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Treatment of 1-(5'-benzyloxy-4'-methoxy-2'-nitrobenzyl)-3,4-dihydroisoquinoline **2** with lithium/ammonia followed by the addition of ethanol gave a mixture of the dibenz[*b,g*]indolizines **3** and **4**. Omission of ethanol resulted in the formation of **3** only. The dihydroisoquinoline from 3,4-dimethoxyphenylethyl amine behaved similarly.

Reduction of **2a** with sodium/ammonia resulted in cleavage to give the nitro-guaiacol **8**. Oxidation of **2a** in the presence of potassium *t*-butoxide gave a complex mixture from which the benzoyldihydroisoquinoline **5** and 2-benzyloxy-5-nitroanisole were isolated in low yield.

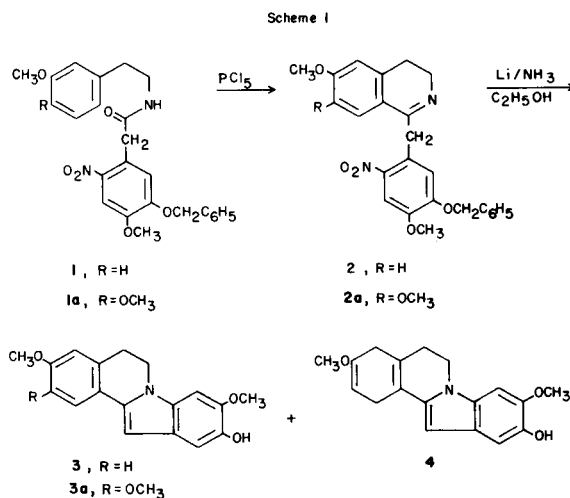
Treatment of the hexahydrobenzylisoquinoline **10** with diazotized sulfanilic acid, followed by reduction and then acetylation gave a diacetyl compound **12** which was hydrolyzed to **13**. Ring closure with boron trifluoride gave the dihydrothebainone **14**.

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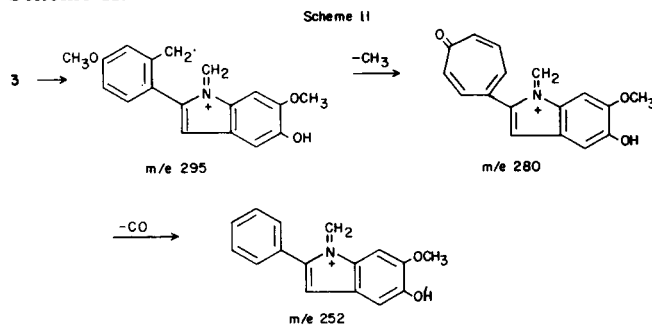
In an attempt to synthesize codeine *via* a route involving a cationic cyclization as a key step, Grewe and Friedrichson (1) cyclized derivatives of the benzylhexahydroisoquinoline **9** in acid media but observed that ring closure occurred primarily *para* to the free phenolic group rather than *ortho*, the desired cyclization mode. Degraw, *et al.* (2), introduced a bromine atom *para* to the hydroxyl to prevent reaction occurring in that position but were unable to effect the desired ring closure on the brominated phenol. Recently, Rice (3) successfully completed a total synthesis of codeine using a modified approach of DeGraw, *et al.* It seemed to us that it should be possible to convert the octahydroisoquinoline **13** to **14** and with the latter in hand complete a synthesis of codeine.

3-Benzyloxy-4-methoxy-6-nitrophenylacetic acid (**4**) was condensed with *m*-methoxyphenylethyl amine in the presence of dicyclohexylcarbodiimide to give the amide **1a** which was cyclized with phosphorus pentachloride to the dihydroisoquinoline **2a**. Reduction using lithium in liquid ammonia followed by treatment with ethanol did not furnish the desired Birch reduction product. Instead, a mixture of two substances were obtained which were assigned structures **3** and **4** (Scheme I). The empirical formula of **3**, C<sub>18</sub>H<sub>17</sub>NO<sub>3</sub> suggested that, *inter alia*, a nitro group had been lost and two aromatic rings were still present. The nmr spectrum showed the required resonance signals. Particularly noteworthy was a one proton signal at  $\delta$  6.64 which was assigned to the indolic proton. A related substance, 5,6-dihydro-2,3,9,10-tetramethoxydibenz[*b,g*]indolizine had a signal for the indole proton at  $\delta$  6.60 (5).

