tende Kupfererz der Mürtschenalp unterscheidet sich von den obenerwähnten Lagerstätten vor allem durch die Anwesenheit von Sr, B, Cr und Mo. Das in Quarzgängen des Triasdolomits eingesprengte Erz des längst aufgelassenen Bergwerks Gnapperkopf[1] ist in bezug auf seine Spurenelemente am ehesten mit demjenigen der Mürtschenalp vergleichbar. Das Kupfer vom Flumser Berg muß als relativ rein angesprochen werden.

TH. HÜGI und W. MEIER

Mineralogisch-petrographisches und Anorganisch-chemisches Institut der Universität Bern, den 1. März 1949.

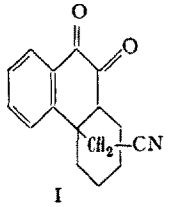
Summary

Spectrographical analysis has been made from several Swiss copper-ore deposits. The results are given in tabular form.

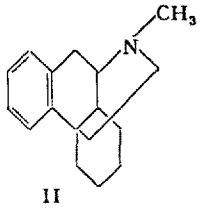
[1] Schweiz. min. u. petr. Mitt. *21*, 80 (1941).

The Synthesis of Ring Systems Related to Morphine. II The Carbon-Nitrogen Ring System

A short time ago the synthesis of 9,10-dioxo-13-cyanomethyl-5, 8, 9, 10, 13, 14-hexahydrophenanthrene (I) was reported[1]. The present communication deals with the conversion of this substance to a saturated cyclic compound whose structure, to a high degree of probability, may be represented by II, and which thus

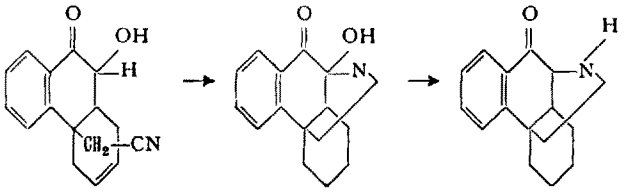


I



II

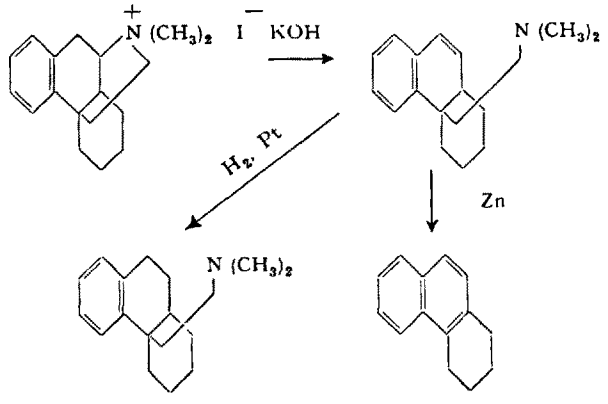
contains the carbon-nitrogen skeleton present in morphine. I on hydrogenation over copper chromite at 135° and moderate pressures is converted to an alkali-insoluble dihydro compound, m. p. 252·5–254° (Calc.: C 75·86; H 5·96; Fd.: C 75·73; H 6·08) in 50% yield. Since the ready alkali-solubility of the parent I must be due to the dicarbonyl system, we have assumed that in the dihydro compound the dicarbonyl system, not the carbon-carbon double bond, has been attacked. Further reduction of this neutral substance over Raney nickel at room temperature and atmospheric pressure produces in 75% yield a saturated basic hexahydro derivative, m. p. 242–243·5° (Calc.: C 74·67, H 7·44; Fd.: C 74·47; H 7·29) with the absorption of two moles of hydrogen. It is not further reduced over either Raney nickel or palladium-carbon at atmospheric pressure. Ring closure at either C 9 or C 10 appears to offer the best explanation of this reaction, since the open chain saturated substance (one isomer of which has been obtained by reduction of I with Raney nickel, m. p. 201–207° with profound decomposition, Calc.: C 74·09, H 8·16; Fd.: C 74·03, H 8·37) is necessarily on octahydro derivative. Of the two possibilities, we regard ring closure at C 9 as much the more probable, since ring closure at C 10 necessitates the formation of a seven-membered ring, but ring closure at C 10 cannot at present be ruled out. The hexahydro compound readily forms a neutral diacetyl derivative (m. p. 137–138·7°, Calc.: C 70·35, H 6·78; Fd.: C 70·10, H 6·71) and is converted by the action of hydrogen iodide and red phosphorus quantitatively into a basic desoxy compound (m. p. 207–208°, Calc.: C 79·63, H 7·93; Fd.: C 79·57, H 8·00) which forms a neutral monoacetyl derivative (m. p. 135·5–137°, Calc.: C 76·29, H 7·47; Fd.: C 76·57, H 7·91). This series of reactions has tentatively been formulated as follows:



Dihydro Compound Hexahydro Compound Desoxy Compound

Carbonyl derivatives of the desoxy compound have not been obtained, but the analytical figures require that the oxygen be present in the form of a carbonyl group. This oxygen is removed by hydrogenation over copper chromite at 200–225° and 140–150 atmospheres pressure to yield an oily oxygen-free base[1] which was not characterized as such but was methylated by the action of formaldehyde and formic acid to the N-methyl derivative II (Calc.: C 84·59, H 9·60; Fd.: C 84·12, H 9·77), purified through its picrate (m. p. 210–212° dec., Calc.: C 58·71, H 5·57; Fd.: C 58·72, H 6·05).

The methylated base II, regenerated from its picrate and distilled, is a stable colorless oil which is saturated to Adams catalyst. It appears to be isomeric with the substance "morphinane", m. p. 62°, obtained by GREWE in his elegant synthesis[2]. Its methiodide (m. p. 232–235° dec. Calc.: C 56·39, H 6·84; Fd.: C 56·43, H 7·15) on short boiling with strong alkali affords an unsaturated oily desbase, soluble in dilute acids (Calc.: C 84·65, H 9·87; Fd.: C 84·09, H 9·43; picrate, m.p.



207–209°, mixed m. p. with picrate of II, 176–195°, Calc.: C 59·49, H 5·82; Fd.: C 59·35, H 6·09) which on hydrogenation over Adams catalyst absorbs one mole of hydrogen and is converted to an oily dihydro-desbase (Calc.: C 83·98, H 10·57; Fd.: C 84·48, H 10·66; picrate, m. p. 191–193° Calc.: C 59·25, H 6·21; Fd.:

[1] M. GATES and W. F. NEWHALL, J. Amer. Chem. Soc. *70*, 2261 (1948).

[1] The complete removal of oxygen from the molecule under these conditions can be taken as evidence of a sort for ring closure at C 9, since if ring closure had taken place at C 10, the oxygen at C 9 would be much more difficultly removable by hydrogenation than one at C 10 adjacent to the aromatic ring. Cf. CH. GRUNDMANN, *Newer Methods of Preparative Organic Chemistry* (Interscience Publishers, New York, 1948), p. 111.

[2] R. GREWE, Naturwissenschaften *33*, 333 (1946); Z. angew. Chem. *A 59*, 194 (1947).

C 59·34, H 6·30). The des-base, on distillation with zinc dust, yields 1,2,3,4-tetrahydrophenanthrene, isolated as its picrate, m. p. 108–110°, not depressed by admixture with authentic 1,2,3,4-tetrahydrophenanthrene picrate, and further characterized as its trinitrobenzene derivative, m. p. 126·5–127·5°, not depressed by admixture with authentic 1,2,3,4-tetrahydrophenanthrene-trinitrobenzene of m. p. 128–129°, (Calc.: C 60·75, H 4·34; Fd.: C 60·67, H 4·96).

If our supposition as to the point of attachment of the nitrogen atom (at C 9) is correct, then the isomerism[1] of our base and GREWE'S morphinane must be the result of isomerism at carbon atoms 13 and 14. Degradative work designed to ascertain the stereochemical nature of the ring juncture in question has been begun in this laboratory.

The 3,4-dimethoxy derivative of I (m. p. 238–239°, Calc.: C 69·44, H 5·51; Fd.: C 69·77, H 5·65) has also been prepared in quantity, and its reduction is under investigation.

M. GATES and W. F. NEWHALL

Park Laboratory, Bryn Mawr College, Bryn Mawr, Pa., January 10, 1949.

Zusammenfassung

9,10-Dioxo-13-cyanmethyl-5,8,9,10,13,14-hexahydro phenanthren wurde durch eine Reihe von Reduktionen, deren Mechanismus nicht vollständig aufgeklärt ist, in eine neue Verbindung übergeführt. Diese besitzt sehr wahrscheinlich das Kohlenstoff/Stickstoffgerüst des Morphins oder eines seiner Stereoisomeren. Es wird über Abbaureaktionen berichtet, die diese Struktur bestätigen können.

[1] Prof. R. GREWE has informed us privately that a by-product of his synthesis, obtained in small amounts[2] appears to be identical with our substance (correspondence in melting points of picrate, methiodide, desbase picrate, dihydrodesbase picrate).

[2] Concerning *Pikrat A* vide R. GREWE, Ber. Dtsch. chem. Ges. *81*, 285 (1948).

