THE ACONITE ALKALOIDS

VIII. ON ATISINE

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(Received for publication, January 26, 1942)

The roots of the Indian plant Aconitum heterophyllum, or atis, have long been known to contain an alkaloid, atisine (1), which belongs in the category of simpler aconite alkaloids or alkamines of low toxicity. The possibility of a structural relationship between this group of alkaloids and the more complicated highly toxic aconitine group makes a study of their chemistry of particular importance. In recent work Lawson and Topps (2) have reported the results of their study of this alkaloid. They revised the older formulation of Wright (3) and of Jowett (4) of C_{22}H_{33}O_{2}N to C_{22}H_{33}O_{2}N and showed that atisine contains an N-methyl group but no methoxyl group. However, their conclusion that a methylenedioxy group is present we have found to be incorrect. Our present work confirms their observations in some respects but in others we have been forced to different conclusions.

Atis root of commercial origin was obtained from India. The isolation of atisine as the hydrochloride followed with minor modifications the procedure used by Lawson and Topps. It was found necessary to employ an excess of NaOH to liberate the alkaloid before extraction of the final crude aqueous mixture. 12 kilos of the root were found to yield about 98 gm. of crude hydrochloride. Analysis of the recrystallized salt supported the formulation C_{22}H_{33}O_{2}N·HCl. The alkaloid itself could not be obtained in crystalline form. It distilled readily in a molecular still. Analysis of such material supported the formulation C_{22}H_{33}O_{2}N. The hydrochloride as obtained by us showed the rotation [α]^{25}_{D} = +28° (c = 1.1 in H_{2}O). This differed considerably from the figures published originally by Jowett; viz., [α]_{D} = +18.46°. A possible explanation for this discrepancy has since been found in the instability of atisine in alkaline solution. Even when the alkaloid as the free base was allowed to stand in alcoholic solution at room temperature, a slow change was found to occur. When, after a number of days, the base was reconverted into the hydrochloride, the latter now showed [α]^{25}_{D} = +13.5°. This change was accelerated by the addition of alkali and led to the formation in part of the substance to be described

1 The rhizomes of commercial Aconitum heterophyllum were purchased from an Indian source through the kind aid of Dr. R. T. Major of Merck and Company, Inc., Rahway, New Jersey.
below. In the procedure used by us for the isolation of the alkaloid from the plant extract the free base was promptly extracted with benzene after liberation with alkali. It is probable that the material for which Jowett reported his rotations was the product of partial rearrangement. This rearrangement may be due to the double bonds of atisine, since the tetrahydro derivative to be described below was not similarly affected by alkali.

Lawson and Topps have described the production of a so called demethylated alkaloid, C_{21}H_{30}O_{3}N (m.p. 147°) by the action of potassium ethoxide on atisine. On repeating the brief directions of these workers we have obtained undoubtedly the substance described by them, but it was found to have retained the N-methyl group of atisine. The same substance was produced by heating the alkaloid in methyl alcoholic NaOH. Although an apparent mixture of substances resulted, the crystalline base was readily isolated first as the hydrochloride. Analyses of the base and its hydrochloride corresponded with the figures for a dihydroatisine, C_{22}H_{35}O_{2}N. On hydrogenation either the base or the hydrochloride was found to absorb but 1 mole of H\textsubscript{2} with the formation of the tetrahydroatisine described below. The production of such a substance from atisine if a dihydro derivative would appear to be the result of a disproportionation of hydrogen. The possibility that atisine itself is really a mixture and that such a dihydro derivative had its origin in one of the components of such a mixture, while still to be considered, appears to be much less likely.

