Lab-Guide

1. 实验安全

1.1 通用安全注意事项

a)实验过程中（反应处理、过柱、旋蒸等）必须佩带防护镜。[Lab goggles or glasses MUST be worn at all times while working in the lab! This is extremely important because even things that seem pretty common and safe (e.g., using the rotovap) involve placing glassware under reduced pressure, which can potentially lead to implosions.]

b)使用危险试剂或者处理特殊反应，必须提前给同实验室同学交涉。

c)任何时候严禁一个人独自在实验室中工作（整理数据，电脑工作除外）。[Don't work in the lab alone! Computer work is okay, but you should plan to have someone else in the lab whenever you need to get something done. This is especially true if you are doing a large scale-up, running reactions with very reactive materials (i.e., strong oxidants or reductants, Grignard reagents, lithium reagents, etc), carrying out reactions requiring high pressure, or running a reaction for the first time. If you do end up working alone, always leave the door open so that someone can get in if there is a problem. Avoid quenching or dispensing large quantities of highly reactive chemicals when no one else is around.]

d)高温过夜实验需要在通风橱贴上标签（实验人员，反应时间，联系方式，反应温度等信息）。

e)牢记灭火器种类与摆放位置以及淋浴等应急处理的位置。

f)地板上不能存放药品，地板需要保持整洁卫生（定期大扫除）。

g)人离开需要拉下通风橱。

h)不允许戴手袋开关门、电梯；不允许穿实验服、戴手套以及携带实验药品进入休息室。

i)每晚最后离开实验室的人员需要仔细检查水、电、门是否正常。

j)实验室万一出现意外事故，请第一时间确保自己的人生安全。

1.2. 反应安全事项

1.2.1. LABEL, LABEL, LABEL all your reactions clearly! This is not only for your safety, but for everyone else's as well. Reaction labels should clearly correspond to your notebooks, such that if something goes wrong and you are not available other lab members or safety personnel can

take appropriate measures.

1.2.2.Reactions under high pressure (e.g., with condensed gases or in super-heated solvents) are explosion hazards and should be treated with extreme caution. A blast shield should be placed in front any system larger than an NMR tube under pressure. NMR tube reactions should also be treated with extreme caution – the hood sash should always be lowered when working with NMR tubes that are under pressure.

1.2.3.Water condenser hoses should be fastened with copper wire, and water flow should be turned as low as possible at night. Remember that the water pressure will increase at night with fewer users in the building.

1.2.4 Oxidants (e.g., bleach, CrVI and MnVII salts, hypervalent iodine reagents, H2O2, etc) should be placed in separate waste from organic reagents/solvents. The oxidation of organics with these reagents can lead to violent exotherms and explosions.

1.2.5.Oxidizing acids (e.g., nitric acid and aqua regia) can react extremely violently with organics, especially acetone, and the resulting explosions and release of corrosive solutions can lead to serious injury. Acids should always be stored in a separate location from organic chemicals. Additionally, waste bottles for acids should be clearly marked and placed in a separate location from organic waste. This will prevent mistakenly pouring acid waste in with organics, which is the most common cause of this type of explosion.

1.2.6. Perchlorate salts can explode without warning, especially when concentrated in the presence of organics (ClO_4^- is a strong oxidant!). Always use a blast shield when concentrating mixtures containing these salts and avoid the use of the ClO_4^- counter anion whenever possible.

1.2.7 Metallic lithium should never be placed in N_2 dry boxes or under a nitrogen atmosphere on your line. A violent and highly exothermic reaction will result from spontaneous "Li_3N" formation.

1.2.8.Remember that even common flash chromatography columns are run under high pressure and can crack or explode unexpectedly.

1.2.9.Examples of toxicity hazards include thallium salts (e.g., TlOEt), alkyl mercury salts (e.g., $HgMe_2$), tin reagents (especially tetra-alkyl or tri-alkyl aryl Sn compounds) and alkylating agents (e.g., MeI).

Exercise extreme caution when using these reagents!! Clean up spills in your hood and in public areas (balances, dry boxes, etc) immediately, using appropriate procedures and dispose of cleaning supplies and gloves in solid waste containers beneath the hood to avoid fume inhalation.

