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(+)-DECUMBENSINE AND (+)-EPI-α-DECUMBENSINE ARE NOT α-HYDROXYBENZYLTETRAHYDROISOQUINOLINES

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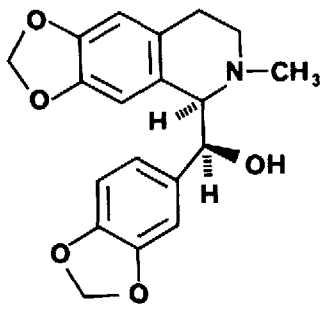
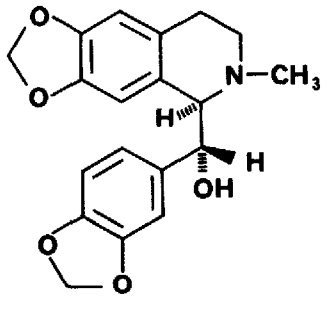
The diastereomeric α-hydroxybenzyltetrahydroisoquinolines 1 and 2 were synthesized from hydrastinine chloride (3) and dithian 4. They were not identical with the two alkaloids (+)-decumbensine and (+)-epi-α-decumbensine. (+)-Epi-α-decumbensine may be identical with the known phthalideisoquinoline hemiacetal (+)-corytensine (7).

The alkaloids: (+)-decumbensine and (+)-epi-α-decumbensine, have recently been isolated from Corydalis decumbens[1], and have been postulated to correspond to the α-hydroxybenzaltetrahydroisoquinolines 1 and 2.



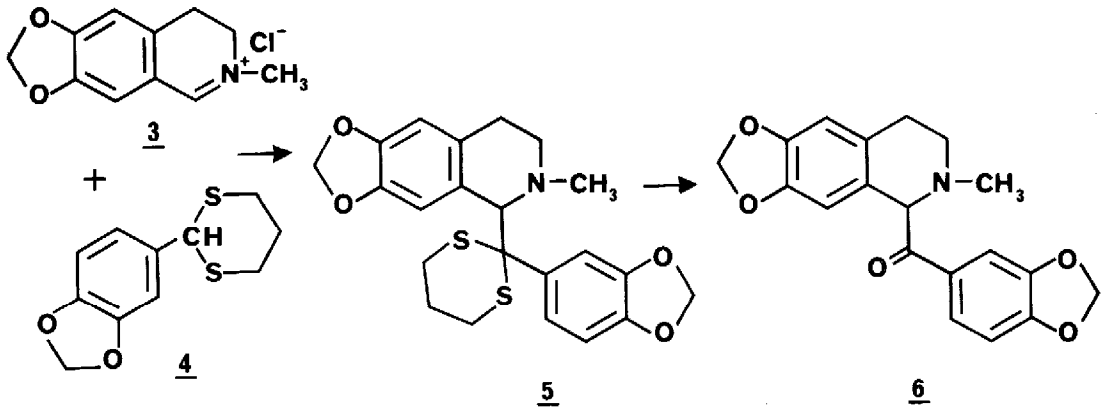
1



2

As a part of an ongoing program on the synthesis of isoquinoline alkaloids, we initiated a total synthesis of the aminoalcohols 1 and 2, for which our dithian strategy[2] seemed to be the method of choice (Scheme). Hydrastinine chloride (3) and piperonal propylenedithioacetal (4) were used as building blocks for the construction of the alkaloids carbon skeleton. Thus treatment of lithiated dithian 4 with iminium salt 3 gave adduct 5; $C_{22}H_{23}NO_4S_2$; m.p. 163-165°C (methanol), whose ^1H NMR spectrum in $CDCl_3$ at 100 MHz revealed the H-1 singlet at 3.95 ppm, besides the peaks characteristic of NCH_3, two methylenedioxy groups and five aromatic pro-

tons. Dithioketal 5 was hydrolyzed with bromine in acetic acid-hydrochloric acid to afford unstable ketone 6 (1670 cm^{-1}, KBr), which was reduced *in situ* with sodium borohydride in methanol, yielding the diastereomeric alcohols 1 and 2; $C_{19}H_{19}NO_5$, as racemates. These were separated on a silica gel column with benzene-ethyl ether (9:1). They spectrally showed satisfactory compliance with known α-hydroxybenzyltetrahydroisoquinolines[3,4].