Some Observations on the Oxidative Degradation of Cholesterol

The oxidation of cholesterol acetatedibromide with chromic acid, as developed by RUZICKA[1], is now classic. From the breaking-down of the aliphatic side-chain of cholesterol by this method a variety of degradation products results, such as dehydroisoandrosterone, pregnenolone, etiocholenic acid, etc.[2], which are important in the synthesis of biologically active steroids. 5-Dehydroisoandrosterone is frequently used as starting material for such syntheses. The mechanism of this oxidative degradation is incompletely understood. Recently BILLETER and MIESCHER[3] advanced a theory on the side-chain fission of cholesterol with chromic acid. They assume that the tertiary carbon-atoms at C_{14}, C_{17}, C_{20}, and C_{25} are the points where the molecule is attacked and from which directly, or indirectly from other intermediate products, tertiary carbinols arise. When split off, these hydroxy groups would yield water while the resulting carbon-carbon double bonds are then disrupted, giving rise to ketones and acids. Many compounds have been isolated and identified that afford confirmation of this theory[2].

[1] L. RUZICKA, Swiss Pat. 182391 (1933). – L. RUZICKA and A. WETTSTEIN, Helv. chim. acta *18*, 987 (1935).

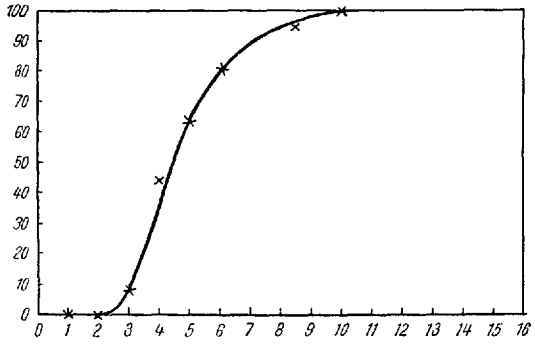
[2] For a review see: J. R. BILLETER and K. MIESCHER, Helv. chim. acta *30*, 1415 (1947).

[3] J. R. BILLETER and K. MIESCHER, Helv. chim. acta *30*, 1414 (1947).

As in this laboratory a similar conclusion as to "intermediate products" had been drawn from other experiments, it was decided to present a few relevant results.

The rate of formation of dehydroisoandrosterone acetate from cholesterol acetatedibromide by oxidation with chromic acid in a solution of glacial acetic acid and dichlorethane was determined. For this purpose the dehydroisoandrosterone acetate formed had to be estimated at various stages of the reaction.

In view of the quantitatively inaccurate and laborious methods available, the isolation of this ketone from the other ketones known to be produced by the oxidation was avoided. Instead of this the colorimetric assay of 17-ketosteroids with the reaction of ZIMMERMANN[1], as adapted by CALLOW and coworkers[2], was used. In this assay advantage is taken of the instability of the coloured reaction products of the 20-, 25-, and other keto-steroids with m-dinitrobenzene in alkaline alcoholic solution, in contradistinction to the more lasting colour



The figure shows the amounts of 5-dehydroisoandrosterone acetate (I), formed by oxidation of cholesterol (as its acetate dibromide) with chromic acid, against time. – The reaction time (in hours) is plotted on the abscissa. The ordinate represents the amounts of (I) expressed in percentage of the total dehydroisoandrosterone acetate formed.

obtained with 17-keto-steroids, e. g., dehydroisoandrosterone acetate. Thus, for instance, the oxidation products of cholesterol, $\Delta^{5,6}$-pregnene-ol-(3β)-acetate-one-20 and $\Delta^{5,6}$-nor-cholestene-ol-(3β)-acetate-one-25 give labile coloured products with colour values of about $^1/_8$ and $^1/_{10}$ respectively of that of dehydroisoandrosterone acetate. These are known to be formed in much smaller amounts than dehydroisoandrosterone acetate. The other known oxidation products gave such faint colours as to be also negligible. The oxidations were performed approximately by the usual procedure[3], using glacial acetic acid distilled over chromic acid and dichlorethane with a negligible chromic acid titre. The reaction temperature was kept constant within $\pm$ 2°. The chromic acid solution was added at a uniform rate over 7 hours and the consumption of the oxidant was controlled iodometrically. At regular intervals aliquot samples were taken and the mixture of reaction components in the samples was "fixed" by reduction of the small excess of chromic acid with methanol. The samples were further worked up by evaporating the dichlorethane *in vacuo*, splitting off the bromine with zinc dust and

[1] W. ZIMMERMANN, Z. physiol. Ch. *233*, 257 (1935); Vitamine und Hormone *5*, 1 (1944); Schweiz. med. Wschr. *76*, 805 (1947).

[2] N. H. CALLOW, R. K. CALLOW, and C. W. EMMENS, Biochem. J. *32*, 1312 (1938).

[3] For experimental details see F.I.A.T. Final Report No. 996. ed. by C. R. ADDINALL, p. 29 (London, 1947).