2.实验卫生

公共卫生（地板、窗台、休息室以及其他公用实验区域）由实验室值日小组负责，个人卫生（实验台、通风橱等）由个人及时清理，至少一周需要进行 1 次大扫除。

3. Ordering Chemicals

Before you order chemicals check if the substances are already in the group or elsewhere in the university.

4. Literature: (建议使用文献订阅功能每天进行最新文献跟踪，如 theoldreader)

It is important to keep up on the current literature in organic and organometallic chemistry – particularly as it relates to your project. Additionally, you will periodically be asked to choose a paper from the current literature to present at group meeting. The following are journals that you should read **every day** and are appropriate sources for group meeting papers:

Angew. Chem. Int. Ed./J. Am. Chem. Soc./Chem. Sci. /Nature Chem.

Org. Lett./Chem. Comm./Chem. Eur. J.

Nature/Science

Organometallics

Nature Comm./Chem/Science Advances

[Note that reading the literature is critical not only to learn more about your project/area of research but also to get you prepared for upcoming seminar speakers, proposal writing, orals, local meetings, writing your own papers, and ultimately getting a job!]

General tips for reading the chemical literature

4.1. You cannot expect to read everything.

4.2. Try to read papers that are (i) the most interesting to you and (ii) the most relevant to your and the group's research projects.

4.3. No one has time to read the entire text of every article. Read the abstract and introduction

and then try to discern the major point of the paper from the Figures and Schemes. If you find something especially interesting or unclear consult the text for further details. Keep in mind when writing your own papers that these are the sections that are usually the most read.

4.4. Whenever possible, discuss with others what you have read! This will solidify your general knowledge as well as improve your understanding of what you have read.

4.5. **Take particular note of papers that describe selective reactions and very strange reaction/mechanism.** These are the most useful in synthetic chemistry and the most difficult to find by traditional searching techniques.

4.6. **Keep an eye out for molecules that could be assembled using the methodology that you are developing**. This will be helpful for those of you who are interested in applying methodology in total synthesis, as well as for writing proposals.

Other journals to keep an eye on (monthly) are:

Org. Process Res. Dev.

Tetrahedron Letters

Tetrahedron

Dalton Transactions

Chem. Rev.

Chem. Soc. Rev.

Acc. Chem. Res.

Synlett

Org. Chem. Frontier

OBC

ChemCatChem

Publications have to be saved as pdf-files. The filenames then contain the journal, the year and the page number.

For example:

J. Am. Chem. Soc. **2017**, *139*, 4246–4249 → ja17-4246.pdf

Supporting Information, Supplementary Material → ja17-4246supp.pdf

5. Lab-Book

Maintaining a clear, well organized, and up-to-date lab notebook is critical for (a) keeping track of your experiments for your thesis, (b) any publications/ patents that you will write and (c) enabling future generations of students to reproduce your work.

General instructions for keeping a lab notebook are as follows.

5.1. Skip 3-4 pages in the beginning for the Table of Contents and update the TOC regularly (monthly, at least).

5.2. Use only non-erasable ink in your notebook. (不能使用铅笔书写)

5.3. Write the reaction/experiment clearly at the top of each page. If you are following a published procedure, indicate the reference from which the procedure was obtained.

5.4. The notes for an experiment contain: Reaction path, molecular formulas, molecular masses of the reactants, the quantity of the experiment, the work-up procedure and the yield(s) of the product(s) and the commercial source/purity of the reagent.

11.2.5. Write a detailed experimental, including the rate/order/time/temperature of addition of each reagent and solvent, and, where appropriate, any color changes that take place during the reaction. Also, detail all work up procedures and TLC data (where appropriate) for the reaction.

5.6. Be sure to weigh the product and determine the % yield for all reactions!!

5.7. NMR/IR/MS spectra should be saved and labeled according to the notebook number.

5.8 The number of the experiment has to be consecutive. If the experiment is done for the second time it has to have a new number and a new page!

Cite also the relevant publications in the lab-book!

After purification the first isolated substance will be A: LWP100A, the second B: LWP100B.

