# THE ULTRAVIOLET SPECTRA OF PROTOBERBERINES[1]

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## Contents



## I. Introduction

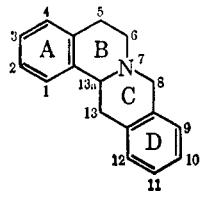
Although more than 60 naturally occurring protoberberines and tetrahydroprotoberberines are presently known, no systematic study of the ultraviolet spectra of these alkaloids has appeared in the literature. This topic was briefly covered in 1964 as part of a much larger review of the uv spectra of all known alkaloids.[2] Since this time, however, enough new data have appeared to warrant a completely separate treatment of the subject. Several spectral examples will be listed here, and generalizations correlating spectra with structures will then be drawn when warranted. Special attention will be given to differences between 9,10- and 10,11-substituted isomers. Ethanolic solutions were used in all cases except where indicated.

## II. Tetrahydroprotoberberines

### A. SIMPLE TYPE

Tetrahydroprotoberberines absorb in the 282–289-m$\mu$ region, with occasionally a shoulder near 230 m$\mu$ (Table I). There is also substantial absorption around 210 m$\mu$, but since this band has either not been reliably recorded or else has gone unmentioned, emphasis will here be placed on the 283–289-m$\mu$ absorption. Inevitably, a minimum is present in the 251–254-m$\mu$ range.

The alkaloid capaurine, which has a hydroxy group at C-1 and corresponds to 1-hydroxy-2,3,9,10-tetramethoxytetrahydroprotoberberine, exhibits a slightly different spectrum with $\lambda_{max}$ 276 and 230 (sh) m$\mu$ (log $\epsilon$ 3.45 and 4.7),[3] but 1-methoxycanadine,[4] mecambridine,[5] and caseadine,[6] which are all substituted at C-1, absorb in the usual range.




Tetrahydroprotoberberines substituted at C-2,3,10,11, sometimes called pseudotetrahydroprotoberberines, again have a maximum between 282 and 289 m$\mu$, and cannot readily be differentiated from their C-2,3,9,10 analogs (Table I).

### B. 13-METHYL SUBSTITUTED

Tetrahydroprotoberberines with a C-13 methyl group may exist in either of two conformations. If the C-13 methyl group and the C-13a hydrogen are *cis* to each other, the B/C quinolizidine ring system is *cis* fused. When the C-13 methyl and the C-13a hydrogen are *trans*, the quinolizidine ring system is also *trans*.[7] These two groups of tetrahydroprotoberberines show maxima between 282 and 288 m$\mu$, in analogy with tetrahydroprotoberberines with no C-13 methyl group. Additionally, no differentiation can be made between the C-13 methyl series with substituents at C-2,3,9,10 and the C-2,3,10,11 series (Table II).

### C. 13-HYDROXY SUBSTITUTED

As expected, C-13 hydroxylated tetrahydroprotoberberines (Table III) have uv spectra very similar to those discussed above. Their maximum absorption falls between 281 and 290 m$\mu$. Differences in stereochemistry at C-13 and C-13a, as well as in the mode of fusion of the B/C rings, appear to have little bearing on the uv absorption.

## III. Dihydroprotoberberines

The measurement of the uv spectra of dihydroprotoberberines is complicated by the fact that these compounds are difficult to purify, and usually contain some of the corresponding

(1) This study was supported by Grant GP-9359 from the National Science Foundation. M. J. H. and C. D. J. are the recipients of Natlona Institutes of Health Fellowships 1-F1-GM-32,921 and 1-F1-GM-33,031 respectively.

(2) A. W. Sangster and K. L. Stuart, *Chem. Rev.*, 65, 69 (1965).

(3) T. Kametani, M. Ihara, K. Fukumoto, H. Yagi, H. Shimanouchi, and Y. Sasada, *Tetrahedron Letters*, 4251 (1968).

