Tetrahedron. Vol. 28. pp. 4299 to 4307. Pergamon Press 1972. Printed in Great Britain

OXIDATIVE TRANSFORMATIONS IN THE APORPHINE ALKALOID SERIES

M. P. CAVA,* A. VENKATESWARLU, M. SRINIVASAN and D. L. EDIE
Department of Chemistry, Wayne State University, Detroit, Michigan 48202
and
Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

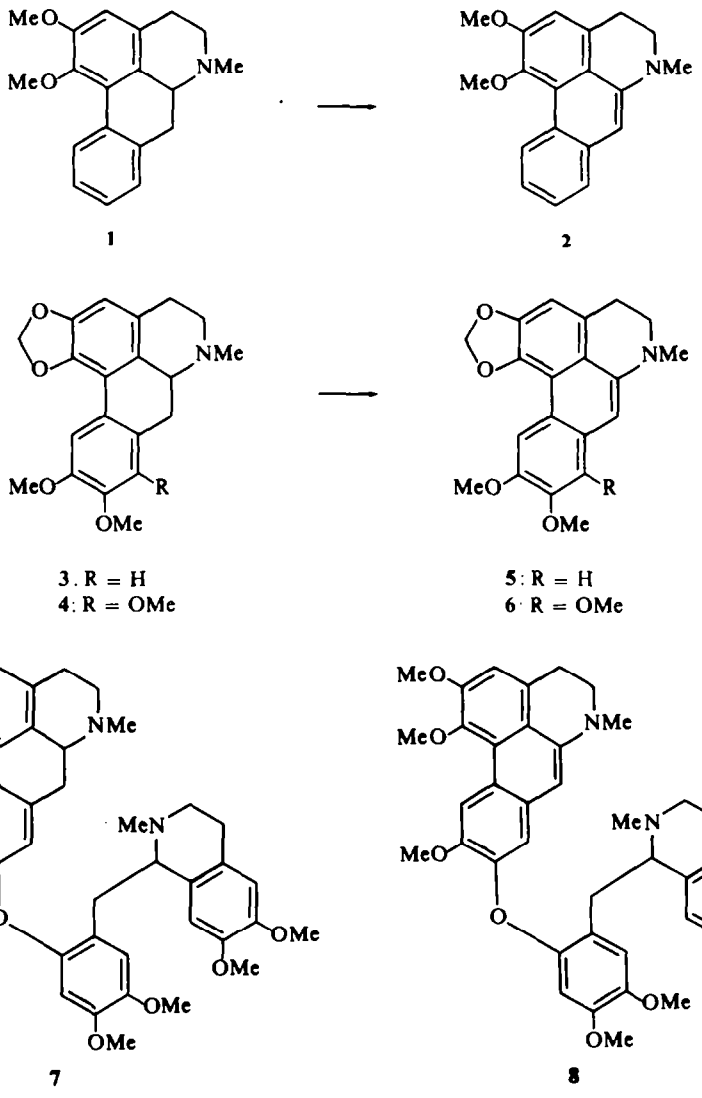
(*Received in the USA* 15 *February* 1972; *Received in the UK for publication* 5 *May* 1972)

Abstract— Oxidation of the non-phenolic aporphines nuciferine (**1**), dicentrine (**3**), ocopodine (**4**) and thalicarpine (**7**) by iodine affords the corresponding dehydroaporphines (**2**, **5**, **6** and **8**). In contrast, iodine oxidation of non-phenolic noraporphines proceeds all the way to the oxoaporphine stage: thus, O-methylnandigerine (**9**), nordicentrine (**11**) and ovigerine (**12**) yield the corresponding oxoaporphines (**10**, **13** and **14**). The phenolic aporphine N-methylnandigerine (**19**) is converted in low yield by iodine to the blue 10,11-*o*-quinone **20**; **20** is formed as the major product of mercuric chloride oxidation of both **19** and its 10,11-isomer bulbocapnine (**21**). The dehydroaporphines dehydronuciferine (**2**) and dehydrodicentrine (**5**) are oxidized by oxygen at pH 6 to give the corresponding oxoaporphines (**23** and **13**); **2** is also rapidly oxidized to **23** by peracetic acid or by benzoyl peroxide, the benzoate ester **24** being an intermediate in the latter reaction.

