

Efficient Palladium-catalyzed Coupling Reactions of Aryl Bromides and Chlorides with Phenols

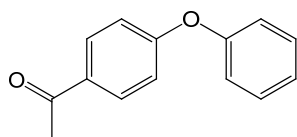
Tongjie Hu,^a Thomas Schulz,^b Christian Torborg,^b Xiaorong Chen,^a Jun Wang,^a Matthias Beller^{b*} and Jun Huang^{a*}

Experimental section:

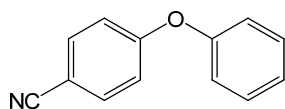
Reagents: All reagents were purchased from Aladdin Reagent Company and Alfa-Aesar Company without further purification. Toluene and dioxane were purified by distillation through a standard procedure.

Analytical Methods: ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker 300 MHz instrument with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. Gas chromatography analyses were performed on a Hewlett Packard 5890 instrument with a FID detector and Hewlett Packard 24 m x 0.2 mm i.d. HP-5 capillary column. Yield refers to isolated yields of compounds greater than 95% purity as determined by capillary gas chromatography (GC) and proton Nuclear Magnetic Resonance spectroscopy (¹H-NMR) analysis.

General procedure for the Pd-catalyzed synthesis of diaryl ethers from aryl halides with phenols. All reactions were carried out under an argon atmosphere in schlenk tubes (containing a stir bar). A schlenk tube containing a stir bar was charged with Pd(OAc)₂ (2.0 mol% Pd), ligand (6.0 mol%) and K₃PO₄ (2.0 equiv.). If the aryl halides (1.0 mmol) and/or phenols (1.2 equiv.) were solids, they were also added at this time. The tube was evacuated and backfilled with argon (this sequence was repeated three times). If the aryl halides and/or phenols were liquids, they were added to the tube at this time along with the solvents. The mixture was stirred in a preheated oil bath (80-100°C) until the aryl halide was consumed as judged by TLC or GC analysis (10-24 h, reaction times were not optimized). The crude material was purified by column chromatography on silica gel (eluting with ethyl acetate/hexane or diethyl ether/hexane mixtures).

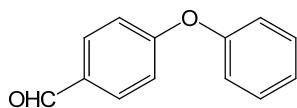


1-(4-Phenoxyphenyl)ethanone¹: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a white solid. M.p. 51°C; ¹H NMR (CDCl₃, 300 MHz): 7.96-7.91 (d, 2H), 7.42-7.36 (t, 2H), 7.22-7.17 (t, 1H), 7.08-7.06 (d, 2H), 7.05-6.97 (d, 2H), 2.57 (s, 3H).

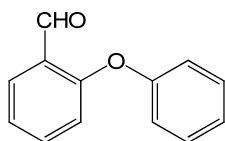


4-Phenoxybenzonitrile²: The crude material was purified by flash chromatography column on

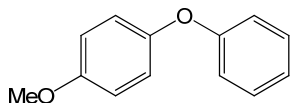
silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a white solid. M.p. 29°C; ^1H NMR (CDCl_3 , 300 MHz): 7.62-7.57 (d, 2H), 7.49-7.38 (t, 2H), 7.25-7.20 (t, 1H), 7.08-7.05 (d, 2H), 7.04-6.95 (d, 2H).



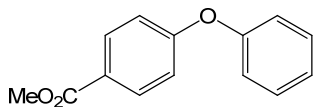
4-Phenoxybenzaldehyde³: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow liquid. ^1H NMR (CDCl_3 , 300 MHz): 9.92 (s, 1H), 7.85-7.82 (d, 2H), 7.43-7.38 (t, 2H), 7.29-7.19 (q, 1H), 7.09-7.04 (t, 4H).



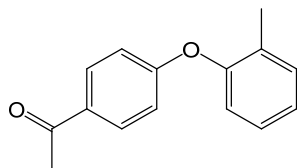
2-Phenoxybenzaldehyde⁴: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow liquid. ^1H NMR (CDCl_3 , 300 MHz): 10.52 (s, 1H), 7.95-7.92 (d, 1H), 7.53-7.47 (t, 1H), 7.41-7.36 (t, 2H), 7.20-7.15 (t, 2H), 7.08-7.05 (d, 2H), 6.91-6.88 (d, 1H).



1-Methoxy-4-phenoxybenzene⁴: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a colorless liquid. ^1H NMR (CDCl_3 , 300 MHz): 7.34-7.27 (m, 2H), 7.07-7.02 (t, 1H), 7.01-6.94 (m, 4H), 6.92-6.84 (m, 2H), 3.81 (s, 3H).

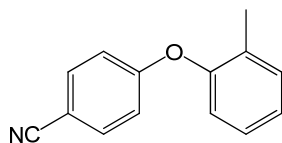


Methyl 4-phenoxybenzoate⁵: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow solid. M.p. 59°C; ^1H NMR (CDCl_3 , 300 MHz): 8.01-7.99 (d, 2H), 7.41-7.36 (t, 2H), 7.21-7.16 (t, 1H), 7.07-7.05 (d, 2H), 7.00-6.97 (d, 2H), 3.89 (s, 3H).

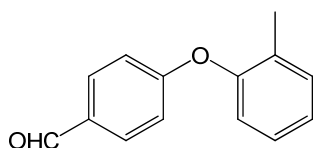


1-(4-(o-Tolxy)phenyl)ethanone⁶: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow solid. M.p. 35°C; ^1H NMR (CDCl_3 , 300 MHz): 7.94-7.89 (d, 2H), 7.29-7.26 (t, 1H), 7.23-7.12 (m, 2H),

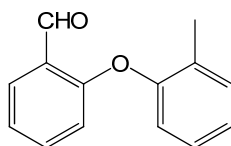
6.98-6.97 (d, 1H), 6.91-6.87 (d, 1H), 2.57 (s, 3H), 2.18 (s, 3H).



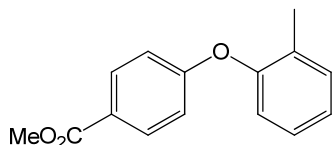
4-(o-Tolyloxy)benzonitrile⁷: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a colorless liquid. ¹H NMR (CDCl₃, 300 MHz): 7.62-7.56 (d, 2H), 7.30-7.26 (t, 1H), 7.24-7.14 (m, 2H), 6.99-6.96 (d, 1H), 6.92-6.89 (d, 2H), 2.17 (s, 3H).



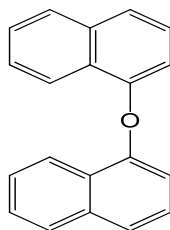
4-(o-Tolyloxy)benzaldehyde⁸: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow liquid. ¹H NMR (CDCl₃, 300 MHz): 9.90 (s, 1H), 7.83-7.80 (t, 2H), 7.30-7.28 (t, 1H), 7.25-7.14 (m, 2H), 7.01-6.94 (q, 3H), 2.18(s, 3H).



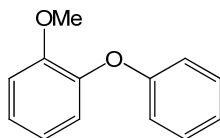
2-(o-Tolyloxy)benzaldehyde⁹: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow solid. M.p. 50°C; ¹H NMR (CDCl₃, 300 MHz): 10.61 (s, 1H), 7.95-7.92 (d, 1H), 7.48-7.42 (t, 1H), 7.30-7.25 (t, 1H), 7.24-7.19 (t, 1H), 7.16-7.10 (m, 2H), 6.96-6.94 (d, 1H), 6.71-6.68 (d, 1H), 2.19 (s, 3H).