(4) M. Ohta, H. Tani, S. Morozumi, and S. Kodaira, *Chem. Pharm. Bull. Japan*, 12, 1080 (1964).

(5) S. Pfeifer and I. Mann, *Tetrahedron Letters*, 83 (1967).

(6) C. Y. Chen, D. B. MacLean, and R. H. F. Manske, *ibid.*, 349 (1968).

(7) M. Shamma, J. A. Weiss, and C. D. Jones, *Tetrahedron*, in press.

*Table I*
**Simple Tetrahydroprotoberberines**[a]

| *Tetrahydroprotoberberines* | *Substituents* C-1 | C-2 | C-3 | C-9 | C-10 | C-11 | $\lambda_{max}$, mμ (log ε) | $\lambda_{min}$, mμ (log ε) |
|---|---|---|---|---|---|---|---|---|
| Canadine (tetrahydroberberine)[b] | | O–$CH_2$–O | | $OCH_3$ | $OCH_3$ | | 284 (3.71) | 252 (2.76) |
| Tetrahydropalmatine[c] | | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | | 281 (3.75), 230 sh (4.25)* | 251 (2.90)* |
| Stepholidine[d] | | OH | $OCH_3$ | $OCH_3$ | OH | | 287 (3.79) | |
| Isocorypalmine[e] | | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | | 282 (3.79), 230 sh (4.4) | 252 (2.85)* |
| Alkaloid HF-1[f] | | $OCH_3$ | OH | OH | $OCH_3$ | | 282 (3.81) | 252 (2.9) |
| Nandinine[g] | | O–$CH_2$–O | | OH | $OCH_3$ | | 286 (3.80), 230 sh (4.1) | 252 (2.3) |
| Tetrahydrocoptisine (stylopine)[h] | | O–$CH_2$–O | | O–$CH_2$–O | | | 289 (3.89), 237 (3.85) | 252 (2.70)* |
| Scoulerine[i] | | OH | $OCH_3$ | OH | $OCH_3$ | | 283 (3.85) 230 (4.20)* | 252 (3.15)* |
| Tetrahydrothalifendine[j] | | O–$CH_2$–O | | $OCH_3$ | OH | | 282 (3.77) | 252 |
| Capaurine[k] | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | | 276 (3.45), 230 sh (4.7)* | 252 (2.8)* |
| 1-Methoxycanadine[l] | $OCH_3$ | O–$CH_2$–O | | $OCH_3$ | $OCH_3$ | | 283.5 (3.47) | |
| Mecambridine (oreophiline)[m] (in methanol) | $OCH_3$ | O–$CH_2$–O | | $CH_2OH$ | $OCH_3$ | $OCH_3$ | 286 (3.74) | 254 (2.89) |
| Caseadine[n] | OH | $OCH_3$ | | | $OCH_3$ | $OCH_3$ | 286 (3.74), 208 sh (4.08), 206 (4.82) | |
| Norcoralydine[o] | | $OCH_3$ | $OCH_3$ | | $OCH_3$ | $OCH_3$ | 287 (3.90) | |
| 2,10-Dihydroxy-3,10-dimethoxy-tetrahydroprotoberberine[p] | | OH | $OCH_3$ | | OH | $OCH_3$ | 289 (3.75) | |
| Descretine[o] | | $OCH_3$ | OH | | $OCH_3$ | $OCH_3$ | 282 (3.77), 228 sh (4.25) | |
| Demethylcoreximine[p] | | OH | $OCH_3$ | | OH | OH | 289 (3.92) | |
| Pseudoepitetrahydro-berberine[q] | | $OCH_3$ | $OCH_3$ | | O–$CH_2$–O | | 288 (3.65), 225 sh (4.09) | 254 (2.67) |
| Coreximine[r] | | OH | $OCH_3$ | | $OCH_3$ | OH | 286 (3.99), 225 sh (4.25)* | 252 (2.95)* |

