10 cc. of water was shaken with 0.30 g. of carbon disulfide in 8 cc. of dioxane, treated successively with 0.24 g. of potassium hydroxide and 1.20 g. of lead nitrate dissolved in a total of 20 cc. of water, and warmed to 60° for fifteen minutes. The lead sulfide was centrifuged, the supernatant evaporated in vacuum, and the residue dissolved with 3 g. of sodium chloride in 15 cc. of water and extracted with 75 cc. of ethyl acetate. The ethyl acetate, washed, dried and evaporated, left 0.38 g. of oil which slowly solidified and was crystallized from ether. There was obtained 0.31 g. (66%) of *d*-5-vinyl-2-thioöxazolidone, m. p. 50–51°, $[\alpha]^{20}D$ +70.5° in methanol (47.0 mg./2.51 cc., 1 dm., +1.32°). A mixture with the *l*-isomer melted at 50.5–52°, solidified instantly when seeded with the racemic compound and melted at 64–66°. A solution of equal parts of the synthetic *d* and natural *l*-compound in methanol, evaporated on a watch glass and scratched, crystallized as *dl*-5-vinyl-2-thioöxazolidone, m. p. 63.5–64.5°, undepressed by an authentic sample.

From *l*-1-amino-3-buten-2-ol *d*-α-bromocamphor-π-sulfonate (monohydrate, 5.08 g.) there was synthesized *l*-5-vinyl-2-thioöxazolidone (0.85 g., 54%), m. p. 50.5–51°, $[\alpha]^{30}D$ −72.8° in methanol (51.6 mg./2.51 cc., 1 dm., −1.45°), identical with the natural product[3] (m. p. 50–50.5°, $[\alpha]^{31}D$ −70.5°).

Acknowledgments.—The author is deeply indebted to Dr. E. B. Astwood for generous collaboration and Dr. R. B. Woodward for useful discussion.

Summary

The natural antithyroid factor *l*-5-vinyl-2-thioöxazolidone has been synthesized from butadiene-1,2-oxide through 1-amino-3-buten-2-ol.

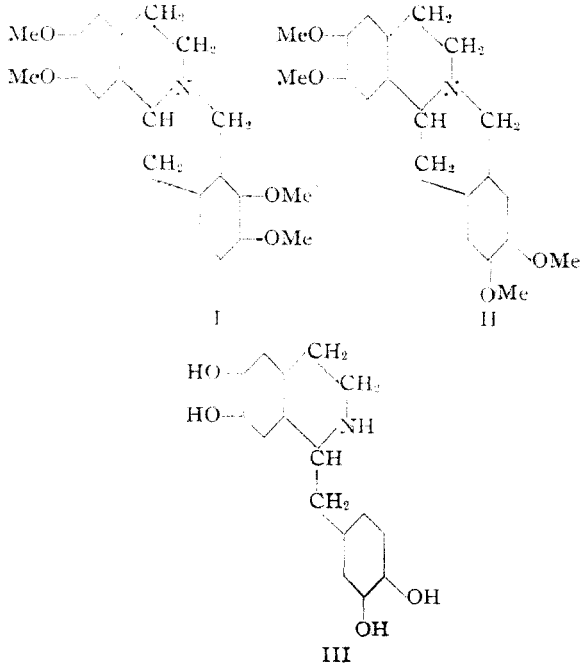
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 31, 1950

[CONTRIBUTION FROM THE RESEARCH LABORATORY, DOMINION RUBBER CO., LTD.]

The Alkaloids of Fumariaceous Plants. XLV. Coreximine, a Naturally Occurring Coralydine

BY RICHARD H. F. MANSKE

The author has recorded the presence of an alkaloid, F29 ($C_{19}H_{21}O_4N$)[1] now termed *coreximine* which has two methoxyls and two phenolic hydroxyls. With diazomethane it yields a dimethyl ether, $C_{21}H_{25}O_4N$, m. p. 177°,[2] and with diazoethane it yields a diethyl ether, $C_{23}H_{29}O_4N$. The former is isomeric but not identical with tetrahydropalmatine (I) and like it is slowly oxidized by air to a quaternary base, a behavior which is characteristic of the tetrahydroprotoberberines. The conclusion, therefore, seemed to be inescapable that coreximine dimethyl ether is a tetramethoxytetrahydroprotoberberine and two formulas seemed *a priori* probable—the most likely of which (II) was already known as norcoralydine.[3] The latter is only known in the racemic form, whereas the dimethyl ether of natural origin is optically active. Racemization of bases of this type, however, is easily achieved by oxidation to the quaternary compound analogous to palmatine and subsequent reduction. When the dimethyl ether was thus racemized it melted at 157° and in admixture with a synthetic specimen of norcoralydine the mixture melted at the same temperature. Späth and Kruta[4] recorded the melting point of synthetic norcoralydine as 152° whereas Pictet and Chou[2] give 157–158°. The writer has obtained the synthetic base in these two forms, presumably isomorphic, but the lower melting form when very slowly heated resolidifies at 151–153° after partial melting and remelts completely at 157°. The picrates prepared from both sources were identical. Coreximine dimethyl ether, therefore, has formula



II and coreximine is one of the four possible bisdesmethyl derivatives of it.