Methyl 4-(o-tolyloxy)benzoate⁸: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a yellow liquid. ¹H NMR (CDCl₃, 300 MHz): 7.99-7.96 (d, 2H), 7.29-7.20 (m, 2H), 7.16-7.11 (t, 1H), 6.99-6.97 (d, 1H), 6.89-6.86 (d, 2H), 3.89 (s, 3H), 2.19 (s, 3H).

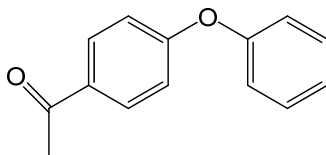


1,1'-Oxydinaphthalene¹⁰: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a white solid. M.p. 109°C; ¹H NMR (CDCl₃, 300 MHz): 8.47-8.28 (d, 2H), 7.98-7.89 (d, 2H), 7.71-7.63 (d, 2H), 7.61-7.56 (m, 4H), 7.54-7.38 (t, 2H), 7.03-6.96 (d, 2H).

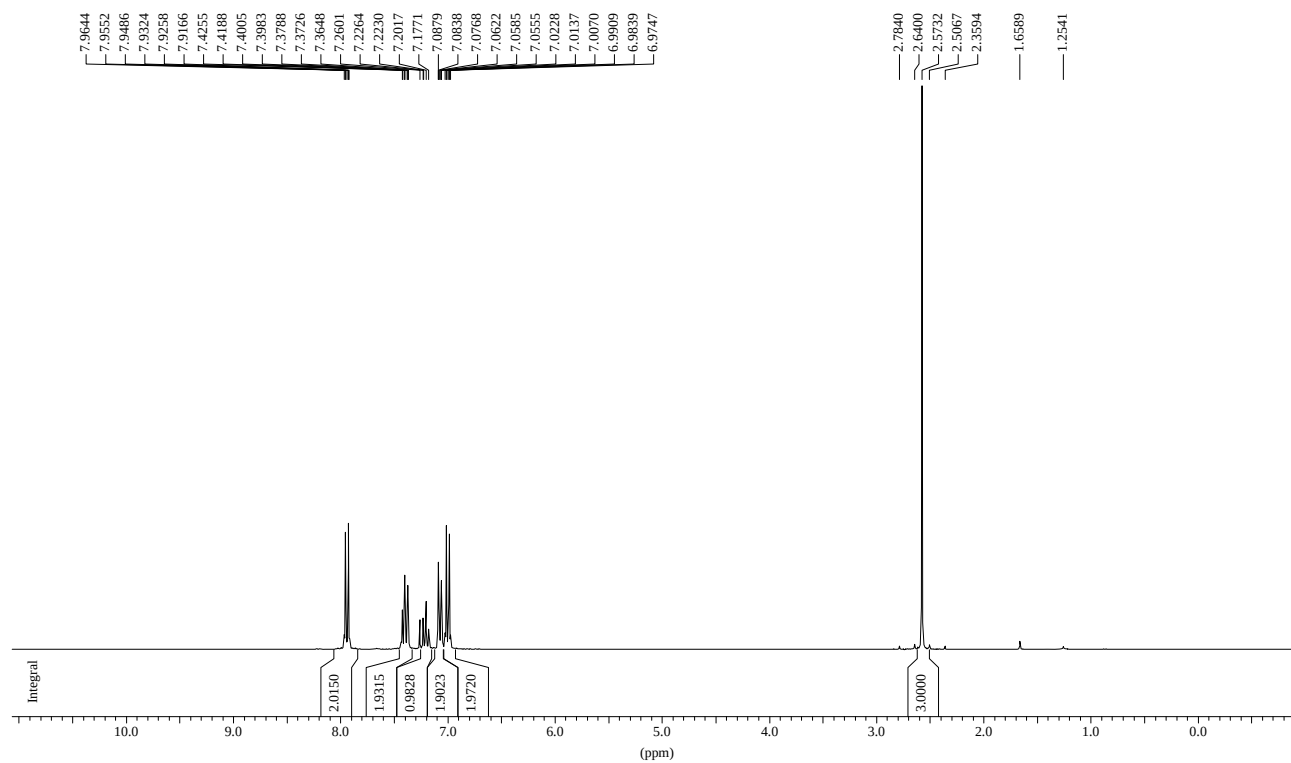


1-Methoxy-2-phenoxybenzene¹¹: The crude material was purified by flash chromatography column on silica gel (10:1 ethyl acetate/hexane) to afford the title compound as a light yellow solid. M.p. 76°C; ¹H-NMR (CDCl₃, 300 MHz): 7.36-7.27 (m, 2H), 7.16-7.10 (m, 1H), 7.07-6.99 (m, 2H), 6.96-6.89 (m, 4H), 3.84 (s, 3H).

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2. Commercially available (Aldrich).
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HJJ-3 1H-NMR CDCl3 300K AV-300



