Experimental

***o*-Nitromandelic Acid.**—A mixture of 7 g. of *o*-nitromandelonitrile and 110 ml. of concentrated hydrochloric acid was warmed to 70–80° under a reflux condenser for 20 hours. The resultant solution was then concentrated to a volume of 20 ml. under reduced pressure. The *o*-nitromandelic acid which had separated at this point was removed by filtration and the filtrate extracted twice with 30-ml. portions of ethyl acetate. The product obtained by filtration was dissolved in the ethyl acetate extracts, which were then dried over magnesium sulfate. Concentration and dilution of the hot solution with cyclohexane caused 5.1 g. of *o*-nitromandelic acid (64.5%), m.p. 137–138°, to be deposited as white crystals on cooling. Grillot and Bashford[4] report an identical melting point for this acid.

Reaction of *o*-Nitromandelic Acid with Formaldehyde and Piperidine.—This reaction was carried out exactly as described by Grillot and Bashford,[4] in order to ensure the identity of the product with that previously obtained. The once recrystallized material was dried over phosphorus pentoxide at reduced pressure and submitted for analysis, in order to confirm its empirical composition.

Anal. Calcd. for $C_{14}H_{20}O_6N_2$: C, 53.75; H, 6.40; N, 8.89. Found: C, 54.20; H, 6.33; N, 8.84.

The melting point of this product did not seem to be a reliable criterion of purity, since it was found to be strongly dependent on the rate of heating. Thus, using a Fisher melting point block, a high rate of heating caused the crystals to melt to a colorless liquid somewhere between 95–105°, whereas very slow heating resulted in some darkening with melting accompanied by decomposition occurring at 152–154°. It seems clear that the rapid heating gives the true melting point of the compound under consideration, while prolonged heating must result in some chemical change. It is perhaps worth noting in passing that repeated recrystallization led to the loss of some of the formaldehyde, with a resultant shift of the infrared spectrum toward that of piperidinium *o*-nitromandelate, and a parallel increase in apparent molecular weight.

Acid Treatment and Recovery of *o*-Nitromandelic Acid.—A 204-mg. sample of twice recrystallized "Mannich base" was dissolved in 5 ml. of water and the solution acidified with 3 drops of concentrated hydrochloric acid. The acidic solution was extracted rapidly with four 5-ml. portions of ether. The combined ether extracts were dried over magnesium sulfate and evaporated. The residue consisted of 125 mg. (94.6%) of *o*-nitromandelic acid, identified by melting point, mixture melting point and a comparison of its infrared absorption spectrum with that of an authentic sample.

Molecular Weight.—The cryoscopic measurements were made using a cell similar to that described by Billings,[8] but using a Western Electric 14B thermistor[9,10] for measuring temperature instead of a Beckmann thermometer. The thermistor circuit was similar to that used by Zemany[11] but somewhat modified to attain the desired precision. The resistance of the thermistor was measured with a Wheatstone bridge, employing a G.E. Photoelectric Recorder for the galvanometer. The apparatus was calibrated against a platinum resistance thermometer and the slope of the curve (in this case 0.00343° per ohm) used in calculating ΔT. The apparatus and method will be discussed fully in a later paper.

Two runs were made, each time diluting to obtain a second concentration. The material for the two runs was obtained from two separate preparations. The results are given in Table I.

TABLE I

APPARENT MOLECULAR WEIGHT OF "MANNICH BASE"

Run	I	Ia	II	IIa
Wt. sample, g.	0.299	0.299	0.192	0.192
Wt. water, g.	19.9	29.9	19.9	29.9
F.p. water, ohms	6441.5	6441.5	6441.5	6441.5
F.p. solution, ohms	6520.0	6593.5	6487.0	6471.0
$\Delta\Omega$	78.5	52.0	45.5	29.5
Apparent mol. wt.	104	104	115	118

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[8] O. B. Billings, Ph.D. Thesis, Cornell University, 1942.

[9] A thermistor is a ceramic resistor having a 4% change in resistance per degree change in centigrade temperature.

[10] K. P. Dowell, Electrical Manufacturing, August, 1948.

[11] P. D. Zemany, *Anal. Chem.*, **24**, 348 (1952).

