
Contents

List of Figures	xiii
List of Tables	xxi
Preface.....	xxiii
Authors	xxv
Chapter 1 General introduction.....	1
Chapter 2 Safety.....	3
2.1 Safety is your primary responsibility.....	3
2.2 Safe working practice.....	4
2.3 Safety risk assessments.....	4
2.4 Common hazards	5
2.4.1 Injuries caused by use of laboratory equipment and apparatus	5
2.4.2 Toxicological and other hazards caused by chemical exposure.....	5
2.4.3 Chemical explosion and fire hazards	6
2.5 Accident and emergency procedures	10
Bibliography.....	10
Chapter 3 Keeping records of laboratory work.....	13
3.1 Introduction.....	13
3.2 The laboratory notebook.....	13
3.2.1 Why keep a lab book?	13
3.2.2 Laboratory records, experimental validity, and intellectual property	14
3.2.3 How to write a lab book: Paper or electronic	15
3.2.4 Paper lab notebook: Suggested lab notebook format	17
3.2.5 Electronic laboratory notebooks.....	20
3.3 Keeping records of data.....	21
3.3.1 Purity, structure determination, and characterization	22
3.3.2 What types of data should be collected?.....	22
3.3.3 Organizing your data records	27

3.4	Some tips on report and thesis preparation	29
3.4.1	Sections of a report or thesis	31
3.4.2	Planning a report or thesis	31
3.4.3	Writing the report or thesis	33
	Bibliography	40
Chapter 4	Equipping the laboratory and the bench	41
4.1	Introduction	41
4.2	Setting up the laboratory	41
4.3	General laboratory equipment	42
4.3.1	Rotary evaporators	42
4.3.2	Refrigerator and/or freezer	42
4.3.3	Glass-drying ovens	42
4.3.4	Vacuum oven	43
4.3.5	Balances	43
4.3.6	Kugelrohr bulb-to-bulb distillation apparatus	43
4.3.7	Vacuum pumps	43
4.3.8	Inert gases	44
4.3.9	Solvent stills	45
4.3.10	General distillation equipment	46
4.3.11	Large laboratory glassware	47
4.3.12	Reaction monitoring	48
4.4	The individual bench	48
4.4.1	Routine glassware	49
4.4.2	Additional personal items	50
4.4.3	Specialized personal items	50
4.4.3.1	Double manifold	50
4.4.3.2	Three-way Quickfit gas inlet T taps	53
4.4.3.3	Filtration aids	54
4.4.3.4	Glassware for chromatography	56
4.5	Equipment for parallel experiments	58
4.5.1	Simple reactor blocks that attach to magnetic stirrer hot plates	59
4.5.2	Stand-alone reaction tube blocks	60
4.5.3	Automated weighing systems	60
4.5.4	Automated parallel dosing and sampling systems	61
4.6	Equipment for controlled experimentation	61
4.6.1	Jacketed vessels	61
4.6.2	Circulating heater-chillers	62
4.6.3	Peltier heater-chillers	63
4.6.4	Syringe pumps	63
4.6.5	Automated reaction control systems	63
4.6.6	All-in-one controlled reactor and calorimeter systems	63

Chapter 5	Purification and drying of solvents	65
5.1	Introduction.....	65
5.2	Purification of solvents	65
5.3	Drying agents.....	66
5.3.1	Alumina, Al_2O_3	67
5.3.2	Barium oxide, BaO	67
5.3.3	Boric anhydride, B_2O_3	67
5.3.4	Calcium chloride, CaCl_2	67
5.3.5	Calcium hydride, CaH_2	68
5.3.6	Calcium sulfate, CaSO_4	68
5.3.7	Lithium aluminum hydride, LiAlH_4	68
5.3.8	Magnesium, Mg	68
5.3.9	Magnesium sulfate, MgSO_4	68
5.3.10	Molecular sieves.....	68
5.3.11	Phosphorus pentoxide, P_2O_5	69
5.3.12	Potassium hydroxide, KOH	69
5.3.13	Sodium, Na	69
5.3.14	Sodium sulfate, Na_2SO_4	70
5.4	Drying of solvents	70
5.4.1	Solvent drying towers.....	70
5.4.2	Solvent stills.....	71
5.4.3	Procedures for purifying and drying common solvents	74
5.4.4	Karl Fisher analysis of water content.....	79
References	79
Chapter 6	Reagents: Preparation, purification, and handling	81
6.1	Introduction.....	81
6.2	Classification of reagents for handling.....	81
6.3	Techniques for obtaining pure and dry reagents	82
6.3.1	Purification and drying of liquids	83
6.3.2	Purifying and drying solid reagents	85
6.4	Techniques for handling and measuring reagents.....	87
6.4.1	Storing liquid reagents or solvents under an inert atmosphere.....	87
6.4.2	Bulk transfer of a liquid under inert atmosphere (cannulation).....	89
6.4.3	Using cannulation techniques to transfer measured volumes of liquid under inert atmosphere	91
6.4.4	Use of syringes for the transfer of reagents or solvents.....	94
6.4.5	Handling and weighing solids under inert atmosphere.....	102

