

Brian Cox and Brian Robinson\*

Department of Pharmacy, University of Manchester,  
Manchester M13 9PL, U. K.

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Reduction of 6-methoxy-9-methyl-11-oxoecchiboline **1a** using lithium aluminium hydride in boiling tetrahydrofuran under reflux affords 6-methoxy-9-methylecchiboline. However, attempts to effect a similar reduction of a suspension of compound **1a** in boiling diethyl ether under reflux, in which it is only very slightly soluble, were unsuccessful and when, under these conditions, a Soxhlet apparatus was employed to effect dissolution, an unexpected reductive ring scission occurred along with reduction of the carbonyl group to afford 4a-(2-aminoethyl)-6-methoxy-9-methyl-1,2,3,4,4a,9a-hexahydrocarbazole **3**.

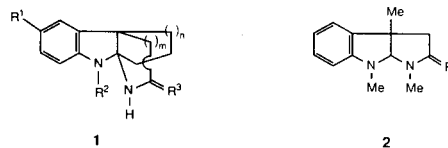
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During the course of our current research, we have investigated the reduction, using lithium aluminium hydride, of 6-methoxy-9-methyl-11-oxoecchiboline **1a** (for the naming and numbering of this ring system, see ref [1]) which was prepared by a method similar to that previously employed to synthesise compounds **1b** [2], **1c** [3] and **1d** [3]. This compound in tetrahydrofuran, in which it is very soluble, is reduced in the presence of excess lithium aluminium hydride under reflux conditions to afford, in good yield, the expected product **1e**. However, attempts to effect this reduction under similar conditions but using diethyl ether in place of tetrahydrofuran were unsuccessful, only starting material, which has a low solubility in diethyl ether, being recovered. This is contrary to previous reports that suspensions of compounds **1b** [2], **1c** [3] and **1d** [3] in boiling diethyl ether under reflux are reduced with lithium aluminium hydride after one, four and four hours, respectively, to afford the products **1f**, **1g** and **1h**, respectively. In an earlier report [4], a similar reduction of compound **2a** into a quantitative yield of product **2b** was effected using lithium aluminium hydride, albeit under unspecified conditions.

In an attempt to overcome this current failure which, in spite of the earlier [2,3] observations, was ascribed to the low solubility of compound **1a** in diethyl ether, the reduction was performed employing a Soxhlet extractor to effect dissolution of the organic reactant. Using an extracting volume of approximately 75 ml, 0.5 g of compound **1a** had eventually completely been dissolved after 21 days. However, subsequent "work up" afforded not the expected product **1e** but 4a-(2-aminoethyl)-6-methoxy-9-methyl-1,2,3,4,4a,9a-hexahydrocarbazole **3**, the structure of which was supported in particular by its C<sub>9</sub>-H atom and tertiary aliphatic C<sub>9</sub>-atom as detected in its <sup>1</sup>H- and <sup>13</sup>C-nmr spectra, respectively, and by its uv spectroscopic properties.

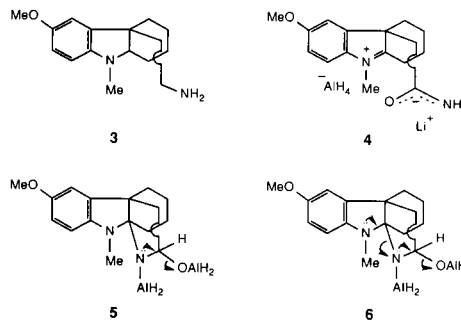
It was unlikely that this product had arisen *via* the in-

termediacy of compound **1e** since it is well-established [5,6,7] that reductive cleavage of the Ph-N-C-N system only occurs under acidic conditions, probably *via* acid-catalysed ring opening to the corresponding 3*H*-indolium cations [7]. Indeed, compound **1e** was recovered unchanged after treatment with excess lithium aluminium hydride in boiling diethyl ether under reflux for 21 days. It is possible that the compound **3** arises *via* initial ring-opening of the lactam ring in compound **1a** to afford the resonance-stabilised intermediate **4** which undergoes subsequent reduction by hydride addition to the 3*H*-indolium cation and at the amidic anionic centre. Alternatively, the reaction may involve the intermediacy of the aluminium hydride addition product, subsequent electron