The base atisine, as well as its tetrahydro derivative, was found to possess 2 active H atoms. These must be contained in two hydroxyl groups, since diacetylatisine hydrochloride was formed on acylation of atisine hydrochloride. Thus the oxygen atoms of atisine have been accounted for by OH groups and not by a methylenedioxy group as suggested by Lawson and Topps.\footnote{These workers reported that the Zerewitinoff determination with atisine hydrochloride was negative. In our repetition of the determination with the salt we have also found no appreciable evolution of CH_{4} at 25°. However, at 95° 0.472 per cent of active H was found. The unsatisfactory behavior of this salt is undoubtedly due to physical complications.}

Atisine on hydrogenation with platinum oxide catalyst absorbed 2 moles of H\textsubscript{2} presumably due to two double bonds. The resulting product proved to be a mixture of apparently isomeric tetrahydroatisines which, unlike atisine itself, readily crystallized. One of these isomers was easily separated because of its sparing solubility and melted at 171–174°. In toluene [\alpha]\textsubscript{D} = -33°; in chloroform [\alpha]\textsubscript{D} = -23°. The same substance was obtained from the dihydroatisine recorded above. Unlike atisine, the tetrahydro derivative is stable toward alkali.
Lawson and Topps reported the hydrogenation of atisine hydrochloride in acetic acid with palladium black to yield a dihydroatisine which was described only as the hydrochloride and concluded that atisine contains but one double bond. In repeating this experiment we found that the hydrogenation with palladium proceeded more slowly than with platinum oxide catalyst but nevertheless continued into the 2 mole stage. From the resulting mixture the above tetrahydroatisine was readily obtained. In an experiment in which the hydrogenation with palladium was interrupted at the 1 mole stage a mixture was obtained which contained unreacted atisine and from which tetrahydroatisine was isolated.

When the attempt was made to reduce atisine with sodium and alcohol, the only crystalline substance which could be isolated appeared to be identical with dihydroatisine. When this substance was in turn catalytically hydrogenated, it yielded a mixture from which the above tetrahydroatisine was isolated. Whether the production of dihydroatisine in this case was due to the reducing action of the sodium and alcohol or due to the transformation of atisine by the resulting sodium ethylate was not determined.

On the assumption of the correctness of the formulation C_{22}H_{33}O_{2}N for atisine, the presence of two hydroxyl groups and two double bonds would indicate that its skeletal structure must be of pentacyclic nature. Since it contains an N-methyl group and apparently at least one C-methyl group, as shown by the Kuhn and Roth (5) determination, such a saturated system cannot be greater than C_{20}H_{33}N. It is probable that three of these rings consist of a hydrogenated phenanthrene. This was supported by the results of dehydrogenation studies.

In the repetition of the dehydrogenation of atisine with selenium already reported by Lawson and Topps we have confirmed in an important respect the observations of these workers. The dehydrogenation product which appeared to be formed in largest amount was the hydrocarbon C_{17}H_{16} reported by them. Their conclusion that it is a substituted phenanthrene hydrocarbon has been supported by absorption spectra measurements carried out at The Rockefeller Institute for Medical Research by Dr. George I. Lavin as shown in Fig. 1. We have previously described (6) the isolation of phenanthrene hydrocarbons from the new aconite alkaloid staphisine and the study of their absorption spectra. The curves of the latter are given, also in Fig. 1, for comparison with the curve of the C_{17}H_{16} hydrocarbon from atisine.

It has since been found that the values of the extinction coefficients as plotted in the curves given in the original paper on staphisine (6) were somewhat too high because of a miscalculation of data. The corrected values are plotted in the curves of Fig. 1.
From the hydrocarbon fraction a substance C_{15}H_{12} has been obtained which agreed in properties with synthetic 1-methylphenanthrene. This was confirmed by comparison of their picrates. From a higher fraction an oily hydrocarbon C_{18}H_{18} was isolated and characterized as the trinitrobenzene derivative (163–166°) and the picrate which melted at 153–156°.

The base C_{17}H_{17}N described by Lawson and Topps as a product from the so called demethylated atisine (dihydroatisine) has not been encountered by us among the products from atisine. Instead a base C_{18}H_{18}N which melted at 83–85° was obtained. This in turn gave a picrate (221–223°) and a methiodide which melted at 233–235°. The absorption spectrum of the base is recorded in Fig. 1.

A possible oxygen derivative of the latter base, the base C_{19}H_{15}ON, was
also obtained which melted at 258–261°. In addition, as recorded in the experimental part, two other crystalline substances and a basic oil isolated as a picrate were encountered in amounts too small for proper and conclusive characterization.

