tionated giving a range of material of b. p. 147–155°, n^{20}_{D} 1.4165–1.4243 (2,2,3,5-tetramethylhexane, b. p. 149°, n^{20}_{D} 1.4147; 2,3,3,5-tetramethylhexane, b. p. 153°, n^{20}_{D} 1.4196)[9] and a main portion boiling at 158°, n^{20}_{D} 1.4265–1.4270 (2,2,3,3-tetramethylhexane, b. p. 158°, n^{20}_{D} 1.4268).[9]

These data strongly indicate that the intermediate material between the principal dienes and ketone contained 2,3,3,5-tetramethyl-1,5-hexadiene (b. p. 155–160°) and that the 180–185° material was 2,2,3,5-tetramethyl-4 or 5-hexene-3-ol. This latter material also had a strong camphoric odor, split off water when heated with $CuSO_4$ giving lower boiling unsaturated products (b. p. 145–155°), decolorized permanganate, absorbed bromine and gave no derivative with 2,4-dinitrophenylhydrazone. It was present in such small quantities however that it was not obtained in a highly purified state, but undoubtedly contained ketone and dienes.

Physical Properties.—The constants determined for the principal compounds synthesized are given in the accompanying table. The boiling points were measured in a small column-type boiling point apparatus, packed with glass helices and having 3–5 theoretical plates, using thermocouples calibrated to 0.03°. Refractive indices were read on a 5-place Valentine no. 454 refractometer. Densities were measured in pycnometers and viscosities in a modified Oswald viscometer, Cannon Type E.

Summary

On treating *t*-butylmagnesium chloride with mesityl oxide, 6.4% of the reaction product was found to be 4,4,5,5-tetramethyl-2-hexanone, a product of 1,4 addition. Other products of the reaction are: 20% recovered mesityl oxide, 35% of the C_{10} dienes, 2-*t*-butyl-4-methyl-1,3-pentadiene and 2,4,5,5-tetramethyl-1,3-hexadiene, as dehydration products of the normal addition product, 1% of which appeared to be the rearranged C_{10} diene, 2,3,3,5-tetramethyl-1,5-hexadiene, and 1% of 2,2,3,5-tetramethyl-4 or 5-hexene-3-ol. A number of the physical properties of the above compounds have been determined.

STATE COLLEGE, PENNA. RECEIVED JUNE 13, 1949

[CONTRIBUTION FROM THE DOMINION RUBBER COMPANY LIMITED, RESEARCH LABORATORIES]

The Alkaloids of Fumariaceous Plants. XLIII. The Structures of Cularine and of Cularimine

BY RICHARD H. F. MANSKE*

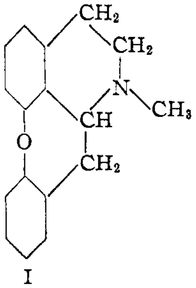
Cularine, $C_{20}H_{23}O_4N$, is an alkaloid which has been isolated from *Corydalis claviculata* and from *Dicentra cucullaria*, *D. eximia*, *D. formosa* and *D. oregana*.[1] It has three methoxyl groups and an indifferent oxygen. Neither oxidation, nor reduction, nor acetylation of the alkaloid yields products which would indicate the presence of alcoholic or ketone groups.

The nitrogen is tertiary and has one methyl group since it is eliminated as trimethylamine in the second step of the Hofmann degradation which also gives rise to a doubly unsaturated compound, $C_{19}H_{18}O_4$, still containing the three methoxyl groups. Cularine on treatment with ethyl chloroformate and alkali yields a compound which is regarded as a urethan, thus indicating the presence of an N-methyltetrahydroisoquinoline nucleus.