- a, R<sup>1</sup> = MeO, R<sup>2</sup> = Me, R<sup>3</sup> = O, m = 1, n = 2  
 b, R<sup>1</sup> = MeO, R<sup>2</sup> = Me, R<sup>3</sup> = O, m = n = 1  
 c, R<sup>1</sup> = H, R<sup>2</sup> = Me, R<sup>3</sup> = O, m = n = 2  
 d, R<sup>1</sup> = H, R<sup>2</sup> = Bz, R<sup>3</sup> = O, m = n = 2  
 e, R<sup>1</sup> = MeO, R<sup>2</sup> = Me, R<sup>3</sup> = H<sub>2</sub>, m = 1, n = 2  
 f, R<sup>1</sup> = MeO, R<sup>2</sup> = Me, R<sup>3</sup> = H<sub>2</sub>, m = n = 1  
 g, R<sup>1</sup> = H, R<sup>2</sup> = Me, R<sup>3</sup> = H<sub>2</sub>, m = n = 2  
 h, R<sup>1</sup> = H, R<sup>2</sup> = Bz, R<sup>3</sup> = H<sub>2</sub>, m = n = 2

- a, R = O  
 b, R = H<sub>2</sub>



movement as shown in **5** leading ultimately to product **1e** and as shown in **6** ultimately affording product **3**. As yet, the reason(s) for the relationship between the nature of reaction product and the reaction conditions is(are) unclear.

### EXPERIMENTAL

Melting points were measured on a Kofler hot-stage and are uncorrected. Ultraviolet, infrared,  $^1\text{H}$ - and  $^{13}\text{C}$ -nuclear magnetic resonance, and mass spectra were recorded on Pye Unicam SP8 500, Pye Unicam SP3 100 and Bruker WP80 pulsed F. T. (in deuteriochloroform with tetramethylsilane as the internal standard,  $^{13}\text{C}$ -Assignments being made using the DEPT technique [8]) spectrophotometers and a Kratos MS-25 instrument connected to a DS-55 data system, respectively. Column chromatography was effected upon Brockmann grade 1 basic alumina (BDH). Organic extracts were dried with magnesium sulphate and evaporated under reduced pressure on a Buchi evaporator. Ether refers to diethyl ether.

#### 6-Methoxy-9-methyl-11-oxoechiboline **1a**.

A solution of a mixture of 6.95 g (0.046 mole) of 4-methoxy- $N_{\alpha}$ -methylphenylhydrazine [2] with 8.79 g (0.048 mole) of ethyl cyclohexanone-2-acetate [9] in 40 ml of benzene containing 3 drops of glacial acetic acid was boiled under reflux with the azeotropic removal of water (Dean-Stark head) for 2 hours. The solvent was then removed to leave the hydrazone as a red-brown-oil. This was dissolved in 25 ml of glacial acetic acid and the solution was boiled under reflux for 1.5 hours. The acetic acid was then removed, the residue was taken up in 500 ml of chloroform and this solution was extracted with 4 x 200 ml of 6*M*-hydrochloric acid. After the addition of 200 g of crushed ice to the combined acidic extracts, they were basified by the addition of ammonia solution (0.88) and the resulting pale-cream precipitate of 3.8 g (31%) of 6-methoxy-9-methyl-11-oxoechiboline **1a** was recrystallised from methanol to afford pale-cream plates, mp 227-229°; ir (potassium chloride disc):  $\nu$  max 1685  $\pm$  5  $\text{cm}^{-1}$  (C=O);  $^1\text{H}$ -nmr:  $\delta$  6.87-6.30 (3H, m,  $\text{H}_5$ ,  $\text{H}_7$ ,  $\text{H}_8$ ), 3.74 (3H, s,  $\text{CH}_3\text{O}$ ), 2.69 (3H, s,  $\text{CH}_3\text{N}$ ), 2.88-2.48 (2H, m,  $\text{COCH}_2$ ), 2.41-1.22 [9H, m, methylene envelope + one deuterium oxide-exchangeable hydrogen (NH)]; ms: m/e 272 ( $\text{M}^+$ , 100), 257 (26.5), 228 (39), 214 (15).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2$ : C, 70.7; H, 7.4; N, 10.3. Found: C, 70.3; H, 7.6; N, 9.9.