[a] Where only volume and spectrum n umber are indicated in the footnotes, the reference is either to J. Holubeck and O. Strouf, "Spectra Data and Physical Constants of Alkaloids," Vol. I, Publishing House of the Czechoslovak Academy of Sciences, Prague, 1965, or to Vol. II by the same authors and publishing house, which appeared in 1966. All values accompanied by an asterisk (*) in Tables I–VI were obtained directly from spectral graphs. [b] I. Sallay and R. H. Ayers, *Tetrahedron*, **19**, 1397 (1963). [c] Volume I, Spectrum No. 264. [d] M. P. Cava, K. Nomura, S. K. Talapatra, M. J. Mitchell, R. H. Schlessinger, K. T. Buck, J. L. Beal, B. Douglas, R. F. Raffauf, and J. A. Weisbach, *J. Org. Chem.*, **33**, 2785 (1968). [e] Volume I, Spectrum No. 147. [f] Volume II, Spectrum No. 343. [g] Volume II, Spectrum No. 369. [h] Volume I, Spectrum No. 260. [i] Volume II, Spectrum No. 244. [j] M. Shamma and M. A. Podczasy, unpublished results. [k] Volume I, Spectrum No. 41. Also T. Kametani, M. Ihara, K. Fukumoto, H. Yagi, H. Shimanouchi, and Y. Sasada, *Tetrahedron Letters*, 4251 (1968). [l] M. Ohta, H. Tani, S. Morozumi, and S. Kodaira, *Chem. Pharm. Bull.* (Tokyo), **12**, 1080 (1964). [m] S. Pfeifer and I. Mann, *Tetrahedron Letters*, 83 (1967). [n] C. Y. Chen, D. B. MacLean, and R. H. F. Manske, *ibid.*, 349 (1968). [o] J. Schmutz, *Helv. Chim. Acta*, **42**, 335 (1959). [p] T. Kametani, I. Noguchi, S. Nakamura, and Y. Konno, *J. Pharm. Soc. Japan*, **87**, 168 (1967). [q] The synthesis of this compound by M.S. and C.D.J. will be reported at a later date. [r] Volume I, Spectrum No. 67.

tetrahydroprotoberberines. There is always a peak between 360 and 375 mμ due to the stilbenoid system, and when a C-13 methyl group is present, a hypsochromic shift of about 5–8 mμ is evident for this long-wavelength band (Table IV).

The alkaloid lambertine actually corresponds to dihydroberberine.[8] The spectrum of the compound has been reported to consist of only a single band at 285 mμ (4.45).[8] This value is inconsistent with the values obtained by Takemoto and Kondo for synthetic dihydroberberine.[9] It is possible, therefore, that the spectral measurement for naturally occurring lambertine was done on an impure sample.

The spectra of two dihydroprotoberberine N-metho salts have been recorded (Table IV), and as expected these differ substantially from the spectra of the free bases. Maxima appear near 250 and 355 mμ, and minima are present around 270 and 315 mμ.

## IV. Protoberberine Salts

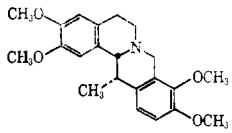
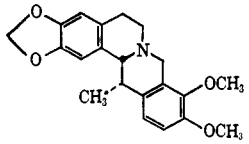
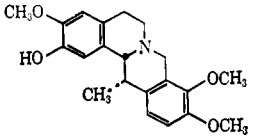
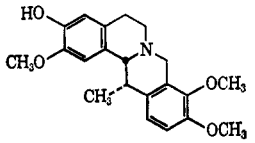
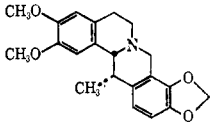
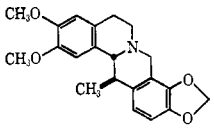
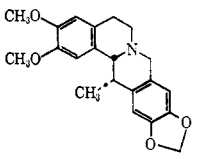
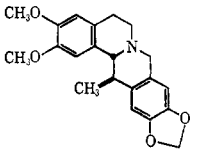
### A. DIFFERENCES BETWEEN C-9,10 AND C-10,11 SUBSTITUTION

A drastic alteration of the spectrum occurs when changing from 9,10 to 10,11 substitution for the protoberberine salts (Table V). The 9,10-substituted salts show a minimum at 301–310 mμ, while their 10,11 counterparts show strong absorption in this region in the form of a peak or a shoulder.