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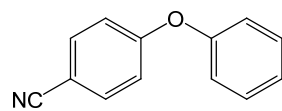
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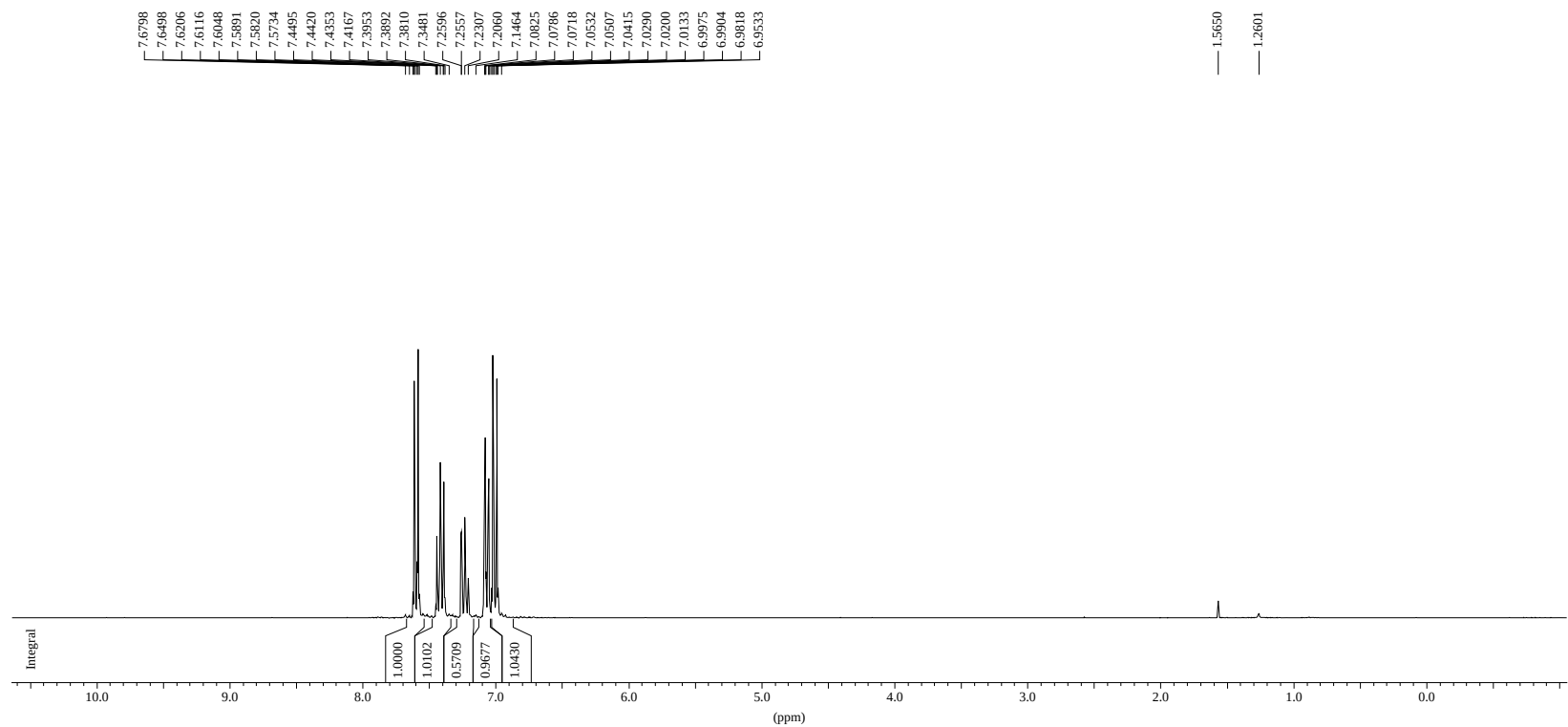
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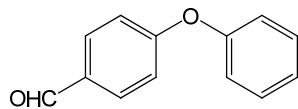
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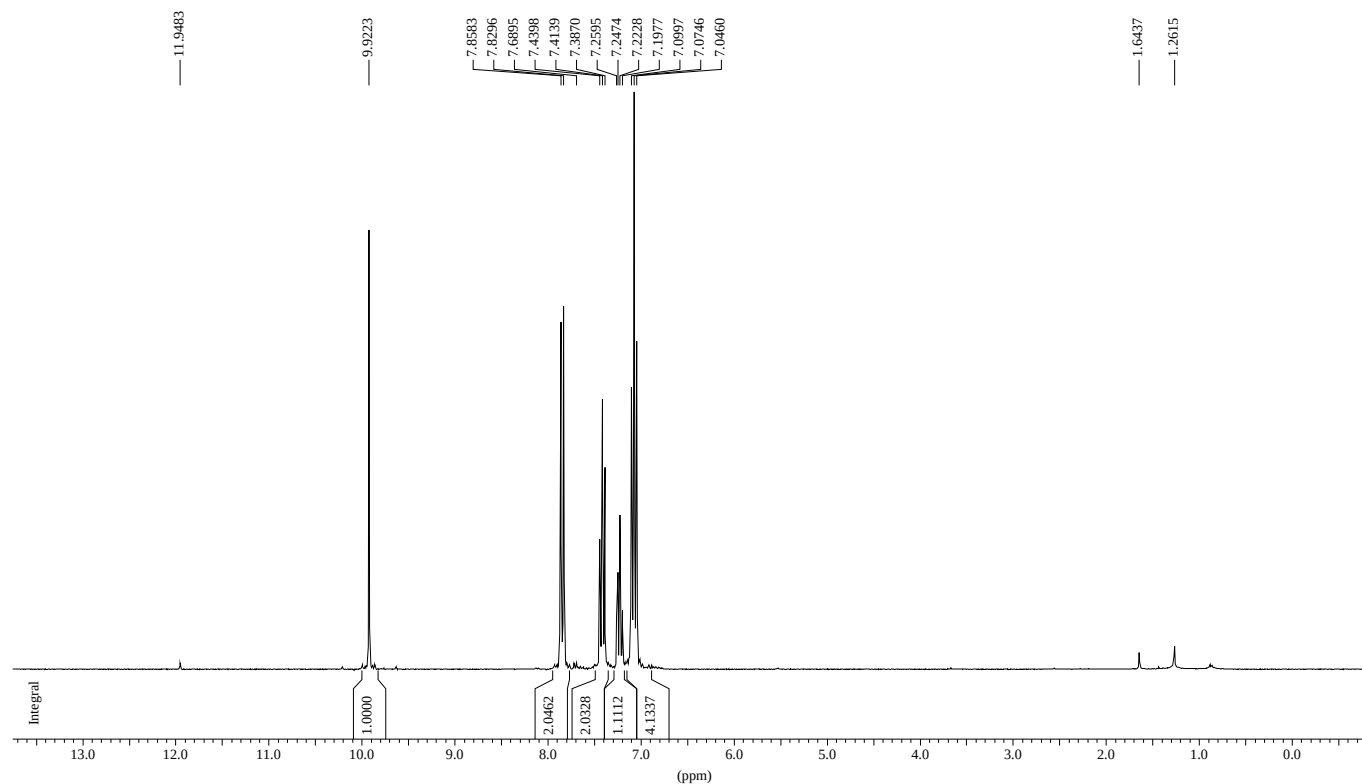


HTJ-4 1H-NMR CDCl3 300K AV-300

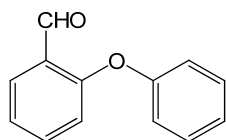




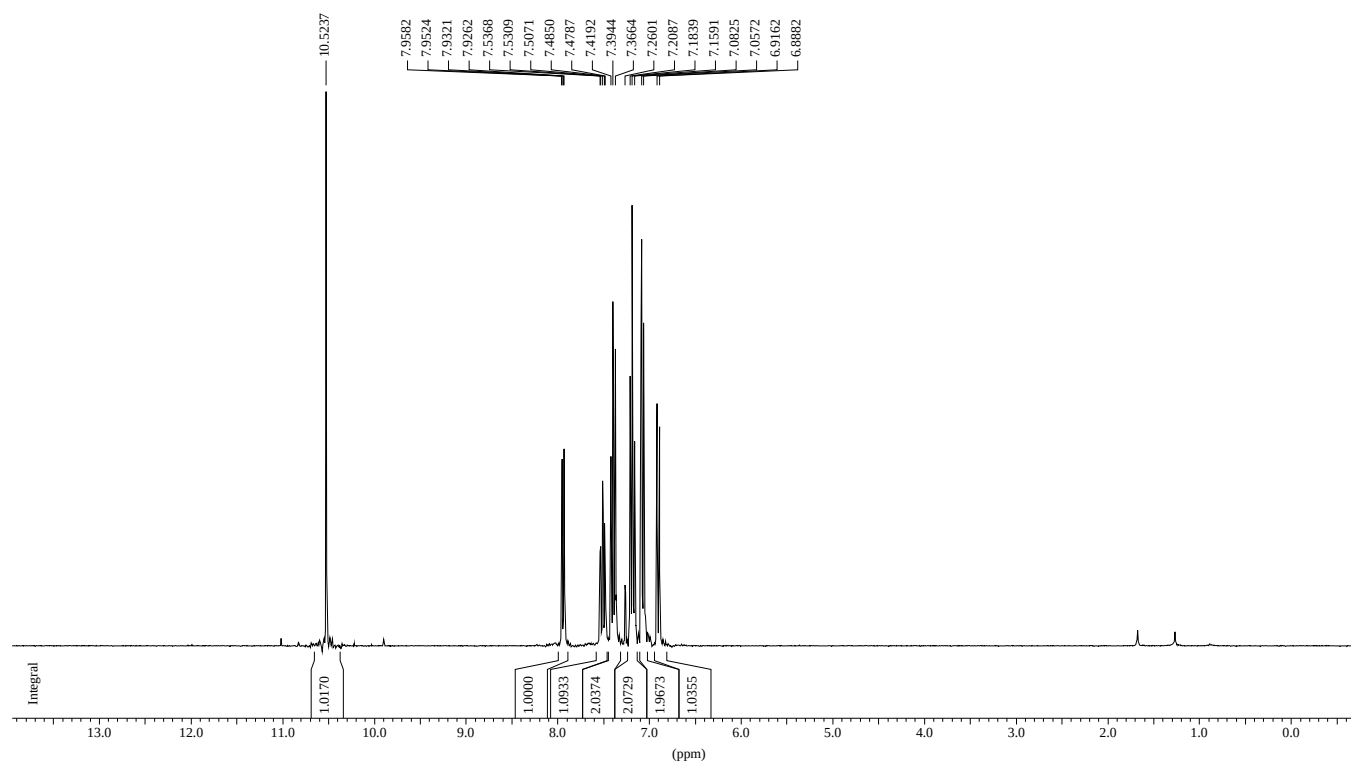
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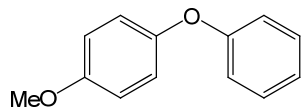