The Properties of Nickel Carbide

BY G. MEYER AND F. E. C. SCHEFFER

RECEIVED JUNE 2, 1952

Browning and Emmett have published[1] a series of equilibrium measurements of the system Ni–C–H_2 and described some properties of a nickel carbide.[1] In their opinion their results disagree with those mentioned in a recent publication.[2]

In the latter a carbide is described which is exothermic (forms from the elements with evolution of heat). Below 419° this carbide is stable, at 700° it decomposes into its elements.[3] The carbide found by Browning and Emmett has quite different properties being endothermic. This follows from the lines of equilibrium in the diagram log *p versus* $1/T$ for the reaction with carbide and the reaction with carbon. These lines intersect at approximately 510°. Thus their carbide is stable above 510°, below this temperature there will be decomposition in carbon and nickel, the compound being unstable. The foregoing is proved by the free energy calculations made by the authors. For the reaction of formation of nickel carbide they find 7127 cal. at 500°K. and 4655 cal. at 600°K. These values being positive the carbide is metastable at these temperatures. Above approximately 783°K. (510°) the value for the free energy of formation becomes zero, the carbide being stable at higher temperatures. So the experiments of Browning and Emmett prove the existence of another carbide, quite different from the carbide described by us 25 years ago. The chemical composition of each carbide is unknown. Bahr and Bahr[4] propose the formula Ni_3C; from their work it is impossible to say whether the carbide they have obtained is the endothermic or the exothermic compound.

[1] L. C. Browning and P. H. Emmett, THIS JOURNAL, **74**, 1680 (1952).

[2] F. E. C. Scheffer, T. Dokkum and J. Al, *Rec. trav. chim.*, **45**, 803 (1926).

[3] G. Meyer and F. E. C. Scheffer, *ibid.*, **46**, 1 (1927).

[4] H. A. Bahr and Th. Bahr, *Ber.*, **61**, 2177 (1928).

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11-Oxygenated Steroids. III. The Preparation of 11β-Hydroxy Pregnanes[1]

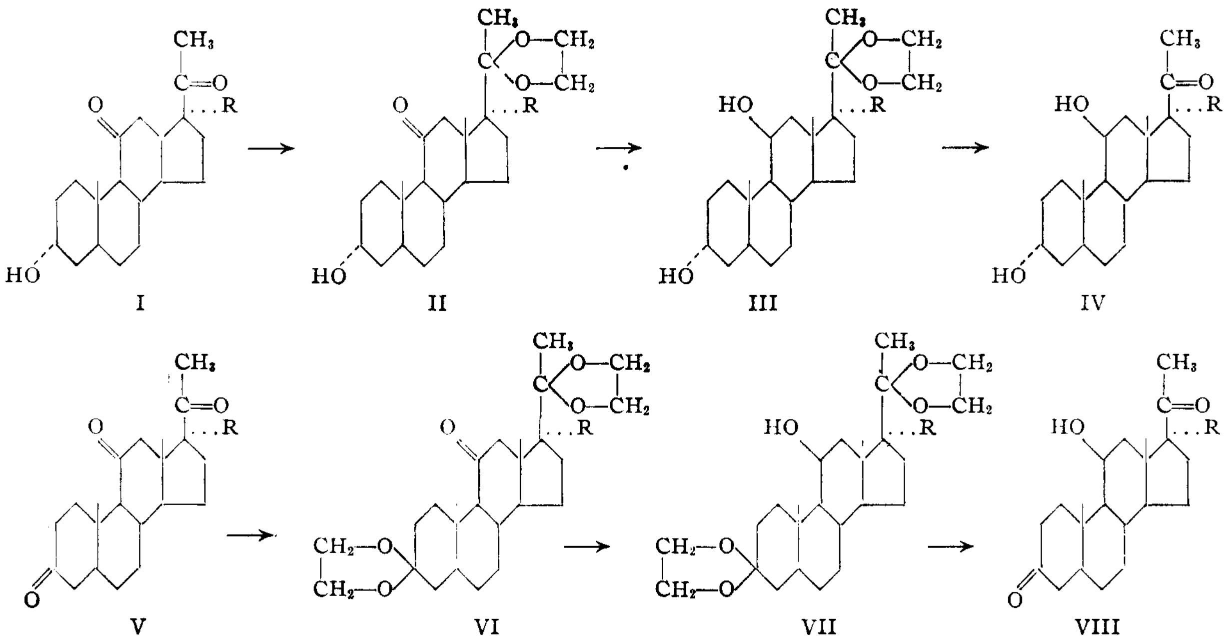
BY EUGENE P. OLIVETO, TEMPLE CLAYTON AND E. B. HERSHBERG

RECEIVED AUGUST 11, 1952

The reported efficacy[2] of 17α-hydroxycorticosterone (Kendall's Compound F) in certain types of arthritis led us to prepare a series of 11β-hy-

[1] For the previous paper in this series, *cf.* H. L. Herzog, M. A. Jevnik and E. B. Hershberg, THIS JOURNAL, **75**, 269 (1953).