IN THE COURSE of searching for new alkaloids from natural sources, we noticed that the development of thin-layer chromatograms of aporphines and noraporphines by iodine vapor led to the development of spots varying in color from blue or green to red, brown or yellow. Others have observed the formation of such colors simply by air oxidation of these alkaloids.[1] In this paper we report the results of the oxidation of some aporphines and noraporphines by iodine and, in part, by certain other mild oxidizing agents.

Iodine oxidation of non-phenolic aporphines. The representative non-phenolic aporphine nuciferine (**1**) was found to react readily with iodine to give dehydronuciferine (**2**); the presence of a mild acid scavenger is necessary for the reaction to proceed to completion. The reaction proceeded best in pure refluxing dioxane containing excess NaOAc. Under these conditions, **1** consumed only one molar equivalent of iodine to give **2** in 87% yield. Similarly dicentrine (**3**) and ocopodine (**4**) gave the naturally occurring[2,3] dehydrodicentrine (**5**) and dehydroocopodine (**6**) in excellent (*ca.* 80%) yield. The dimeric aporphine–benzylisoquinoline alkaloid thalicarpine (**7**) reacted somewhat less smoothly with iodine to give a fair yield (45%) of dehydrothalicarpine (**8**).[4,5] In general, iodine oxidation appears to be the simplest and cleanest preparative procedure for the conversion of a non-phenolic aporphine to the corresponding dehydroaporphine. This type of conversion has been achieved previously by careful permanganate oxidation,[6] by a quinone (DDQ) dehydrogenation,[4] or by mercuric chloride oxidation.[7] The superiority of the iodine oxidation was supported by examining the conversion of **1** into **2** by these other methods. The

* To whom all inquiries should be addressed: Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104.

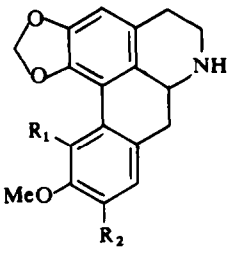


yields of **2** using permanganate, DDQ, and mercuric chloride were 65%, 56%, and 31%, respectively.

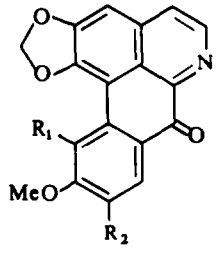
Iodine oxidation of non-phenolic noraporphines. The representative non-phenolic noraporphine O-methylnandigerine (**9**)[8] was found to consume three molar equivalents of iodine when heated in refluxing 95% EtOH in the presence of excess NaOAc to give the corresponding completely aromatic oxoaporphine **10**. The reaction was slow (16 h) but intermediates in the oxidation could not be isolated by using shorter reaction times. Under the same conditions, iodine oxidation of nordicentrine (**11**)*

* Nordicentrine has so far been found naturally only in *Ocotea macropoda*: M. P. Cava, Y. Watanabe, J. Kunitomo, K. Bessho, M. J. Mitchell, A. I. daRocha, B. Hwang, J. A. Weisbach, and B. Douglas, Abstracts of Papers, The Second Natural Products Symposium, Mona, Kingston, Jamaica, 1968, p. 3.

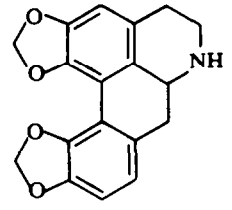
and ovigerine (**12**)[8] gave the natural oxoaporphines dicentrinone (**13**)[3] and hernandonine (**14**),[9] respectively. The oxoaporphine yields in these three cases were in the 47–53% range, making this the best route available from a non-phenolic noraporphine to an oxoaporphine. By contrast, the chromic acid oxidation of **11** is reported to give **13** in only 2% yield.[10] Light-catalyzed air oxidation of non-phenolic noraporphines affords oxoaporphines in fair yield (~ 25%), although products are difficult to purify; an example is the conversion of **12** into **14**.[3]



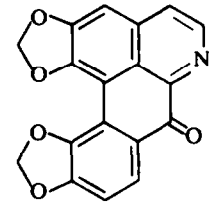
9: R_1 = OMe, R_2 = H
11: R_1 = H, R_2 = OMe