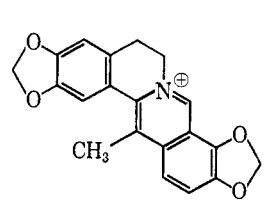
Since tetrahydroprotoberberines can be easily oxidized with either iodine or mercuric acetate to the corresponding quaternary salts, it follows that uv spectroscopy can assist in the establishment of the ring D substitution pattern for the tetrahydroprotoberberine bases.

(8) R. Chatterjee and P. C. Maiti, *J. Indian Chem. Soc.*, **32**, 609 (1955); *Chem. Abstr.*, **50**, 5993 (1956).
(9) T. Takemoto and Y. Kondo, *J. Pharm. Soc. Japan*, **82**, 1408 (1962).

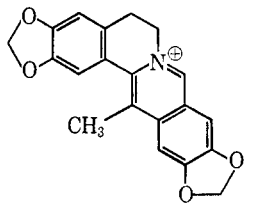
*Table II*[a]
**13-Methyltetrahydroprotoberberines**

| *Base* | *Structure* | $\lambda_{max}$, $m\mu$ (*log* $\epsilon$) | $\lambda_{min}$, $m\mu$ (*log* $\epsilon$) |
|---|---|---|---|
| Corydaline[b] |  | 282, 230 sh (3.76, 4.30)* | 252 (3.0)* |
| Corybulbine[c] |  | 282, 230 sh (3.76, 4.25)* | 252 (3.10)* |
| Isocorybulbine[d] |  | 283, 225 sh (3.80, 4.25)* | 252 (3.10)* |
| Thalictricavine[e] |  | 287, 230 sh (3.6, 4.2)* | 254 (2.9) |
| Base II[e] |  | 283, 230 sh (3.7, 4.1)* | 254 (3.2) |
| Thalictrifoline[e,g] |  | 283, 235 sh (3.7, 4.15)* | 254 (3.3) |
| (±)-α-13-Methyl-2,3-dimethoxy-10,11-methylenedioxy-5,6-13,β13a-tetrahydro-8H-dibenzo[*a*,*g*]quinolizine[f] |  | 287, 230 sh (3.84, 4.5) | 254 (2.70) |
| (±)-β-13-Methyl-2,3-dimethoxy-10,11-methylenedioxy-5,6,13,β13a-tetrahydro-8H-dibenzo[*a*,*g*]quinolizine[f] |  | 288, 230 (3.81, 4.4) | 254 (2.74) |

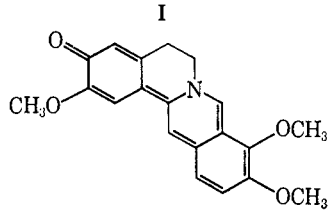
[a] See footnote *a*, Table I. [b] Volume I, Spectrum No. 73. [c] Volume I, Spectrum No. 71. [d] Volume I, Spectrum No. 145. [e] H. Taguchi and I. Imaseki, *J. Pharm. Soc. Japan*, **84**, 955 (1964). [f] The synthesis of this compound by M. S. and C. D. J. will be reported at a later date. [g] No absolute configuration implied.