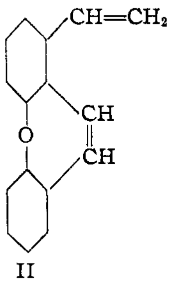
The compound $C_{19}H_{18}O_4$ on oxidation with permanganate yields a tribasic acid, $C_{18}H_{16}O_{10}$, as chief product, and therefore one of the double bonds must be extracyclic and the other in a ring. The loss of only one carbon atom shows that the extracyclic double bond is present as $RCH{=}CH_2$. Such degradations are characteristic of aporphine alkaloids but the above acid still contains the indifferent oxygen and the three methoxyl groups. The only carbon atoms lost are those of the N-methyl group and of the terminal methylene.

Isoquinoline alkaloids containing ether-linked oxygen are generally of the type containing two isoquinoline nuclei and therefore the determination of molecular weights was of some importance but in such types the cryoscopic method of determining them is generally unreliable. Nevertheless the cryoscopic method with camphor gave values which indicated the single molecular formula without question but, more important, the degradation unsaturated compound gave a Rast value of 298 whereas theory demands 310 for the single formula.

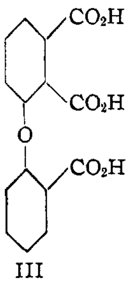
It was therefore obvious that a structure must be written in which there is present a benzylisoquinoline nucleus containing an ether bridge between the two benzene nuclei (I). Such a formula serves to explain adequately the degradation *via* (II) to the acid (III) (plus three methoxyls in each case). Along with the acid (III) there was always encountered a monobasic acid, $C_{17}H_{14}O_7$, which contained, in addition to the carboxyl and three methoxyls, two extra oxygen atoms. The formation of this acid involved the loss of two



I



II



III

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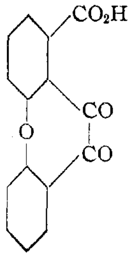
(1) Manske, *Can. J. Research*, **B16**, 81 (1938).

carbons from (II) and alternate formulas were considered for (II) until it was realized that (II) could oxidize to (IV). Such a compound would be expected to present an element of instability and therefore undergo the benzilic acid rearrangement to (V) with extraordinary facility. The last, being a xanthydrol-9-carboxylic acid would then undergo decarboxylation and oxidation to the xanthone (VI). This series of reactions is strictly analogous to the oxidation of phenanthraquinone to fluorenone.[2]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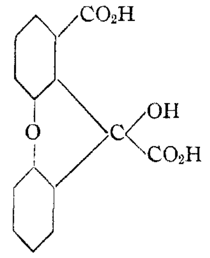
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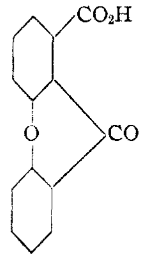
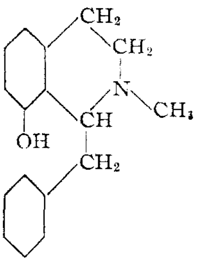
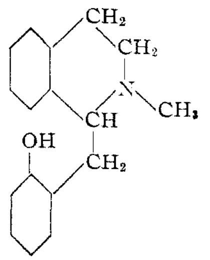
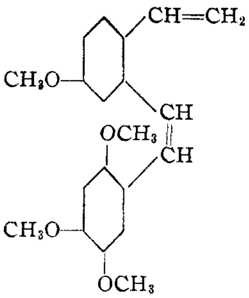

VI

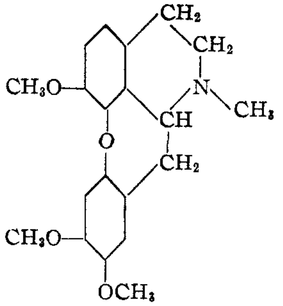
Attempts to synthesize acids of the type of (III) with methoxyls in probable positions failed entirely when the starting materials were bromometahemipinic acid and *o*-vanillic acid and it was not expected that compounds of type II (or its reduction product) could be readily prepared. Pschorr and Knöffler[3] have prepared a dibenz(b,f)oxepine (no. 2070 in The Ring Index)[4] but no other examples of a compound analogous to (II) containing the seven-membered ether ring appear to be known.