The mass spectrum of **3** showed three major peaks: a molecular ion, *m/e* 295, a parent peak, *m/e* 280 and a smaller peak, *m/e* 252. A possible fragmentation pattern which closely resembles that of the cryptaustoline alka-



loids (**6**) which are dibenzindolizine derivatives is shown in Scheme II.

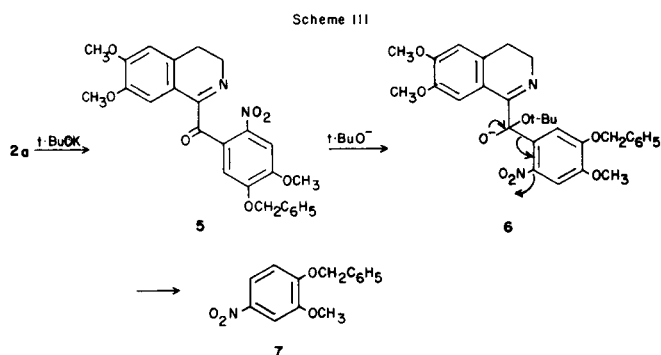


The other product of the reaction **4** had the empirical formula, C<sub>18</sub>H<sub>19</sub>NO<sub>3</sub>. The nmr spectrum strongly suggested that it was the Birch reduction product of **3**, a con-

clusion supported by the fact that if the reduction were carried out without addition of ethanol to the lithium-ammonia reaction medium, **4** was not obtained.

A similar result was obtained where **1a**, prepared from 3,4-dimethoxyphenylethyl amine, was converted to **2a** and the latter subjected to the action of lithium-ammonia. The elementary analysis, the ir and nmr spectra were compatible with structure **3a** for the product of the reaction.

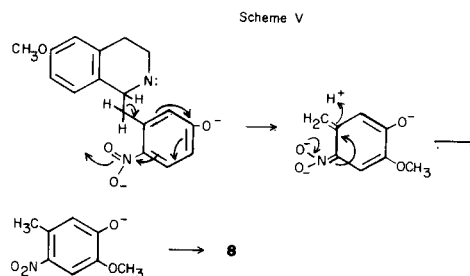
To eliminate the possibility that **3** and **3a** resulted from a base-catalyzed cyclization followed by the elimination of the nitro group **2a** was treated with potassium *t*-butoxide in THF at zero degrees. A complex mixture of products resulted from which two crystalline substances were isolated by chromatography: the benzoylisoquinoline **5** and 2-benzyloxy-5-nitroanisole **7**. The formation of **5** and **7** can be rationalized as shown in Scheme III.



The elemental analysis, nmr and ir spectra were in agreement with the assignment of structure **5**. It has been known for some time that base-catalyzed air oxidation of 3,4-dihydro-1-benzylisoquinolines converts them to the corresponding benzoyl derivatives (7,8). Cleavage with *t*-butoxide of **5** via the intermediacy of **6** as shown in Scheme III can result in **7** whose structure was secured by direct comparison with an authentic sample (9).