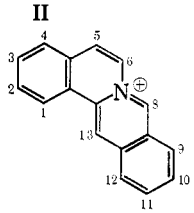
I



II



III



IV

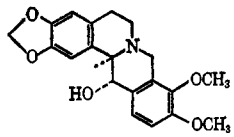
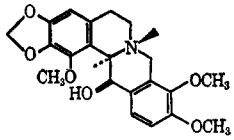
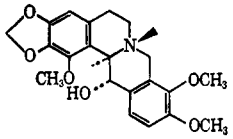
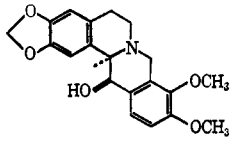
The quaternary alkaloid worenine presents an interesting problem. It had originally been formulated as I, but this structure was then assigned to corysamine which is a different material from worenine.[10,11] It follows that worenine might instead be formulated as II. Unfortunately, no uv spectrum of worenine is recorded in the literature, and no sample of the alkaloid is available to verify such a hypothesis.

## B. PHENOLIC SALTS

The phenolic protoberberines columbamine and jatrorrhizine iodide deserve special attention. Although dilute ethanolic solutions of these alkaloids are both yellow under neutral

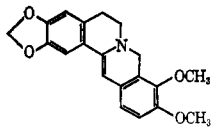
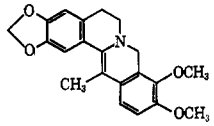
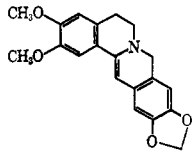
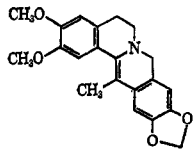
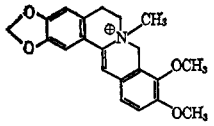
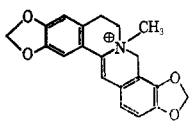
(10) Z. Kitasato, *J. Pharm. Soc. Japan*, No. 542, 48 (1927).
(11) C. Tani and N. Takao, *ibid.*, **82**, 599 (1962).

*Table III*[a]
**13-Hydroxytetrahydroprotoberberines**

| *Base* | *Structure* | $\lambda_{max}$, $m\mu$ (*log* $\epsilon$) | $\lambda_{min}$, $m\mu$ (*log* $\epsilon$) |
|---|---|---|---|
| Ophiocarpine[b,c] |  | 290, 230 (3.78, 4.25)* | 252 (2.95)* |
| 13-Epiophiocarpine[c] |  | 286 (3.76) | |
| (−)-β-13-Hydroxy-2,3-methoxylenedioxy-1,9,10-trimethoxy-5,6,13,α13a-tetrahydro-8H-dibenzo-[a,g]quinolizine[d] |  | 281.5 (3.47) | |
| (−)-α-13-Hydroxy-2,3-methylenedioxy-1,9,10-trimethoxy-5,6,13,α13a-tetrahydro-8H-dibenzo-[a,g]quinolizine[d] |  | 282 (3.51) | |

[a] See footnote *a*, Table I. [b] Volume I, Spectrum No. 200. [c] M. Ohta, H. Tani, and S. Morozumi, *Chem. Pharm. Bull.* (Tokyo), **12**, 1072 (1964). [d] Reference 4.

*Table IV*
**Dihydroprotoberberines**

| *Base* | *Structure* | $\lambda_{max}$, $m\mu$ (*log* $\epsilon$) | $\lambda_{min}$, $m\mu$ (*log* $\epsilon$) |
|---|---|---|---|
| Dihydroberberine[a] |  | 368, 280 (4.25, 4.10) | 305 (3.70) |
| 13-Methyldihydro-berberine[a] |  | 360, 280 (4.5, 4.0) | 305 (3.8) |
| Dihydropseudoepi-berberine[b] |  | 375, 280, 260 (4.2, -, -) | — |
| 13-Methyldihydro-pseudoepiberberine[b] |  | 370, 283, 262 (4.1, -, -) | — |
| Dihydroberberine methochloride[c] (in water) |  | 350, 250–240 (4.39, 3.97) | 362, 300–320, 270 (3.31, 3.97, 3.34) |
| Dihydrocoptisine methochloride ("Substance R")[d] |  | 375, 357, 343 sh, 306, 255, 215 (4.33, 4.38, 4.26, 3.88, 3.84, 4.42) | 367, 314, 274, 244 (4.30, 3.85, 3.41, 3.81) |