Consideration was therefore directed to scission of the alkaloid at the ether linkage. While diphenyl ethers can be split by a number of reactions most of the methods involve conditions which are likely to bring about deep-seated changes and therefore of doubtful value. However, Sartoretto and Sowa[5] have shown that metallic sodium dissolved in liquid ammonia hydrogenolyzes diaryl ethers with the formation of a phenol and a hydrocarbon. It was therefore considered probable that the compound (I) would give rise to (VII) or (VIII) or both under the same conditions.


VII


VIII


IX


X

Only a single product could be isolated in pure form from the reaction mixture. It yielded a sparingly-soluble oxalate and when oxidized with permanganate it gave only 4-methoxyphthalic acid. Therefore the phenolic hydroxyl must be in the benzyl portion as in (VIII) and the one methoxyl in cularine must be in position 7 (of I). The alternate possibility, position 6, is discarded on the grounds that when two oxygens are present in the same ring in an alkaloid they are always vicinal. The compound (VIII), though soluble in aqueous alkali, could not be methylated with diazomethane. It was therefore boiled with a large excess of dimethyl sulfate and alkali to bring about methylation and Hofmann degradation at the same time. A small yield of nitrogen-free and alkali-insoluble unsaturated compound was obtained. This is the tetramethoxy derivative (IX) because on oxidation with permanganate it yielded 4-methoxyphthalic acid and asaronic acid (2,4,5-trimethoxybenzoic acid). These two fragments serve to locate the position of the methoxyl groups in cularine without ambiguity as in (X) which is therefore the correct structure. One point which may be mentioned is the fact that had the ether bridge from the benzyl moiety been located at either of the positions 6 or 7 in the isoquinoline ring it could still have given the compound (VIII). To build such compounds with models proved to be impossible because of the large strains involved. Even the unsaturated compound (II) with the ether bridge in other positions than that shown could not be constructed with models.

The writer has described an alkaloid (F30) from *Dicentra eximia*[1] which was regarded as N-desmethylcularine and which is now termed cularimine. This relationship has been confirmed. The ultimate unsaturated hydrocarbon from the Hofmann degradation was oxidized and yielded the acids (III) and (VI) identical with those obtained from cularine. Furthermore, during this degradation a base was obtained whose picrate and methiodide were identical with the picrate and methiodide, respectively, of cularinemethine. Finally, the secondary nature of the nitrogen in cularimine was indicated by the fact that its crude methiodide is not entirely quaternary, and confirmed by the fact that cularimine instantly yields an insoluble precipitate when its solution in dilute acetic acid is treated with sodium nitrite. Accordingly, cülari-

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[2] Anschütz and Japp, *Ber.*, **11**, 211 (1878).

[3] Pschorr and Knöffler, *Ann.*, **382**, 53 (1911).

[4] Patterson and Capell, "The Ring Index," Reinhold Publishing Corp., New York, N. Y., 1940.

[5] Sartoretto and Sowa, THIS JOURNAL, **59**, 603 (1937).

mine was methylated with a mixture of formic acid and formaldehyde.[6] The resulting base was identical with cularine. It also yielded a crystalline N-benzoyl derivative of the correct elementary composition but its reaction with acetic anhydride gave a compound of unknown structure. This is the first recorded case of a secondary base occurring in the entire *Papaveraceae* family.

The formula of cularine, which contains a new type of ether bridge, presents some features of biogenic interest. It may be assumed that the protoberberines and the aporphines are derived from the benzylisoquinolines by condensation or oxidation ring closures. In such cases the alkoxyl substituents are always in the 6- and 7-positions of the isoquinoline portion. The ring closure to the benzylisoquinoline however can theoretically give rise to 7,8-dialkoxyisoquinolines which have not hitherto been found. It seems reasonable that the precursor of cularine is an 8-hydroxy-7-methoxybenzylisoquinoline from which the ether bridge is formed by dehydrogenation. Other orientations of the hydroxyl group cannot undergo similar ring closures. In the bis-benzylisoquinolines the problem of strain is not encountered, but even here many of the ether bridges are in the 8-position. It is pertinent to note that the methoxyl groups in the benzyl moiety are in positions which are usual in the benzylisoquinoline types.