[2] J. L. Hollander, *J. Am. Med. Assoc.*, **147**, 1629 (1951).



R = H, OH

droxylated pregnanes for pharmacological testing. The biological results will be reported elsewhere.

The appropriate pregnan-11,20-dione or -3,11,20-trione (I and V, respectively) was refluxed overnight in benzene or toluene solution with an excess of ethylene glycol and *p*-toluenesulfonic acid catalyst while water was removed continuously from the reaction. The 11-ketone failed to react but the 20-monoketal (II) or 3,20-bisketal (VI) was formed and could be isolated easily in excellent yield after the removal of the excess glycol and the acid catalyst.

These ketals were readily reduced to the 11β-hydroxy compounds (III and VII) with sodium borohydride[1] in aqueous methanol.

Although the reduction of an 11-ketone to the 11β-hydroxy compound can be effected by platinum and hydrogen,[3] lithium aluminum hydride[4] and lithium borohydride,[5] experience in these laboratories has shown that, because of greater ease of handling and more satisfactory solubility characteristics, sodium borohydride is preferable for the reduction.

Although Chaikin and Brown[6] stated that all four hydrogens in $NaBH_4$ are available for reductive purposes (*i.e.*, one mole of $NaBH_4$ will reduce four moles of a ketone) it was found that a large excess of the reducing agent was necessary for optimum results. When one mole of sodium borohydride for each mole of 11-ketopregnane was used (theoretically a fourfold excess) and the solution allowed to stand at room temperature overnight it was possible to recover significant quantities, in some cases up to 40%, of starting material. Excellent results were obtained by refluxing the ketone overnight with four moles of reducing agent per mole of ketone. Possibly the steric hindrance of the 11-ketone is the factor which necessitates the use of such a large excess of reducing agent, for with a slow reaction the decomposition of the reagent by boiling the solvent assumes appreciable proportions.

The 11β-hydroxy ketals (III and VII) were readily cleaved to the corresponding 11β-hydroxy ketones (IV and VIII) upon brief warming with aqueous acetic acid.

As expected, none of the 11β-hydroxy compounds formed an acetate at that position using acetic anhydride and pyridine.

Experimental[7]

The four starting ketones, pregnan-3α-ol-11,20-dione,[8] pregnan-3α,17α-diol-11,20-dione,[9] pregnan-3,11,20-trione[10] and pregnan-17α-ol-3,11,20-trione,[9] have been previously synthesized.

The following procedure for the conversion of pregnan-17α-ol-3,11,20-trione (V, R = OH) to pregnan-11β,17α-diol-3,20-dione (VIII, R = OH) has been used for the preparation of all the members of the series whose physical constants are described in Table I.

3,20-Bisethylene Glycol Ketal of Pregnan-17α-ol-3,11,20-trione.—A solution of 15 g. of pregnan-17α-ol-3,11,20-trione in 300 ml. of benzene containing 30 ml. of ethylene glycol and a trace of *p*-toluenesulfonic acid was refluxed overnight; water was removed during this time by means of a Dean-Stark tube. A solution of 1 g. of potassium hydroxide in methanol was then added and the benzene layer washed three times with water. After drying over Drierite and removal of the solvent under reduced pressure, the solid residue was crystallized from aqueous methanol; yield 17.5 g. (93%), m.p. 175–178°. The analytical sample, crystallized once more for analysis, had a m.p. of 182.5–183.5°.

3,20-Bisethylene Glycol Ketal of Pregnan-11β,17α-diol-3,20-dione.—A solution of 10 g. of the 11-ketobisketal and 4 g. of sodium borohydride in 150 ml. of methanol and 30 ml.

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(3) A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **26**, 586 (1943).

(4) L. H. Sarett, M. Feurer and K. Folkers, This Journal, **73**, 1777 (1951).

(5) N. L. Wendler, Huang-Minlon and M. Tishler, *ibid.*, **73**, 3818 (1951).

(6) S. W. Chaikin and W. G. Brown, *ibid.*, **71**, 122 (1949).

(7) We are indebted to Mr. Edwin Conner, Mrs. Alice Barrella, Miss Betty Blasko, Mrs. Elizabeth McEntire and Miss Joan Mustachio for the analytical and rotational data.

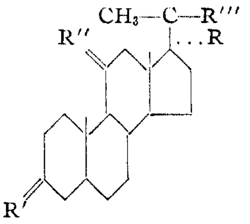
(8) J. von Euw, A. Lardon and T. Reichstein, *Helv. Chim. Acta*, **27**, 821 (1944).