**EXPERIMENTAL**

*Atisine*—The isolation of the alkaloid from atis root has been based essentially on that of Jowett and of Lawson and Topps, with a few modifications.

13 kilos of ground root were extracted twice with 39 liters of 70 per cent alcohol. In each case the extracted root was squeezed dry in a press. The extract was concentrated under diminished pressure to remove the alcohol and the remaining thin aqueous syrup was treated with one-fourth of its volume of 10 per cent H₂SO₄. The mixture, which was strongly acid to Congo red, was extracted with chloroform several times and the remaining clear aqueous solution was carefully treated with Na₂CO₃ solution until slightly alkaline to litmus. The mixture was extracted repeatedly with benzene and the extract was set aside. The aqueous phase was then shaken with fresh benzene, made strongly alkaline with NaOH solution, and promptly and repeatedly extracted with benzene. The washed and dried benzene extract on concentration yielded a light brown resin of mixed alkaloids. This was dissolved in alcohol and, while chilling, carefully treated with HCl (1.19) until barely acid to Congo red. During this operation a copious mass of colorless needles formed which were collected with 95 per cent alcohol. 35.3 gm. were obtained. On concentration of the mother liquor successive additional crops of crystals brought the yield to 46 gm. In a later experiment 24 kilos yielded four crops of crystals which totaled 98 gm. Analyses of these fractions indicated that they consisted essentially of atisine hydrochloride. From the ultimate mother liquor on longer standing additional material was obtained which was found to consist of salts of at least two new alkaloids as described in Paper IX.

After recrystallization from 50 per cent alcohol the salt formed flat needles which melted with decomposition at 311–312° (uncorrected).

\[ [\alpha]_D^{25} = +28° \ (c = 1.10 \text{ in } H_2O) \]

C₇₂H₄₈O₂NCl. Calculated. C 69.52, H 9.02

Found. (a) " 69.92, " 9.16

(b) " 69.74, " 8.79

(c) " 69.50, " 9.06

(d) " 69.78, " 8.79

Attempts to crystallize the free base obtained by decomposition of the salt were not successful. However, the residue obtained on concentration of the benzene solution of the base distilled rapidly and quantitatively
under 0.01 μ and at a bath temperature of 140°. It formed a white opaque film on the condenser which could be removed as a powder. It melted at 57–60°.

\[ \text{C}_{22}\text{H}_{33}\text{O}_{2}\text{N}. \text{ Calculated, C 76.91, H 9.69; found, C 76.72, H 9.65} \]

The molecular weight was determined in camphor by the method of Rast. Calculated, 343.27; found, 342.5.

A C-methyl determination according to Kuhn and Roth (5) was as follows: 0.0376 gm. of base after three distillations consumed a total of 0.74 cc. of 0.105 N NaOH. Calculated for one CH₃, 1.045 cc.

The Tschugaeff-Zerewitinoff determination was as follows: 11.92 mg. of base gave 1.45 cc. of CH₄ (20°, 739 mm.). At 95° there was no change. Found, H 0.487; calculated for 2H, 0.587.

**Diacetylatisine Hydrochloride**—0.1 gm. of atisine hydrochloride and 2 cc. of acetic anhydride were refluxed for 10 minutes. The alkaloid salt gradually dissolved. The clear solution was repeatedly concentrated in vacuo after addition of alcohol. The reaction product crystallized from alcohol-ether in delicate needles which melted at 241–243° (uncorrected) with decomposition.

\[ \text{C}_{22}\text{H}_{35}\text{O}_{2}\text{N}. \text{ Calculated, C 67.27, H 8.26; found, (a) 66.97, H 8.45; (b) C 66.89, H 8.53} \]

**Atisine and Alkali. Dihydroatisine(?)**—3m. of atisine hydrochloride were sealed in a tube with a saturated solution of NaOH (15 to 20 gm.) in 35 cc. of methyl alcohol. The mixture was heated at 100° for 6 hours. The colorless mixture after dilution was extracted with chloroform. The extract was washed and dried over K₂CO₃ and then concentrated. Residual chloroform was boiled off with 95 per cent alcohol. On careful addition of HCl (1.19) until the mixture was just acid to Congo red, the hydrochloride rapidly crystallized. After collection with cold alcohol 1.36 gm. of the salt were obtained. A portion of this salt on recrystallization by solution in hot 95 per cent alcohol followed by concentration separated as thin or broad flat needles which melted with decomposition at 261–263°.