[a] Reference 9. [b] The synthesis of this compound by M. S. and C.D. J. will be reported at a later date. [c] P. B. Russell, *J. Am. Chem. Soc.*, 78, 3115 (1956). [d] A. Klasek, V. Simanek, and F. Santavy, *Tetrahedron Letters*, 4549 (1968).

*Table V*
**Protoberberine Salts**

| Salt | Substituents C-2 | C-3 | C-9 | C-10 | C-11 | C-13 | C-5 | $\lambda_{max}$, mμ (*log* ε) | $\lambda_{min}$, mμ (*log* ε) |
|---|---|---|---|---|---|---|---|---|---|
| Columbamine iodide[a] | OH | $OCH_3$ | $OCH_3$ | $OCH_3$ | | | | 438, 352, 268* (3.7, 4.4, 4.4) | 388, 304, 248 (3.4, 3.8, 4.3) |
| Jatrorrhizine iodide[a] | $OCH_3$ | OH | $OCH_3$ | $OCH_3$ | | | | 442, 347, 266* (3.7, 4.4, 4.4) | 388, 301, 248 (3.4, 3.8, 4.3) |
| Berberine iodide[b] | O—$CH_2$–O | | $OCH_3$ | $OCH_3$ | | | | 423, 345, 263 (3.7, 4.4, 4.4) | 370, 305, 250 (3.7, 3.8, 4.1) |
| Palmatine iodide[c] | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | | | | 425, 355, 265* (4.0, 4.5, 4.4) | 380, 305, 250 (3.0, 4.4, 4.3) |
| Coptisine chloride[d] | O–$CH_2$–O | | O–$CH_2$–O | | | | | 357, 265, 241, 225* (4.4, 4.4, 4.36, 4.4) | 390, 310, 252* (3.1, 3.7, 4.3) |
| Thalifendine chloride[e] | O–$CH_2$–O | | $OCH_3$ | OH | | | | 348, 269, 231 (4.1, 4.2, 4.2) | |
| Berberastine chloride[b] | O–$CH_2$–O | | $OCH_3$ | $OCH_3$ | | | OH | 424, 344, 265, 228 (4.63, 4.41, 4.35, 3.71) | 377, 302.5, 250, 212 |
| Thalidastine chloride[f] | O–$CH_2$–O | | $OCH_3$ | OH | | | OH | 348, 269, 233 (4.1, 4.2, 4.2) | |
| Dehydrothalictrifoline iodide[g] | $OCH_3$ | $OCH_3$ | O–$CH_2$–O | | | $CH_3$ | | 445, 350, 260 (3.7, 4.3, 4.4) | 385, 310, 250* (3.3, 3.8, 4.3) |
| Dehydrothalictricavine iodide[h] | O–$CH_2$–O | | $OCH_3$ | $OCH_3$ | | $CH_3$ | | 340, 260* (4.4, 4.5) | 305, 250* (3.9, 4.3) |
| Corysamine chloride[d] | O–$CH_2$–O | | O–$CH_2$–O | | | $CH_3$ | | 345, 275* (4.6, 4.7) | 380, 310, 252* (3.6, 3.3, 4.25) |
| Pseudoepiberberine iodide[i] | $OCH_3$ | $OCH_3$ | O–$CH_2$–O | | | | | 365, 338, 310 sh, 287, 262, 238 (3.8, 4.2, 4.4, 4.4, 4.3, 4.3) | 332, 270, 247 (4.1, 4.2, 4.2) |
| Pseudopalmatine iodide[c] | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | | | | 375, 345, 310 sh, 287, 265* (4.0, 4.3, 4.5, 4.7, 4.3) | 365, 335, 270, 250* (3.9, 4.3, 4.3, 4.1) |
| 13-Methylpseudoepiberberine iodide[i] | $OCH_3$ | $OCH_3$ | O–$CH_2$–O | | | $CH_3$ | | 365, 338 sh, 305 sh, 287, 260, 218 (3.8, 4.1, 4.4, 4.5, 4.4, 4.4) | 270, 247 (4.3, 4.2) |

