Supporting Information

Easy-to-Execute Carbonylations: Microwave Synthesis of Acyl Sulfonamides using Mo(CO)₆ as a Solid Carbon Monoxide Source

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EXPERIMENTAL SECTION

Procedures

Analytical TLC was performed using glass-backed 0.2 mm silica gel 60 F-254 plates. Visualization was done with UV light. NMR spectra were recorded for ^1H at 400 MHz and for ^{13}C at 100 MHz at 25 °C. Chemical shifts for ^1H and ^{13}C were referenced to CHCl_3 and CDCl_3 for those samples with neat CDCl_3 as solvent, respectively. For those samples with $\text{CD}_3\text{OD}/\text{CDCl}_3$ as the solvent system chemical shifts were referenced to CD_2HOD (^1H) or CD_3OD (^{13}C). Preparative HPLC was performed using a reversed-phase C8 (Zorbax SB-C8 (5 μm , 21.2 x 150 mm) column with a $\text{MeCN}/\text{H}_2\text{O}$ (0.05% HCOOH) gradient. Analytical HPLC-MS spectra were recorded in positive or negative ESI mode on an instrument equipped with a reversed-phase Chromolith SpeedROD RP-18e (4.6 x 50 mm) column using $\text{MeCN}/\text{H}_2\text{O}$ (0.05% HCOOH) as gradient. Alternatively, a GC-MS instrument equipped with a CP-Sil 8 CB capillary column (30 m x 0.25 mm, 0.25 μm) operating at an ionization energy of 70 eV was used. The oven temperature (GC) was 150-300 °C or 70-300 °C. Exact molecular masses were determined on a mass spectrometer equipped with an electrospray ion source. Microwave heated reactions were performed in a SmithSynthesizer. Reaction temperatures were determined using the built-in, on-line IR-sensor. The specific temperature data for the amidocarbonylations of the aryl iodides were: ramp time (0-110 °C): 80 s; hold time at 110 °C: 820 s and for the aryl bromides: ramp time (0-140 °C): 100 s; hold time at 140 °C: 800 s.

Materials

Palladium(II) acetate, tri-*t*-butylphosphonium tetrafluoroborate, 1,8-diazabicyclo[5.4.0]-undec-7-en, Herrmann's palladacycle {*trans*-di(μ -acetato)bis[*o*-tolylphosphino)benzyl]-dipalladium(II)}, $\text{Mo}(\text{CO})_6$, and anhydrous 1,4-dioxane were purchased from commercial

suppliers. Compounds **1a-i**, **2a-i** and **3a-f** were accordingly purchased from commercial sources. Compounds **4a-e**^{1,2}, **h**¹, **j**³, **k**⁴, **m**⁵, **n**⁶, **o**¹ and **7**⁷ are known, while structures **4f,g,i,l,p**, **5**, **6** and **8** are new. All known products gave satisfactory analytical data corresponding to the reported literature values except for the ¹³C NMR spectra of compound **4n**, which was found not consistent with the literature report⁶ (although the ¹H NMR was in accordance with the report). A listing of ¹³C NMR resonances for **4n** is provided.

Spectroscopic and analytical data for new compounds **4f,g,p**.

N-(4-Benzoyl-benzoyl)-4-methyl-benzenesulfonamide (**4f**)

Following the general procedure, compound **4f** was prepared in 70% yield, 106 mg from the aryl iodide. ¹H NMR (400 MHz, CD₃OD/CDCl₃): δ 2.36 (s, 3H), 7.27 (apparent d, *J* = 7.6 Hz, 2H), 7.40-7.47 (m, 2H), 7.54-7.61 (m, 1H), 7.67-7.74 (m, 4H), 7.94 (apparent d, *J* = 8.4 Hz, 2H), 7.98 (apparent d, *J* = 8.4 Hz, 2H); ¹³C NMR (100 MHz, CD₃OD/CDCl₃): δ 21.7, 128.2, 128.96, 128.99, 129.8, 130.2, 130.5, 133.7, 137.2, 137.4, 137.9, 141.2, 144.7, 168.1, 197.2; ESI⁺-MS (*m/z*, relative intensity) 380 ([M+H]⁺, 100), 759 ([2M+H]⁺, 45), 1138 ([3M+H]⁺, 20); HRMS [M+H]⁺ Calcd for C₂₁H₁₈NO₄S: 380.0957. Found: 380.0974.