It should be pointed out that a number of O-desmethyl derivatives of cularine have been encountered[7] and at one time some of these were oxidized with permanganate on the assumption that one benzene ring would survive and that a recognizable fragment might be isolated, but oxalic acid and carbon dioxide were the only products ever obtained. This observation offers independent if indirect proof of the assigned structure because the destruction of one of the nuclei would yield a phenolic product which would be subject to further and complete oxidation.

Experimental

Cularine Methiodide and Methine.—A suspension of 5 g. of cularine in 5 cc. of methanol was treated at room temperature with 4 g. of methyl iodide. The alkaloid dissolved readily and the methiodide then slowly separated in colorless crystals which when recrystallized from hot methanol melted at 205°.[7a]

The main portion of the methiodide was dissolved in water (readily soluble) after the organic solvents had been boiled out and a turbidity removed by filtration. The solution (*ca.* 75 cc.) was then heated for twenty-four hours on a steam-bath with 10 g. of potassium hydroxide. The separated oil was extracted with ether and the residue when dried *in vacuo* weighed 5.2 g. This could not be induced to crystallize, but the picrate crystallized readily from methanol in pale yellow needles melting sharply at 167°. *Anal.* Calcd. for $C_{27}H_{28}O_{11}N_4$: C, 55.48; H, 4.78; N, 9.59. Found: C, 55.27; H, 4.85; N, 9.55.

Methine Methiodide and the Compound II.—The methine (5.2 g.) was treated with an excess of methyl iodide in methanol and after twenty-four hours the solvents boiled out. The sparingly-soluble methine methiodide which separated in long colorless needles when washed with methanol melted sharply at 213° without decomposition. *Anal.* Calcd. for $C_{21}H_{26}O_4NI$: C, 52.17; H, 5.38; N, 2.90. Found: C, 52.12; H, 5.62; N, 2.93. The residue was dissolved in 125 cc. of hot water, a turbidity removed by filtration and 10 g. of potassium hydroxide added. The mixture was heated on the steam-bath for five hours, cooled and extracted with large successive amounts of ether. The aqueous solution was again heated for five hours and again extracted with much ether. A total of twenty hours of heating was necessary before all of the methiodide had decomposed. The combined ether extract was shaken with a little dilute acid (the acid extracted a small amount of base which was identified as the methine by the melting point of its picrate), dried over potassium carbonate and evaporated to a small volume. Even while the ether was boiling the unsaturated compound began to crystallize in stout prisms. It melted sharply at 123° and recrystallization from methanol–ether did not change its melting point. The yield of pure product was 4.2 g. *Anal.* Calcd. for $C_{19}H_{18}O_4$: C, 73.55; H, 5.81; $3OCH_3$, 30.00; mol. wt., 310. Found: C, 73.65, 73.72; H, 5.99, 5.95; OCH_3, 30.07; mol. wt. (Rast in camphor), 298, 298.

In one experiment the vapors evolved in the decomposition of the methine methiodide were absorbed in alcoholic hydrogen chloride and the concentrated solution treated with platinic chloride. The platinichloride which separated melted with decomposition at 240–241° and on ignition yielded 36.97% of platinum. Trimethylamine platinichloride requires 36.99% platinum.

When a small portion of the above hydrocarbon was hydrogenated in the presence of platinum oxide it readily absorbed hydrogen. The reduced compound was recrystallized from hexane containing a trace of ether. Large single crystals, probably hexagonal, melting sharply at 77° were obtained. *Anal.* Calcd. for $C_{19}H_{22}O_4$: C, 72.61; H, 7.01. Found: C, 72.63, 72.79; H, 7.00, 7.01.