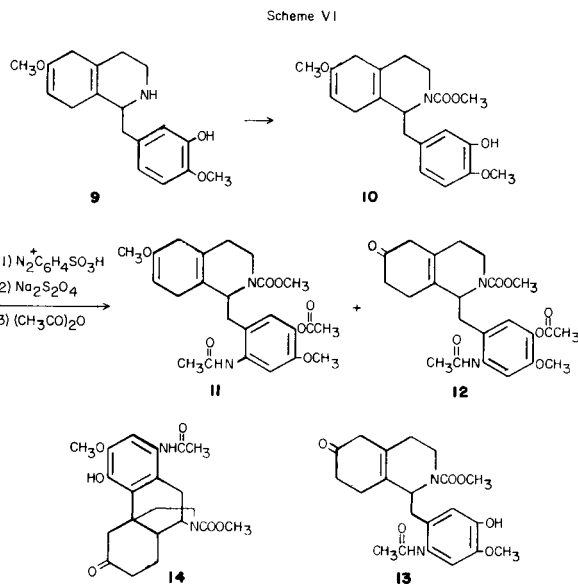
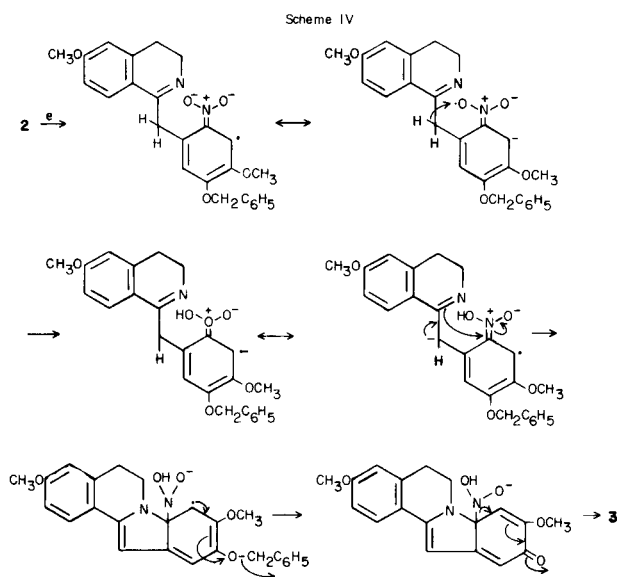
The formation of **3** and **3a** can be explained by involving a reductive cyclization-elimination process as outlined in Scheme IV. This scheme is compatible with the experimental results; for example, when the reaction was attempted with an analogue wherein the benzyloxy group was replaced by a methoxyl no dibenzindolizine was obtained.

The reaction took an entirely different course when lithium was replaced by sodium. In this case the major product that was isolated was **8** as shown in Scheme V. This observation is similar to the one noted by Neumeyer (10) who reported a similar cleavage when 1-(*o*-nitrobenzyl)isoquinoline methiodides were reduced with potassium borohydride.



The difference between the lithium and sodium reactions is that in the latter case the C=N is reduced first, thereby excluding cyclization which depends on the maintenance of the integrity of this double bond. When lithium was used, an addition of an electron to the nitro group took precedence over reduction of the double bond. With the latter intact, cyclization could proceed as shown in Scheme IV.

The nitrogen functionality was introduced into the isoquinoline ring system after the Birch reduction but prior to cyclization as outlined in Scheme VI.



The Birch reduction product **9** prepared by a slight modification of the method of Grewe (11) was converted to the *N*-carbomethoxy derivative **10**. Treatment of the latter with sulfanilic acid gave a red azo compound which was reduced *in situ* to the amino compound. Acetylation with acetic anhydride in pyridine furnished a mixture of **11** and **12** which were separated chromatographically. Compound **12** was hydrolyzed to **13** which was converted to **14** with the aid of boron trifluoride etherate. Although **14** is isomeric with **13**, it can easily be distinguished from its precursor by melting point and nmr data, since **14** has only one aromatic proton whereas **13** has two.

## EXPERIMENTAL

Melting points were taken on a Laboratory Devices Mel-Temp apparatus and are corrected. Infrared spectra were obtained on a Perkin-Elmer model 137 spectrometer. The nmr spectra were recorded on a Varian T-60A spectrometer in deuteriochloroform solution with TMS as an internal standard. Mass spectra were run on a Hitachi-Perkin Elmer RMU-GE spectrometer. Elementary analyses were determined by Instranal Laboratories, Rensselaer, N. Y. 12144.

