MAGNOFLORINE AND *N,N*-DIMETHYLLINDCARPINE

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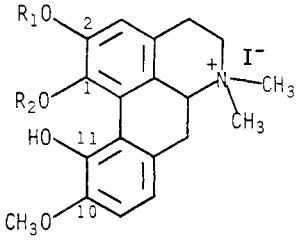
ABSTRACT.—Authentic magnoflorine and *N,N*-dimethyllindcarpine iodides were prepared and their spectral physical properties compared. The two compounds were easily distinguishable spectrally and by chromatography. A literature report of isolation of *N,N*-dimethyllindcarpine from *Menispermum canadense* L. was proven incorrect. The equivocal identification of a quaternary aporphine from *Caltha leptosepala* as either *N,N*-dimethyllindcarpine or magnoflorine was resolved in favor of the latter.

One of us isolated from *Caltha leptosepala* DC. (1) a small amount of a quaternary aporphine alkaloid iodide whose uv and ^{1}H nmr spectra were identical to those reported (2) for N,N-dimethyllindcarpine iodide, **1**, (isolated from *Menispermum canadense* L.). A definitive structural assignment could not be made because these data also closely matched those of magnoflorine **2**. Magnoflorine is a very common alkaloid which has been reported from a wide variety of plant



1: $R_1 = H$; $R_2 = CH_3$

2: $R_1 = CH_3$; $R_2 = H$

3: $R_1 = R_2 = CH_3$

genera. If **2** is not easily distinguishable from *N,N*-dimethyllindcarpine, many of the isolation reports for magnoflorine could be in error. As far as we are aware, the quoted paper (2) is the only report of isolation of *N,N*-dimethyllindcarpine as a natural product. It has been prepared (3) by methylation of natural *N*-methyllindcarpine, but was characterized only by melting point, optical rotation, and elemental analysis.

RESULTS

(+)-*N,N*-Dimethyllindcarpine iodide, **1**, was obtained by treatment of authentic (+)-*N*-methyllindcarpine with methyl iodide and had mp 188–190° (lit. mp 187° (3) and $[\alpha]^{25}$D+166°, c 0.71 MeOH (lit. $[\alpha]^{25}$D+151°). In the original preparation (3) of **1** iodide it was reported as the 1.5 H_2O hydrate. Our sample was recrystallized from abs ethanol and dried over P_2O_5 for two days at 110°/8mm, but ^{1}H nmr analysis indicated that it, too, must be a hydrate. Our (+)-*N*-

methyllindcarpine had been isolated (4) from *Glaucium flavum* Cr. var. *vestitum*. Its structure was proven by uv, ir, ^1H and ^{13}C nmr*, mp and mass spectrum. These correlated with data partially available from the literature (3, 5). In addition, the (+)-*N*-methyllindcarpine was converted quantitatively to (+)-isocorydine by O-methylation as described in (6).

(+)-Magnoflorine iodide, **2**, was obtained by selective O-demethylation of (+)-*N*-methylisocorydine iodide, **3**. The latter had been isolated from *Zanthoxylum coriaceum* A. Rich. (6), and its structure was assured by uv, ir, mass spectrum,

TABLE 1. Comparison of *N,N*-dimethyllindcarpine (**1**) and magnoflorine (**2**) iodides.

	1	**2**
R_f[a] 7:7:4:1 (MeOH/$CHCl_3$/$HCONH_2$/H_2O)	0.50	0.62
15:3:1 (MeOH/H_2O/NH_4OH)	0.13	0.29
Tlc visualization (short wave length)	dark purple-black with no fluorescence	purple-blue with fluorescence
(long wave length)	nil	bright, light blue fluorescence
UV, EtOH[b]	265, 270, 307	270, 276sh, 320
EtOH, H^-	227, 270, 304	225, 270, 304
EtOH, OH^-	330	275sh, 312, 330sh
^1H nmr DMSO-d_6 (60 MHz)	N-CH_3: 2.87, 3.26[c] OCH_3: 3.60, 3.76 Aromatics: 6.76 (1H), 6.93	N-CH_3: 2.98, 3.42 OCH_3: 3.88, 3.91 Aromatics: 7.02 (3H)[d]
DMSO-d_6+D_2O (60 MHz)	not taken	N-CH_3: 2.83, 3.28 OCH_3: 3.82 (6H) Aromatics: 6.90 (1H), 6.95 (2H)
DMSO-d_6 (100 MHz)	N-CH_3: 2.90, 3.31[e] OCH_3: 3.63, 3.80 Aromatics: 6.79 (1H), 6.93 (2H, center of AB quartet; δ_A=7.08, δ_B=6.86, J_{AB}=7Hz)	N-CH_3: 2.92, 3.36 OCH_3: 3.82, 3.86 Aromatics: 6.95 (1H), 6.97 (2H, center of AB quartet; δ_A=7.03; δ_B=6.91, J_{AB}=8Hz)
DMSO-d_6+TFA-d_1 (80 MHz)	N-CH_3: 2.93, 3.36 OCH_3: 3.63, 3.80 Aromatics: 6.80 (1H), 6.91 (2H)	not taken