HTJ-8 1H-NMR CDCl3 300K AV-300

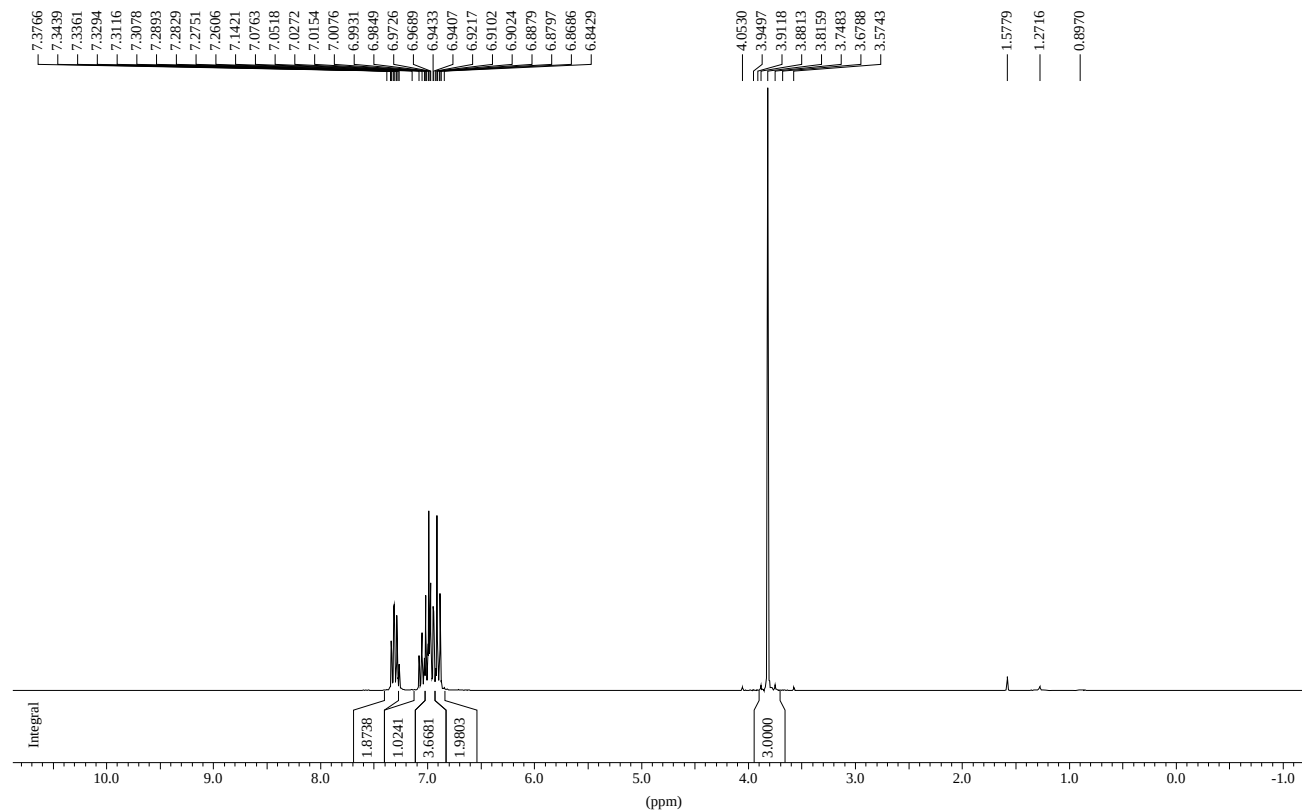


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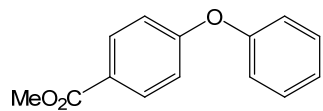
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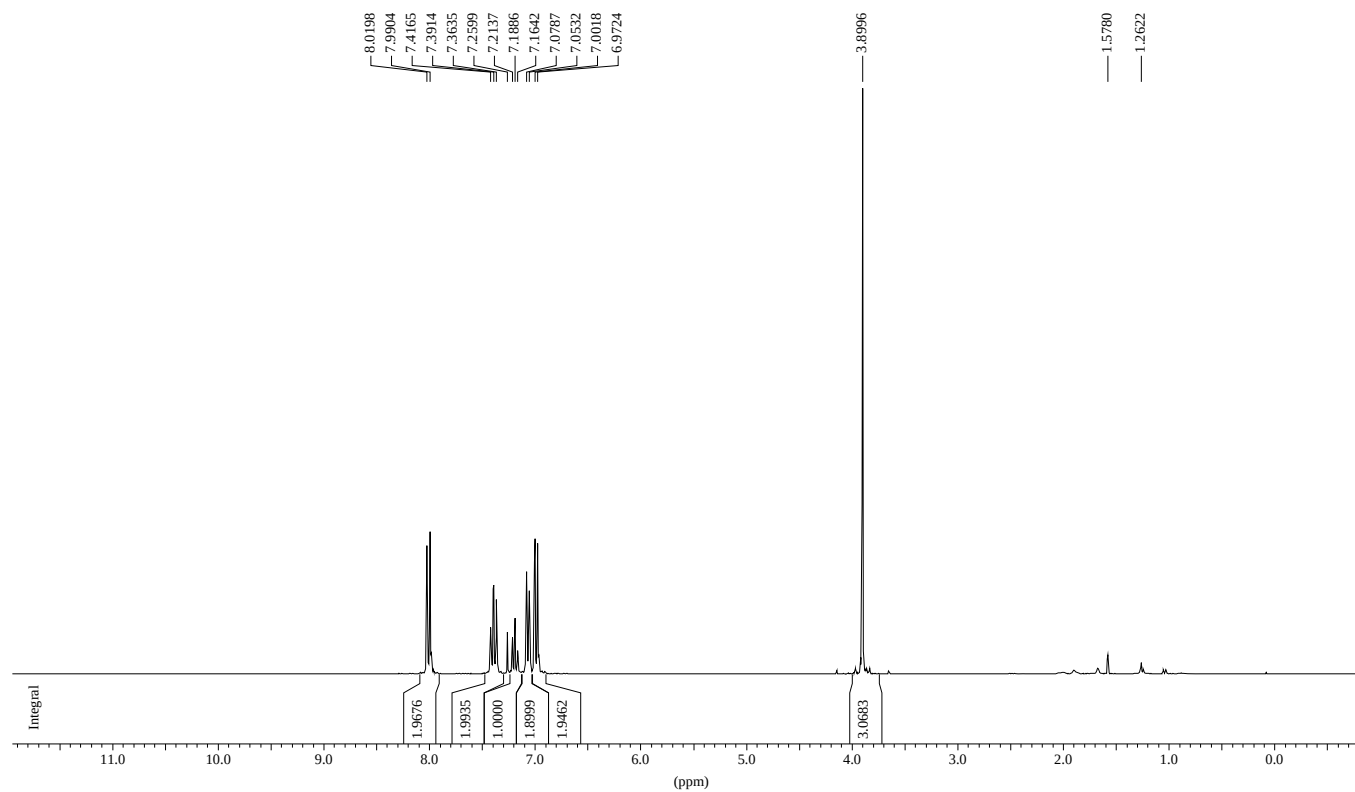
HJJ-2 1H-NMR CDCl3 300K AV-300