NMR experiments should be named: XX20170404(date)LWP100A. **After the experiment is completed and the products are characterised, save all spectra as unprotected pdf-files or in a word-file!**

Requirements for the characterization of new compounds. 1. Yield in mg and %. 2. Appearance (m.p) and color. 3. NMR (^{1}H, ^{13}C, dept135, dept 90 (or HSQC-me), if necessary ^{31}P, ^{19}F, H,H-COSY, HMBC. 4. MS, GC-MS, HRMS. 5. IR. 6. X-ray, UV-, CD-, Fluorescence- and CV-spectra.

For already published compounds a ^{1}H-NMR is sufficient, cite the publication!

Label, Label, Label your products with your experiment number on NMR tubes, HRMS, ESI vials and flasks.

Do all the necessary analytical work immediately after purification of the compounds!

科技论文写作步骤

1. Create a Useful Outline (确定课题前需要明确这个课题所解决的问题和重要性：very important, highly important or important?并合理列出提纲)

Gather some data, determine the major advances of the project

ASK yourself: WHY? WHAT? HOW?

Carefully organize the data by importance (not chronology)

Consider possible figures and where they should appear in the text

Review your outline with a colleague to see if you missed a key point (in the group seminar)

2. Choose the Journal Carefully (depending on the topic the journal prefers to)

3. Tell a story not chemistry

Make sure the paper has a main theme and punchline

AVOID "data dumping"

Provide context to prior literature, and **cite** the **original work** in the reference section

Explain why the problem is important (it's better to explain in mechanistic pathway; if only the others don't do this work, it's not enough for a good paper)

Analyze the data accurately and objectively

Provide a STRONG conclusion, describing how your work moves the field forward, but be realistic

4. Draw Graphics with Care (very very important, check and discuss with others, correct and correct)

Be clear an precise, simple but informative

Graphics should complement the text and support your story

Color is better if possible

Graphics must be original, unpublished artwork created by the author

5. Attract the Readers with a STRONG TITLE

Craft a compelling title: Describe your results/findings in as few words as possible, in an evocative and exciting way (the title is shorter, the manuscript is better)

Avoid buzz words and hard-to-justify claims like "first" and "only"

Avoid asking a question in the title: be clear on what was accomplished

6. Check-Discuss-Correct-Discuss-Consider-Correct (usually this step takes a long time, at least 10 times before submission)

7. White a strong cover letter

论文投稿前自查清单

序号	内容	Y/N
1	论文题目是否精炼准确，无拼写、概念错误。	
2	所有作者的姓名，地址是否准确无误。	
3	论文中的分子式是否符合规范，尺寸要一致。(出版社要求)	
4	论文中的化合物的相对构型是否正确。	
5	论文中化合物编号有无重复、漏编。（是否与 SI 对应）	
6	论文中化合物命名是否正确规范。	
7	论文中所用缩写是否正确规范，是否已给出全名。	
8	正文所用数据，实验演进是否符合科学逻辑。	
9	正文所用数据与支持材料、原始记录本是否一致。	
10	实验步骤是否真实详尽、无歧义，不刻意放大或缩小实验规模	
11	基金名称是否翻译规范，基金号是否正确。	
12	文献引用是否全面、必要，有无遗漏。（特别是最直接相关的）	
13	文献引用格式是否符合所投杂志的要求。	
14	论文页数是否符合所投杂志要求。（Word 检查字数）	
15	论文内容没有违反相关法律，不涉及有关伦理问题。	
16	论文中所有数据、图表是否自己原创	
支持信息检查核对表		
17	文章题目、作者和通讯地址是否和正文一致	
18	目录	
19	通用步骤是否和实验记录一致	
20	是否每个化合物的 ^{1}H NMR,^{13}C NMR, IR 和 HRMS 齐全	
21	已知化合物是否引用了文献	
22	核磁谱图是否按照正文顺序排列	

实验室人员姓名缩写

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张崧琳 zsl

<实验记录本,检测等均采用姓名缩写编号>

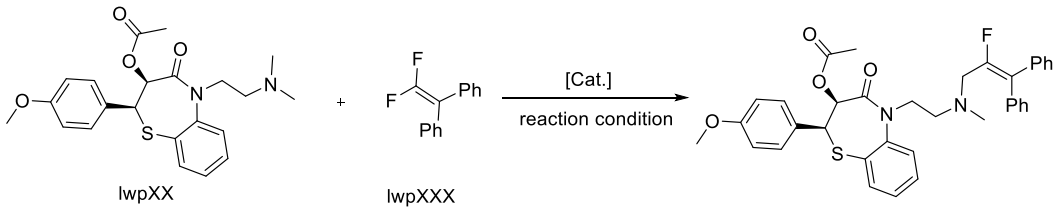
过夜反应模板(贴通风橱上)

