A 400 MHz ^{1}H NMR STUDY OF FOUR BASIC RESERPINE ALKALOIDS

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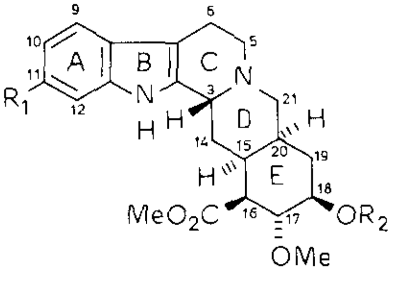
Abstract — The chemical shifts and most of the main coupling constants of four basic reserpine alkaloids 1 - 4 have been determined in a 400 MHz ^{1}H NMR study.

Introduction

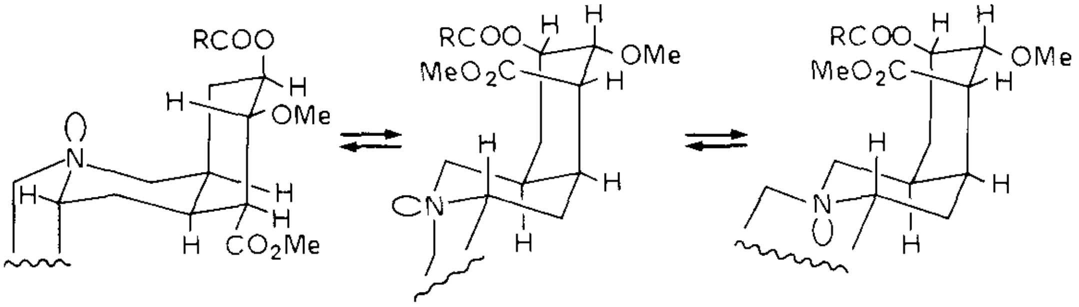
With the enormous progress in ^{1}H NMR instrumentation and techniques during the past few years, it is now often possible to recognize individual protons in the spectra of even complicated molecules. In the present communication we describe the results obtained in a 400 MHz ^{1}H NMR study of the four basic reserpine alkaloids *reserpine* 1, *rescinnamine* 2, methyl reserpate 3 and deserpidine 4. For earlier fragmentary ^{1}H NMR data on the reserpine alkaloids under investigation, see Ref. 1.



1 R_1 = OMe, R_2 = 3,4,5-trimethoxybenzoyl
2 R_1 = OMe, R_2 = 3,4,5-trimethoxycinnamoyl
3 R_1 = OMe, R_2 = H
4 R_1 = H, R_2 = 3,4,5-trimethoxybenzoyl

Stereochemical considerations

The generally accepted configuration for the four reserpine alkaloids under investigation is represented in formulae 1 - 4.[2] However, the stereochemical considerations are complicated by the fact that several conformations are possible. Considering as a first approximation only the conformations where the C ring is in the half-chair form and the D and E rings in the chair form, three conformations (a, b, c) (Scheme 1), due to *cis*-decalin type ring interconversion and nitrogen inversion,[3-4] are in theory possible.



a b c

Scheme 1.

Results and Discussion

Application of the normal consecutive single and multi-line decoupling techniques permitted all the protons in the four reserpine alkaloids 1 - 4 to be discovered and the coupling constants presented in Table 1 to be determined. As far as we know, this is the first time such has been achieved in the reserpine series.

The coupling constants found (Table 1) and the dihedral angles in different H-C-C-H systems, measured with the aid of Dreiding models, for the three conformations under consideration, clearly support the strong preponderance of conformer a in which all three ring E substitutients are equatorial. This is in good agreement with earlier stereochemical suggestions.[1,2] The contribution of conformer c is very small and that of conformer b can be considered negligible. It has been shown[5] that the *trans* diequatorial juncture (*cf*. C and D rings of conformer c) of quinolizine itself is 10.9 kJ/mol (2.6 kcal/mol) more stable than the *cis* juncture (*cf*. C and D rings of conformer b).

Table 1. ^{1}H NMR data of the four reserpine alkaloids 1 - 4.

Chemical shifts	1	2	3	4
H-3	4.48 br s	4.48 br s	4.42 br s	4.52 br s
H-5α	3.17 m	3.18 m	3.17 m	3.20 m
H-5β	3.17 m	3.18 m	3.17 m	3.20 m
H-6α	2.95 ddd	2.96 ddd	2.94 ddd	2.98 ddd
H-6β	2.49 br d	2.50 br d	2.50 br d	2.54 br d
H-9	7.33	7.34	7.32	7.48
H-10	6.78	6.78	6.77	7.12
H-11	-	-	-	7.17
H-12	6.84	6.85	6.84	7.32
H-14α	1.81 ddd	1.79 ddd	1.75 ddd	1.86 ddd
H-14β	2.29 ddd	2.32 ddd	2.23 ddd	2.33 ddd
H-15	2.05 dddd	2.03 dddd	1.97 dddd	2.04 dddd
H-16	2.69 dd	2.66 dd	2.52 dd	2.70 dd
H-17	3.89 dd	3.83 dd	3.52m	3.90 dd
H-18	5.05 ddd	4.95 ddd	3.55 m	5.07 ddd
H-19α	1.98 dddd	1.95 dddd	2.20 m	1.98 dddd
H-19β	2.34 m	2.26 m	2.25 m	2.34 m
H-20	1.89 ddd	1.87 ddd	1.75 br dd	1.90 br dd
H-21α	2.46 dd	2.46 dd	2.45 dd	2.47 dd
H-21β	3.05 dd	3.05 dd	3.02 dd	3.04 dd
CH_3O-	3.90 s	3.91 s	-	3.89 s
CH_3O-	3.90 s	3.91 s	-	3.89 s
CH_3O-	3.90 s	3.89 s	-	3.89 s
CH_3O-	3.81 s	3.84 s	3.83 s	-
CH_3O-	3.80 s	3.82 s	3.80 s	3.80 s
CH_3O-	3.49 s	3.53 s	3.58 s	3.49 s
H-2'	7.32 s	6.76 s	-	7.33 s
H-6'	7.32 s	6.76 s	-	7.33 s
H-α	-	6.37 d	-	-
H-β	-	7.63 d	-	-
NH	7.67 br s	7.67 br s	7.58 br s	7.83 br s