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HTJ-11 H1-NMR CDCl3 300K AV-300



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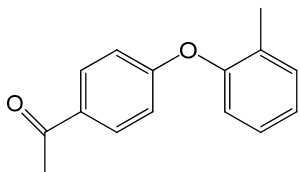
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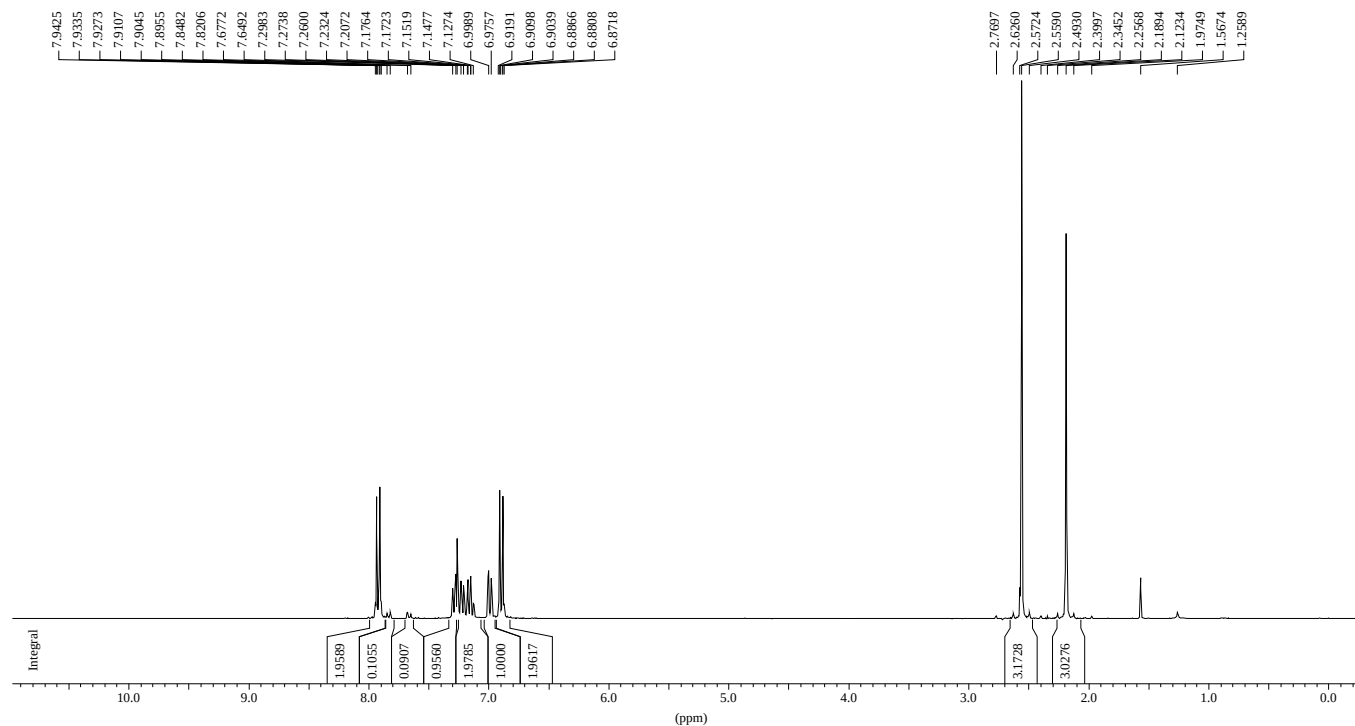
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HTJ-5 1H-NMR CDCl3 300K AV-300



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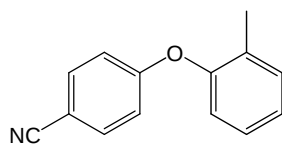
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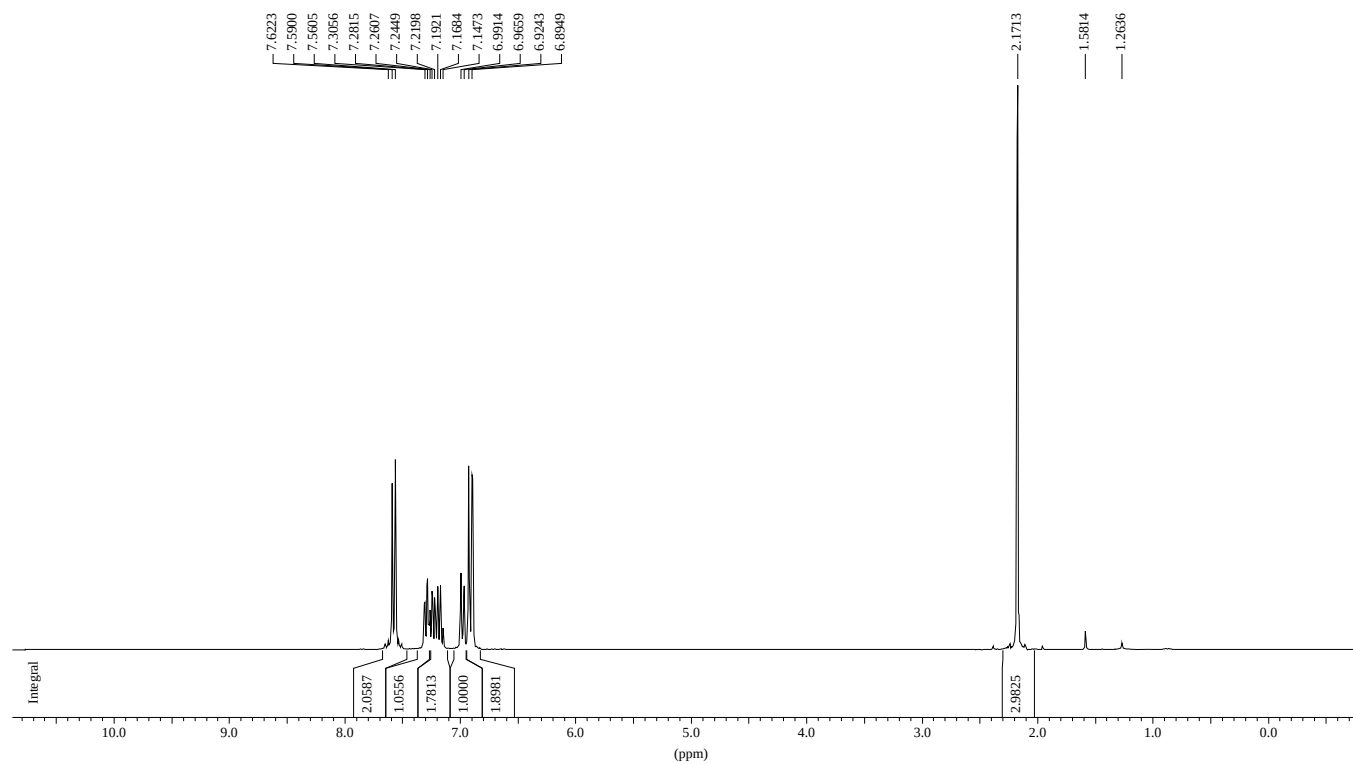
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HTJ-6 1H-NMR CDCl3 300K AV-300



