

Contents

Preface							
In	troduc	tion .		2			
1	Stero	Steroids: a Brief History					
1	1.1	Structure Determination	Squices of Prograterane	10 10			
	1.1	1.1.1 Cholesterol and Cholic Acid	Rivatered do Not more S.o.	10			
		1.1.2 The Sex Steroids	6.2.2 By Total Synthesis	13			
		1.1.3 Corticosteroids		16			
		1.1.5 Corneosteroids		10			
2	Sources of Steroids						
	2.1	Biosynthesis		20 20			
	2.2	Commercial Steroid Starting Materials		22			
		2.2.1 Diosgenin		23			
		2.2.2 Soybean Sterols		25			
		and the state of t		0.00			
3	Estra	nes: Steroids in Which Ring A is Aromatic		28			
	3.1	Biological Activity		28			
	3.2	Sources of Estranes		28			
		3.2.1 From Androstanes		28			
		3.2.2 Estrogens by Total Synthesis		32			
	3.3	Chemical Reactions of Estranes		37			
		3.3.1 Aromatic A-ring Reactions		37			
		3.3.2 Modifications on Ring B		40			
		3.3.3 Modifications on Ring C		41			
		3.3.4 Modifications on Ring D		42			
	3.4.	Some Drugs Based on Estranes		45			
4	Gona	nes or 19-nor-Steroids		48			
	4.1	Preparation of Gonane Starting Materials		48			
		4.1.1 Birch Reduction		48			
		4.1.2 Synthesis by Sequential Annulation React	ions	49			
	4.2	Anabolic-Androgenic Gonanes		50			
		4.2.1 Biological Activity		50			
		4.2.2 Synthesis of 19-Norandrogens		51			
	4.3	Progestational Gonanes		55			
		4.3.1 Biological Activity	distribution of the contract o	55			
		4.3.2 Preparation of 19-Norprogestins	on monorable a may abounce will be stressed to be seen to be	55			
	4.4	Some Drugs Based on Gonanes		67			
		4.4.1 Androgenic–Anabolic Agents		67			
		4.4.2 Progestins		67			
		4.4.3 Progestin Antagonists		67			
			or kiba oli Bornandi dan kibana kan es				
5		ostanes, C ₁₉ Steroids and Their Derivatives	(musika deskad)) es dandas hababailana bele d	68			
	5.1	Biological Activity		68			
	5.2	Sources of Androstanes		68			
		5.2.1 From Pregnenolone		68			
		5.2.2 Fermentations		69			
		5.2.3 Total Synthesis		69			

	5.3	Modifie	d Anabolic-Androgenic Androstanes	69	
		5.3.1	17-Desalkyl Compounds	69	
		5.3.2	17-Alkyl Compounds	73	
		5.3.3	Modifications on Ring B	77	
		5.3.4	Modifications on Ring C	79	
		5.3.5	Modifications on Ring D	80	
	5.4		obutyrolactone Aldosterone Antagonists	83	
	5.5		rugs Based on Androstanes	85	
		5.5.1	Androgens	85	
		5.5.2	Spirobutyrolactones	85	
6	Pregn	anes, Par	rt 1: Progestins	86	
	6.1		eal Activity	86	
	6.2		of Progesterone	86	
		6.2.1	From Phytochemicals	86	
		6.2.2	By Total Synthesis	87	
		6.2.3	From Dehydroepiandrosterone (DHEA) Acetate	88	
	6.3		d Pregnanes	88	
		6.3.1	17-Hydroxy and Acyloxy Derivatives	88	
		6.3.2	Modifications on Ring A	89	
		6.3.3	Modifications on Ring B	90	
		6.3.4	General Methods for Modifications on Ring D	94 96	
		6.3.5	More Progesterone Analogues	100	
	6.4		rugs Based on Progestins	100	
		6.4.1	Medroxyprogesterone Acetate (10-2)	100	
		6.4.2	Megestrol Acetate (10-3)	101	
		6.4.3	Melengestrol Acetate (26-7)	101	
7	Pregn	anes, Par	rt 2: Corticosteroids	102	
	7.1		eal Activity	102	
	7.2		of Corticoids	102	
		7.2.1.	Introduction of Oxygen at C ₁₁	102	
		7.2.2	Construction of the Dihydroxyacetone Side Chain	103	
	7.3		d Corticoids	105	
		7.3.1	Unsaturation	105	
		7.3.2	Additional Alkyl Groups	106	
		7.3.3	Halogenated Corticoids	109	
		7.3.4	Hydroxylation: 16,17-Diols	111	
		7.3.5	Corticoids with Multiple Modifications	112	
	o <u>r</u> yerd	7.3.6	Miscellaneous Corticoids	117 119	
	7.4	Some D	rugs Based on Corticoids	119	
8	Misce	llaneous	Steroids	122	
	8.1		yclic Steroids	122	
		8.1.1	Introduction	122	
		8.1.2	Steroids with a Heteroatom in Ring A	122	
		8.1.3	Steroids with a Heteroatom in Ring B	124	
		8.1.4	Steroids with a Heteroatom in Ring C	126	
		8.1.5	Steroids with a Heteroatom in Ring D	128	
	8.2	Cardeno		129	
		8.2.1	Actodigin Aglycone	130	
		8.2.2	Synthesis from a Bile Acid	130	
	8.3	Compou	ands Related to Cholesterol	132	
-				135	
Subject Index Reactions Index					
R	eactions	Index		141	

Steroid Chemistry at a Glance

Daniel Lednicer

The term steroid has become virtually synonymous with drug abuse in sport to the majority of the public. However these steroids —androgens— actually comprise only a single relatively small class of biologically active steroids, and are overshadowed by a large collection of compounds, a sizeable number of which are commercial drugs, that share the same structural carbon skeleton. The development of these drugs has led to a large body of organic chemistry often denoted as "Steroid Chemistry".

Steroid Chemistry at a Glance provides a concise overview of the main principles, biological activity, chemical synthesis, and reactions of steroid chemistry. Topics covered include:

- history, isolation and structure determination of steroids
- steroid nomenclature and stereochemistry
- natural sources of steroids
- estranes
- gonanes (19-nor steroids)
- androstanes
- progestins
- corticosteroids
- heterocyclic steroids

Based on the highly successful and student friendly "at a glance" approach, *Steroid Chemistry at a Glance* provides students with a resource with which they can quickly, concisely and confidently acquire, regularly review and revise the basic facts that underpin the properties, synthesis and reactions of this important class of natural product-derived compounds. It will also serve as a handy bench reference for postgraduates and professional chemists.

Daniel Lednicer's career in both the private and public sectors has been devoted to the search for new therapeutic agents. He spent two decades at the bench as a chemist at the Upjohn Company. Following that, he served as director of chemical research at Mead Johnson, director of pharmaceutical sciences at Adria Laboratories, and pharmaceutical manager at Analytical Biochemistry Laboratories. Most recently, he was a project officer at the National Cancer Institute. Daniel Lednicer is the author of several books on drug synthesis and discovery, including seven volumes of the series "Organic Chemistry of Drug Synthesis".