\[ [\alpha]_D^{12} = -16° (c = 1.02 \text{ in H}_2\text{O}) \]

\[ \text{C}_{22}\text{H}_{35}\text{O}_{2}\text{N} \cdot \text{HCl}. \text{ Calculated, C 69.16, H 9.50; found, (a) 69.23, H 9.29; C 69.01, H 9.36; (b) 69.32, H 9.50} \]

The major portion of the above unrecrystallized salt was directly decomposed with dilute NaOH and the base was extracted with ether. The dried extract on concentration readily yielded large, well formed prisms of
the base which melted at 150–153° after preliminary sintering. The micro melting point was 156–158° (corrected).

\[
\alpha = -45° (c = 1.02 \text{ in toluene})
\]

\[\text{C}_{22}\text{H}_{25}\text{O}_{2}\text{N}}. \text{ Calculated. } \text{C 76.46, H 10.22, N(CH}_3 \text{) 4.35}
\]

\[\text{Found. (a) } \text{C 76.42, H 10.11; C 76.35, H 10.07}
\]

\[\text{“ (b) } \text{C 76.74, H 10.27, N(CH}_3 \text{) 2.64}
\]

A portion of the base was reconverted into the hydrochloride. The latter again crystallized from alcohol-ether in needles which melted at 261–262°.

\[
\alpha = -17° (c = 1.00 \text{ in H}_2\text{O})
\]

\[\text{Found. C 69.20, H 9.62}
\]

The attempt was made to repeat the reported demethylation of atisine as described by Lawson and Topps. Potassium ethylate was prepared from 1.4 gm. of K and 19 cc. of absolute alcohol in an atmosphere of nitrogen. 0.5 gm. of atisine hydrochloride was then added and the mixture was refluxed for 5.5 hours. During the operation much of the alcohol was carried off by the nitrogen, so that the actual mixture became more concentrated, which more than compensated for the partial neutralization of the HCl. After dilution the dried ether extract yielded a colorless resin which did not crystallize directly. It was converted into the HCl salt, several fractions of which crystallized readily. The salt formed needles from alcohol and melted with effervescence at 303° (uncorrected).

\[
\alpha = -2° (c = 0.98 \text{ in H}_2\text{O})
\]

\[\text{Found. C 69.61, H 8.95, N(CH}_3 \text{) 2.37}
\]

A second fraction was obtained from the mother liquor. Found, N(CH$_3$) 2.55.

The above melting point, rotation, and analytical data definitely point to a mixture. When the base was recovered from the salt with alkali, the ether extract on concentration readily crystallized as characteristic prisms which melted at 152° and were identical with the above base obtained with alcoholic NaOH.

\[\text{C}_{22}\text{H}_{25}\text{O}_{2}\text{N}}. \text{ Calculated. } \text{C 76.46, H 10.22; Found, C 76.51, H 10.01}
\]

**Tetrahydroatisine**—0.25 gm. of atisine hydrochloride was hydrogenated with 50 mg. of platinum oxide catalyst in methyl alcoholic solution under approximately 3 atmospheres pressure. The reaction was rapid and practically completed within 10 minutes after a total of 45 cc. of H$_2$ or about 32 cc. by the substance was absorbed. Calculated for 2 moles of H$_2$, 31.5 cc. After filtration and removal of the solvent the free base was liberated with alkali and extracted with ether. The extract on concentration to small volume readily crystallized after chilling. 0.145 gm. of substance
was collected in the cold with ether. It melted partly at 155°-156°, but did not clear until above 165°.

\[ \text{C}_{22}\text{H}_{37}\text{O} \text{PN} \]. Calculated, C 76.02, H 10.74; found, C 76.21, H 10.85

This was shown to be a mixture. On recrystallization from 95 per cent alcohol it crystallized as flat needles which melted at 171°-174°. The melting point was not changed by further recrystallization. The yield was about one-third of the starting material.