4-Methyl-N-(4-Trifluoromethyl-benzoyl)-benzenesulfonamide (4g)

Following the general procedure, compound **4g** was prepared in 76% yield, 104 mg from the aryl iodide and in 95% yield, 132 mg from the aryl bromide. ^1H NMR (400 MHz, $\text{CD}_3\text{OD}/\text{CDCl}_3$): δ 2.31 (s, 3H), 7.15 (apparent d, $J = 8.0$ Hz, 2H), 7.49 (apparent d, $J = 8.0$ Hz, 2H), 7.85 (apparent d, $J = 8.0$ Hz, 2H), 8.13 (apparent d, $J = 8.0$ Hz, 2H); ^{13}C NMR (100 MHz, $\text{CD}_3\text{OD}/\text{CDCl}_3$): δ 21.4, 124.6 (q, $J = 270.6$ Hz, CF_3), 125.1 (q, $J = 3.6$ Hz), 126.7, 129.6, 130.0, 133.2 (q, $J = 32.3$ Hz), 140.8, 141.1, 142.9, 172.7; ESI-MS (m/z , relative intensity) 342 ($[\text{M}-\text{H}]^-$, 90), 685 ($[\text{2M}-\text{H}]^-$, 100), 1028 ($[\text{3M}-\text{H}]^-$, 95); HRMS $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{13}\text{F}_3\text{NO}_3\text{S}$: 344.0568. Found: 344.0582.

N-(4-Cyano-benzoyl)-4-methyl-benzenesulfonamide (4p)

Following the general procedure, compound **4p** was prepared in 83% yield, 100 mg from the bromide. ^1H NMR (400 MHz, $\text{CD}_3\text{OD}/\text{CDCl}_3$): δ 2.33 (s, 3H), 7.18 (apparent d, $J = 8.4$ Hz, 2H), 7.57 (apparent d, $J = 8.8$ Hz, 2H), 7.85 (apparent d, $J = 8.4$ Hz, 2H), 8.13 (apparent d, $J = 8.8$ Hz, 2H); ^{13}C NMR (100 MHz, $\text{CD}_3\text{OD}/\text{CDCl}_3$): δ 21.5, 114.8, 119.1, 126.8, 129.7, 130.3, 132.2, 140.9, 142.2, 143.1, 172.1; ESI-MS (m/z , relative intensity) 299 ($[\text{M}-\text{H}]^-$, 10), 599 ($[\text{2M}-\text{H}]^-$, 100), 899 ($[\text{3M}-\text{H}]^-$, 65), 1199 ($[\text{4M}-\text{H}]^-$, 45); HRMS $[\text{M}+\text{H}]^+$ Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_3\text{S}$: 301.0647. Found: 301.0652.

APPENDIX

¹³C NMR and LC-UV (254 nm) or GC-MS chromatograms for new compounds 4f,g,i,l,p,
5, 6 and 8.

N-(4-Benzoyl-benzoyl)-4-methyl-benzenesulfonamide (4f)

4-Methyl-N-(4-Trifluoromethyl-benzoyl)-benzenesulfonamide (4g)

Automation directory:
Sample id: s200106_12
Sample : sulphonamide_2_2_C
Pulse Sequence: s2pul
Solvent: cd3od
Temp: 26.0 C / 299.1 K
Sample #40, Operator: wu
File: sulphonamide_2_2_C_04
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
2000 repetitions
OBSERVE CH3, 100.5234459 MHz
DECOUPLE CH1, 399.7770416 MHz
Power 39 dB, continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 19 min, 48 sec

4-Methyl-N-(thiophene-3-carbonyl)-benzenesulfonamide (4i)

Automation directory:
Sample id : s_20041115_10
Sample : sulphonamide_9_C
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 24.9 C / 297.1 K
Sample #40, Operator: wu
File: sulphonamide_9_C.01
Mercury-400BB "mach167.orgfarm.uu.se"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
2000 repetitions
OBSERVE CH3, 100.534890 MHz
DECOUPLE H1, 399.7734664 MHz
Power 39 dB,
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 19 min, 48 sec

***N*-(4-Methyl-benzoyl)-methanesulfonamide (4l)**

Std Carbon experiment
Automation directory:
Sample : sulphonamide_7_C_-
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 24.0 C / 297.1 K
Operation: waltz16
File: sulphonamide_7_C_02
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 30.2 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
2000 repetitions
OBSERVE C13, 100.5704608 MHz
DECOUPLE H1, 399.9637083 MHz
SOLVENT
continuous on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 19 min, 48 sec

Chromatogram Plot

File: i:\wu_meso2ntoul_p 11-12-2004.sms

Sample: wu_MeSO2NToul_p

Scan Range: 1 - 1548 Time Range: 0.00 - 14.98 min.