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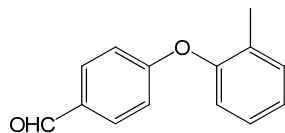
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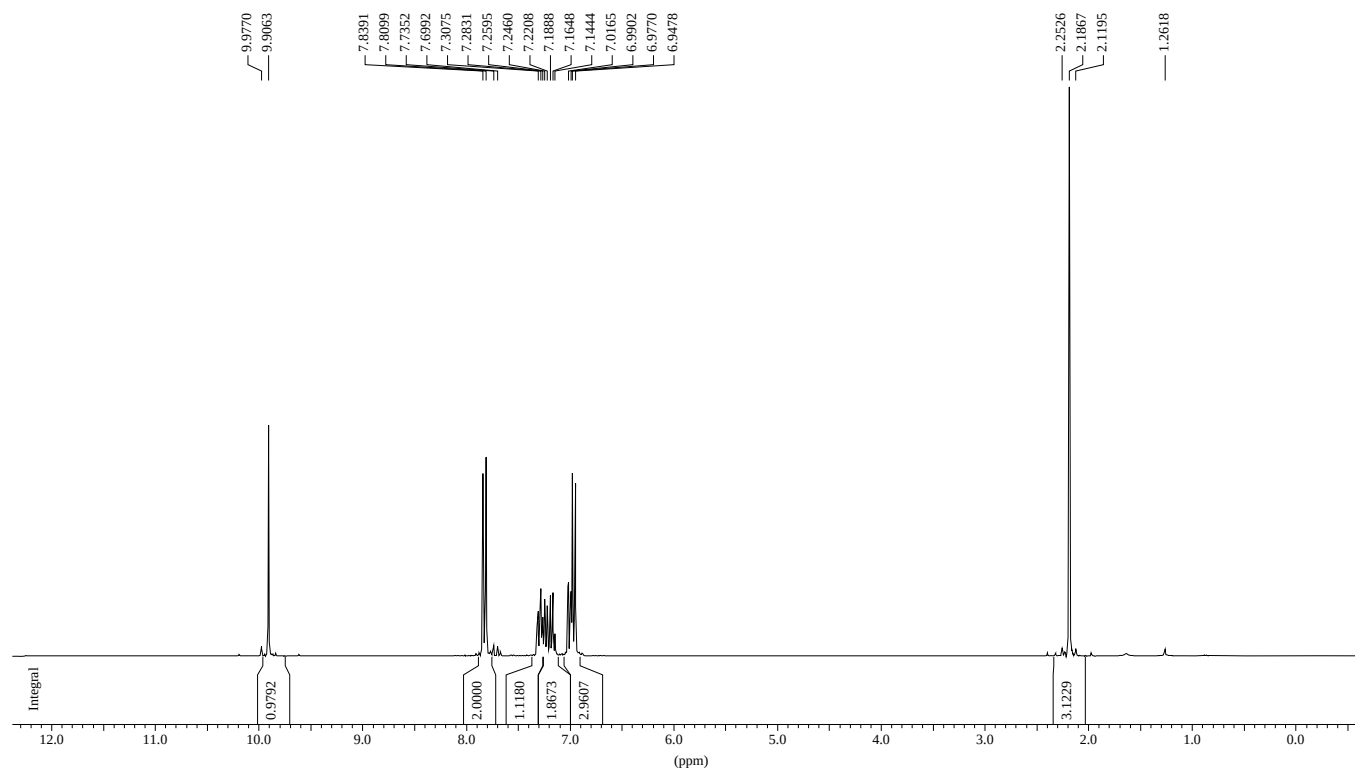
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HTJ-7 1H-NMR CDCl3 300K AV-300



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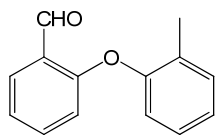
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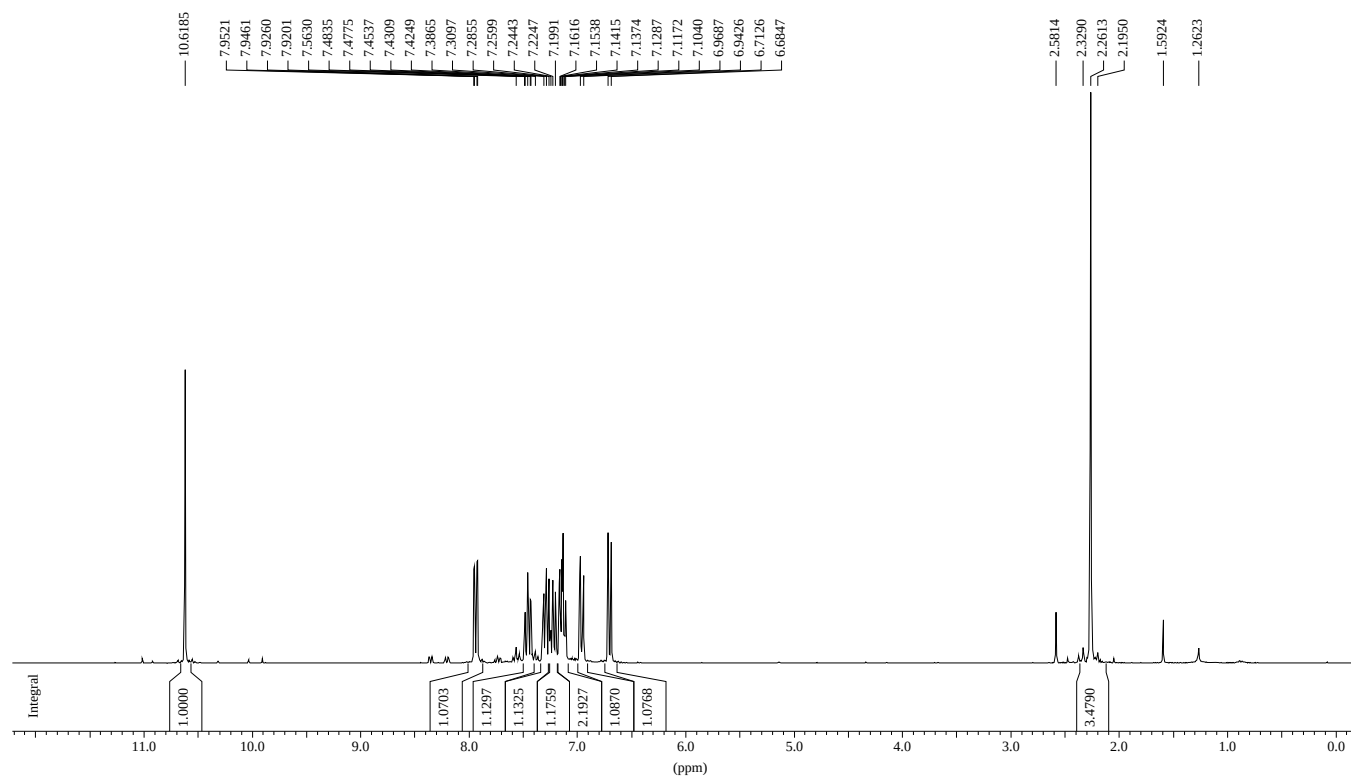
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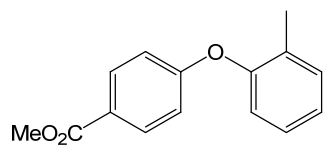