Found. \( \langle a \rangle \) C 75.90, H 10.52; \( \langle b \rangle \) C 76.37, H 10.68

\[ [\alpha]_b^\circ = -33° (c = 1.03 \text{ in toluene}); -23° (c = 1.00 \text{ in chloroform}) \]

The Tschugaeff-Zerewitinoff determination was as follows: 11.53 mg. gave 1.68 cc. of CH₄ (25°, 750 mm.); at 95° there was no change. Found, H 0.593; calculated, 2H 0.581.

From the original ether mother liquor on further concentration additional crystallization was obtained in small amount (11 mg.) which consisted mostly of small glistening prisms. The melting point also indicated non-homogeneity. It began to soften above 155° but did not form a clear melt under 168°.

\[ [\alpha]_b^\circ = -57° (c = 0.77 \text{ in toluene}) \]

0.25 gm. of atisine hydrochloride was hydrogenated in acetic acid solution with 50 mg. of Pd black under 3 atmospheres pressure. The absorption was much slower than in the above case with platinum catalyst. Although after 6 hours about 1 mole in excess of that required by the catalyst had been absorbed, absorption continued and after 24 hours was interrupted. 28 cc. of H₂ were absorbed by the substance.

After liberation of the base it crystallized from ether as an obvious mixture of isomers which gradually and incompletely melted at 138°-139° and became clear somewhat higher. Found, C 76.10, H 10.57.

After repeated recrystallization from 95 per cent alcohol, it melted at 171°-174° and showed no depression when mixed with the above tetrahydroatisine obtained with platinum catalyst.

In an experiment in which the hydrogenation with Pd was interrupted at the 1 mole stage the only product which crystallized as the free base was obtained in small yield. Found, C 76.16, H 10.65.

After repeated recrystallization from alcohol, it melted at 171°-174° and showed no depression with tetrahydroatisine.

0.1 gm. of dihydroatisine with 50 mg. of platinum oxide catalyst in methanol rapidly absorbed 1 mole of H₂ in excess of the requirements of the catalyst. The crystalline reaction product proved to be a mixture which after several recrystallizations from alcohol gave 23 mg. of characteristic
needles of the tetrahydro derivative which melted at 172–173°. Found, C 76.02, H 10.50.

A similar result was obtained when the hydrochloride of dihydroatisine was hydrogenated. The hydrogenated base recovered from the reaction mixture after repeated recrystallization melted at 172–173°. Found, C 76.29, H 10.73.

Atisine and Sodium—2 gm. of sodium were added in portions to a refluxing solution of 0.5 gm. of atisine hydrochloride in 30 cc. of absolute alcohol. The diluted reaction mixture was extracted with ether. The washed, dried, and concentrated extract on careful addition of petroleum ether gradually crystallized. 0.14 gm. of glistening, flat, often diamond-shaped prisms was obtained which after recrystallization melted at 153–155°. A mixture with dihydroatisine melted at 150–153°.

\[ \alpha_d^\text{ii} = -45.5^\circ \text{ (c = 1.01 in toluene)} \]

C\text{22H35O2N}. Calculated. C 76.46, H 10.22, N(CH\text{3}) 4.35

<table>
<thead>
<tr>
<th>Found.</th>
<th>(a)</th>
<th>76.26,</th>
<th>10.08</th>
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<tbody>
<tr>
<td>(b)</td>
<td>76.11,</td>
<td>10.06,</td>
<td>N(CH\text{3}) 2.74</td>
</tr>
</tbody>
</table>

The Tschugaeff-Zerewitinoff determination was as follows: 15.475 mg. gave 2.0 cc. of CH\text{4} (26°, 739 mm.); there was no change at 95°. Found, H 0.517; calculated for 2H, 0.584.

0.1 gm. of this substance was hydrogenated with 50 mg. of platinum oxide catalyst in methyl alcohol. The substance absorbed 10 cc. of H\text{2}. The resulting base crystallized as needles from alcohol, melted at 170–172°, and showed no depression when mixed with tetrahydroatisine.

C\text{22H31O2N}. Calculated, C 76.02, H 10.74; found, C 78.39, H 10.67

12.90 mg. of substance gave 1.78 cc. of CH\text{4} (26°, 739 mm.); there was no change at 95°. Found, H 0.552; calculated, 2H 0.581.