Sample Notes: Routine

Operator: Org Farm Kemi

Date: 11/12/04 13:02

***N*-(4-Cyano-benzoyl)-4-methyl-benzenesulfonamide (4p)**

Automation directory:
Sample id : s_20041106_14
Sample : sulphonamide_13_C
Pulse Sequence: s2pu1
Solvent: cd3od
Temp: 26.0 C / 299.1 K
Sample #41, Operator: wu03
File: sulphonamide_13_C
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.000 sec
Acq. time 1.300 sec
Width 24154.6 Hz
2000 repetitions
OBSERVE C13, 100.5234328 MHz
DECOUPLE H1, 399.7770416 MHz
Power 39 dB
continuously on
Antenna coupled
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 1 hr, 19 min, 48 sec

[(*S*)-1-(4-Bromo-benzenesulfonylaminocarbonyl)-butyl]-carbamic acid *tert*-butyl ester
(5)

**[(S)-1-(4-Methanesulfonylaminocarbonyl-benzenesulfonylaminocarbonyl)-butyl]-
carbamic acid *tert*-butyl ester (6)**

{(S)-1-[(2S, 4R)-2-[(S)-1-(4-Methanesulfonylaminocarbonyl-benzenesulfonylaminocarbonyl)-butylcarbamoyl]-4-(7-methoxy-2-phenyl-quinoline-4-yloxy)-pyrrolidine-1-carbonyl]-2-methyl-propyl}-carbamic acid *tert*-butyl ester (8)

¹³C NMR and LC-UV (254 nm) or GC-MS chromatograms for known compounds 4a-e,h,j,k,m,n,o and 7.

N-(4-Methoxy-benzoyl)-4-methyl-benzenesulfonamide (4a)

N-(4-Methyl-benzoyl)-4-methyl-benzenesulfonamide (4b)

Automation directory:
Sample : 500428.04
Sample : sulphonamide_2_C
Pulse Sequence: szpul
Solvent: cdcl3
Temp: 26.0 C / 299.1 K
Sample #40, Operator: wu
File: sulphonamide_2_C.01
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
512 repetitions
OBSERVE C13, 100.5231045 MHz
DECOUPLE H1, 399.7754664 MHz
Spectrum 1
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FI size 65536
Total time 20 min, 25 sec

***N*-(2-Methyl-benzoyl)-4-methyl-benzenesulfonamide (4c)**

Automation directory:
Sample id : s_20041028_25
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 26.0 C / 299.1 K
Sample #40, Operator: wu
File: 01
Mercury-400SB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.814 sec
Width 2414.8 Hz
1000 repetitions
OBSERVE C13, 100.5231075 MHz
DECOUPLE H1, 399.7754664 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
Fft size 83936
Total time 0 min, 0 sec

Chromatogram Plot

File: i:\wu_o_methyl_carbsul.sms

Sample: wu_O_Methyl_CarbSul

Scan Range: 1 - 1548 Time Range: 0.00 - 14.99 min.

Sample Notes: ROUTINE

Operator: Operator

Date: 11/10/04 15:16

N-Benzoyl-4-methyl-benzenesulfonamide (4d)

Automation directory:
Sample id : s_20041029_04
Sample : sulphonamide_5_2_C
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 26.0 C / 299.1 K
Sample #48, Operator: wu
File: sulphonamide_5_2_C_01
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24134.6 Hz
SFO 100.6261300 MHz
OBSERVE C13, 100.6231073 MHz
DECOUPLE H1, 399.7754664 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 20 min, 25 sec

4-Methyl-N-(naphthalene-1-carbonyl)-benzenesulfonamide (4e)