*N*-[2-(*m*-Methoxyphenylethyl)]-5-benzyloxy-4-methoxy-2-nitrophenylacetamide (**1**).

To a cooled, stirred slurry of 5.2 g. (15.4 mmoles) of 5-benzyloxy-4-methoxy-2-nitrophenylacetic acid (**4**) in 135 ml. of dichloromethane, a solution of 3.7 g. (18 mmoles) of dicyclohexylcarbodiimide in 90 ml. of dichloromethane was added dropwise over a period of 15 minutes. The solution was cooled and then 2.5 g. (16.5 mmoles) of 2-(*m*-methoxyphenyl)ethyl amine in 90 ml. of dichloromethane was added in the next 40 minutes. The mixture was stirred at room temperature for 1 hour and filtered. The filtrate was washed with water and dicyclohexylurea was removed by filtration. The dichloromethane was washed successively with 150 ml. of 3 *N* hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride and then dried. Evaporation of the dichloromethane left a crystalline residue which was crystallized from ethyl acetate to give 6.37 g. of the amide **1**, m.p. 142-144°. Concentration of the mother liquors gave another crop of crystals, 560 mg., m.p. 142-143°. The combined yield was 6.93 g. (94%); nmr:  $\delta$  2.70 (t, 2H, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 3.20 (q, 2H, NHCH<sub>2</sub>), 3.70 (d, 6H, OCH<sub>3</sub>), 3.90 (s, 2H, COCH<sub>2</sub>), 5.20 (s, 2H, OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 6.6-7.2 (m, 4H, aromatic), 7.30 (s, 1H aromatic), 7.40 (s, 5H, aromatic).

*Anal.* Calcd. for C<sub>25</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>: C, 66.65; H, 5.81; N, 6.22. Found: C, 66.44; H, 5.74; N, 6.12.

*N*-2-(3,4-Dimethoxyphenylethyl)-5-benzyloxy-4-methoxy-2-nitrophenylacetamide (**1a**).

A suspension of 20.0 g. of 5-benzyloxy-4-methoxy-2-nitrophenylacetic acid in 455 ml. of dichloromethane was cooled to 0° and treated with a solution of 14.1 g. of dicyclohexylcarbodiimide in 300 ml. of dichloromethane. A solution of 12.0 g. of 3,4-dimethoxyphenylethylamine in 122 ml. of dichloromethane was added dropwise and the mixture was left overnight. It was worked up in the above-described way to give the desired amide **1a** which after crystallization from methanol melted at 162-164°, weight 28 g., (92%).

*Anal.* Calcd. for C<sub>26</sub>H<sub>28</sub>N<sub>2</sub>O<sub>7</sub>: C, 64.98; H, 5.87; N, 5.83. Found: C, 64.81; H, 5.79; N, 5.84.

1-(5'-Benzyloxy-4'-methoxy-2'-nitrobenzyl)-3,4-dihydro-6-methoxyisoquinoline (**2**).

Four grams of **1** dissolved in 50 ml. of dichloromethane was added, with stirring to a suspension of 9.2 g. of phosphorus pentachloride in 50 ml. of dichloromethane cooled to zero degrees. The mixture was stirred

in a nitrogen atmosphere for one hour and then at room temperature for 24 hours. The suspended solid was collected on a filter and then shaken with 150 ml. of cold water and 200 ml. of chloroform. The aqueous phase was treated with ammonium hydroxide and extracted with chloroform. The combined chloroform layers were dried over potassium carbonate and evaporated to leave a yellow oil which solidified. The solid was dissolved in ether and treated with dry hydrogen chloride to give the hydrochloride salt of **2** which, after crystallization from ethanol, melted at 211-214°, weight 1.4 g. (36%).

A portion of the salt was converted to the free base which melted at 129-131° after crystallization from ethanol; nmr:  $\delta$  2.60 (m, 2H, CH<sub>2</sub>), 3.70 (m, 2H, NCH<sub>2</sub>), 3.90 (d, 6H, OCH<sub>3</sub>), 4.40 (s, 2H, CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 5.20 (s, 2H, OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 6.90 (m, 4H, aromatic), 7.5 (s, 5H, aromatic), 7.70 (s, 1H, aromatic).