#### Reduction of 6-Methoxy-9-methyl-11-oxoechiboline **1a** to 6-Methoxy-9-methylechiboline **1e**.

A solution of 3.00 g (0.011 mole) of 6-methoxy-9-methyl-11-oxoechiboline **1a** in 500 ml of tetrahydrofuran was added over a period of 30 minutes to a stirred suspension of 2.85 g (0.075 mole) of lithium aluminium hydride in 200 ml of tetrahydrofuran which was boiling under reflux. The mixture was then boiled under reflux for 16 hours, after which the excess lithium aluminium hydride was decomposed by the dropwise addition of a saturated aqueous solution of sodium sulphate. The suspended white solid was removed by filtration and washed well with ether. The organic phase was collected, the aqueous phase was extracted with 3 x 100 ml of ether, and the combined organic phases were dried and evaporated to afford 2.17 g (75%) of 6-methoxy-9-methylechiboline **1e** as a pale-brown oil, the spectroscopic properties of which were identical with those of a sample purified *via* the picrate salt.

The picrate was obtained from ethanol as orange needles, mp 170-172°.

*Anal.* Calcd. for  $\text{C}_{22}\text{H}_{25}\text{N}_5\text{O}_8$ : C, 54.2; H, 5.2; N, 14.4. Found: C, 54.6; H, 5.4; N, 14.6.

The free base was liberated from the picrate by treatment with aqueous sodium hydroxide, extraction into chloroform, passage of the chloroform solution through a short alumina column, and removal of the solvent to afford compound **1e** as a clear pale-yellow oil, bp 150°/0.4 mm of Hg; ir (liquid film):  $\nu$  max 3330  $\pm$  10  $\text{cm}^{-1}$  (broad) (NH), transparent

between 1800-1610  $\pm$  5  $\text{cm}^{-1}$  (absence of C=O); uv (96% ethanol):  $\lambda$  max 319, 252;  $\lambda$  min 282, 225 nm (log  $\epsilon$  3.36, 3.84, 2.93, 3.44, respectively) (4-MeO-C<sub>6</sub>H<sub>4</sub>-N-C-N system); (96% ethanol + concentrated hydrochloric acid):  $\lambda$  max 316, 247;  $\lambda$  min 266, 233 (log  $\epsilon$  3.62, 3.61, 3.13, 3.51, respectively) (5-methoxy-3*H*-indolium cation- cf refs. [7], [10], [11]);  $^1\text{H}$ -nmr:  $\delta$  6.67-6.29 (3H, m,  $\text{H}_5$ ,  $\text{H}_7$ , and  $\text{H}_8$ ), 3.75 (3H, s,  $\text{CH}_3\text{O}$ ), 2.65 (3H, s,  $\text{CH}_3\text{N}$ ), 2.07-1.22 [13H, m, methylene envelope + one deuterium oxide-exchangeable hydrogen (NH)]; ms: m/e 258.1731 ( $\text{M}^+$ , 57) ( $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}$  requires 258.1732), 243 (12), 228 (16), 215 (28), 122 (100).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{22}\text{N}_2\text{O}$ : C, 74.4; H, 8.6; N, 10.8. Found: C, 74.0; H, 8.5; N, 10.4.