[a] Reference 12. [b] M. M. Nijland, *Pharm. Weekblad*, **98**, 301 (1963). [c] W. Wiegrebe, *Arch. Pharm.*, **301**, 25 (1968). [d] Reference 11. [e] M. Shamma, M. A. Greenberg, and B. S. Dudock, *Tetrahedron Letters*, 3595 (1965). [f] M. Shamma and B. S. Dudock, *ibid.*, 3825 (1965). [g] H. Taguchi and I. Imaseki, *J. Pharm. Soc. Japan*, **84**, 955 (1964). [h] Reference 9. [i] The synthesis of this compound by M. S. and C. D. J. will be reported at a later date.

*Table VI*
**Dehydroprotoberberine Salts**

| Salt | Substituents C-2 | C-3 | C-9 | C-10 | C-11 | $\lambda_{max}$, *mμ* (*log* ε) | $\lambda_{min}$, *mμ* (*log* ε) |
|---|---|---|---|---|---|---|---|
| Dehydropalmatrubine bromide[a] | $OCH_3$ | $OCH_3$ | OH | $OCH_3$ | | 477, 354, 281, 248 | 412, 337, 263 |
| Dehydropalmatine bromide[a] | $OCH_3$ | $OCH_3$ | $OCH_3$ | $OCH_3$ | | 464, 355, 328, 285, 246 | 404, 344, 306, 268 |
| Dehydroberberubine bromide[a] | O–$CH_2$–O | | OH | $OCH_3$ | | 470, 352, 281, 249 | 415, 334, 268 |
| Deoxythalidastine chloride[b] | O–$CH_2$–O | | $OCH_3$ | OH | | 463, 348, 308, 378, 270, 247 (3.68, 3.71, 4.08, 4.18, 4.18, 4.24) | |
| Dehydroberberine chloride[a] | O–$CH_2$–O | | $OCH_3$ | $OCH_3$ | | 460, 348, 310, 278, 246 | 405, 332, 290.5, 257 |
| 2,3-Dimethoxy-9,10-methylenedioxybenz[*a*]-acridizinium chloride[c] | $OCH_3$ | $OCH_3$ | O–$CH_2$–O | | | 492, 358, 327, 275, 248 | 417, 340, 304, 262 |
| Dehydrocoptisine chloride[c] | O–$CH_2$–O | | O–$CH_2$–O | | | 490, 356, 317, 248 | 418, 337, 294, 264 |
| 10,11:2,3-Bismethylenedioxybenz[*a*]acridizinium chloride[d] | O–$CH_2$–O | | | O–$CH_2$–O | | 417, 332, 317, 306, 282 | 368, 326, 312, 292, 254 |
| Dehydropseudoberberine chloride[d] | O–$CH_2$–O | | | $OCH_3$ | $OCH_3$ | 422, 326, 312, 302, 278, 235 | 376, 320, 306, 290, 262 |
| Dehydropseudoepiberberine chloride[c] | $OCH_3$ | $OCH_3$ | | O–$CH_2$–O | | 413, 322, 309, 276 | 367, 317, 285, 250 |
| Dehydronorcoralydine chloride[c] | $OCH_3$ | $OCH_3$ | | $OCH_3$ | $OCH_3$ | 417, 322, 309, 278 | 370, 318, 286, 250 |

[a] Reference 15. [b] Reference 13. [c] Reference 16. [d] Reference 17.

