Electrophilic activation of carboxylic anhydrides for nucleophilic acylation reactions

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2. Characterization attempts for intermediate

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3.2. UPLC data corresponding to entries of table 1
1. Anhydride activation using Reagent Tf$_2$O, Ms$_2$O and MsCl (Scheme 2):

To a solution of benzoic anhydride (0.113g, 0.5 mmol) in DCM (5 mL) at 0 °C was added Reagent (0.52 mmol, 1.1 eq), base (1.1 mmol, 2.2 eq). Reaction mixture was stirred for 30 minutes at 0 °C and piperidine (1.1 mmol, 2.2 eq) was added. Progress of the reaction was monitored by TLC. After 2 h, reaction mixture was diluted with DCM (20 ml) and washed with 1N aq HCl (10 mL) followed by NaHCO$_3$ (10 mL) and brine (10 mL). Organic layer was dried over anhydrous sodium sulfate and was concentrated to afford phenyl(piperidin-1-yl)methanone as transparent oil (130mg, 70%).

2. Characterization of intermediate: To a solution of benzoic anhydride (0.122g, 0.5 mmol, 1.0 equiv) in DCM (10 mL) at -78 °C was added MsCl (1.1 mmol, 1.1 eq), triethylamine (2.2 mmol, 2.2 eq). Reaction mixture was stirred for 30 minutes -78 °C and mass spectra was recorded using Orbitrap Fusion mass spectrometer (Thermo) in positive ion mode through direct infusion by syringe. This analysis showed a peak corresponding to intermediate B at m/z 206.1558 consistent with empirical formula C$_{13}$H$_{20}$NO (206.1538) (see spectra attached below).
3.1. $^1$H and $^{13}$C Spectra of compounds

$^1$H spectra of Phenyl(piperidin-1-yl)methanone (2a):
$^1$H spectra of phenyl(pyrrolidin-1-yl)methanone (2b):
$^1$H spectra of N-methylbenzamide (2c):
$^1$H spectra of N-benzylbenzamide (2d):
$^1$H spectra of N-phenylbenzamide (2e):
$^1$H spectra of N-isopropylbenzamide (2f):
$^1$H spectra of $N,N$-diethylbenzamide (2g):
$^1$H spectra of $N,N$-diisopropylbenzamide (2h):
$^1$H spectra of $N,N$-dimethylbenzamide (2i):
$^1$H spectra of phenyl(thiomorpholino)methanone (2j):
$^1$H spectra of morpholino(phenyl)methanone (2k):
$^{1}H$ spectra of Benzamide (2l):
$^1$H spectra of Benzoyl azide (2m):
$^1$H spectra of S-methyl benzothioate (2n):
$^1$H spectra of S-phenyl benzothioate (2o):
$^1$H spectra of Phenyl benzoate (2p):
$^1$H spectra of Methyl benzoate (2q):
$^1$H spectra of (4-methoxyphenyl)(pyrrolidin-1-yl)methanone (3b):
$^1$H spectra of pyrrolidin-1-yl(thiophen-3-yl)methanone (4b):
$^1$H, $^{13}$C, HRMS and IR spectra of (4-(dimethylamino)phenyl)(pyrrolidin-1-yl)methanone (5b):
$^1$H spectra of (4-methylphenyl)(pyrrolidin-1-yl)methanone (6b):
$^1$H spectra of furan-2-yl(pyrrolidin-1-yl)methanone (7b):
$^1$H spectra of cyclohexyl(pyrrolidin-1-yl)methanone (8b):
$^1$H spectra of 4-(pyrrolidine-1-carbonyl)benzonitrile (9b):
$^1$H spectra of 2-phenyl-1-(pyrrolidin-1-yl)ethanone (10b):
$^1$H spectra of 1-(4-(pyrrolidine-1-carbonyl)phenyl)ethan-1-one (11b):
$^1$H spectra of 4-(pyrrolidine-1-carbonyl)benzaldehyde (12b):
$^1$H, $^{13}$C, HRMS and IR spectra of $N,N$-dimethylterephthalamide (13b):
$^1$H spectra of Boc-Phenylalanine pyrrolidine amide (14b):
$^1$H, $^{13}$C and HRMS spectra of tert-butyl(1-((2-morpholinophenyl)amino)-1-oxo-3-phenylpropan-2-yl)carbamate (15b):
$^1$H, $^{13}$C and MS spectra of tert-butyl (4-(azidocarbonyl)phenyl)carbamate (16b):
3.2. UPLC DATA CORRESPONDING TO ENTRIES OF TABLE-1