10 R_1 = OMe, R_2 = H
13: R_1 = H, R_2 = OMe

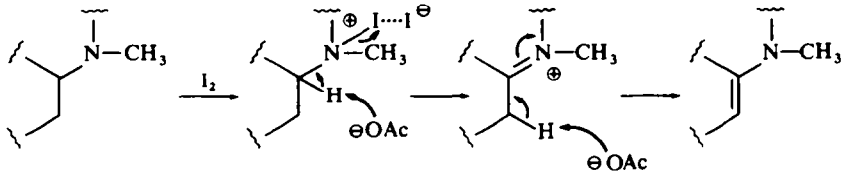


12



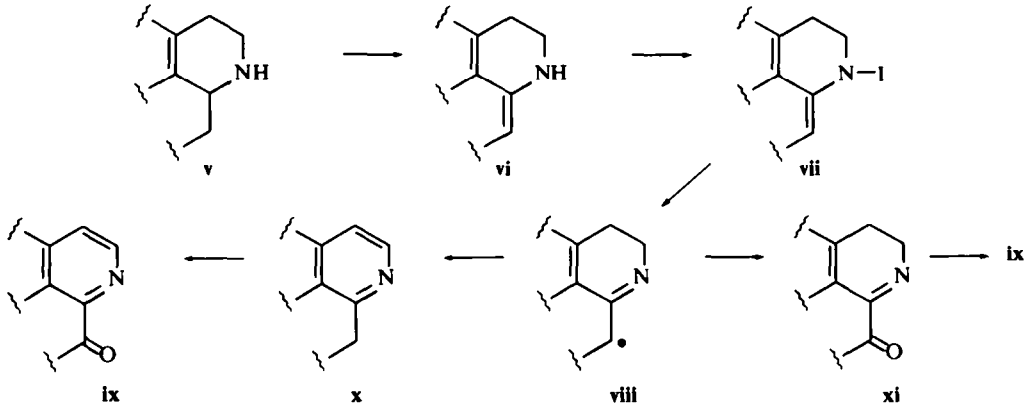
14

A rather straightforward mechanism can be proposed for the iodine-NaOAc oxidation of a non-phenolic aporphine (**i**). Interaction of the basic nitrogen with an iodine molecule gives a charge-transfer complex, a dipolar resonance contributor to which may be drawn as **ii**. Acetate ion-catalyzed loss of HI from **ii** yields the conjugated immonium ion **iii**, converted to a dehydroaporphine (**iv**) by loss of a proton.



i **ii** **iii** **iv**

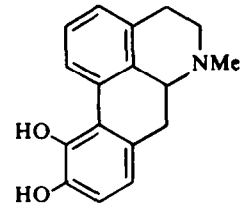
In the case of non-phenolic noraporphine (**v**), similar steps would give a dehydronoraporphine (**vi**). Iodination of **vi** could give a highly labile N-iodo derivative **vii**, homolysis of which would produce the delocalized radical **viii**. Further oxidation steps would transform **viii** into a oxoaporphine **ix**, either by way of an isoquinoline intermediate (**x**) or by way of a 4,5-dihydrooxoaporphine (**xi**).



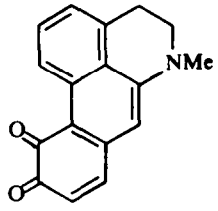
Iodine oxidation of phenolic aporphines. In general, little is known concerning the oxidation products of phenolic aporphines. Apomorphine (**15**) is readily converted by various oxidizing agents (best by $HgCl_2$) to the deep blue *o*-quinone **16**.[7] Oxidation of isothebaine (**17**) by iodine and other oxidizing agents has been reported to give the unusual green dipolar structure **18**.[1] Our preliminary investigations have indicated that phenolic aporphines can give quite complex reaction mixtures on treatment with iodine. In the case of N-methylnandigerine (**19**),[8] it was possible, after laborious purification, to isolate in low yield (~ 9%) a deep greenish-blue crystalline compound, $C_{18}H_{13}NO_4$ which was assigned the demethylated *o*-quinonoid structure **20**, on the basis of a comparison of its spectral properties with those reported for the blue apomorphine quinone **16**. This same quinone **20** could be prepared more easily and in better yield (33%) by $HgCl_2$ oxidation of **19**. Qualitative oxidation of the 11-hydroxyaporphines bulbocapnine (**21**) and isocorydine (**22**) by either iodine or $HgCl_2$ showed, on TLC analysis, that each aporphine formed a deep blue product similar to **20**. Preparative $HgCl_2$ oxidation of **21** proceeded in reasonable yield (39%) to give a blue quinone which proved to be identical with quinone **20**. Oxidation of a 10-hydroxy-11-methoxyaporphine and of a 10-methoxy-11-hydroxyaporphine therefore both take place with demethylation to give the same 10,11-quinone.