[a]Si gel F254.
[b]In our hands, the direct EtOH uv of quaternary phenolic aporphines show variable behavior at long wave lengths. This is most likely due to the presence of zwitter ion forms. A consistent spectrum results with added acid.
[c]Partially obliterated by an H_2O peak.
[d]This absorption appears as a "singlet" but is broad at the base with a hint of side absorptions.
[e]Obliterated by a H_2O peak.

optical rotation, mp, and ^1H nmr in three different solvents including DMSO-d_6 with added base. The demethylation procedure was as follows: **3**, 473 mg, was dissolved in 4 ml HCl and heated at reflux for 4 hrs. To this solution, 4 mls of 1:1 water/methanol was added; some black solid which did not show a positive iodoplatinate test for alkaloids was removed by filtration. The remaining solution was evaporated to yield a light tan foam. Tlc (7:7:4:1 methanol/chloroform/formamide/water with iodoplatinate visualization) showed small alkaloidal

*^{13}C nmr data will be published in detail subsequently.

spots at the origin and solvent front, but only a large R_f 0.62 spot in between. Tlc of **1** in the same solvent gave only a spot at R_f 0.50. The foam was dissolved in methanol (2 mls) with a little potassium iodide and, after two precipitations, yielded 65 mg of pure magnoflorine iodide, **2**, mp 256° with prior softening at 243° (capillary). The capillary literature (7) mp is 249–250°. Tlc of the dark mother liquors showed **2** to be the major remaining component with several lower R_f trace spots also present. There is ample precedence in the literature for selective O-demethylation of the most hindered methoxy group. A close analog to our reaction is the selective removal of the methoxyl at C–1 in nornuciferine (8).

The ^{1}H nmr, uv, KBr ir and tlc (two solvent systems) for this isolated **2** were identical with those of the isolated (2) *Caltha leptosepala* alkaloid and with a supplied sample (9) from *Menispermum canadense*, which was purported to be a mixture of **1** and **2**. In particular, the KBr ir spectrum of the prepared **2** was superimposable (same position and intensity for 46 ir peaks) with the supplied sample. The KBr ir spectrum of **1** showed numerous peak intensity and position differences compared with our **2** (or the supplied sample from *M. canadense*).

Tlc, uv and ^{1}H nmr data for **1** and **2** are given in table 1.

DISCUSSION

Spectrally, the two most obvious distinctions between **1** and **2** are in the ^{1}H nmr; **1** shows a methoxyl absorption at 3.60, which is characteristic (10) of aporphines with methoxy groups at the hindered (1 or 11) positions. Methoxyls at positions 2 and 10, as in **2**, are generally in the 3.8–4.0 region. The downfield 6.76 aromatic singlet for the C–3 proton is also common for 1-methoxy-2-hydroxy aporphines (10).

The quaternary aporphine reported (1) from *Caltha leptosepala* is clearly magnoflorine, not *N*,*N*-dimethyllindcarpine. The latter remains unknown as a natural product since the data reported here for authentic **1** do not match those quoted (2) for **1** from *Menispermum canadense*. This leaves some question as to the identity of the substance from *M. canadense* which was erroneously assigned the structure of **1**. Since the purported **1** was isolated from mother liquors which had yielded **2**, it seems possible that these mother liquors simply gave additional **2**. Magnoflorine shows rather distinct ^{1}H nmr shifts when D_2O is added to DMSO-d_6 (see table 1), so perhaps an inadvertent nmr solvent change led to the misidentification.

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