*Anal.* Calcd. for C<sub>25</sub>H<sub>24</sub>N<sub>2</sub>O<sub>5</sub>: C, 69.42; H, 5.59; N, 6.48. Found: C, 69.25; H, 5.63; N, 6.38.

1-(5'-Benzyloxy-4'-methoxy-2'-nitrobenzyl)-3,4-dihydro-5,6-dimethoxydihydroisoquinoline (**2a**).

A mixture of 3.0 g. of the amide **1a**, 6.9 g. of phosphorus pentachloride and 30 ml. of dichloromethane was stirred at zero degrees for one hour and then overnight at ambient temperature. The mixture was poured into ice and 50 ml. of benzene was added. The whole was made basic with ammonium hydroxide and the benzene-dichloromethane layer was separated. The aqueous phase was extracted once with benzene and the combined extracts were dried and evaporated to leave 2.5 g. (87%) of **2a**, m.p. 166-167.5° after crystallization from ethanol.

*Anal.* Calcd. for C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>: C, 67.52; H, 5.68; N, 6.06. Found: C, 67.09; H, 5.54; N, 5.98.

5,6-Dihydro-3,9-dimethoxy-10-hydroxydibenz[*b,g*]indolizine (**3**).

Approximately 200 ml. of ammonia was collected in a flask kept at -80°. Sodium (0.5 g.) was added to the liquid and the ammonia was distilled into the reaction vessel protected from moisture. Then 0.1 g. of lithium was added and after about 30 minutes 2.0 g. of the isoquinoline **2**, dissolved in 50 ml. of dry tetrahydrofuran was added with stirring to the deep blue solution, kept at -80°. After 2 hours, the cooling bath was removed and the ammonia was allowed to evaporate. To the residue there was added 100 ml. of water followed by 30 g. of ammonium chloride. The mixture was extracted with 3 x 100 ml. of chloroform. The dried extract was evaporated and the residue was chromatographed on silica gel using chloroform as the eluant. A crystalline material was obtained which after crystallization from ethanol melted at 211-212°, weight 300 mg. (22%); nmr:  $\delta$  3.07 (t, 2H, CH<sub>2</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 3.90 (s, 3H, OCH<sub>3</sub>), 4.07 (t, 2H, CH<sub>2</sub>N), 5.40 (s, 1, OH), 6.64 (s, 1H, indole H), 6.44-7.77 (m, 5H, aromatic H); ms: m/e 295 (80%), 280 (M<sup>+</sup>-15) (100%), 252 (M<sup>+</sup>-43) (10%).

*Anal.* Calcd. for C<sub>18</sub>H<sub>17</sub>NO<sub>3</sub>: C, 73.20; H, 5.80; N, 4.75. Found: C, 73.23; H, 5.78; N, 4.76.

1,4,5,6-Tetrahydro-3,9-dimethoxy-10-hydroxydibenz[*b,g*]indolizine (**4**).

A solution of 5.0 g. of **2** in 50 ml. of dry THF was added dropwise to a stirred solution of 2.3 g. of lithium in 250 ml. of liquid ammonia (distilled over sodium) kept at -80°. The mixture was stirred for 2.5 hours and then 50 ml. of absolute ethanol was added slowly. After 2.5 hours the cooling bath was removed and the ammonia was allowed to evaporate. The residue was treated with water and then 50 g. of ammonium chloride was added. The residue was extracted with chloroform, washed with water, dried and concentrated. The chromatography on silica gel gave some **3** and another crystalline compound **4**, which after recrystallization from ethanol melted at 190-191°, weight 650 mg.; nmr:  $\delta$  2.50-3.17 (m, 6H, CH<sub>2</sub>), 3.57 (s, 3H, OCH<sub>3</sub>), 3.90 (s, 3H, OCH<sub>3</sub>), 4.00 (t, 2H, NCH<sub>2</sub>), 5.40 (s, 1H, OH), 6.10 (s, 1H, vinyl H), 6.60 (s, 1H, indole H), 7.00, 7.20 (2s, 2H, aromatic).