Oxidation of dehydroaporphines to oxoaporphines. It was noticed that solutions of dehydronuciferine (**2**) in $CHCl_3$ or MeOH easily undergo discoloration on exposure to air. In order to ascertain the nature of this aerial oxidation, oxygen was passed through a solution of **2** in *t*-BuOH. Analysis by TLC showed the slow appearance of the corresponding oxoaporphine, lysicamine (**23**); after four days, however, only about 2% of **23** could be isolated and most of the starting material was recovered unchanged. By varying the experimental conditions it was found that the conversion of **2** to **23** by oxygen takes place most rapidly at about pH 6 in a mixed aqueous-organic solvent. Thus, **2** was consumed completely in 48 hr when oxygen was passed through its solution in a mixture of pH 6 buffer and dioxane or *t*-BuOH; lysicamine (**23**) was isolated in preparatively useful yields (40–45%). In a similar experiment, dehydrodicentrine (**5**) was converted into dicentrinone (**13**) in 30% yield.*

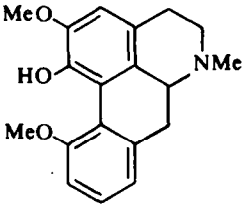
* See reference 4 for the isolation of two oxoaporphines which were apparently formed by the action of air on a mixture containing the corresponding dehydroaporphines.



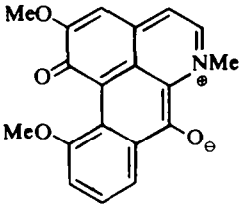
15



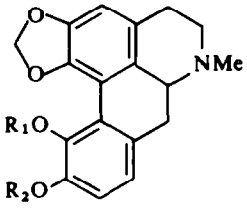
16



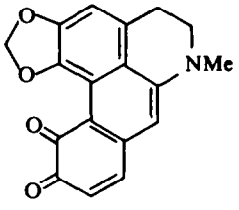
17



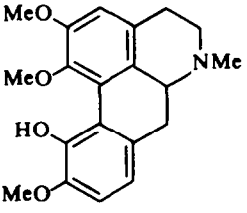
18



19 : R_1 = Me, R_2 = H
21 : R_1 = H, R_2 = Me



20

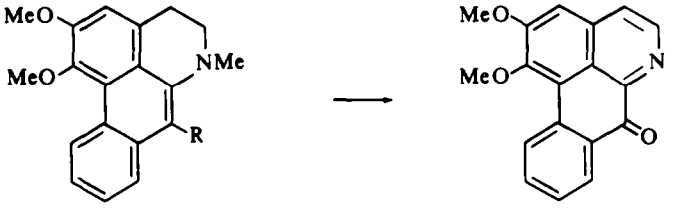


22

The reaction of dehydronuciferine (2) with oxygen was considerably slower in a more strongly acid medium: after reaction for 10 days, the starting material was only half consumed in the presence of pH 2·5 buffer. In the presence of alkali, a solution of 2 showed no conversion to 23 after treatment with oxygen for 5 days.

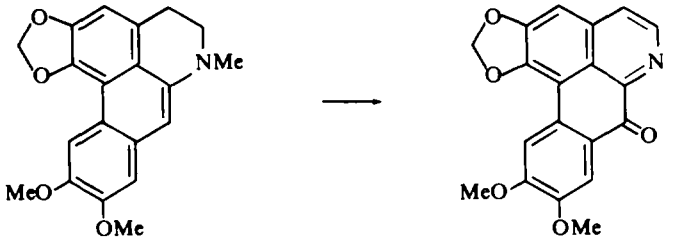
An attempt was made to carry out the direct conversion by oxygen of the aporphine nuciferine (1) to the oxoaporphine lysicamine (23). This conversion was indeed observed at pH 6, but the reaction was very slow and of no preparative interest. Thus, after 15 days reaction with oxygen, dehydronuciferine (2) and lysicamine (23) were isolated in yields of 10% and 25%, respectively, in addition to 18% of unreacted nuciferine (1).

Two alternate procedures were found for the oxidation of **2** to **23**. In the first of these, treatment of **2** with benzoyl peroxide (1·5 equivalents) in benzene gave, after 30 min at room temperature, a mixture of **23** (19%) and a new compound, 7-benzoyloxydehydronuciferine (**24**), formed in 30% yield. Although ester **24** was sensitive to light and air and gave erratic elemental analyses, its structure was in accord with both spectral and chemical evidence. Its NMR spectrum differed from that of the parent **2** mainly by the absence of the C-7 singlet at δ 6·53 and the presence of five additional lower field aromatic protons; its mass spectrum showed the expected molecular ion peak at *m/e* 413, as well as a peak due to loss of a benzoyl group (103) at 308. Finally further reaction of **24** with benzoyl peroxide in benzene afforded lysicamine (**23**), showing that ester **24** is an intermediate in the oxidation of **2** to **23** by benzoyl peroxide.