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**BENZOIC ANHYDRIDE STANDARD**

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- **Sample Type:** Unknown
- **Vial:** 1A,2
- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 5.0 Minutes

**Acquired By:** System
**Sample Set Name:** 60 40 water acetonitrile
**Acq. Method Set:** ACQUITY TUV ChA
**Processing Method:** ACQUITY TUV ChA 254nm

**Date Acquired:** 5/24/2017 12:04:46 PM IST
**Date Processed:** 5/25/2017 12:28:59 PM IST

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**CHROMATOGRAM**

**BENZOYL PIPERIDINE**

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- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 4.0 Minutes

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**Sample Set Name:**
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**Date Acquired:** 5/29/2017 12:25:24 PM IST
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- **Vial:** 2:A,5
- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 4.0 Minutes
- **Acquired By:** System
- **Sample Set Name:**
- **Acq. Method Set:** at
- **Processing Method:** 60:40 water acetonitrile
- **Channel Name:** ACQUITY TUV ChA
- **Proc. Chnl. Descr.:** ACQUITY TUV ChA 254nm

**Date Acquired:** 5/30/2017 12:03:56 PM IST
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Date Acquired: 5/26/2017 3:49:54 PM IST
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- **Vial:** 2.B.1
- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 4.0 Minutes

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- **Vial:** 2 A,7
- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 4.0 Minutes

- **Acquired By:** System Name
- **Sample Set Name:** at
- **Acq. Method Set:** 60 40 water acetonitrile
- **Processing Method:** ACQUITY TUV ChA
- **Channel Name:** ACQUITY TUV ChA 254nm
- **Proc. Chnl. Descr.:**

**Date Acquired:** 5/25/2017 12:38:22 PM IST

**Date Processed:** 5/25/2017 2:18:04 PM IST

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52
**SAMPLE INFORMATION**

- **Sample Name:** VK-088-288
- **Sample Type:** Unknown
- **Vial:** 1A,5
- **Injection #:** 1
- **Injection Volume:** 1.00 ul
- **Run Time:** 4.0 Minutes
- **Acquired By:** System
- **Sample Set Name:**
- **Acq. Method Set:** at
- **Processing Method:** 60:40 water acetonitrile
- **Channel Name:** ACQUITY TUV ChA
- **Proc. Chnl. Descr.:** ACQUITY TUV ChA 254nm

- **Date Acquired:** 5/24/2017 4:10:27 PM IST
- **Date Processed:** 5/25/2017 12:34:42 PM IST

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Sample Type: Unknown
Vial: 2, C, 8
Injection #: 1
Injection Volume: 1.00 ul
Run Time: 4.0 Minutes

Acquired By: System
Sample Set Name: LT093207AW
Acq. Method Set: at
Processing Method: ACQUITY TUV ChA
Channel Name: ACQUITY TUV ChA 254nm
Proc. Chnl. Descr.: ACQUITY TUV ChA 254nm

Date Acquired: 5/30/2017 4:05:43 PM IST
Date Processed: 5/31/2017 9:45:37 AM IST

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- **Channel Name:** ACQUITY TUV ChA 254nm

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- **Run Time:** 4.0 Minutes

- **Acquired By:** System
- **Sample Set Name:**
- **Acq. Method Set:** at
- **Processing Method:** 60 40 water acetonitrile
- **Channel Name:** ACQUITY TUV ChA
- **Proc. Chnl. Descr.:** ACQUITY TUV ChA 254nm

- **Date Acquired:** 5/25/2017 3:00:53 PM IST
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