Scheme

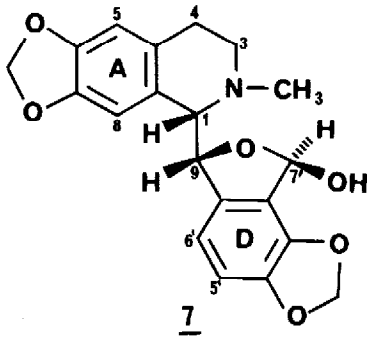
Compound 2 was eluted first; m.p. 89-90°C (ethyl ether); 3345 cm^{-1} (KBr). ^1H NMR spectrum revealed the presence of NCH_3 singlet at 2.56 ppm, four-proton multiplet between 2.25 and 3.32 ppm typical for reduced tetrahydroisoquinoline moiety, and two methylenedioxy signals at 5.81 and 5.96 ppm. One of the five aromatic protons was strongly shielded and appeared as a singlet at 5.54 ppm. The most important feature of the spectrum derived from the H-1 and H-α vicinal protons which gave rise to two one-proton doublets at 3.37 and 4.28 ppm with a coupling constant J=8.9 Hz, indicating the l-(threo) configuration[3-5].

Compound 1; m.p. 97-99°C (ethyl ether), exhibited spectral characteristics quite similar to those of 2 except for the ^1H NMR spectrum. The H-1 and H-α protons were responsible for two doublets at 3.70 and 4.99 ppm with a coupling constant J=4.0 Hz confirming the u-(erythro) configuration[3-5].

It is clear that 1 and 2 are not identical with the natural products (+)-decumbensine and (+)-epi-α-decumbensine.

We were not able to establish the structure of (+)-decumbensine and (+)-epi-α-decumbensine on the grounds of the published spectral data[1].Epi-

α-decumbensine is probably identical with the known phthalideisoquinoline hemiacetal (+)-corytensine (7)[6]. The ^{1}H NMR chemical shift assignments for (+)-corytensine (7) as well as those recently reported for (+)-epi--α-decumbensine[1] but adapted to a phthalideisoquinoline hemiacetal structure are listed in the Table. The similarity between the values is striking. We, of course, realize that (+)-corytensine (7) and our new tentative structure for (+)-epi-α-decumbensine have different molecular formulas and molecular wight. This difference, however, would be difficult to detect by mass spectroscopy because of the very facile cleavage of the central double benzylic bond in phthalideisoquinoline hemiacetals, resulting on the one hand in a massive base peak representing rings A and B. On the other hand, the molecular ion is hard to detect and identify.



7

Table. **^{1}H NMR data of (+)-corytensine (7) and (+)-epi-α-decumbensine**

Position Number	Corytensine	Epi-α-decumbensine
1	3.68	3.66
3	2.54* ddd (J=13.0;10.5;3.0 Hz)	2.99 ddd (J=12.4;3.8;2.0 Hz)
	3.00 dt (J=10.5;3.0 Hz)	3.18* ddd (J=15.3;12.4;3.1 Hz)
4	2.47 dt (J=15.5;3.0 Hz)	2.45 ddd (J=15.3;3.1;2.0 Hz)
	3.20* ddd (J=15.5;13.0;3.0 Hz)	2.53* dt (J=15.3;3.8 Hz)
5	6.60	6.59
8	6.71	6.07
9	5.29	5.27
5'	6.85 d (J=8 Hz)	6.82
6'	6.83 d (J=8 Hz)	6.82
7'	6.25	6.23
$-NCH_3$	1.96	1.95
$-OCH_2O-$(A)	5.90 d (J=1.7 Hz) 5.94 d (J=1.7 Hz)	5.91 m
$-OCH_2O-$(D)	6.04 d (J=1.5 Hz) 6.08 d (J=1.5 Hz)	6.04 m

*interchangeable

(+)-Decumbensine itself is reported to be diastereomeric with (+)--epi-α-decumbensine, and is thus also another probable phthalideisoquinoline hemiacetal.

With the probable assignment of phthalideisoquinoline hemiacetal structure to (+)-decumbensine and (+)-epi-α-decumbensine, it becomes evident that this relatively new class of phthalideisoquinolines[6-8] is fairly common in nature.

Acknowledgment. We wish to express our gratitude to professor Maurice Shamma and to Dr. Belkis Gözler of the Pennsylvania State University for valuable discussion, for directing our attention to the resemblance of (+)-epi-α-decumbensine to corytensine and for encouraging us to publish these results.

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