Dehydrogenation of Atisine—18 gm. of atisine hydrochloride were decomposed with NaOH solution and the free base was extracted with ether. The dried extract was concentrated to dryness in a dehydrogenation apparatus. 50 gm. of selenium powder were then added, and the mixture was heated in a current of nitrogen for 2 hours in a salt bath kept at 340°.

The resulting distillate was examined for basic, phenolic basic, phenolic, and neutral fractions. Only a small amount of basic material was obtained, which had the odor of pyridine derivatives, but nothing crystalline could be isolated. Appreciable amounts of phenolic or basic phenolic fractions were not present. The neutral fraction contained more material but appeared to consist largely of unstable selenium derivatives of unpromising nature.

The residue which remained in the dehydrogenation flask was finely ground and exhaustively extracted with ether. Evaporation of the extract
yielded a residue of about 11 gm. It was redissolved in ether and 35 cc. of 10 per cent HCl were added. After thorough shaking, the ether phase was separated from the acid layer, which contained considerable insoluble sticky tar. Investigation of the ether solution for acid or phenolic products proved negative. The dried ether solution yielded a residue of 5.9 gm. This was dissolved in benzene and passed through a chromatograph prepared with 1 pound of Brockmann's alumina suspended in benzene. Approximately 3 gm. of material passed through the column with the benzene. This hydrocarbon fraction was set aside to be treated as described below.

2.6 gm. of material were subsequently eluted with 5 per cent methyl alcohol in benzene. This fraction was sublimed in an apparatus under 0.2 mm. pressure up to an oil bath temperature of 250°. 2 gm. of resinous sublimate were obtained which contained free selenium. This was removed with

<table>
<thead>
<tr>
<th>Fraction No.</th>
<th>Bath temperature</th>
<th>Column temperature</th>
<th>Weight of fraction</th>
<th>Analysis</th>
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<td>°C.</td>
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<td>mg.</td>
<td>C (%)</td>
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<td>9</td>
<td>266</td>
<td>238</td>
<td>150</td>
<td>80.21</td>
</tr>
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Table I

Fractionation of Neutral or Weakly Basic Heterocyclic Fraction

bone-black in ether solution. After removal of the solvent, the residue was resublimed with heating not higher than 200°. The sublimate weighed 1.8 gm. This was fractionally distilled in a fractionating apparatus with a column 21 cm. in length as shown in Table I.

Fractions 7 and 8 crystallized from ether. Fraction 8 gave 26 mg. of delicate curved needles which showed a rather indefinite melting point of 180–190°. Its properties made further purification very difficult, especially with the small amount of material available.

C₁₂H₁₁ON. Calculated. C 80.45, H 9.97, N 4.47
C₂₅H₂₉ON. “ “ 80.20, “ 9.77, “ 4.68

The analytical data approximated the figures for a formulation C₂₁H₃₁ON.
The C figure for the formula \( \text{C}_{21}\text{H}_{31}\text{ON} \) is somewhat low, but the fractions from Nos. 4 to 9 more or less approach the theory and it appears possible that this material could have been formed from atisine by the loss of an oxygen atom and a \( \text{CH}_2 \) group with a rearrangement which rendered the nitrogen atom no longer strongly basic.

The insoluble sticky tar suspended in the above acid extract was extracted with chloroform. The latter was then shaken with 10 per cent NaOH. Solid material separated at the interface and was removed mechanically after standing for some time. The chloroform layer was separately investigated as given below. The solid material was dissolved in sufficient chloroform and the solution was dried over \( \text{K}_2\text{CO}_3 \). Upon evaporation a residue of 220 mg. remained, which was partly crystalline. After successive recrystallizations from acetone and chloroform pale yellow needles were obtained which melted at 258–261°. The analytical data proved to be in agreement with the calculated data for an oxygen derivative of the \( \text{C}_{16}\text{H}_{15}\text{N} \) base reported below.