2,3,8-Trimethoxyxanthone-5-carboxylic Acid (VI) and 4,5,5′-Trimethoxydiphenyl ether-2,2′,5-tricarboxylic Acid (III).—The crystalline unsaturated compound (II) was dissolved in a liberal volume of acetone and the solution treated with finely powdered potassium permanganate until the pink color was permanent. Water in small amounts and more permanganate were added until the color again was permanent. Hot water was then added, the acetone boiled out, and the hot mixture filtered. The cooled mixture was acidified with hydrochloric acid and shaken with ether whereupon a very sparingly soluble acid crystallized. This was filtered off, washed with water and with ether. When recrystallized from boiling acetic acid it separated in very pale yellow fine needles which melted at 304°. This is the trimethoxy derivative of VI. *Anal.* Calcd. for $C_{17}H_{14}O_7$: C, 61.81; H, 4.24; $3OCH_3$, 28.18; neut. equiv., 330. Found: C, 62.15; H, 4.71; OCH_3, 26.77; neut. equiv., 329. The acid forms sparingly-soluble sodium and potassium salts and a readily-soluble ammonium salt. It dissolved to a yellow-colored solution in sulfuric acid which shows a deep sea-green fluorescence. The methyl ester was prepared by suspending the acid in methanol in which it is only sparingly soluble and adding an ethereal solution of diazomethane. Partial removal of the solvents and cooling yielded well-formed needles, sparingly soluble in methanol, which melted sharply at 252°. *Anal.* Calcd. for $C_{18}H_{16}O_7$: C, 62.79; H, 4.65; $4OCH_3$, 36.05. Found: C, 62.48, 62.34; H, 4.84, 4.79; OCH_3, 35.27, 35.38.

The aqueous filtrate from the xanthone carboxylic acid was repeatedly extracted with ether and the extract evaporated to dryness. The residue was extracted with cold acetone, which left a small amount of the sparingly-soluble acid (VI), and the somewhat concentrated solution further evaporated with the portionwise addition of benzene. In the course of several days a crop of colorless dense crystals separated which melted at 187° with the evolution of vapors—presumably due to anhydride formation. *Anal.* Calcd. for $C_{18}H_{16}O_{10}$: C, 55.10; H, 4.08;

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(6) Hess, Merck and Uibrig, *Ber.*, **48**, 1886, 1974 (1915).

(7) Manske, *Can. J. Research*, **B18**, 97 (1940).

(7a) All melting points are corrected.

$3OCH_3$, 23.72. Found: C, 55.11, 54.87; H, 4.44, 4.44; OCH_3, 22.73. This acid (III) was obtained in large prisms melting at 113° when recrystallized from water, and in fine needles melting at 152°, when recrystallized from ether and under some conditions when recrystallized from water. These forms are evidently different hydrates and when dried at 100° *in vacuo* over phosphorus pentoxide lost variable amounts of water, the form melting at 113° losing three molecules; but the dehydrated compound gave analytical figures in good agreement with $C_{18}H_{16}O_{10}$. Furthermore, each of the acids gave the same *trimethyl ester* when treated with ethereal diazomethane. The esters from the acids of the three different melting points all melted at 152° when recrystallized separately from methanol–ether. The ester is moderately soluble in warm methanol and only sparingly so in ether. *Anal.* Calcd. for $C_{21}H_{22}O_{10}$: C, 58.06; H, 5.07; $6OCH_3$, 42.86. Found: C, 58.13; H, 5.12; OCH_3, 41.86.