*Anal.* Calcd. for C<sub>18</sub>H<sub>19</sub>NO<sub>3</sub>: C, 72.70; H, 6.43; N, 4.71. Found: C, 72.20; H, 6.53; N, 4.56.

5,6-Dihydro-10-hydroxy-2,3,9-trimethoxydibenz[*b,g*]indolizine (**3a**).

Two grams of the dihydroisoquinoline (**2a**) dissolved in 20 ml. of dry THF was added to a solution of 150 mg. lithium in 100 ml. of liquid ammonia distilled over sodium. The reaction and subsequent work-up was set similar to that described for **3**. Chromatography on silica gel gave in addition to 1.3 g. of recovered starting material 150 mg. of **3a**, m.p. 215-217° after recrystallization from ethanol; nmr:  $\delta$  3.05 (t, 2H, CH<sub>2</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 3.92 (s, 6H, OCH<sub>3</sub>), 4.10 (t, 2H, CH<sub>2</sub>N), 6.60 (s, 1H, indole H), 7.0, 7.2 (2s, 2H, aromatic).

*Anal.* Calcd. for C<sub>19</sub>H<sub>19</sub>NO<sub>4</sub>: C, 70.13; H, 5.89; N, 4.31. Found: C, 70.07; H, 5.89; N, 4.22.

Reactions of 1-(5'-Benzyloxy-4'-methoxy-2'-nitrobenzyl)-3,4-dihydro-5,6-dimethoxyisoquinoline (**2a**).

#### A. Sodium in Ammonia.

Two grams of **2a** in 20 ml. of dry THF was added dropwise to a stirred solution of 0.6 g. of sodium in 100 ml. of dry ammonia kept at -80°. After 3 hours, 25 g. of ammonium chloride was added and the mixture was allowed to stand overnight. Water was added to the residue and the suspension was extracted with chloroform. The dried organic extract was evaporated and the concentrate was chromatographed on silica gel using chloroform as the eluant. There was obtained 300 mg. of yellow needles which melted at 170-171°. Oxford (12), reported that the nitroguaiacol **8** melted at 168-170°; nmr:  $\delta$  2.57 (s, 3H, CH<sub>3</sub>), 3.98 (s, 3H, OCH<sub>3</sub>), 6.06 (s, 1H, OH), 6.82, 7.68 (2s, 2H, aromatic).

*Anal.* Calcd. for C<sub>9</sub>H<sub>9</sub>NO<sub>4</sub>: C, 52.16; H, 4.92; N, 7.61. Found: C, 51.96; H, 4.90; N, 7.40.

#### B. Potassium *t*-Butoxide.

To a stirred solution of potassium *t*-butoxide in 50 ml. of THF kept at 0° there was added 4.62 g. of **2a** over a 15 minute period. The purple reaction mixture was kept at 0° for six days, protected from moisture but exposed to air. The mixture was acidified with acetic acid, diluted with water and made faintly alkaline with 15% sodium hydroxide solution. The layers were separated and the aqueous layer was extracted with chloroform. The combined organic layers were dried and concentrated. The residue was chromatographed on silica gel using ether-chloroform as the eluant. Two crystalline materials were obtained. The less polar compound was 2-benzyloxy-5-nitroanisole **7**, m.p. 75-78° undepressed when admixed with an authentic sample prepared according to the method of Drake, *et al.* (9), weight 70 mg. The more polar compound, melted at 154-155° after crystallization from methanol, weight 34 mg. It was the benzoyldihydroisoquinoline **5**;  $\nu$  (potassium bromide): 1685 cm<sup>-1</sup> (C=O); nmr:  $\delta$  3.50-3.90 (m, 4H, CH<sub>2</sub>), 4.00-4.20 (3s, 9H, OCH<sub>3</sub>), 5.20 (s, 2H, OCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>), 7.10-8.60 (m, 9H, aromatic).