实验 人员	时 间	反应 温度
（试剂、底物、溶剂、反应条件等基本信息）		
联系电话		

实验 人员	时 间	反应 温度
（试剂、底物、溶剂、反应条件等基本信息）		
联系电话		

实验记录本模板（每页只记录一个实验）

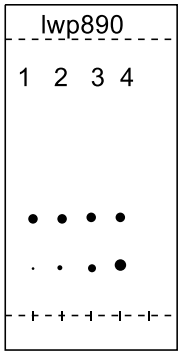
20170404　　lwp890



lwpXX　　lwpXXX

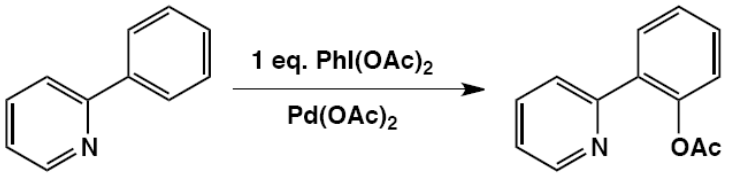
lwpxx: MW 442.53 g/mol, 0.5 mmol, 1 equiv, 221.3 mg
lwpxxx: MW 216.23 g/mol, 1 mmol, 2 equiv, 216.2 mg
[Cat.]: MW 800.56 g/mol, 0.05 mmol, 0.01 equiv, 4.0 mg （Sigma）

lwp890-1: DMF (1 mL)
89% ^{19}F NMR yield.
Wash with 10 mL water and extract with EA (3 mL) three times. Purified on flash CC (SiO2) (PE/EA = 1:10 to 1:3)
262.6 mg, 86%.
lwp890-2: MeCN (1 mL)
95% ^{19}F NMR yield.
lwp890-3: MeCN (0.5 mL)
87% ^{19}F NMR yield
lwp890-4: MeCN (0.2 mL)
70% ^{19}F NMR yield



Rf = 0.3 (PE/EA = 1:5)

500 MHZ：lwp890 (H,C,F)　(核磁图及时解析并用 Word 文档保存数据，word 或者 pdf 文档保存对应谱图)。
HRMS: lwp890 found:611.2374 (M+H)（同时使用文件夹按照编号顺序保存谱图或者保存电子文档）
IR: lwp890　ν = 3038, 2987, 1685, 1569……（同时使用文件夹按照编号顺序保存谱图）
white solid; mp. 105-106 °C;
（备注：所有样品检测结束后需转移到样品瓶放冰柜-20 °C 保存至文章接收，并拷贝该文章所有实验数据到课题组共用电脑备份）



Chemical	Source	Mol. Weight	Amount	mmol (eq)
$Pd(OAc)_2$	Pressure	224 g/mol	0.014 g	0.064 (0.05)
2-phenylpyridine	Aldrich	155.20 g/mol	0.200 g	1.29 (1.0)
$PhI(OAc)_2$	Acros	322.10 g/mol	0.415 g	1.29 (1.0)
AcOH (Solvent)	Fisher		8.0 mL	

Procedure

$Pd(OAc)_2$, $PhI(OAc)_2$ and 8-methylquinoline were placed in a 20 mL vial in that order. Acetic acid (8 mL) was added.

Mixture is a clear suspension with yellow solids at bottom of vial. Placed in oil bath at 100°C and heated for 1 hr. After 5 min, color changes to black.

Removed vial from bath and allowed to stand at 5 min at room temperature. Opened and removed ~10 mL for GC analysis.

GC shows 8% starting material (retention time 4 min) and 80% of a new peak at 6 min. Other unidentified peaks were observed at 7 and 9 min (5% each). GC labeled lwp891.

Rotovapped vial to dryness. Some of the material bumped into the rotovap trap. Recovered material by rinsing the trap with acetone (3 x 5 mL). Some remained stuck in the rotovap trap.