conditions, they show different color changes upon the addition of base. Columbamine is unaffected by the addition of sodium bicarbonate, and becomes tan in the presence of sodium hydroxide. Jatrorrhizine becomes deep red in the presence of sodium hydroxide or even sodium bicarbonate. Jatrorrhizine is therefore more easily converted to the corresponding zwitterion, and one of the canonical contributors to this species is the highly conjugated but neutral quinonoid structure III. By contrast, only dipolar forms of the columbamine zwitterion can be drawn.[12]

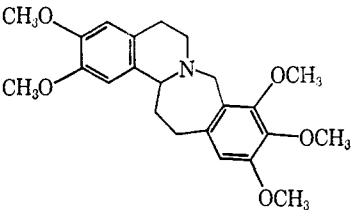
## V. Dehydroprotoberberine Salts

Dehydroprotoberberine salts, as exemplified by structure IV, have not been isolated from natural sources, but can be readily obtained through the dehydration of naturally occurring 5-hydroxylated protoberberine salts such as berberastine[13] and thalidastine.[14] Alternatively, they are available synthetically through preparative routes developed by Bradsher and Dutta.[15–17]

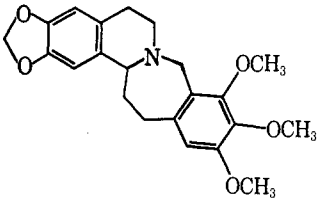
There is a substantial difference between the spectra of 9,10- and 10,11-substituted dehydroprotoberberine salts as shown in Table VI, even though extinction coefficients are often not available. In particular, 2,3,9,10-substituted salts always exhibit a maximum in the 248–258-mμ range. On the other hand, dehydroprotoberberines with substituents at 2,3,10,11 show a maximum between 322 and 332 mμ. Additionally, in the 2,3,9,10 series, a $\lambda_{min}$ is present between 404 and 418 mμ, whereas the 2,3,10,11-substituted compounds show a $\lambda_{max}$ between 413 and 422 mμ. These facts can be turned to advantage in the structural elucidation of 5-hydroxyprotoberberine salts (*e.g.*, berberastine or thalidastine) which can be easily dehydrated to dehydro salts.[13,14]

## VI. Homotetrahydroprotoberberines

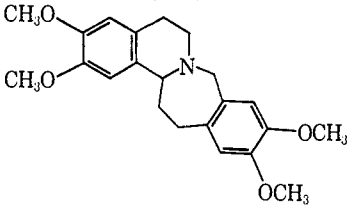
Homotetrahydroprotoberberines are derivatives of phenylethyltetrahydroisoquinoline. They have as yet to be isolated from natural sources, but so far three of them have been prepared in the laboratory. Their spectra bear a pronounced similarity to those of the tetrahydroprotoberberines.[18]




$\lambda_{max}$ 282, 230 sh (3.62, 4.15)




$\lambda_{max}$ 289, 230 sh (3.75, 4.13)




$\lambda_{max}$ 282, 226 sh, 210 (3.75, 4.20, 4.34)

(12) M. P. Cava, T. A. Reed, and J. L. Beal, *Lloydia*, **28**, 73 (1965).
(13) M. Shamma and B. S. Dudock, *Tetrahedron Letters*, 3825 (1965).
(14) M. M. Nijland, *Pharm. Weekblad*, **98**, 301, (1963).
(15) N. L. Dutta and C. K. Bradsher, *J. Org. Chem.*, **27**, 2213 (1962).
(16) C. K. Bradsher and N. L. Dutta, *ibid.*, **26**, 2231 (1961).
(17) C. K. Bradsher and N. L. Dutta, *J. Am. Chem. Soc.*, **82**, 1145 (1960).
(18) A. Brossi, A. I. Rachlin, S. Teitel, M. Shamma, and M. J. Hillman, *Experientia*, **24**, 766 (1968).