2: R = H
24: R = OCOPh

23



5 **13**

In the second procedure, reaction of **2** with three molar equivalents of peracetic acid at room temperature for 5 min gave **23** in 50% yield. The latter reaction constitutes the most convenient method reported for the conversion of a dehydroaporphine to an oxoaporphine; it is particularly useful in total oxoaporphine syntheses in view of the synthetic availability of dehydroaporphines from non-natural precursors.[11]

Examples of syntheses using this reaction will be reported elsewhere.

EXPERIMENTAL

All m.ps. were determined in open tubes using a Thomas–Hoover Uni-melt apparatus and are uncorrected. Specific rotations were measured on a Perkin–Elmer Model 141 Polarimeter. UV and visible spectra were measured in 95% EtOH with a Perkin–Elmer Model 202 spectrophotometer. IR spectra were recorded in KBr with a Perkin–Elmer Model 137 spectrophotometer. The NMR spectra were obtained in $CDCl_3$ (unless otherwise noted), using a Varian A-60A instrument; chemical shifts are reported as ppm (δ) downfield from TMS. Microanalyses were performed by Midwest Microlab, Inc., Indianapolis, Indiana.

The identity of all known alkaloidal products was confirmed by direct comparison (IR, TLC, rotation) with authentic samples from our collection.

Dehydroaporphines by iodine oxidation of aporphines

Dehydronuciferine (**2**). A solution of iodine (0·51 g, 2 mmole) in dioxane (40 ml, reagent grade) was added dropwise during 30 min to a refluxing solution of nuciferine (**1**, 0·60 g, ~2 mmole) in dioxane (35 ml, reagent grade) containing suspended anhydrous NaOAc (0·65 g, 8 mmole). The stirred mixture was refluxed gently for an addition 2 hr and then evaporated *in vacuo* to dryness. Extraction of the residue with $CHCl_3$ (3 × 75 ml) and evaporation of the extract gave an oil which crystallized from absolute EtOH to give lemon-yellow needles of dehydronuciferine (**2**, 0·527 g, 87%), m.p. 130–131° (lit[11] m.p. 126–130°).

The yield of **2** from **1** dropped when technical grade dioxane was used. When EtOH was employed as solvent, a 50% increase in iodine consumption was noted, and pure **2** (60% yield) was obtained only after silica chromatography.

Dehydrodicentrine (**5**). A solution of iodine (0·28 g, 1·1 mmole) in pure dioxane (30 ml) was added dropwise during 25 min to a stirred refluxing solution of dicentrine (**3**, 0·339 g, 1 mmole) in pure dioxane (30 ml) containing anhydrous NaOAc (0·205 g, 2·5 mmole). After a further 45 min refluxing, the mixture was cooled, filtered, and the precipitate washed with $CHCl_3$. Evaporation of combined filtrates gave a residue which was shaken for 5 min with 5% aqueous $NaHSO_3$ (10 ml). NH_3 was added and the solid $CHCl_3$ extracted. Evaporation of the extract and crystallization from $CHCl_3$–EtOH afforded yellow needles of dehydrodicentrine (**5**, 0·195 g), m.p. 216–217° (lit[2] m.p. 218°). Silica chromatography of the mother liquor residues gave an additional 0·08 g of **5**, bringing the total yield to 81%.

A 63% yield of **5** was obtained when technical dioxane was employed.

Dehydroocopodine (**6**). A solution of iodine (0·56 g, 2·2 mmole) in pure dioxane (45 ml) was added dropwise during 35 min to a stirred refluxing solution of ocopodine (**4**, 0·738 g, 2 mmole) in pure dioxane (70 ml) containing anhydrous NaOAc. After 45 min of additional refluxing, the mixture was worked up as described for dehydrodicentrine. Crystallization from absolute EtOH gave dehydroocopodine (**6**, 0·585 g, 79%) as golden yellow plates, m.p. 112–114 (lit[3] m.p. 113°).