*Anal.* Calcd. for C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>7</sub>: C, 65.54; H, 5.08; N, 5.88. Found: C, 65.35; H, 4.78; N, 5.74.

#### 6-Methoxy-1-(3-hydroxy-4-methoxybenzyl)-1,2,3,4,5,8-hexahydroisoquinoline (**9**).

Approximately 600 ml. of liquid ammonia was collected in a three-necked flask equipped with a dry ice condenser and stirrer and cooled to -80°. Anhydrous ether (100 ml.) and 16.0 g. of lithium was added and then 20 g. of 1-(benzyloxy-4-methoxybenzyl)-3,4-dihydroisoquinoline (**11**) was added portionwise. The mixture was stirred at -80° for 4 hours and 200 ml. of ethanol was added dropwise. The cooling bath was removed and the mixture was left overnight to permit the ammonia to evaporate. A solution of 150 g. of ammonium chloride in 500 ml. of water was added slowly at 0°. After two hours the suspension was filtered and the crystalline solid crystallized from methanol to give 12.5 g. (92%) of **9**, m.p. 193-195° [Grewe (11) reported m.p. 182°].

#### 6-Methoxy-1-(3-hydroxy-4-methoxybenzyl)-2-carbomethoxy-1,2,3,4,5,8-hexahydroisoquinoline (**10**).

A suspension of 7.0 g. of **10** in 50 ml. of acetone and 120 ml. of 2*N* sodium hydroxide was stirred at -10° during the dropwise addition of 15 ml. of methyl chloroformate. After 2 hours the mixture was quenched with 200 ml. of ice water and the crystalline solid was collected and wash-

ed with water and crystallized from methanol, weight 6.4 g., m.p. 126-128° [lit. (11) m.p. 134-135°].

*Anal.* Calcd. for C<sub>22</sub>H<sub>27</sub>NO<sub>7</sub>: C, 63.29; H, 6.52; N, 3.35. Found: C, 63.26; H, 6.60; N, 3.31.

The above *N,O*-dicarbomethoxy derivative was suspended in a solution of 150 ml. of 1*N* sodium hydroxide and 50 ml. of methanol and heated with stirring at 50-60° under nitrogen for 2 hours. The suspension was cooled to -5° and treated with a solution of 30 g. of ammonium chloride in 150 ml. of water. The crystals were filtered, washed with water and crystallized from methanol, weight 5.6 g., m.p. 143-144° [lit. (11) m.p. 144°].

*Anal.* Calcd. for C<sub>20</sub>H<sub>25</sub>NO<sub>5</sub>: C, 66.83; H, 7.01; N, 3.90. Found: C, 66.95; H, 7.21; N, 3.85.

#### 6-Methoxy-1-(2-acetamido-5-acetoxy-4-methoxybenzyl)-2-carbomethoxy-1,2,3,4,5,8-hexahydroisoquinoline (**11**) and 1-(2-acetamido-5-acetoxy-4-methoxybenzyl)-2-carbomethoxy-6-oxo-1,2,3,4,5,6,7,8-octahydroisoquinoline (**12**).

A solution of 1.6 g. of sulfanilic acid monohydrate and 445 mg. of sodium carbonate in 9.0 ml. of water was cooled to 0° and added dropwise with stirring. This solution was then added slowly to a stirred cold solution of 2.1 ml. of concentrated hydrochloric acid in 10 ml. of water. This diazonium suspension was kept at 0° for 15 minutes before being added slowly to a cold solution of 1.5 g. of **10**, in 30 ml. of methanol and 1.5 g. of sodium hydroxide in 45 ml. of water. The suspension of the red azo compound was stirred at 0° for 30 minutes and then 3.9 g. of sodium hydrosulfite was added portionwise. The mixture was warmed on the steam bath for about 15 minutes; during this time the color changed to yellow.