Dissolved reaction mixture in methylene chloride. Ran TLC's in 40%/60% and 50%/50% and 60%/40% hexanes/ethyl acetate. Optimal conditions were 50%/50% hexanes/ethyl acetate (product Rf =0.2).

Mistakenly dropped vial on bench and spilled approximately 1/4 of material. Yield is expected to be low as a result.

Rotovapped to dryness and redissolved in 50% hexanes/50% ethyl acetate)

Loaded onto silica column (50 g silica, wet-packed in 50%/50% hexanes/ethyl acetate), and collected 100 fractions.

Every other fraction was TLCed and fractions lwp891A, lwp891B, and lwp891C (each of the three spots were collected and rotovapped to dryness. Obtained 114 mg of fractions lwp891A, 10 mg of fractions lwp891B and 212 mg of fractions lwp891C.

^1H NMR spectra of each fraction was obtained in $CHCl_3$. Fractions lwp891A;lwp891B;lwp891C

Conclusions from 1H NMR and GC analysis:

Fractions lwp891A are iodobenzene with some other solvent impurities.

Fractions lwp891B contain aromatic and aliphatic peaks. Need to do more analysis.

Fractions lwp891C are the expected product. No solvent is present.

Molecular weight of product: 213.2 g/mol

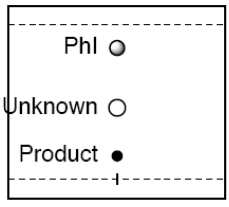
Amount Expected: 275 mg

Amount Obtained: 212 mg

% Yield: 77% yield

Colorless oil

Rf= 0.2 (PE/EA=1:1)



化合物数据表征模板

IR, ^{1}H NMR, ^{13}C NMR, HRMS

If solid, mp should be given.

^{1}H NMR （保留小数点后两位，严禁使用核磁软件自动解析读取数据）

s (singlet); brs (broad singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet) and m (multiplet)

^{13}C NMR（保留小数点后一位，严禁使用核磁软件自动解析读取数据）

For example

According to the general procedure 1, the crude product was purified by flash chromatography on SiO_2 (100% PE to PE:EA= 30:1). 8 h, 48 mg, 81%

Rf= 0.2 (PE/EA = 1:1)

White solid, mp = 117 ^{o}C.

IR (ATR): *v* = 3031, 2956, 2903, 2857, 1834, 1648, 1600, 1574, 1505, 1462, 1430, 1369, 1347, 1299, 1256, 1188, 1157, 1103, 1082, 1055, 1035, 994, 973, 955, 938, 899, 863, 835, 749, 690, 671, 640, 620 cm^{-1}

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.15-7.06 (m, 2H), 6.63 (t, *J* = 7.2 Hz, 1H), 6.38 (d, *J* = 8.1 Hz, 2H), 5.18 (dd, *J* = 8.7, 3.9 Hz, 1H), 3.62-3.51 (m, 1H), 3.46-3.36 (m, 1H), 2.58-2.43 (m, 1H), 2.20-1.96 (m, 3H) ppm

^{13}C NMR(75 MHz, $CDCl_3$): δ= 145.5, 143.5 (dddd, *J* = 246.6, 15.1, 12.0, 2.0 Hz), 141.0-138.6 (m), 137.4 (tt, *J* =12.3, 1.6 Hz), 129.4, 117.0, 111.7, 54.1, 48.5 (d, *J* = 1.6 Hz), 33.9, 24.5 ppm

^{19}F NMR (470 MHz, $CDCl_3$): δ= -91.9 – -91.2 (m, 2F), -145.8 – -146.0 (m, 2F) ppm

HRMS (EI) calcd. for $C_{15}H_{12}N_2F_4$ $[M]^+$: 296.09311, found: 296.09312.