(9) T. H. Kritchevsky, D. L. Garmaise and T. F. Gallagher, This Journal, **74**, 483 (1952).

(10) P. Hegner and T. Reichstein, *Helv. Chim. Acta*, **26**, 721 (1943).

TABLE I

PHYSICAL CONSTANTS AND YIELD DATA:



R'	R''	R'''	Yield, %	M.p. °C.[a]	$[\alpha]_D$[b]	Empirical Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Recrystallization solvent
					R = H						
OH H	O	O—CH$_2$ O—CH$_2$	85	128.4–129.6	+ 55.1	$C_{23}H_{36}O_4$	73.36	73.68	9.64	9.96	Methanol–water
OH H	OH H	O—CH$_2$ O—CH$_2$	87	159.8–160.4	+ 67.1	$C_{23}H_{38}O_4$	72.97	72.86	10.12	10.45	Methanol–water
OH H	OH H	O	85	216.0–217.6[c]	+132.9	$C_{21}H_{34}O_3$	75.40	75.22	10.25	10.55	Methanol–water
O—CH$_2$ O—CH$_2$	O	O—CH$_2$ O—CH$_2$	91	125.4–127.0	+ 53.9	$C_{25}H_{38}O_5$	71.74	71.92	9.15	8.84	Methanol–water
O—CH$_2$ O—CH$_2$	OH H	O—CH$_2$ O—CH$_2$	91	138.5–139.5	+ 61.0	$C_{25}H_{40}O_5$	71.39	71.10	9.59	9.91	Methanol–water
O	OH H	O	85	174.0–175.0	+135.0	$C_{21}H_{32}O_3$	75.86	75.68	9.70	9.79	Methanol–water
OAc H	OH H	O		178.8–179.6[d]	+135.9	$C_{23}H_{36}O_4$	73.36	73.64	9.64	9.84	Methanol–water
					R = OH						
OH H	O	O—CH$_2$ O—CH$_2$	94	149.6–150.4	+ 28.7	$C_{23}H_{36}O_5$	70.37	70.33	9.25	9.55	Acetone–hexane
OH H	OH H	O—CH$_2$ O—CH$_2$	100	179.0–180.5	+ 21.7	$C_{23}H_{38}O_5$	70.01	70.00	9.71	9.50	Acetone–water
OH H	OH H	O	95	224.0–227.0	+ 70.6	$C_{21}H_{34}O_4$	71.96	71.73	9.78	9.57	Acetone–water
O—CH$_2$ O—CH$_2$	O	O—CH$_2$ O—CH$_2$	93	182.5–183.5	+ 30.8	$C_{25}H_{38}O_6$	69.09	69.38	8.81	9.13	Methanol–water
O—CH$_2$ O—CH$_2$	OH H	O—CH$_2$ O—CH$_2$	96	181.0–182.4	+ 30.1	$C_{25}H_{40}O_6$	68.77	68.97	9.24	9.56	Methanol
O	OH H	O	95	213.2–214.4	+ 69.6	$C_{21}H_{32}O_4$	72.38	72.37	9.26	9.44	Methanol
OAc H	OH H	O		189.0–190.4	+ 82.7	$C_{23}H_{36}O_5$	70.37	70.20	9.25	9.19	Methanol–water

[a] All m.ps. are corrected. [b] All rotations in acetone, in a one-decimeter tube, at a concentration of *ca.* 1%. [c] Reported (ref. 8), m.p. 222–225°. [d] Reported (ref. 8) m.p. 182–184°, $[\alpha]_D$ +147.5° (acetone).

of water was refluxed overnight. The solution was filtered hot, water added to incipient crystallization and the mixture was chilled and filtered; yield 9.6 g., m.p. 181.0–182.4°.

Pregnan-11β,17α-diol-3,20-dione.—A solution of 8.5 g. of the 11β-hydroxybisketal in 25 ml. of acetic acid and 10 ml. of water was warmed on the steam-bath for 0.5 hour. Water was added to induce crystallization and the mixture was chilled and filtered. There was formed 6.1 g. (95%) of dione, m.p. 213.2–214.4°.

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11-Oxygenated Steroids. IV. The Selective Reduction of Steroidal 11,20-Diketones with Sodium Borohydride[1]

BY EUGENE P. OLIVETO AND E. B. HERSHBERG

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The selective reducing action of sodium borohydride toward steroidal diketones has been re-

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[1] For the previous paper in this series, *cf.* E. P. Oliveto, T. Clayton and E. B. Hershberg, THIS JOURNAL, **75**, 486 (1953).