HTJ-10 H1-NMR CDC13 300K AV-300

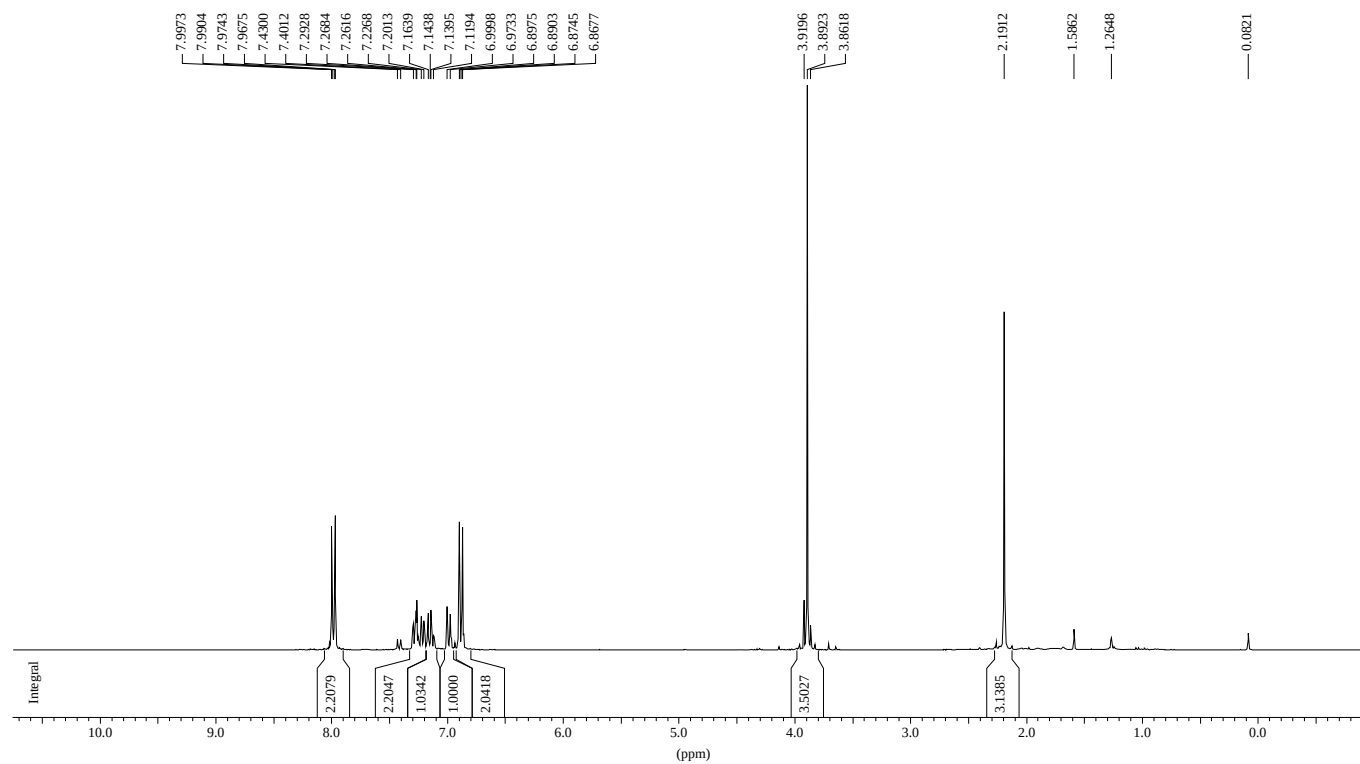


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DATE_d     : Mar 12 2010
DE         : 6.0 usec
INSTRUM    : av300
NS         : 16
PULPROG    : zg30
SFO1       : 300.1318644 MHz
SW_h       : 4496.403 Hz
TD         : 23980
TE         : 298.0 K
*** Processing Parameters ***
GB         : 0.0000000
LB         : 0.50 Hz
PC         : 1.00
PPARMOD    : 1D
SF         : 300.1300060 MHz
SI         : 32768
SSB        : 0.0000000
SW_p       : 4496.4028777
TDefeff    : 23980
WDW        : EM
*** 1D NMR Plot Parameters ***
XOffset    : 1.00 cm
YOffset    : 4.00 cm
Start      : 12.22 ppm
Stop       : -0.30 ppm
AQ_time    : 2.6665760 sec
  
```



HTJ-12 H1-NMR CDCl3 300K AV-300



*** Current Data Parameters ***

NAME : 100312

EXPNO : 64

PROCNO : 1

*** Acquisition Parameters ***

DATE_t : 01:05:43

DATE_d : Mar 12 2010

DE : 6.0 usec

INSTRUM : av300

NS : 16

PULPROG : zg30

SFO1 : 300.1314689 MHz

SW_h : 3531.073 Hz

TD : 23980

TE : 298.0 K

*** Processing Parameters ***

GB : 0.0000000

LB : 0.50 Hz

PC : 1.00

PPARMOD : 1D

SF : 300.1300060 MHz

SI : 32768

SSB : 0.0000000

SW_p : 3531.0734463

TDeff : 23980

WDW : EM

*** 1D NMR Plot Parameters ***

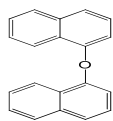
XOffset : 1.00 cm

YOffset : 4.00 cm

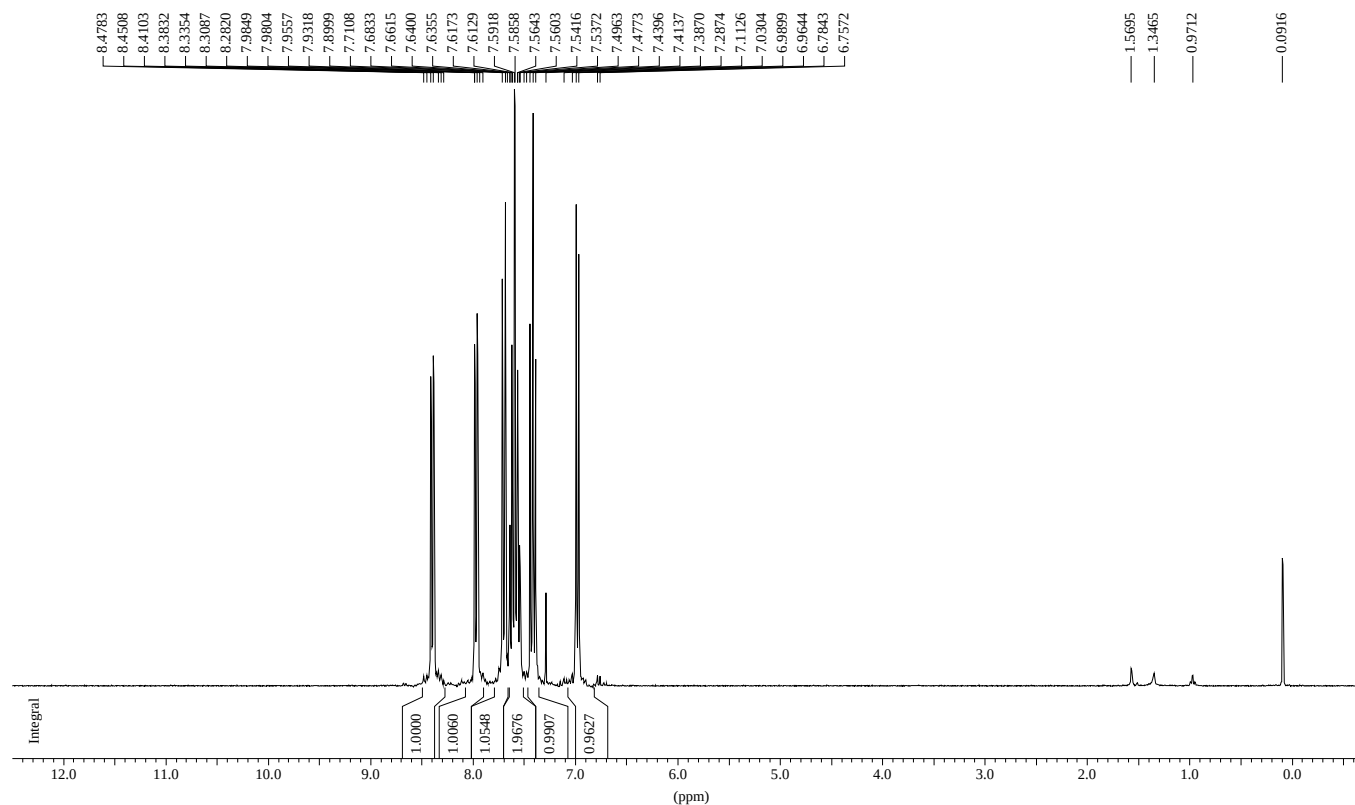
Start : 10.76 ppm

Stop : -1.01 ppm

AQ_time : 3.3955680 sec