Table 1. continues

Coupling constants

1: $J_{3,14\alpha} \approx 3$ Hz; $J_{3,14\beta} = 5$ Hz; $J_{5\alpha,6\alpha} = 7$ Hz; $J_{5\alpha,6\beta} < 1$ Hz; $J_{5\beta,6\alpha} = 12$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 14$ Hz: $J_{14\alpha,15} = 3$ Hz; $J_{14\beta,15} = 14$ Hz; $J_{15,16} = 5$ Hz; $J_{15,20} \approx 3$ Hz; $J_{16,17} = 12$ Hz; $J_{17,18} = 9$ Hz; $J_{18,19\alpha} = 5$ Hz; $J_{18,19\beta} = 12$ Hz; $J_{19\alpha,19\beta} = 12$ Hz; $J_{19\alpha,20} = 4$ Hz; $J_{19\beta,20} = 12$ Hz; $J_{20,21\alpha} \approx 2$ Hz; $J_{20,21\beta} = 4$ Hz; $J_{21\alpha,21\beta} = 12$ Hz.

2: $J_{3,14\alpha} \approx 3$ Hz; $J_{3,14\beta} = 5$ Hz; $J_{5\alpha,6\alpha} = 7$ Hz; $J_{5\alpha,6\beta} < 1$ Hz; $J_{5\beta,6\alpha} = 12$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 14$ Hz: $J_{14\alpha,15} = 3$ Hz; $J_{14\beta,15} = 14$ Hz; $J_{15,16} = 5$ Hz; $J_{15,20} \approx 3$ Hz; $J_{16,17} = 12$ Hz; $J_{17,18} = 9$ Hz; $J_{18,19\alpha} = 5$ Hz; $J_{18,19\beta} = 12$ Hz; $J_{19\alpha,19\beta} = 12$ Hz; $J_{19\alpha,20} = 4$ Hz; $J_{19\beta,20} = 12$ Hz; $J_{20,21\alpha} \approx 2$ Hz; $J_{20,21\beta} = 4$ Hz; $J_{21\alpha,21\beta} = 12$ Hz.

3: $J_{3,14\alpha} \approx 3$ Hz; $J_{3,14\beta} = 5$ Hz; $J_{5\alpha,6\alpha} = 7$ Hz; $J_{5\alpha,6\beta} < 1$ Hz; $J_{5\beta,6\alpha} = 12$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 14$ Hz; $J_{14\alpha,15} = 3$ Hz; $J_{14\beta,15} = 14$ Hz; $J_{15,16} = 5$ Hz; $J_{15,20} \approx 3$ Hz; $J_{16,17} = 12$ Hz; $J_{19\alpha,20} \approx 4$ Hz; $J_{20,21\alpha} \approx 2$ Hz; $J_{20,21\beta} = 4$ Hz; $J_{21\alpha,21\beta} = 12$ Hz.

4: $J_{3,14\alpha} \approx 3$ Hz; $J_{3,14\beta} = 5$ Hz; $J_{5\alpha,6\alpha} = 7$ Hz; $J_{5\alpha,6\beta} < 1$ Hz; $J_{5\beta,6\alpha} = 12$ Hz; $J_{6\alpha,6\beta} = 16$ Hz; $J_{14\alpha,14\beta} = 14$ Hz; $J_{14\alpha,15} = 3$ Hz; $J_{14\beta,15} = 14$ Hz; $J_{15,16} = 5$ Hz; $J_{15,20} \approx 3$ Hz; $J_{16,17} = 12$ Hz; $J_{17,18} = 9$ Hz; $J_{18,19\alpha} = 5$ Hz; $J_{18,19\beta} = 12$ Hz; $J_{19\alpha,19\beta} = 12$ Hz; $J_{19\alpha,20} \approx 4$ Hz; $J_{19\beta,20} = 12$ Hz; $J_{20,21\alpha} \approx 2$ Hz; $J_{20,21\beta} = 4$ Hz; $J_{21\alpha,21\beta} = 12$ Hz.

Spectra were run in $CDCl_3$ at 400 MHz. Values are in ppm (TMS = 0), s, singlet, d, doublet, m, multiplet, br, broad. The sample temperatures used were 20°C for compounds 1, 2, and 4, and 56°C for compound 3. The coupling constant between the cinnamic protons (- CH = CH -) in compound 2 is 17 Hz. The coupling constants between the aromatic protons are not included.

Supplementary evidence for the preponderance of conformer a is furnished by the H-3 chemical shifts (Table 1).[1,4]

The ^{1}H NMR data presented should be useful in the determination of similar reserpine alkaloid structures. We would underline, however, that caution is *needed in the application of the present* results to the isoreserpine series where the conformational conditions are very different.

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