4-Methyl-N-(thiophene-2-carbonyl)-benzenesulfonamide (4h)

Automation directory:
Sample id: 152004103_05
Sample : sulphonamide_42
Pulse Sequence: s2pul
Solvent: acetone
Temp: 26.0 C / 299.1 K
Sample #40, Operator: wu
File: sulphonamide.4.2.02
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
128 repetitions
OBSERVE C13, 100.5231473 MHz
DECOUPLE H1, 399.7775413 MHz
Cont. decoupling on
continuously on
VATZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 20 min, 25 sec

***N*-(4-Methyl-benzoyl)-benzenesulfonamide (4j)**

Automation directory:
Sample id : S2004115_09
Sample : sulphonamide_I0_H
Pulse Sequence: s2pul
Solvent: cdc13
Temp. 24.0 C / 297.1 K
Sample #41, Operator: wu
File: sulphonamide_I0_C_02
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
Sweep rate 100.000 MHz
Observation frequency 500.136300 MHz
Decouple H1, 399.7754664 MHz
Power 39 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 20 min, 25 sec

Std Carbon experiment

Automation directory:
Sample : sulphonamide_12_C_

Automation directory:
Sample : sulphonamide_12_C_

pulse Sequence: s2pu1

solvent: cdc13

Temp: 24.0 C / 297.1 K
Operator: wu

File: sulphonamide_12_C_01

mercury-400bb "mach16/.orgtafm.uu.se"

elax. delay 1.000 sec

pulse 45.0 degrees
ca time 1.300 sec

idth 24154.6 Hz

12 repetitions
SERVE C13 100 570443

DECOUPLE H1, 399.9637083 MHZ

power 31 dB continuously on

ALTZ-16 modulated

TA PROCESSING
ine broadening 0.5 Hz

size 65536

total time 20 min, 25 sec

C,C,C-Trifluoro-N-(4-methyl-benzoyl)-methanesulfonamide (4m)

Automation directory:
Sample id : s_20041115_11
Sample : sulphonamide_11_2_C
Pulse Sequence: s2pul
Solvent: cdcl3
Temp: 24.0 C / 297.1 K
Sample #42, Operator: wu
File: sulphonamide_11_2_C_01
Mercury-400BB "mach167.orgfarm.uu.se"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24154.6 Hz
3392 repetitions
OBSERVE C13, 100.5230985 MHz
DECODE H1, 399.7734664 MHz
Pulse 59 dB, continuously on
VATZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 65536
Total time 6 hr, 38 min, 50 sec

Chromatogram Plot

File: i:\wu_cf3so2ntoul_p 11-12-2004001.sms
Sample: wu_CF3SO2NToul_p
Scan Range: 1 - 1631 Time Range: 0.00 - 15.99 min.
Sample Notes: Routine

Operator: Org Farm Kemi
Date: 11/12/04 15:37

***N*-Methyl-*N*-(4-methyl-benzoyl)-benzenesulfonamide (4n)⁶**

¹³C NMR (100 MHz, CDCl₃): δ 21.7, 35.9, 128.5, 128.9, 129.09, 129.11, 131.5, 133.8, 138.3, 143.0, 171.6.

***N*-(2-Methoxy-benzoyl)-4-methyl-benzenesulfonamide (4o)**

Automation directory:
 Sample id : s_20041103_15
 Sample : sulphonamide_15_C
 Pulse Sequence: s2pul
 Solvent: cdcl3
 Temp: 25.0 C / 299.1 K
 Sample #2, Operator: uu
 File name: sulphonamide_15_C_03
 Mercury-400BB "mach167.Orgfarm.uu.se"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 1.300 sec
 Width 24154.6 Hz
 512 repetitions
 OBSERVE C13, 100.523116 MHz
 DECOUPLE H1, 399.7754664 MHz
 Power 39 dB
 continuously on
 continuously on
 DATA ACQUISITION
 DATA PROCESSING
 Line broadening 0.5 Hz
 FT size 65536
 Total time 20 min, 25 sec

(2*S*, 4*R*)-1-((*S*)-2-*tert*-Butoxycarbonylamino-3-methyl-butyryl)-4-(7-methoxy-2-phenyl-quinoline-4-yloxy)-pyrrolidine-2-carboxylic acid (7)

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