\[
\begin{align*}
\text{C}_{16}\text{H}_{15}\text{ON} & \quad \text{Calculated.} \quad \text{C} \ 80.97, \ \text{H} \ 6.38, \ \text{N} \ 5.90 \\
& \quad \text{Found.} \quad \text{C} \ 80.97, \ \text{H} \ 6.13, \ \text{N} \ 6.02
\end{align*}
\]

The above chloroform layer after drying and concentration yielded a residue which weighed 4.9 gm. It was dissolved in 50 cc. of benzene and chromatographed through 300 gm. of alumina in benzene. Only a small amount of material passed through the column with benzene or with anhydrous ether alone. However, when 5 per cent methyl alcohol was added to the ether, a total of approximately 2.4 gm. of material was eluted from the column. This material was sublimed and all was collected that would distil under 0.2 mm. pressure and an oil bath temperature of 200°. The sublimate weighed 2.2 gm. It was fractionated with a fractionating column 21 cm. in length at 0.2 mm. The record of the fractionation is given in Table II.

Each fraction contained approximately 150 mg. of material. Fraction 5 was sharply crystalline, while Fractions 3 and 4 were largely crystalline. The fractions from Nos. 7 to 11, as directly obtained, were resins, but Fractions 8, 9, and 10 crystallized partially on standing.

The Base \( \text{C}_{16}\text{H}_{15}\text{N} \) –After two recrystallizations from ether, Fraction 5 formed broad leaves and melted at 83–85°. It did not contain active hydrogen and was therefore a tertiary base.

\[
\begin{align*}
\text{C}_{16}\text{H}_{15}\text{N} & \quad \text{Calculated.} \quad \text{C} \ 86.83, \ \text{H} \ 6.84, \ \text{N} \ 6.33 \\
& \quad \text{Found.} \quad \text{C} \ 87.01, \ \text{H} \ 7.08, \ \text{N} \ 6.15
\end{align*}
\]

The crystalline base with the calculated amount of picric acid gave a picrate from acetone as long well formed needles. It appeared to melt partially and change form under the microscope at 180° with the major
portion of the material melting at approximately 221–223°. A few crystals persisted to a higher temperature.

\[
\text{C}_{16}\text{H}_{13}\text{N} \cdot \text{C}_{8}\text{H}_{4}\text{O}_{7}\text{N}_{4} \quad \text{Calculated, C 58.64, H 4.03; found, C 58.60, H 4.08}
\]

20 mg. of the crystalline base were dissolved in 2 cc. of methyl iodide. Crystalline material soon separated. After 4 hours at room temperature the theoretical weight of the methiodide as long rods was collected. The melting point, 233–235°, was not changed by recrystallization.

\[
\text{C}_{17}\text{H}_{15}\text{NI} \quad \text{Calculated, C 56.19, H 5.00; found, C 56.16, H 5.02}
\]

Fractions 1 and 2 appeared from the analysis to contain material which was not completely dehydrogenated. Fraction 2 was treated with 170 mg. of picric acid, in 8 cc. of acetone. 70 mg. of yellow needles were ob-

<table>
<thead>
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<td>Fractionation of Basic Material</td>
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<th>Column temperature</th>
<th>(n_D^20)</th>
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<tr>
<td></td>
<td>°C.</td>
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...tained which appeared to consist mostly of the picrate of the \(\text{C}_{16}\text{H}_{15}\text{N}\) base. On concentration the mother liquor gave an additional 164 mg. of yellow needles which after recrystallization melted at 210–213°. Analytical data obtained with this material, however, suggested the picrate of a base \(\text{C}_{20}\text{H}_{29}\text{N}\).

\[
\text{C}_{20}\text{H}_{29}\text{N} \cdot \text{C}_{8}\text{H}_{4}\text{O}_{7}\text{N}_{3} \
\quad \text{Calculated, C 60.90, H 6.30; found, C 61.03, H 6.66}
\]

Fraction 11 crystallized directly from a concentrated solution of ether. After recrystallization rosettes of needles were obtained which did not possess a sharp melting point. However, the analytical data did not differ much from those directly obtained with Fraction 9 and suggested a formulation of \(\text{C}_{20}\text{H}_{29}\text{ON}\).
C_{20}H_{21}ON. Calculated, C 80.75, H 9.15; found, C 80.64, H 9.38

The previously mentioned main hydrocarbon fraction was sublimed at an oil bath temperature of 200° and under 0.2 mm. pressure. The sublimate was fractionated in a distillation apparatus with a column 21 cm. in length under 0.2 mm. pressure as recorded in Table III. Each fraction contained approximately 130 mg. of material except Fractions 1 and 20 which contained much less.

