495(3)
C(9)-C(8)	1.381(3)
C(6)-C(7)	1.376(3)
C(6)-C(5)	1.385(3)
C(12)-C(13)	1.497(3)
C(7)-C(8)	1.378(3)

C(11)-O(2)-C(12)	116.23(14)
C(1)-N(2)-N(1)	104.82(15)
C(3)-N(1)-N(2)	111.62(14)
C(3)-N(1)-C(4)	128.90(15)
N(2)-N(1)-C(4)	119.44(15)
C(3)-C(2)-C(1)	103.94(16)

C(3)-C(2)-C(11)	122.39(16)
C(1)-C(2)-C(11)	133.59(17)
C(5)-C(4)-C(9)	120.64(18)
C(5)-C(4)-N(1)	119.38(17)
C(9)-C(4)-N(1)	119.97(17)
N(2)-C(1)-C(2)	111.76(16)
N(2)-C(1)-C(10)	117.05(16)
C(2)-C(1)-C(10)	131.05(16)
N(1)-C(3)-C(2)	107.86(15)
C(8)-C(9)-C(4)	119.2(2)
O(1)-C(11)-O(2)	123.28(17)
O(1)-C(11)-C(2)	123.08(17)
O(2)-C(11)-C(2)	113.64(15)
C(7)-C(6)-C(5)	120.5(2)
C(4)-C(5)-C(6)	119.41(19)
F(2)-C(10)-F(3)	107.13(17)
F(2)-C(10)-F(1)	105.76(17)
F(3)-C(10)-F(1)	106.05(18)
F(2)-C(10)-C(1)	113.98(17)
F(3)-C(10)-C(1)	111.71(16)
F(1)-C(10)-C(1)	111.69(16)
O(2)-C(12)-C(13)	107.13(17)
C(6)-C(7)-C(8)	119.49(18)
C(7)-C(8)-C(9)	120.8(2)

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$). The anisotropic displacement factor exponent takes the form: $-2p^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U ¹¹	U ²²	U ³³	U ²³	U ¹³	U ¹²
O(2)	38(1)	55(1)	44(1)	-20(1)	-8(1)	-7(1)
N(2)	34(1)	50(1)	41(1)	-13(1)	-8(1)	-13(1)
N(1)	31(1)	46(1)	37(1)	-12(1)	-4(1)	-14(1)
F(1)	102(1)	120(1)	43(1)	-2(1)	-12(1)	-55(1)
F(2)	97(1)	70(1)	71(1)	-26(1)	-35(1)	-23(1)

O(1)	38(1)	77(1)	59(1)	-33(1)	-18(1)	4(1)
F(3)	57(1)	118(1)	75(1)	-47(1)	-37(1)	19(1)
C(2)	35(1)	41(1)	38(1)	-11(1)	-6(1)	-13(1)
C(4)	34(1)	47(1)	39(1)	-14(1)	2(1)	-19(1)
C(1)	34(1)	44(1)	40(1)	-12(1)	-6(1)	-13(1)
C(3)	32(1)	43(1)	41(1)	-9(1)	-8(1)	-11(1)
C(9)	40(1)	63(1)	43(1)	-15(1)	-4(1)	-12(1)
C(11)	38(1)	45(1)	41(1)	-12(1)	-8(1)	-11(1)
C(6)	41(1)	56(1)	58(1)	-24(1)	1(1)	-12(1)
C(5)	39(1)	56(1)	47(1)	-17(1)	-6(1)	-13(1)
C(10)	40(1)	54(1)	48(1)	-17(1)	-11(1)	-6(1)
C(12)	43(1)	53(1)	50(1)	-21(1)	1(1)	-7(1)
C(7)	52(1)	61(1)	47(1)	-23(1)	9(1)	-26(1)
C(13)	69(2)	63(1)	45(1)	-20(1)	0(1)	-21(1)
C(8)	53(1)	77(2)	40(1)	-21(1)	-2(1)	-22(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$).

	x	y	z	U(eq)
H(3)	2642	848	5113	47
H(9)	1121	2145	6716	60
H(6)	-4933	6646	6198	62
H(5)	-3389	5055	4646	57
H(12A)	5977	-3403	2136	60
H(12B)	6562	-1784	1401	60
H(7)	-3466	5988	8004	61
H(13A)	4103	-3089	530	88
H(13B)	6298	-3551	84	88
H(13C)	4781	-1539	-207	88
H(8)	-424	3775	8246	67

NOE difference spectra for 2,5-Diphenyl-3-amino-pyrazole (Entry 14, Table 2):

Gradient shimmed ^1H spectrum of 2,5-Diphenyl-3-amino-pyrazole at 500 MHz in DMSO