

*Lutz F. Tietze, Theophil Eicher,
Ulf Diederichsen, Andreas Speicher*

Reactions and Syntheses

in the Organic Chemistry Laboratory



WILEY-VCH Verlag GmbH & Co. KGaA

Contents

1 C–C Bond formation

Introduction	1
1.1 Nucleophilic addition to aldehydes, ketones, carboxylic acid derivatives (esters, anhydrides), and α,β-unsaturated carbonyl compounds; carbonyl olefination	4
1.1.1 (<i>E</i>)-Acetoxy-2-methyl-2-butenal	4
1.1.2 (<i>S</i>)-2,3-Dimethylhex-5-en-3-ol	10
1.1.3 (<i>S</i>)-5-Oxo-3,5-diphenylpentanoic acid methyl ester	16
1.1.4 (<i>S</i>)-3-Phenylheptanoic acid	22
1.1.5 Ethyl 8-chloro-4-methyl naphthalene-2-carboxylate	28
1.1.6 ($\pm$)-4-Hydroxy- <i>ar</i> -himachalane	33
1.1.7 Methylenecyclododecane	41
1.2 Alkylation of aldehydes/ketones, carboxylic acids, and β-dicarbonyl compounds	46
1.2.1 (+)-(<i>S</i>)-4-Methylheptan-3-one	46
1.2.2 (<i>S</i>)-2-Isopropylhex-4-yn-1-ol	50
1.2.3 3-Oxo-5-phenylpentanoic acid methylester	59
1.3 Reactions of the aldol and Mannich type	62
1.3.1 Olivetol	62
1.3.2 (+)-(<i>7aS</i>)-7,7a-Dihydro-7a-methyl-1,5(<i>6H</i>)-indanedione	66
1.3.3 Cyclohexyl 2-benzoylamino-2-(2'-oxocyclohexyl) acetate	71
1.3.4 (<i>S</i>)-1-Hydroxy-1,3-diphenyl-3-propanone	78
1.3.5 [(1 <i>S</i> ,2 <i>R</i> ,6 <i>R</i>)-2-Hydroxy-4-oxo-2,6-diphenyl]cyclohexane carboxylic acid ethyl ester	85
1.4 Electrophilic and nucleophilic acylation	92
1.4.1 (–)-Ethyl (1 <i>R</i>)-1-methyl-2-oxocyclopentane-1-carboxylate	92
1.4.2 Ethyl (<i>S</i>)- and (<i>R</i>)-2-hydroxy-4-phenylbutanoate	97
1.4.3 Naproxen	104
1.4.4 3-Benzoylcyclohexanone	114
1.5 Reactions of alkenes via carbenium ions	119
1.5.1 Piperine	119
1.5.2 Cicloxilic acid	126
1.5.3 β -Ionone	131

1.6	Transition-metal-catalyzed reactions	138
1.6.1	(<i>E</i>)-4-Chlorostilbene	138
1.6.2	2-Cyanomethyl-3',4'-dimethoxybiphenyl	143
1.6.3	(2-Phenylethynyl)aniline	149
1.6.4	3,3-Dimethylcyclohexanone	152
1.7	Pericyclic reactions	156
1.7.1	Tranlycypromine	156
1.7.2	11,11-Difluoro-1,6-methano[10]annulene	162
1.7.3	Dimethyl heptalene-1,2-dicarboxylate	167
1.7.4	Dimethyl 1,8-bishomocubane-4,6-dicarboxylate	172
1.7.5	α -Terpineol	177
1.7.6	Bicyclo[2.2.2]octene derivative	187
1.8	Radical reactions	191
1.8.1	Ethyl 4,6,6,6-tetrachloro-3,3-dimethylhexanoate	191
1.8.2	3-Bromophenanthrene	195
2	Oxidation and reduction	
2.1	Epoxidation of C=C bonds	199
2.1.1	Sharpless–Katsuki epoxidation	199
2.1.2	Jacobsen epoxidation	202
2.2	Dihydroxylation of C=C bonds	210
2.2.1	Sharpless dihydroxylation	211
2.3	Oxidation of alcohols to carbonyl compounds	214
2.3.1	Swern oxidation	215
2.3.2	Dess–Martin oxidation	217
2.3.3	Perruthenate oxidation	220
2.3.4	TEMPO oxidation	222
2.4	Enantioselective reduction of ketones	224
2.4.1	BINAL-H -Reduction of butyrophenone	227
2.4.2	CBS-Reduction of acetophenone	228