In a paper dealing with the structure of cularine the writer[5] has called attention to the fact that ring closure of the isoquinoline nucleus in natural alkaloids can proceed in two ways. When the benzylisoquinoline first forms there is the possibility of yielding either a 6,7 or a 7,8-dihydroxy compound. The latter can then undergo oxidative ring closure to yield cularine. The former (III) can also undergo oxidative ring closure, but

(1) Manske, *Can. J. Research*, **B16**, 81 (1938)
(2) All melting points are corrected.
(3) Pictet and Chou, *Ber.*, **49**, 370 (1916).
(4) Späth and Kruta, *Monatsh.*, **50**, 341 (1928)
(5) Manske, THIS JOURNAL, **72**, 55 (1950).

this ring closure can take place either ortho or para to a hydroxyl yielding an aporphine related to corydine or to glaucine. *Dicentra eximia* (Ker) Torr. the source plant of coreximine yields not only cularine, indicating a 7,8-dihydroxybenzylisoquinoline as a precursor, but also corydine as well as glaucine, the related glaucentrine, and dicentrine.[6] Furthermore, III can undergo condensation and ring closure with formaldehyde to yield compounds of type II[3] or a mixture of type I and II.[4] It had generally been assumed that in the plant this ring closure is possible only in a position ortho to a hydroxyl. The present example of coreximine supplies an example of such a ring closure para to a hydroxyl and lends very convincing proof to the theory that the protoberberines are formed in the plant from the benzylisoquinolines. It should be noted that the balance between the two types of ring closure must be a delicate one. Instead of yielding coreximine the closely related *D. oregana* Eastwood yields corypalmine (type I)[7,8] as well as cularine, corydine, glaucine, etc.

Experimental

A solution of 50 mg. of coreximine O,O-dimethyl ether in 10 cc. of dilute acetic acid was heated on a steam-bath for five hours with an excess of mercuric acetate. The resultant deep yellow solution containing mercurous acetate in suspension was treated with an excess of zinc dust and a little hydrochloric acid and digestion on a steam-bath continued until the solution was colorless. The mixture was filtered and the clear filtrate shaken with ether in the presence of an excess of ammonia. The washed ether extract was freed of solvent, rapidly dried *in vacuo* and redissolved in a little dry ether. There was an almost immediate separation of nearly colorless fine prismatic crystals which when washed with a little ether and dried melted sharply at 157°. Small portions of this were mixed with various amounts of norcoralydine[2] similarly crystallized and in all cases the mixture melted at 157°.

The picrate of the base of natural origin melted either alone or in admixture with that of synthetic coralydine at 140° with some previous shrinking at 138°.

(6) Manske, *Can. J. Research*, **8**, 592 (1933).
(7) Manske, *ibid.*, **10**, 765 (1934).
(8) Manske, *ibid.*, **B14**, 348 (1936).

Summary

1. The alkaloid previously recorded as F29, and now termed coreximine, has been shown to be a dihydroxydimethoxyprotoberberine which when O-methylated and racemized yields norcoralydine.

2. This is the first recorded example of a natural base of this type.

3. It is pointed out that the natural occurrence of an alkaloid of the type of norcoralydine is in harmony with, and in substantiation of, the theory that the benzylisoquinolines are biosynthetic intermediates in the formation of alkaloids of more complex types such as cularine, the aporphines, the protoberberines, etc.

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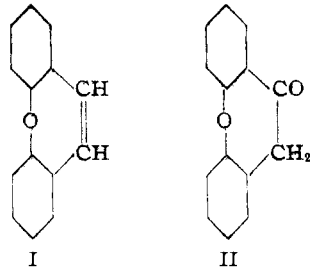
Synthesis and Reactions of Some Dibenzoxepins

BY RICHARD H. F. MANSKE AND ARCHIE E. LEDINGHAM

It has been shown[1] that a portion of the molecular structure of cularine includes the 10,11-dihydrodibenz[*b*,*f*]oxepin nucleus and on exhaustive methylation yields a derivative of dibenz[*b*,*f*]oxepin (I). Oxidation of the latter



I II

yielded the expected dibasic acid but there was also obtained about 10% of a compound formulated as a xanthone derivative. Since there came to mind no simple syntheses of a highly substituted xanthone it was of interest to prepare model substances and observe their behavior on oxidation. For this purpose it was desirable to have *o*-phenoxybenzaldehyde readily available. It had already been prepared by Lock and Kempter[2] but the reactions were involved, gave low yields, and were not adaptable to highly substituted derivatives. A Stephen's reaction on *o*-phenoxybenzonitrile[3] gave some of the material but this method did not seem adaptable to highly substituted derivatives either. It was observed, however, that the copper salt of salicylaldehyde when boiled with iodobenzene or when heated in an autoclave with bromobenzene to 220° gave a 25% yield of *o*-phenoxybenzaldehyde. Similarly *o*-bromoanisole gave a 40% yield of *o*-(2-methoxyphenoxy)-benzaldehyde. Both of these aldehydes were converted to the corresponding arylacetic acids via their azlactones and the arylpyruvic acids. When the chloride of *o*-phenoxyphenylacetic acid was reacted upon by aluminum chloride in nitrobenzene it gave a good yield of 10,11-dihydrodibenz[*b*,*f*]oxepin-10[11 *H*]one (II). Reduction of the ketone (II) to the corresponding carbinol was readily

(1) Manske, THIS JOURNAL, **71**, 55 (1950).
(2) Lock and Kempter, *Monatsh.*, **67**, 24 (1935).
(3) Suter, THIS JOURNAL, **51**, 2581 (1929).