Hydrogenolysis of Cularine to 1-Benzyl-2′-hydroxy-7,4′,5′-trimethoxy-2-methyltetrahydroisoquinoline (VIII).—A solution of 3.4 g. of cularine in 75 cc. of anhydrous ether was prepared by dissolving it under reflux in a much larger volume and rapidly evaporating some of the solvent. To this was added 50 cc. of liquid ammonia and then a very dilute freshly-prepared solution of sodium in liquid ammonia was slowly run in with stirring. The blue color disappeared immediately and gave rise to a fugitive but brilliant carmine-colored solution. Sodium in liquid ammonia was added until the blue color was permanent for several minutes. After standing overnight, during which time the ammonia had evaporated, water was added and the mixture repeatedly extracted with ether. (The alkaline aqueous solution on saturation with carbon dioxide yielded only a trace of amorphous base. Although it was subsequently shown that all of the base in the ether extract was phenolic and soluble in aqueous sodium hydroxide it is readily extracted from such solutions by ether.) The washed and dried extracts yielded a pale yellow resin when the ether was evaporated but attempts to obtain crystals failed. However, the tetroxalate crystallized readily (3 g.) from hot water in which it is moderately soluble. It is only very sparingly soluble in cold water and melts at 141°. *In vacuo* at 100° over phosphorus pentoxide it lost 10.00% of its weight, the trihydrate requiring 10.32% water. The dried oxalate gave C, 55.53, 55.32; H, 5.54, 5.62; N, 3.18, 3.11. Calcd. for $C_{20}H_{25}O_4N{\cdot}2(CO_2H)_2$: C, 54.69; H, 5.54; N, 2.68. The free base, regenerated from the recrystallized oxalate, was obtained as a colorless brittle resin which did not crystallize.

There was present in the aqueous mother liquor from the preparation of the oxalate a small amount of base which was oxidized with potassium permanganate, first in dry acetone, and then in the presence of water. This mixture of acids obtained from the oxidation was freed of oxalic acid by means of ammoniacal calcium chloride and then yielded a very small amount of an acid which was only sparingly soluble in ether. When it was recrystallized from a large volume of ether it was obtained in colorless fine needles which melted at 186° and on admixture with succinic acid melting at 188° it melted at 186–187°. The formation of succinic acid by the oxidation of (VIII) is not understandable. It may, however, be assumed that the slight excess of sodium used in the scission caused some nuclear reduction and that such reduction products might give rise to succinic acid on oxidation. No succinic acid was encountered when the purified base was oxidized.

4-Methoxyphthalic Acid.—A solution of the resin base (VIII) in cold alkaline solution was treated with potassium permanganate until the color due to the latter was permanent for two hours. The excess permanganate was destroyed with a little methanol and the heated solution treated with an excess of calcium chloride and ammonium chloride to remove oxalic acid. The aqueous filtrate from the mixture was acidified with hydrochloric acid and exhausted with ether. The residue from the ether extract crystallized readily and, since it proved to be readily soluble in water, it was assumed to be a phthalic acid. It was therefore dissolved in ethylamine, evaporated to dryness, and sublimed *in vacuo*. The colorless crystalline sublimate was recrystallized from hot water and then obtained in colorless elongated plates which melted sharply at 81°. On admixture with a synthetic specimen of N-ethyl-4-methoxyphthalimide[8] melting at 79° it melted at 79–80°. N-Ethyl-metahemipinimide also melts at 81°, but when admixed with the above imide the mixture was completely liquid at 65–70°.

Asaronic Acid.—When the base (VIII) is treated with diazomethane in ether alone or in ether–methanol there is no evolution of nitrogen and the mixture standing for one week in the refrigerator yielded no non-phenolic base whatever. The base (0.6 g.) was therefore dissolved in methanol, treated with excess methyl iodide, and then, while boiling, gradually treated with potassium hydroxide pellets. Most of the methanol was then evaporated and methylation continued by heating with excess of dimethyl sulfate and strong potash. At intervals the mixture was cooled and extracted with ether. There was ultimately obtained about 0.2 g. of resinous product which was soluble neither in acid nor in alkali. It was oxidized in acetone containing 10% of water with potassium permanganate, the acids isolated in the normal way by ether extraction after precipitating the oxalic acid as calcium oxalate. The crystalline product proved to be a mixture from which boiling hexane extracted a small amount of acid which was recrystallized from hot water. It was obtained in colorless prisms melting sharply at 142°. In admixture with a specimen of asaronic acid, m. p. 143–144°, kindly submitted for purposes of comparison by Professor A. Robertson, Liverpool University, England, it melted at 142–143°. The melt readily crystallized on slight cooling and remelted at the same temperature.