HTJ-13 H1-NMR CDCl3 300K AV-300



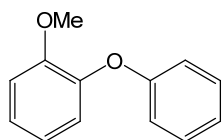
*** Current Data Parameters ***

NAME : 100315
EXPNO : 78
PROCNO : 1
*** Acquisition Parameters ***
DATE_t : 01:56:36
DATE_d : Mar 15 2010
DE : 6.0 usec
INSTRUM : av300
NS : 8
PULPROG : zg30
SFO1 : 300.1317584 MHz
SW_h : 3980.892 Hz
TD : 23980
TE : 298.0 K

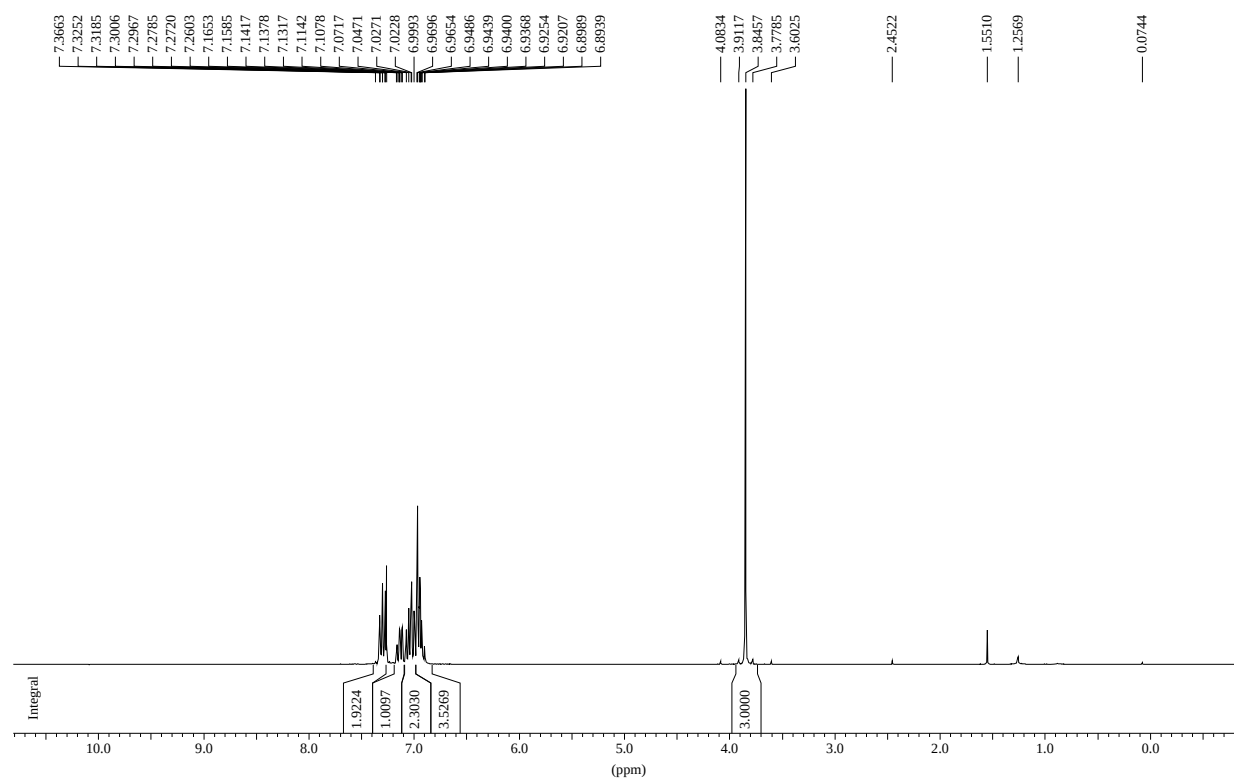
*** Processing Parameters ***
GB : 0.0000000
LB : 0.10 Hz
PC : 1.00
PPARMOD : 1D
SF : 300.1299973 MHz
SI : 32768
SSB : 0.0000000
SW_p : 3980.8917197
TDeff : 23980
WDW : EM

*** 1D NMR Plot Parameters ***

XOffset : 1.00 cm
YOffset : 4.00 cm
Start : 12.50 ppm
Stop : -0.76 ppm
AQ_time : 3.0118880 sec



HJJ-1 1H-NMR CDCl3 300K AV-300



```

*** Current Data Parameters ***
NAME      : 100301
EXPNO     : 12
PROCNO    : 1
*** Acquisition Parameters ***
DATE_t    : 07:00:44
DATE_d    : Mar 01 2010
DE        : 6.0 usec
INSTRUM   : av300
NS        : 32
PULPROG   : zg30
SFO1      : 300.1314951 MHz
SW_h      : 3511.236 Hz
TD        : 18380
TE        : 298.0 K
*** Processing Parameters ***
GB        : 0.0000000
LB        : 0.50 Hz
PC        : 1.00
PPARMOD   : 1D
SF        : 300.1300062 MHz
SI        : 32768
SSB       : 0.0000000
SW_p      : 3511.2359551
TDeff     : 18380
WDW       : EM
*** 1D NMR Plot Parameters ***
XOffset   : 1.00 cm
YOffset   : 4.00 cm
Start     : 10.81 ppm
Stop      : -0.89 ppm
AQ_time   : 2.6173120 sec
  
```