Dioxo-2,5-méthyl-4-hydroxy-4-N-phénylpyrrolidine (**18**). 25,8 g de **16** sont portés à reflux 4 h dans 200 ml d'eau. **18** cristallise à froid. Rdt.: 10,5 g. F. 162–164° (éthanol). – ^{1}H-RMN. (60 MHz, DMSO-d_6): 1,52 ppm (*s*, 3 H: $-CH_3$); 2,9 ppm (*q*, 2 H: $-CH_2-$); 6,12 ppm (*s*, 1 H: –OH); 7,38 ppm (*m*, 5 H arom.). – SM.: *m/e* 205 (M^+); 187 ($M^+ - H_2O$); 177 ($M^+ - CO$); 119 ($C_6H_5NCO^+$); 58 ($CH_3C^+(OH)CH_2$); 43 (CH_3CO^+).

$C_{11}H_{11}NO_3$ (205,22) Calc. C 64,30 H 5,41 N 6,83% Tr. C 64,18 H 5,25 N 6,78%

Dioxo-2,5-méthyl-4-Δ^3-N-phénylpyrroline (**19**). 2 g de **18** sont portés à reflux 2 h dans 20 ml d'anhydride acétique avec 2 g d'acétate de sodium anhydre. Le mélange réactionnel est alors refroidi, versé dans de l'eau glacée et extrait à l'éther. Après évaporation de l'éther il précipite 1,2 g de **19**. F. 96–97° (éthanol) (échantillon de référence **12** [6], F. 97–98° (éthanol), Litt. [8] 98–99°).

Acide N-phényl-succinamique (**21**). 2 g de **10** (ou de **13**) sont portés $^1/_2$ h à reflux dans 10 ml de KOH 18%. La solution qui dégage une forte odeur d'ammoniac est refroidie et extraite à l'éther pour éliminer les produits neutres. Les eaux sont acidifiées à pH 4 avec de l'acide sulfurique et extraites à nouveau à l'éther. Après évaporation on obtient 0,9 g de **21**. F. 143–145° (eau) (échantillon de référence [7] F. 144–145°). – ^{1}H-RMN. (60 MHz, acétone-d_6): 4,33 ppm (*s*, 4 H: $-CH_2-CH_2-$); 7,33 ppm (*m*, 5 H arom.); 9,13 (*s*, 1 H: –NH).

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77. Steroids

Part I

Selective Hydrogenation of Ergosterol and its Acetate

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(14. VIII. 74)

Summary. Selective hydrogenation of ergosterol or its acetate in solution in different solvents over *Raney* nickel to give 5α-ergosta-7,22-dien-3β-ol or its acetate can be controlled by the addition of paraformaldehyde, acetaldehyde, benzaldehyde, 4-dimethylaminobenzaldehyde, and dimethylaniline, the latter 2 giving the best yield. When using pure solvents 5α-ergost-7-en-3β-ol or its acetate can be obtained in almost quantitative yield.

Selective catalytic hydrogenation of ergosterol (I) or its acetate (IV) in ethyl acetate over *Raney* nickel to give γ-ergostenol or its acetate (resp. III and VI)

has been repeatedly described (*e.g.* I → III by *Ciba* Ltd. [1]; IV → VI by *Bladon et al.* [2]). We failed to realise these reactions using commercial ethyl acetate as solvent, but we found soon that this was due to the presence of about 2% acetaldehyde in the commercial product. This failure promoted the following research on the effect of certain ingredients on the catalytic hydrogenation of ergosterol and its acetate over *Raney* nickel. When using pure ethyl acetate, hydrogenation of IV gave after 20 minutes 55% of pure 5,6-dihydroergosteryl acetate (V), increasing to about 63% after 35 minutes; but with longer time a mixture of V and VI was formed, the latter gradually increasing in quantity to give after 6 h pure VI in 65% yield. On the other hand, on the addition of acetaldehyde (0.5% w/v), paraformaldehyde (0.2% w/v), benzaldehyde (0.5% w/v), 4-dimethylaminobenzaldehyde (0.5% w/v), or dimethylaniline (0.5% w/v) to the pure solvent, shaking IV with hydrogen for 6 h, compound V was mainly obtained. The inhibitory effect of certain compounds on olefinic catalytic hydrogenation has been related to the presence of a lone pair of electrons in the inhibitory molecules [3]. The presence of a free lone pair of electrons is evident in dimethylaniline and 4-dimethylaminobenzaldehyde which gave the best yield (95%) of V. Higher yields of pure V can be obtained on addition of an inhibitory ingredient rather than shortening the time of hydrogenation when using pure ethyl acetate [1]. The same results were obtained with thiophene-free benzene (*cf.* [4]) (see experimental). In this connection, it may be noted that *Ruyle et al.* [5] reported that the hydrogenation of IV in solution in thiophene-free benzene over *Raney* nickel gave, after 3 h at room temperature and a pressure of 3 atm. compound V in 90% yield. The solvent benzene used by *Ruyle et al.* was probably not rigorously purified.