The writer is deeply indebted to Dr. F. W. Matthews, Canadian Industries, Limited, McMasterville, Que., for comparing the degradative and synthetic asaronic acids by X-ray diffraction patterns. The two samples checked well with each other. The following data are for the purified acid (powder camera diameter, 143.2 mm.; chromium kα X-radiation $\lambda = 2.291$ Å.; filter, V_2O_5; specimen mount, capillary, 20° oscillation; intensities, visual estimation).

Å.	I/I^0	Å.	I/I^0
8.2	0.60	3.63	0.05
7.2	.90	3.52	1.00
6.8	.90	3.47	0.05
5.50	.50	3.38	.10
4.12	.20	3.25	.30
3.97	.10	3.13	.20
3.90	.05	3.06	.05
3.79	.10	2.77	.10

The hexane-insoluble acid consisted substantially of 4-methoxyphthalic acid because it readily yielded the ethylimide described above.

Action of Ethyl Chloroformate.—A solution of cularine in purified ether was treated with an excess of ethyl chloroformate and then shaken with excess aqueous potassium hydroxide until the excess ethyl chloroformate was destroyed. The washed solution was extracted with dilute hydrochloric acid and with water, dried over potassium carbonate, and the solvent removed. The colorless resin thus obtained could not be induced to crystallize.

A portion was treated in acetone solution with potassium permanganate until the color of the latter was permanent for one hour. The filtered solution was largely freed of acetone on the steam-bath and the residue dissolved in ether. The ethereal solution was washed with aqueous potassium hydroxide, and with dilute acid, dried with potassium carbonate, and evaporated to a resin which in contact with methanol crystallized readily. When

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[8] Manske, *Can. J. Research*, **B16**, 76 (1938).

recrystallized from methanol this neutral compound was obtained in short stout prisms melting sharply at 120°. The mean of good quadruplicate analyses was C, 61.81; H, 6.15; N, 3.62; OCH_3, 25.86.

Cularimine.—A solution of cularimine (0.4 g.) in ether was treated with an excess of methyl iodide and after twenty-four hours the solvents boiled out. The residue which was sparingly soluble in cold water was digested on the steam-bath with an aqueous suspension of freshly precipitated silver chloride. The cooled filtrate from the insoluble silver salts on rendering alkaline with potassium hydroxide yielded some oily precipitate indicating the presence of non-quaternary salts in solution. The mixture was extracted with ether, the aqueous solution treated with a large excess of potassium hydroxide, and heated on a steam-bath. The liberated base yielded a picrate melting at 167° and a methiodide melting at 213°. These derivatives were proved identical with cularinemethine picrate and cularinemethine methiodide, respectively, by mixed melting point determinations. Nevertheless, the methiodide was decomposed with alkali and the resultant hydrocarbon oxidized as above described for (II). The acids (III) and (VI) were obtained and proved to be identical with those obtained from cularine.

Cularine from Cularimine.—A mixture of 40 mg. of cularimine, 0.1 cc. of formic acid and 0.1 cc. of 35% formaldehyde was heated on a steam-bath for four hours. The resultant resin was dissolved in 20 cc. of boiling dilute aqeuous oxalic acid and the filtered solution cooled. The sparingly-soluble oxalate was separated and decomposed in aqueous suspension with ammonia in the presence of ether. The washed ether solution was evaporated to dryness and the residue crystallized from boiling pentane containing a trace of ether. The colorless stout prisms then obtained melted at 115° either alone or in admixture with cularine. The yield was 27 mg.