The cooled mixture was extracted with 3 x 100 ml. portion of chloroform and the pooled extracts were dried and concentrated. The residue was dissolved in 30 ml. of dry pyridine, cooled to 0° and treated with 15 ml. of acetic anhydride. The mixture was left in the refrigerator overnight before being poured onto ice. The aqueous suspension was extracted with chloroform and the extracts were washed successively with 5% sulfuric acid, 5% sodium carbonate and water. After drying with magnesium sulfate, the chloroform solution was evaporated and the residue was chromatographed on silica gel using ether as the eluant. The first fraction was the enol ether **11**, weight 1.5 g. After crystallization from methanol it melted at 163-164°; nmr:  $\delta$  2.17 (s, 6H, OCCH<sub>3</sub>), 3.74 (s, 3H, OCH<sub>3</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 6.21 (s, 1H, vinyl H), 6.65 (s, 2H, aromatic).

*Anal.* Calcd. for C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>O<sub>7</sub>: C, 62.86; H, 6.60; N, 6.11. Found: C, 62.60; H, 6.29; N, 5.98.

The more polar fraction was the ketone **12**, weight 1.4 g. After crystallization from acetone-petroleum ether, it melted at 143-144°; nmr:  $\delta$  2.23 (s, 6H, OCCH<sub>3</sub>), 3.49 (s, 3H, OCH<sub>3</sub>), 3.80 (s, 3H, OCH<sub>3</sub>), 6.69 (s, 1H, aromatic), 7.90 (s, 1H, aromatic).

*Anal.* Calcd. for C<sub>23</sub>H<sub>28</sub>N<sub>2</sub>O<sub>7</sub>: C, 62.14; H, 6.35; N, 6.30. Found: C, 62.28; H, 6.53; N, 6.12.

#### 1-(2-Acetamido-5-hydroxy-4-methoxybenzyl)-2-carbomethoxy-6-oxo-1,2,3,4,5,6,7,8-octahydroisoquinoline (**13**).

A mixture of 600 mg. of the oxo compound **12**, 100 mg. of potassium carbonate, 28 ml. of methanol and 8 ml. of water was stirred at room temperature for 30 minutes. The mixture was diluted with 100 ml. of water and extracted with chloroform. The dried extract was concentrated and the residue was crystallized from acetone-petroleum ether, weight 502 mg., m.p. 178-179°;  $\nu$  (potassium bromide): 3500 (OH), 3300 (NH), 1710 (C=O), 1667 cm<sup>-1</sup> (CONH); nmr:  $\delta$  2.17 (s, 3H, OCCH<sub>3</sub>), 3.50 (s, 3H, OCH<sub>3</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 5.71 (s, 1H, OH), 6.57 (s, 1H, aromatic), 7.37 (s, 1H, aromatic).

*Anal.* Calcd. for C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>: C, 62.67; H, 6.51; N, 6.96. Found: C, 62.73; H, 6.51; N, 6.68.

#### 1-Acetamido-17-carbomethoxydihydrothebainone (**14**).

A mixture of 300 mg. of **13** and 20 ml. of boron trifluoride etherate was stirred under nitrogen at room temperature for 2 hours. The mixture was

poured into ice water and extracted with chloroform. The extract was washed, dried over magnesium sulfate and concentrated to dryness to leave a residue which was chromatographed on preparative silica gel plates using chloroform-methanol (19:1) as the developing solvent. The band  $R_f = 0.3$  was removed and extracted to leave crystals, weight 200 mg., m.p. 110-112°, after crystallization from chloroform-petroleum ether; nmr:  $\delta$  2.57 (s, 3H, OCH<sub>3</sub>), 3.80 (s, 6H, OCH<sub>3</sub>), 6.64 (s, 1H, aromatic).

*Anal.* Calcd. for C<sub>21</sub>H<sub>26</sub>N<sub>2</sub>O<sub>6</sub>: C, 62.67; H, 6.51; N, 6.96. Found: C, 62.58; H, 6.64; N, 6.68.

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