Table 1. *Hydrogenation of ergosterol* (I) *and ergosteryl acetate* (IV) *in different solvents over* Raney *nickel*

I	Solvent	*Raney* nickel	Time	Products (g)			IV	Solvent	*Raney* nickel	Time	Products (g)		
(g)	(ml)	(~g)	(h)	II	III	others	(g)	(ml)	(~g)	(h)	V	VI	others
1	50[a]	1	6	0.92	–	–	2.0	150[a]	2	6	1.70	–	–
1	50[b]	1	6	–	0.85	–	1.9	150[a]	0.7	20	1.60	–	–
1	18[c]	1.5	3	–	0.90	–	0.5	25[b]	0.5	0.33	0.28	–	0.13[k]
1	18[d]	1.5	3	mixture[j]			0.5	25[b]	0.5	0.55	0.32	–	0.05[l]
1	18[e]	1.5	3	0.82[i]	–	–	1	50[h]	1	1	0.2	0.1	0.30[k]
1	50[f]	1	6	–	0.70	–	1	50[h]	1	6	–	0.65	–
0.5	25[g]	0.5	6	mixture[k]			10	85[h]	10	0.33	5	–	2.5[m]
							7	60[h]	7	3.50	mixture[l]		

[a]) Ethyl acetate contaminated with acetaldehyde; [b]) Pure ethyl acetate as attested by GLC.; [c]) Freshly purified dioxane [9]; [d]) Technical, dioxane contaminated with glycollic aldehyde or glyoxal (3.5 mg in 100 g) (identified as glyoxal bis-2,4-dinitrophenylhydrazone, m.p. & mixed m.p. with an authentic sample 315°); [e]) Mixture of pure & technical dioxane 1:1; [f]) Pure absolute ethanol; [g]) Technical 95% ethanol; [h]) Thiophene-free benzene; [i]) Indicating the effect of concentration of impurities on hydrogenation; *cf.* product obtained by *Pfizer* [7]; [j]) Neosterol [6] (0.58 g), and unchanged ergosterol; [k]) Inseparable mixture; [l]) (Probably V + VI as shown by comparison with products obtained by crystallizing a mixture of equal parts of V & VI from ethyl acetate/methanol and chloroform/methanol); [m]) Unchanged ergosteryl acetate.

Hydrogenation of I in solution in technical dioxane gave after 3 h neosterol (previously prepared synthetically from I & II by *Barton* & *Cox* [6]). We soon discovered the contamination of the commercial dioxane with glycollic aldehyde or/and glyoxal (3.5 mg in 100 g). Hydrogenation of I in solution in freshly purified dioxane gave III in almost quantitative yield after 3 h. When we used equal volumes of the purified and the technical dioxane, 5,6-dihydroergosterol (II) was obtained almost quantitatively. The process of removing the peroxide did not apparently affect other impurities such as glycollic aldehyde or glyoxal probably contaminating the dioxane used by

Table 2. *Hydrogenation of ergosteryl acetate* (IV) (1g) *in ethyl acetate* (50 ml) *with ingredients added* (0.5% w/v) *over* Raney *nickel* (1 g) for 6 h

Ingredient	Products (g)		
	V	VI	others
Acetaldehyde	0.70	0.06	0.20[b]
Paraformaldehyde[a]	0.85	–	–
Benzaldehyde	0.65	–	0.25[b]
4-Dimethylaminobenzaldehyde[c]	0.95	–	–
Dimethylaniline[c]	0.90	–	–

a) 0.20% w/v was only added.

b) A mixture similar to that of k in Table 1.

c) Hydrogenation of ergosterol (I) under the same conditions using 4-dimethylaminobenzaldehyde or dimethylaniline gave II in about 90% yield.

Laubach & *Brunings* [7] who reported that hydrogenation of I over *Raney* nickel gave after 3 h compound II.