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Fraction 2 crystallized directly in largest part and Fractions 9 to 15 crystallized on standing. The analytical data in general agreed with the figures for the C_{17}H_{16} hydrocarbon reported by Lawson and Topps (calculated, C 92.68, H 7.32). Fractions 19 and 20 contained free selenium. Fraction 20 was found also to contain crystalline hydrocarbon material.

1-Methylphenanthrene—Fraction 2 after two recrystallizations from ether melted at 117–121°.

C_{13}H_{12}. Calculated. C 93.70, H 6.25, mol. wt. 192.1
Found. " 93.37, " 6.49, " 195.2
Synthetic 1-methylphenanthrene (which melted at 122–124°) gave a mixture with the above hydrocarbon which melted at 119–121°.

8 mg. of the hydrocarbon yielded 12 mg. of picrate from ethyl alcohol as well formed, orange needles which melted at 137–139°.

\[ \text{C}_{15}\text{H}_{12}\cdot\text{C}_6\text{H}_4\text{O}_7\text{N}_3 \] Calculated, C 59.84, H 3.59; found, C 60.00, H 3.87

The picrate prepared from synthetic 1-methylphenanthrene melted at 138–140° and showed no depression when mixed with that from the above hydrocarbon.

The \( \text{C}_{17}\text{H}_{16} \) Hydrocarbon—Fraction 14 was somewhat sticky at room temperature but did not melt until a temperature of 40° was reached. Upon recrystallization from isopentane it formed square plates which melted at 41–43°.

\[ \text{C}_{17}\text{H}_{16} \] Calculated, C 92.68, H 7.32; found, C 92.61, H 7.30

The picrate crystallized from acetone as orange needles which melted at 129–131°.

\[ \text{C}_{17}\text{H}_{16}\cdot\text{C}_6\text{H}_4\text{O}_7\text{N}_3 \] Calculated, C 61.44, H 4.26; found, C 61.54, H 4.28

The earlier fractions also appeared to consist largely of this hydrocarbon. Although Fraction 6 could not be induced to crystallize directly, it formed in good yield a 1,3,5-trinitrobenzene derivative which after recrystallization melted at 145–148°.

\[ \text{C}_{17}\text{H}_{16}\cdot\text{C}_6\text{H}_4\text{O}_7\text{N}_3 \] Calculated, C 63.71, H 4.42; found, C 63.79, H 4.11

The \( \text{C}_{18}\text{H}_{18} \) Hydrocarbon—The major part of Fraction 18 was treated with 70 mg. of 1,3,5-trinitrobenzene in acetone. The product which crystallized after recrystallization formed fuzzy needles which melted at 163–166°.

\[ \text{C}_{18}\text{H}_{18}\cdot\text{C}_6\text{H}_4\text{O}_7\text{N}_3 \] Calculated, C 64.40, H 4.73; found, C 64.58, H 4.50

The hydrocarbon recovered from the trinitrobenzene derivative by reduction with Zn and HCl formed an oil which was distilled under 0.2 mm. pressure. The distillate did not crystallize. It gave the correct analytical figures for \( \text{C}_{18}\text{H}_{18} \).

\[ \text{C}_{18}\text{H}_{18} \] Calculated, C 92.25, H 7.75; found, C 92.17, H 7.92

A portion of the oily hydrocarbon was treated with an equivalent of picric acid. After two recrystallizations from a mixture of acetone and ethyl alcohol, small orange needles of the picrate were obtained which melted at 153–156°.

\[ \text{C}_{18}\text{H}_{18}\cdot\text{C}_6\text{H}_4\text{O}_7\text{N}_3 \] Calculated, C 62.18, H 4.56; found, C 62.50, H 4.45
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THE ACONITE ALKALOIDS: VIII. ON ATISINE
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