Dehydrothalicarpine (**8**).* A solution of iodine (0·127 g, 0·5 mmole) in pure dioxane (20 ml) was added to a stirred and refluxing solution of thalicarpine (**7**, 0·348 g, 0·5 mmole) and anhydrous NaOAc (0·45 g) in pure dioxane (25 ml) during 0·5 hr. After an additional 0·5 hr of refluxing the crude product was worked up in the usual manner and was partially purified by column chromatography on silica with MeOH–$CHCl_3$. The still impure product (0·315 g) was subjected to PLC on one 2 mm, 20 × 40 cm Merck SGF plate, developed successively with 0·25%, 1%, 2·5% and 5% MeOH–$CHCl_3$. Elution of the major band (*ca* R_f 0·3) gave, on ether trituration, deyhdrothalicarpine (**8**, 0·149 g, 43%), m.p. 181–183° (lit[4] m.p. 186–187°).

Oxoaporphines by iodine oxidation of noraporphines

Dicentrinone (**13**). To a refluxing solution of nordicentrine (**11**, 0·044 g, 0·14 mmole) in 95% EtOH (6 ml) containing NaOAc (0·041 g, 0·5 mmole) was added dropwise a solution of iodine (0·085 g, 0·3 mmole) in 95% EtOH (10 ml) during 10 min. After refluxing for 6 hr, additional NaOAc (0·02 g) and iodine (0·043 g in 5 ml of 95% EtOH) were added and refluxing was continued for a further 10 hr. The residue remaining after evaporation of solvent was shaken with $NaHSO_3$aq, made basic with NH_3 and $CHCl_3$ extracted. Evaporation of the extract gave a dark yellow solid which was purified by chromatography on silica (5 g), the product (bright orange band) being eluted by 5% MeOH in $CHCl_3$. Crystallization from $CHCl_3$–EtOH gave bright yellow needles of dicentrinone (**13**, 0·021 g, 47%) m.p. 300° dec. (lit[3] m.p. 300° dec.).

Hernandonine (**14**). Ovigerine (**12**, 0·060 g, ~ 0·2 mmole) was oxidized with iodine and the product isolated as described in dicentrinone. Crystallization from $CHCl_3$–EtOH gave bright yellow needles of hernandonine (**14**, 0·032 g, 51%), m.p. 300° dec. (lit[3] m.p. 298–300° dec.).

1,2-*Methylenedioxy*-10,11-*dimethoxy*-7-*oxodibenzo*[de,g]*quinoline* (**10**). A solution of iodine (0·2 g, ~ 0·8 mmole) in 95% EtOH (40 ml) was added dropwise during 1·5 hr to a refluxing solution of O-methylnandigerine[6] (**9**, 0·065 g, 0·2 mmole) in 95% EtOH (20 ml) containing NaOAc (0·164 g, 2 mmole). After refluxing for an additional 13 hr, the mixture was worked up for the product by the procedure used for dicentrinone. Crystallization from $CHCl_3$–EtOH gave orange-yellow needles of oxoaporphine **10** (0·037 g,

* This experiment was carried out by Dr. M. J. Mitchell.

53%), m.p. 238–241°. One additional crystallization gave the analytical sample, m.p. 240–241°. UV spectrum: λ_{max}223 mμ (log ε 4·52), 255 (4·31), 272 sh (4·25), 360 (4·29), 410 (4·25). Calcd. for $C_{19}H_{13}NO_5$: C, 68·06: H, 3·91: N, 4·18. Found: C, 68·18: H, 4·20: N, 3·90%).

1,2-*Methylenedioxy*-6a,7-*dehydroaporphine*-10,11-*quinone* (**20**)

From N-methylnandigerine (**19**) *and mercuric chloride.* $HgCl_2$ aq (5%, 15 ml) and pH 6 McIlvain buffer (25 ml) were added to a solution of N-methylnandigerine hydrobromide[3] (0·15 g, 0·38 mmole) in water (13 ml). The turbid yellow mixture was heated with stirring at 70–75° for 35 min. The blue product was extracted into $CHCl_3$ (400 ml), and the extract was washed with 2 N H_2SO_4 (4 × 30 ml) followed by water (2 × 25 ml). Evaporation of the dried extract and crystallization of the residue from $CHCl_3$–EtOH gave deep blue–green prisms of quinone **20** (0·038 g, 33%), m.p. 208–210°. Recrystallization from the same solvent gave analytical sample, m.p. 218–220°. The IR spectrum showed bands in the carbonyl region at 1685, 1650, 1590 and 1580 cm^{-1}. UV and visible spectrum: λ_{max} 227 mμ (log ε 4·35), 286 (4·02), 347 (4·23), 405 (3·75), 626–660 (3·67): no alkali shift. NMR spectrum: 3·21 (3 H, s, N–Me), 2·9–3·6 (4 H, m, C-4 and C-5), 6·06 (2 H, s, methylenedioxy), 6·11, 6·73 (2 × 1 H, s, C-7 and C-3, respectively), 6·21 and 7·10 (2 × 1 H, d, J = 10 Hz, C-8 and C-9 H). (Calc. for $C_{18}H_{13}NO_4$: C, 70·35: H, 4·26: N, 4·56. Found: C, 70·56: H, 4·34: N, 4·64%).