6.5	Preparation and titration of simple organometallic reagents and lithium amide bases	107
6.5.1	General considerations	107
6.5.2	Preparation of Grignard reagents (e.g., phenylmagnesium bromide)	109
6.5.3	Titration of Grignard reagents	109
6.5.4	Preparation of organolithium reagents (e.g., <i>n</i> -butyllithium)	110
6.5.5	Titration of organolithium reagents (e.g., <i>n</i> -butyllithium)	111
6.5.6	Preparation of lithium amide bases (e.g., lithium diisopropylamide)	112
6.6	Preparation of diazomethane	113
6.6.1	Safety measures	113
6.6.2	Preparation of diazomethane (a dilute ethereal solution)	113
6.6.3	General procedure for esterification of carboxylic acids	115
6.6.4	Titration of diazomethane solutions	115
	References	115
Chapter 7 Gases.....		117
7.1	Introduction.....	117
7.2	Use of gas cylinders.....	117
7.2.1	Fitting and using a pressure regulator on a gas cylinder.....	118
7.3	Handling gases	120
7.4	Measurement of gases.....	122
7.4.1	Measurement of a gas using a standardized solution.....	122
7.4.2	Measurement of a gas using a gas-tight syringe	123
7.4.3	Measurement of a gas using a gas burette.....	123
7.4.4	Quantitative analysis of hydride solutions using a gas burette	125
7.4.5	Measurement of a gas by condensation	126
7.4.6	Measurement of a gas using a quantitative reaction.....	126
7.5	Inert gases	127
7.6	Reagent gases	127
7.6.1	Gas scrubbers	128
7.6.2	Methods for preparing some commonly used gases	128
	References	130

Chapter 8 Vacuum pumps.....	131
8.1 Introduction.....	131
8.2 House vacuum systems (low vacuum).....	131
8.3 Medium vacuum pumps	131
8.3.1 Water aspirators	131
8.3.2 Electric diaphragm pumps.....	132
8.4 High vacuum pumps	133
8.4.1 Rotary oil pumps	133
8.4.2 Vapor diffusion pumps.....	134
8.5 Pressure measurement and regulation	135
8.5.1 Units of pressure (vacuum) measurement.....	136
Chapter 9 Carrying out the reaction	137
9.1 Introduction.....	137
9.2 Reactions with air-sensitive reagents	138
9.2.1 Introduction.....	138
9.2.2 Preparing to carry out a reaction under inert conditions	138
9.2.3 Drying and assembling glassware.....	139
9.2.4 Typical reaction setups using a double manifold	140
9.2.5 Basic procedure for inert atmosphere reactions.....	140
9.2.6 Modifications to basic procedure	144
9.2.7 Use of balloons for holding an inert atmosphere	149
9.2.8 Use of a "spaghetti" tubing manifold.....	152
9.3 Reaction monitoring.....	153
9.3.1 Thin layer chromatography	153
9.3.2 High performance liquid chromatography	160
9.3.3 Gas-liquid chromatography (GC, GLC, VPC).....	164
9.3.4 NMR	167
9.4 Reactions at other than room temperature.....	167
9.4.1 Low-temperature reactions	168
9.4.2 Reactions above room temperature	170
9.5 Driving equilibria.....	177
9.5.1 Dean-Stark traps	177
9.5.2 High-pressure reactions	178
9.6 Agitation	178
9.6.1 Magnetic stirring	179
9.6.2 Mechanical stirrers.....	180
9.6.3 Mechanical shakers and vortexers.....	182
9.6.4 Sonication.....	183
9.7 Use of controlled reactor systems.....	184
9.7.1 Jacketed vessels.....	185
9.7.2 Parallel reactors.....	186
References	189