#### Reduction of 6-Methoxy-9-methyl-11-oxoechiboline **1a** to 4a-(2-Aminoethyl)-6-methoxy-9-methyl-1,2,3,4,4a,9a-hexahydrocarbazole **3**.

Into a 30 x 100 mm Whatman extractor thimble was placed 0.50 g (0.0018 mole) of compound **1a**. This was extracted using a Soxhlet apparatus into a suspension of 2.0 g (0.053 mole) of lithium aluminium hydride in 150 ml dry ether. After 21 days, during which time the volume of the reaction mixture was maintained steady by the occasional addition of small volumes of dry ether, the extraction was complete. "Work-up" of the reaction mixture, following the procedure described above for the isolation of **1e**, afforded 0.344 g (72%) of 4a-(2-aminoethyl)-6-methoxy-9-methyl-1,2,3,4,4a,9a-hexahydrocarbazole **3** as a pale-brown oil, the spectroscopic properties of which were identical with those of a sample purified *via* the formate salt.

The formate was obtained from ethanol-water as colourless needles, mp 168-172°.

*Anal.* Calcd. for  $\text{C}_{17}\text{H}_{25}\text{N}_2\text{O}_3$ : C, 66.9; H, 8.3; N, 9.2. Found: C, 67.0; H, 8.7; N, 9.3.

The free base was liberated from the formate by a method similar to that described above for the liberation of compound **1e** from its picrate and was obtained as a pale-yellow oil, bp 165°/0.7 mm of Hg; ir (liquid film):  $\nu$  max 3330  $\pm$  10  $\text{cm}^{-1}$  (broad) (NH<sub>2</sub>), transparent between 1800-1610  $\pm$  5  $\text{cm}^{-1}$  (absence of C=O); uv: (96% ethanol):  $\lambda$  max 311, 247;  $\lambda$  min 279, 225 nm (log  $\epsilon$  3.72, 4.19, 3.26, 3.83, respectively) (5-methoxyindoline); (96% ethanol + concentrated hydrochloric acid):  $\lambda$  max 281, 275, 230;  $\lambda$  min 278, 263, 216;  $\lambda$  inf 252 (log  $\epsilon$  3.47, 2.48, 4.14, 3.46, 3.36, 3.96, 3.46, respectively) (5-methoxyindolinium cation);  $^1\text{H}$ -nmr:  $\delta$  6.88-6.62 (3H, m,  $\text{H}_5$ ,  $\text{H}_7$ , and  $\text{H}_8$ ), 3.74 (3H, s,  $\text{CH}_3\text{O}$ ), 3.48-3.42 (1H, m,  $\text{C}_{9a}\text{H}$ ), 2.82 (3H, s,  $\text{CH}_3\text{N}$ ), 3.22-3.14 (1H, m), 2.98-2.80 (2H, m), 2.35-1.80 (6H, m), 1.56-1.30 (4H, m), 1.20-1.00 (1H, m) (methylene envelope + NH<sub>2</sub>);  $^{13}\text{C}$ -nmr:  $\delta$  151.28, 141.83, 132.19 (quat aromatic), 115.53, 112.20, 110.72 (tert aromatic), 60.86 (tert aliphatic, C-9a), 55.69 (prim aliphatic), 46.59 (quat aliphatic), 43.76, 39.38 (sec aliphatic), 31.81 (primary aliphatic), 30.97, 26.78, 22.47, 21.26 (sec aliphatic); ms: m/e 260.1887 ( $\text{M}^+$ , 40.5) ( $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}$  requires 260.1888), 245 (2.5), 216 (100).

*Anal.* Calcd. for  $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}$ : C, 73.8; H, 9.3; N, 10.8. Found: C, 74.1; H, 9.3; N, 11.2.

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