From bulbocapnapnine (**21**) *and mercuric chloride.* Hg Cl_2 aq (5%, 8 ml) and pH 6 McIlvain buffer (13 ml) were added to a solution of bulbocapnine hydrochloride (0·074 g, 0·2 mmole) in water (10 ml), and the mixture heated at 80° for 4 hr with stirring. Work-up as above, followed by crystallization from $CHCl_3$–EtOH, gave blue–green prisms of quinone **20** (0·024 g, 39%), m.p. 208–210°, identical (IR, TLC) with material prepared from N-methylnandigerine.

From N-methylnandigerine (**19**) *and iodine.* A refluxing solution of N-methylnandigerine (**19**, 0·115 g, 0·33 g) and anhydrous NaOAc (0·082 g, 1 mmole) in pure dioxane (20 ml) was treated during 20 min with a solution of iodine (0·085 g, 0·33 mmole) in pure dioxane (10 ml). After refluxing for a further 15 min, additional NaOAc (0·045 g) and iodine (0·085 g in 10 ml of dioxane) were added. After 15 min, the same amounts of NaOAc and iodine solution were added and refluxing was continued for an additional 0·5 hr. The solvent was evaporated and the residue was treated with dilute NH_3 and $CHCl_3$. Evaporation of the organic extract and chromatography on silica (2% MeOH in $CHCl_3$ eluant) gave a green solid which was again purified by preparative TLC (silica) to give blue–green crystals of quinone **20** (0·010 g, 9%), m.p. 208–210°, identical (IR, TLC) with material prepared above.

Autoxidation of dehydroaporphines and a representative aporphine

Dehydronuciferine (**2**). A slow stream of oxygen was passed through a solution of dehydronuciferine (**2**, 0·100 g, 0·33 mmole) in dioxane (25 ml) and pH 6 McIlvain buffer (15 ml) for a period of 48 hr. The dioxane was removed *in vacuo*, the mixture made basic with NH_3, and the product extracted into $CHCl_3$. Chromatography on silica (6 g) gave unchanged **2** (0·011 g) in the $CHCl_3$ eluate. Further elution with 2% MeOH in $CHCl_3$ gave, after crystallization from EtOH, orange–yellow needles of lysicamine (**23**, 0·045 g, 45%), m.p. 211–212° dec. (lit[12] m.p. 210–211° dec.).

The autoxidation of **2** in *t*-BuOH containing either pH 6 McIlvain buffer or 5% NH_4Cl aq also gave **23** in yields of 35–40%.

Dehydrodicentrine (**5**). A stream of oxygen was passed through a solution of dehydrodicentrine (**5**, 0·067 g, 0·2 mmole) in dioxane (40 ml) and pH 6 McIlvain buffer (15 ml) for a period of 20 hr. The reaction mixture was worked up as for dehydronuciferine above, and the product chromatographed on silica (6 g). Elution with 1% MeOH in $CHCl_3$ gave unchanged **5** (0·018 g). Subsequent elution with 4% MeOH in $CHCl_3$ gave, after crystallization from $CHCl_3$–EtOH, yellow needles of dicentrinone (**13**, 0·019 g, 30%); the yield of pure **13** based upon unrecovered **5** was 36%.

Nuciferine (**1**). Nuciferine (**1**, 0·100 g, ~0·33 mmole) was dissolved in *t*-BuOH (25 ml) and the solution diluted with pH 6 McIlvain buffer (10 ml). A slow stream of oxygen was passed through the solution for 15 days: organic solvent lost by vaporization was replenished when necessary. The solvent was concentrated, aqueous NH_3 added, and the product $CHCl_3$ extracted. Extraction of the $CHCl_3$ solution with 1 N H_2SO_4 removed unchanged **1** (0·018 g), which was recovered after basification with NH_3. The products in the $CHCl_3$ phase were chromatographed on silica to give dehydronuciferine (**2**, 0·010 g from the $CHCl_3$ eluate) and lysicamine (**23**, 0·030 g, from the 4% MeOH in $CHCl_3$ eluate).