Chapter 10 Working up the reaction	191
10.1 Introduction.....	191
10.2 Quenching the reaction	191
10.2.1 Strongly basic nonaqueous reactions.....	192
10.2.2 Near neutral nonaqueous reactions.....	192
10.2.3 Strongly acidic nonaqueous reactions	193
10.2.4 Nonaqueous reactions involving Al(III) reagents.....	193
10.2.5 Reactions involving oxidizing mixtures that may contain peroxide residues.....	195
10.2.6 Acidic or basic aqueous reactions	195
10.2.7 Liquid ammonia reactions	195
10.2.8 Reactions involving homogeneous transition metal catalysts	197
10.3 Isolation of the crude product.....	198
10.3.1 Typical isolation from an aqueous work-up	199
10.3.2 Isolation from a reaction involving nonvolatile polar aprotic solvents	203
10.3.3 Using an acid/base aqueous work-up to separate neutral organics from amines.....	203
10.3.4 Using an acid/base aqueous work-up to separate neutral organics from carboxylic acids	204
10.3.5 Nonaqueous work-ups	205
10.3.6 Work-ups using scavenger resins.....	206
10.3.7 Use of scavengers to remove heavy metal residues	207
10.4 Data that need to be collected on the crude product prior to purification	208
Chapter 11 Purification	209
11.1 Introduction.....	209
11.2 Crystallization.....	209
11.2.1 Simple crystallization.....	209
11.2.2 Small-scale crystallization.....	212
11.2.3 Crystallization at low temperatures	214
11.2.4 Crystallization of air-sensitive compounds.....	217
11.3 Distillation	218
11.3.1 Simple distillation.....	218
11.3.2 Distillation under an inert atmosphere.....	220
11.3.3 Fractional distillation	221
11.3.4 Distillation under reduced pressure.....	223
11.3.5 Small-scale distillation.....	226
11.4 Sublimation.....	228
11.5 Flash chromatography	229

11.5.1	Equipment required for flash chromatography	230
11.5.2	Procedure for running a flash column	232
11.5.3	Recycling silica for flash chromatography	239
11.6	Dry-column flash chromatography	240
11.7	Preparative TLC	241
11.8	Medium pressure and prepacked chromatography systems.....	242
11.9	Preparative HPLC.....	245
11.9.1	Equipment required	245
11.9.2	Running a preparative HPLC separation.....	246
References	248

Chapter 12 Small-scale reactions..... 249

12.1	Introduction.....	249
12.2	Reactions at or below room temperature	250
12.3	Reactions above room temperature	252
12.4	Reactions in NMR tubes.....	253
12.5	Purification of materials	255
12.5.1	Distillation	255
12.5.2	Crystallization.....	255
12.5.3	Chromatography.....	255

Chapter 13 Large-scale reactions..... 259

13.1	Introduction.....	259
13.2	Carrying out the reaction	261
13.2.1	Using standard laboratory equipment	261
13.2.2	Using a jacketed vessel	261
13.3	Work-up and product isolation.....	263
13.4	Purification of the products	266

Chapter 14 Special procedures..... 267

14.1	Introduction.....	267
14.2	Catalytic hydrogenation	267
14.3	Photolysis	270
14.4	Ozonolysis.....	272
14.5	Flash vacuum pyrolysis (FVP).....	273
14.6	Liquid ammonia reactions	274
14.7	Microwave reactions	275
References	276

Chapter 15 Characterization..... 277

15.1	Introduction.....	277
15.2	NMR spectra	277
15.3	IR spectra	280

15.4	UV spectroscopy	280
15.5	Mass spectrometry	281
15.6	Melting point (m.p.) and boiling point (b.p.).....	281
15.7	Optical rotation	281
15.8	Microanalysis	282
15.9	Keeping the data	283
Chapter 16 Troubleshooting: What to do when things don't work.....		285
Chapter 17 The chemical literature.....		289
17.1	Structure of the chemical literature	289
17.2	Some important paper-based sources of chemical information	290
17.2.1	<i>Chemical Abstracts</i>	290
17.2.2	<i>Beilstein</i>	291
17.2.3	Science Citation Index (paper copy).....	292
17.3	Some important electronic-based sources of chemical information.....	294
17.3.1	SciFinder	295
17.3.2	Reaxys	295
17.3.3	Web of Science and SCOPUS	295
17.3.4	Cambridge Structural Database (CSD).....	296
17.3.5	The World Wide Web	296
17.4	How to find chemical information.....	296
17.4.1	How to do searches	296
17.4.2	How to find information on specific compounds.....	297
17.4.3	How to find information on classes of compounds	297
17.4.4	How to find information on synthetic methods	298
17.5	Current awareness.....	298
	References	299
	Appendix 1: Properties of common solvents	301
	Appendix 2: Properties of common gases.....	305
	Appendix 3: Approximate pK_a values for some common reagents versus common bases	309
	Appendix 4: Common Bronsted acids	311
	Appendix 5: Common Lewis acids	313
	Appendix 6: Common reducing reagents	315
	Appendix 7: Common oxidizing reagents.....	319
	Index	323