The hydrogenation of I in solution in technical 95% ethanol gave a mixture of II & III. When using purified absolute ethanol, compound III was the main product.

It is apparent that the contaminants acetaldehyde, glyoxal or added ingredients such as dimethylaniline etc. (see above) will not interfere with hydrogenation of the ethylenic bond at position 5(6), and inhibit or at least retard that at position 22(23). It has been noted [8] that the side chain double bonds (*e.g.* at the 22(23)-position) are next in order of susceptibility (compared with the double bond at the 5,6-position) to catalytic hydrogenation.

Experimental Part

The $[\alpha]_D$-values were determined in chloroform at 20°.

Raney nickel was prepared from nickel-aluminium alloy (30 g) digested on steam bath for 4 h with sodium hydroxide (40 g) in distilled water (100 ml), and then thoroughly washed with distilled water.

Ergosterol (I) (from *British Drug House*) was crystallised from alcohol/benzene 2:1: m.p. 162°, $[\alpha]_D = -127°$.

Ergosteryl acetate (IV) was prepared from ergosterol by classical procedures and crystallised from ethyl acetate: m.p. 173–174°, $[\alpha]_D = -92°$.

Hydrogenation experiments (Tables 1 and 2) were carried out at room temperature and atmospheric pressure. After hydrogenation, the solution was decanted and the catalyst was treated with chloroform twice. The combined solutions were filtered. The solvent was eliminated under reduced pressure, and the residue was crystallised from ethyl acetate-methanol or chloroform-methanol.

The products were *5α-ergosta-7,22-dien-3β-ol* (II), m.p. 174–175°, $[\alpha]_D = -21°$; *5α-ergost-7-en-3β-ol* (III), m.p. 149–150°, $[\alpha]_D = -1°$; *3β-acetoxy-5α-ergosta-7,22-diene* (V), m.p. 182°, $[\alpha]_D = -20°$; *3β-acetoxy-5α-ergost-7-ene* (VI), m.p. 159–161°, $[\alpha]_D = -3°$.

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78. Dynamische *Jahn-Teller* Verzerrungen und chemische Bindungsverhältnisse in orbitalentarteten Sandwichkomplexen[1])

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Summary. In order to derive information on the *Jahn-Teller* effect and on chemical bonding in orbitally degenerate sandwich molecules, the low-spin $d^5(^2E_{2g})$ metallocenes $Mn(cp)_2$ and $Fe(cp)_2^+$ as well as the $d^7(^2E_{1g})$ metallocenes $Co(cp)_2$ and $Ni(cp)_2^+$ have been diluted in a variety of diamagnetic host systems and studied by ESR. at liquid helium temperature and slightly higher temperatures. Analysis of the measured anisotropic *Zeeman* and hyperfine data leads to the conclusions that the *Jahn-Teller* distortions remain entirely dynamic in all four cases ($E_{JT} \lesssim h\nu$), and that the covalent delocalization of the singly occupied degenerate metal 3d orbital over the ligand rings correlates well with the observed *Jahn-Teller* distortion increasing strongly along the series $Fe(cp)_2^+ < Mn(cp)_2 < Co(cp)_2 < Ni(cp)_2^+$. This finding agrees with the expectation that the ligand components of the singly occupied $e_{2g}(e_{1g}^*)$ orbitals are mainly responsible for the dynamic $e_{1g}(e_{2g})$ distortions in the cyclopentadienyl rings.

1. Einleitung. – Metallorganische Sandwichkomplexe vom Typ der Metallocene, $Me(C_5H_5)_2$, und der Dibenzolkomplexe, $Me(C_6H_6)_2$, (siehe Fig. 1), haben aufgrund ihrer hochsymmetrischen Struktur und ihrer aussergewöhnlichen Bindungscharakteristik seit der Zeit ihrer Entdeckung vor ungefähr 25 Jahren die besondere Aufmerksamkeit der Chemiker auf sich gezogen (siehe z.B. [1] [2]). Besonders intensiv untersucht – sowohl experimentell als auch theoretisch – wurden die relativ stabilen diamagnetischen d^6-Repräsentanten Ferrocen, $Fe(cp)_2$, und Dibenzol-Chrom, $Cr(bz)_2$. Dieser Aufsatz befasst sich mit den viel reaktiveren paramagnetischen d^5-

[1]) Vorgetragen an der Herbstversammlung der Schweizerischen Chemischen Gesellschaft am 11. Oktober 1974 in Neuchâtel.