3 Heterocyclic compounds

Introduction	233
3.1 Three- and four-membered heterocycles	236
3.1.1 (<i>S</i>)-Propranolol	236
3.1.2 Oxetane derivative	241
3.1.3 Azetidin-2-one derivative	245
3.2 Five-membered heterocycles	249
3.2.1 2,4-Diphenylfuran	249
3.2.2 3,4-Dimethylpyrrole	255
3.2.3 4,6-Dimethoxybenzo[b]thiophene	262
3.2.4 2-Phenylindole	268
3.2.5 Melatonin	272
3.2.6 3-(4-Methylbenzoylamino)-1-phenyl-4,5-dihydropyrazole	279
3.2.7 Camalexin	284
3.2.8 Microwave-assisted pyrazole synthesis	289
3.3 Six-membered heterocycles	293
3.3.1 Azine and diazine syntheses with acetoacetate	293
3.3.2 (<i>R</i>)-Salsolidine	302
3.3.3 Epirizole	308
3.3.4 Ras farnesyltransferase inhibitor	313
3.3.5 ($\pm$)-Dihydrexidine	322
3.4 Condensed heterocycles	333
3.4.1 6-Ethoxycarbonylnaphtho[2,3- <i>a</i>]indolizine-7,12-quinone	333
3.4.2 EGF-R-Pyrrolo[2,3- <i>d</i>]pyrimidine	341
3.4.3 7-Phenyl-1,6-naphthyridine	347
3.4.4 Caffeine	351
3.4.5 Nedocromil analogon	357
3.4.6 High-pressure reaction	366
3.5 Other heterocyclic systems; heterocyclic dyes	372
3.5.1 ($\pm$)-Samin	372
3.5.2 Dibenzopyridino[18]crown-6	380
3.5.3 Indigo	385
3.5.4 Pyrvinium iodide	389
3.5.5 2,3,7,8,12,13,17,18-Octamethylporphyrin	396
3.5.6 Synthesis of a rotaxane	399

4	Selected natural products	
4.1	Alkaloids	404
	Introduction	404
4.1.1	Hirsutine	407
4.1.2	<i>rac</i> -2,3-Dimethoxyberbine	419
4.1.3	Buflavine	426
4.2	Isoprenoids	432
	Introduction	432
4.2.1	($\pm$)- <i>trans</i> -Chrysanthemic acid	436
4.2.2	Nerol	443
4.2.3	(-)-Menthol	450
4.2.4	Artemisia ketone	455
4.2.5	Veticadinol	459
4.2.6	all- <i>trans</i> -Vitamin A acetate	469
4.3	Carbohydrates	476
	Introduction	476
4.3.1	Synthesis of glycosyl donors	479
4.3.2	Glycosylations of glucosyl donors with cyclopentanol	485
4.4	Amino acids and peptides	489
	Introduction	489
4.4.1	<i>N</i> -Boc- <i>N</i> -methyl-(<i>S</i>)-alanyl nucleo amino acid	493
4.4.2	(<i>S</i>)-Homoproline	498
4.4.3	Amino acid resolution with amino acylase	507
4.4.4	γ,δ -Unsaturated α -amino acids	512
4.4.5	Passerini hydroxyamide	518
4.4.6	Aspartame	525
4.4.7	Ugi dipeptide ester	533
4.4.8	Solid-phase synthesis of β -peptides	537
4.5	Nucleotides and oligonucleotides	542
	Introduction	542
4.5.1	2',3'-Dibenzoyl-6'- <i>O</i> -DMT- β - <i>D</i> -glucopyranosyl-uracil 4'- <i>O</i> -phosphoramidite	546
4.5.2	Solid-phase Synthesis of Nucleic acids	556
5	Index of reactions	561
6	Index of products	566
7	Subject Index	573