N-Benzoylcularimine.—A solution of 50 mg. of cularimine in 50 cc. of ether was treated with an excess of benzoyl chloride and then shaken with successive portions of strong aqueous potassium hydroxide. A little pyridine was added and the ethereal solution washed with several successive portions of water. Evaporation of the ether left a pale-colored oil which was dissolved in a little methanol, treated with a few drops of aqueous potassium hydroxide and after a short time diluted with much water. The precipitate which crystallized readily was washed, dried, and recrystallized from its concentrated solution in methanol by the addition of ether. The colorless rhombic plates of N-benzoylcularimine thus obtained melted sharply at 174°. *Anal.* Calcd. for $C_{26}H_{25}O_5N$: C, 72.39; H, 5.80. Found: C, 72.66; H, 6.20.

Treatment of Cularine with Acetic Anhydride.—When 50 mg. of cularine was treated with 0.2 cc. of acetic anhydride it dissolved at once, but in the course of several minutes the solution crystallized for the greater part. The mixture was washed several times by decantation with ether and then with cold methanol. The crystalline residue was then recrystallized twice from hot methanol in which it is only moderately soluble. Colorless elongated plates melting sharply at 217° were thus obtained. Found: C, 70.44, 70.22; H, 6.73, 6.66; N, 4.23. These analyses do not agree with acetylcularine but fit $C_{20}H_{23}O_4N$ which requires C, 70.38; H, 6.75; N, 4.11. When heated on the steam-bath for two hours with 5 parts of hydrochloric acid to 25 parts of methanol it was unchanged.

Summary

1. Hofmann degradation of cularine has yielded an unsaturated compound which still contains the three methoxyl groups and the indifferent oxygen of the alkaloid. Oxidation of this compound yielded a tribasic acid which is regarded as a derivative of diphenyl ether and a monobasic acid which is probably a derivative of xanthone.

2. Cleavage of cularine with metallic sodium dissolved in liquid ammonia yielded a phenolic base which is a benzylisoquinoline derivative. The latter on oxidation yielded 4-methoxyphthalic acid and on exhaustive methylation followed by oxidation yielded the above acid and asaronic acid.

3. The structure of cularine is therefore that of a diphenyl ether with a seven-membered ring and an isoquinoline nucleus. The positions of the methoxyl groups are fixed by the degradation products.

4. Cularimine, an alkaloid not hitherto named, is N-desmethylcularine.

5. Cularine is the first representative of a new class of isoquinoline alkaloids with a diphenyl ether bridge related biogenetically to the benzylisoquinolines.

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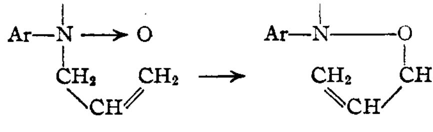
Thermal Rearrangement of Allyl-type Sulfoxides, Sulfones and Sulfinates[1]

BY ARTHUR C. COPE,* DWIGHT E. MORRISON[1a] AND LAMAR FIELD[1b]

The rearrangement of allyl groups from nitrogen to oxygen in amine oxides has been reinvestigated recently[2] and explained on the basis of an intramolecular, cyclic mechanism. The reaction resembles the Claisen rearrangement,[3] except for differences which distinguish dyad from triad systems.



This paper reports the preparation of a group of allyl-substituted sulfur compounds, and an investigation of their susceptibility to rearrangement.

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(1) Abstracted from portions of the doctoral theses of Dwight E. Morrison (Columbia University) and Lamar Field (Massachusetts Institute of Technology).

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(2) Kleinschmidt and Cope, THIS JOURNAL, **66**, 1929 (1944); Cope and Towle, *ibid.*, **71**, 3423 (1949).

(3) Tarbell, *Chem. Rev.*, **27**, 495 (1940).