TLC Stains

Stain	Uses	Recipe
p-Anisaldehyde	General purpose stain, particularly good with groups with nucleophilic properties.	Add 15 ml of AcOH and 3.5 mL of *p*-Anisaldehyde to 350 mL ice cold EtOH. Cautiously add 50 mL concentrated H2SO4 dropwise over 60 minutes. Store unused portion at 0°C.
Ninhydrin	Particularly good for amino acids.	Dissolve 1.5 g ninhydrin in 100mL of *n*-butanol and add 3 mL AcOH.
KMnO4	Olefins and other readily oxidized groups.	Dissolve 1.5 g KMnO4, 10 g K2CO3, and 1.25 mL 10% NaOH in 200 mL water.
Cerium Sulfate	General stain, particularly useful for alkaloids.	Make an aqueous solution of 10% Cerium (IV) sulfate and 15% H2SO4.
Morin Hydrate	General reagent. Fluorescently active.	Make up a 0.1 wt% solution in methanol.
Cerium Molybdate	General purpose stain. Requires heating to visualize. aka Hanessian's stain.	Dissolve 0.5g Ce(NH4)2(NO3)6 and 24.0 g of (NH4)6Mo7O24·4H2O. Carefully add 28 mL H2SO4, stir for 1 hour and filter if necessary.
2,4-DNP	aldehydes and ketones	Dissolve 12 g of 2,4-dinitrophenylhydrazine, 60 mL of H2SO4, and 80 mL of H2O in 200 mL 95% EtOH.
Bromocresol Green	Acidic (pKA <5) groups	Add 0.04g bromocresol green to 100 mL absolute EtOH. Slowly drip in a 0.1M solution of NaOH until the solution just turns pale blue.
Phosphomolybdic Acid	General purpose	Dissolve 10 g PMA in 100 mL absolute ethanol

核磁管清洗（很重要）

1.Rinse the contents of your NMR tubes into organic (or aqueous) waste, depending of the contents of the tube.

2.Rinse tubes at least one to two more times with a wash bottle into your waste before using the NMR tube cleaner. These steps are important to avoid cross contamination of the NMR tube cleaner with everyone's samples.

3.Note that you should never stick the tip of a wash bottle into an NMR tube to wash it out. This will inevitably lead to breaking the end off the tube. Instead, always hold the bottle several cm away from the end of the tube to spray the solvent in.

4.If solids or precipitated metals remain in the tube at this point, clean it out with some solvent (typically acetone) and a pipe cleaner.

5.**Use the NMR tube washer to finish cleaning the tube. Typical solvent rinses might involve methanol followed by acetone, then ethyl acetate then dichloromethane.**

6.Note that aqueous washings (i.e., bleach, water, acid, etc.) are sometimes necessary to remove toxic reagents like Sn and or other water-soluble reagents. However, these washings need to be separated from the organic washings, and disposed of appropriately.(对于金属残留物，用王水浸泡 12 小时后用水洗净，然后用 NMR tube washer)。

Also, washes with H_2O or aqueous solutions should be followed by copious rinsing with methanol before the introduction of immiscible organics like dichloromethane or hexanes.

7.Place NMR tubes flat in the oven to dry. Do not leave them in the oven for more than ~6-8 hrs (after which they should be placed in a dessicator for storage). Leaving the NMR tubes in the oven for longer than this can lead to warping, which may cause problems with spinning, shimming, and/or result in breakage in the NMR instruments.

8.For an excellent reference regarding an NMR tube cleaning system see, Org. Process Res. Dev., 2016, 20 (2), pp 319–319.

有机化学资源

1. Periodic Table （https://www.webelements.com/）

2. Organic Chemistry Resources （http://www.organicworldwide.net/）

3. Aldrich Substructure Search （http://www.sigmaaldrich.com/chemistry.html）

4. Nobel Prize Internet Archive （http://www.almaz.com/nobel/nobel.html）

5. pKa Table （http://www.chem.wisc.edu/areas/reich/pkatable/index.htm）

6.免费文献直达 http://sci-hub.cc/

7.文献链接 http://chemsearch.kovsky.net/

8. Organic Chemistry Conferences
（http://www.chemistry-conferences.com/topics/organic-chemistry.htm）

9.有机合成方法学论文写作（http://www.lac.dicp.ac.cn/pdf/lwxz.pdf）

Group seminar

个人工作报告每两周一次

文献报告每周一次（最新文献详细讲解；新兴话题；有机材料；有机化学家；反应机理讲解）

组内随机考核（元素周期表基础知识、新文献阅读情况、常用反应机理书写、实验记录本考察等方式）