Further oxidations of dehydronuciferine (**2**)

Peracetic acid. A solution of AcOOH in AcOH (25 ml, containing 0·50 g of pure peracid) was added slowly

at room temp with stirring to a solution of dehydronuciferine (**2**, 0·500 g) in AcOH (25 ml). After 5 min at room temp, the solvent was removed *in vacuo* (*ca.* 50°). The red residue was taken in a few ml of MeOH, aqueous NH_3 added, and the crude product $CHCl_3$ extracted. Evaporation of the reddish extract gave a residue which was extracted with boiling ether. Evaporation of the ether, followed by chromatography on a short column of netural alumina (1% MeOH in $CHCl_3$) gave, after crystallization ($CHCl_3$-hexane), pure lysicamine (**23**, 0·0250 g, 50%).

Benzoyl peroxide. A solution of benzoyl peroxide (1·210 g, 5 mmoles) in a minimal amount of benzene was added at room temp to a solution of dehydronuciferine (**2**, 1·000 g, 3·30 mmoles) in benzene (50 ml). After 30 min at room temp, the brown solution was chromatographed on silica to give 0·192 g (19%) of lysicamine (**23**), and 0·429 g (30%) of 7-benzoyloxydehydronuciferine (**24**), m.p. 174–175° (tan chunks from MeOH $CHCl_3$). (Calc. for $C_{26}H_{23}O_4N$: N, 3·39. Found: N, 3·44%). When ester **24** (0·050 g) was submitted to the action of excess benzoyl peroxide under the original reaction conditions, lysicamine (**23**, 0·020 g, 57%) was isolated after silica chromatography.

Potassium permanganate, DDQ, and mercuric chloride. In each reaction, 0·100 g of **1** was oxidized using the exact experimental conditions reported in the literature for the conversion of other aporphines into the corresponding dehydroaporphines.[4,6,7] The dehydronuciferine (**2**) formed was isolated by preparative TLC (silica gel). Yields of **2** from **1** using permanganate, DDQ and $HgCl_2$ were 65%, 56%, and 31%, respectively.

Acknowledgement—We thank the National Institutes of Health for a grant (CA 11445) in support of the portions of this work carried out at the University of Pennsylvania. The remaining portion of the work (at Wayne State University) was generously supported by Smith, Kline and French Laboratories, Philadelphia, Pennsylvania.

REFERENCES

[1] V. Preininger, J. Hrbek Jr., Z. Samek and F. Santavy, *Arch. Pharmazie* **302**, 808 (1969)
[2] M. P. Cava, Y. Watanabe, K. Bessho, M. J. Mitchell, A. I. daRocha, B. Hwang, B. Douglas and J. A. Weisbach, *Tetrahedron Letters* 2437 (1968)
[3] M. P. Cava and A. Venkateswarlu, *Tetrahedron* **27**, 2639 (1971)
[4] S. M. Kupchan, T.-H. Yang, M. L. King and R. T. Borchardt, *J. Org. Chem.* **33**, 1052 (1968)
[5] H. B. Dutschewska and N. M. Mollov, *Chem. Ind.* (London), 770 (1966)
[6] N. M. Mollov and H. B. Dutschewska, *Tetrahedron Letters* 853 (1966)
[7] H. A. Linde and M. S. Ragab, *Helv. Chim. Acta* **51**, 683 (1968)
[8] M. P. Cava, K. Bessho, B. Douglas, S. Markey, R. F. Raffaul and J. A. Weisbach, *Tetrahedron Letters* 1577 (1966)
[9] K. Ito and H. Furukawa, *Tetrahedron Letters* 3023 (1970)
[10] M. P. Cava, K. V. Rao, B. Douglas and J. A. Weisbach, *J. Org. Chem.* **33**, 2443 (1968)
[11] M. P. Cava, M. J. Mitchell, S. C. Havlicek, A. Lindert and R. J. Spangler, *J. Org. Chem.* **35**, 175 (1970)
[12] N. Katsui, K. Sato, S. Tobinaga and N. Takenchi, *Tetrahedron Letters* 6257 (1966)