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LOUISFIESERONE, AN UNUSUAL FLAVANONE DERIVATIVE FROM *INDIGOFERA SUFFRUTICOSA*, Mill.

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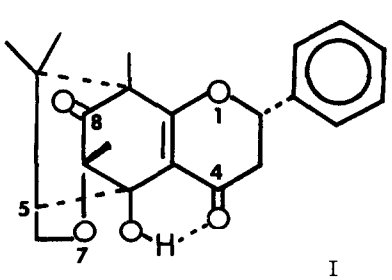
Indigofera suffruticosa, Mill., 'jiquelite', is a shrubby leguminosae which has found use in Mexico as a folk medicine to treat convulsions and dizziness.[1] The species *Indigofera tintori*, the source of indigo, and *Indigofera endecaphylla* have been studied extensively[2]; however, there is little information on the compounds or phytochemistry of *Indigofera suffruticosa*.

Indigofera suffruticosa, Mill. was collected near Monterrey, Mexico and the whole plant (roots and aereal parts) was extracted with petroleum ether. Upon concentration, the petroleum ether extract yielded a precipitate (6 g) from which 2.447 g of a pale yellow solid were obtained by column chromatography over silica gel. The rest of the extract was percolated through a silica gel column yielding β-sitosterol (200 mg) and a second crop (110 mg) of the pale yellow solid louisfieserone (I), [2S,4bS,5R,7aR,9S]-5,6,7a,9-tetrahydro-4b-hydroxy-7a,9,10,10-tetramethyl-2-phenyl-5,9-methano-2H-furo[2,3-f][1]benzopyran-4,8(3H)-dione.



I

Louisfieserone exhibits the following properties: $C_{22}H_{24}O_5$, m.p. 217°C. $[\alpha]_{589}^{25}$, +379°; $[\alpha]_{578}$, +405°; $[\alpha]_{546}$, +509°; $[\alpha]_{436}$, +1616°; $[\alpha]_{365}$, +60°; conc. 2 mg/ml $CHCl_3$. IR: ν_m, 3300 (OH), 3020, 2920, 1724 (C=O), 1613, 1587 (aromatic ring), 1450, 1429 (CH_2), 1375, 1365 (gem $(CH_3)_2C$), 1260, 1124, 1076, 1002, 964, 819, 763, 629 cm^{-1}. UV: λ_m(EtOH), 207 (46,400), 285 (30,600), 329 (9,100) nm. No shifts were observed upon addition of $AlCl_3$, HCl or sodium acetate.[3] λ_m(EtOH-CH_3ONa), 207 (60,800), 280 (53,100), 303sh (45,500), 383 (57,400). MS, m/e (relative abundance). 368 (4), 353 (1), 341 (27), 340 (13), 322 (15), 307 (12), 288 (6), 286 (8), 284 (6), 278 (6), 270 (6), 265 (5), 221 (20), 208 (6), 193 (5), 177 (6), 173 (16), 164 (5), 163 (6), 161 (6), 153 (6), 150 (55), 144 (6), 142 (4), 133 (5), 130 (6), 125 (7), 107 (7), 105 (10), 103 (30), 97 (27), 94 (6), 91 (18), 83 (17), 81 (11), 79 (16), 77 (32), 72 (5), 69 (41), 66 (3), 57 (5), 43 (100), 41 (84), 28 (7). Louisfieserone gave a negative ferric chloride test and could not be acetylated even under drastic conditions. Elemental analasis. Found: C, 71.58; H, 6.56; O, 21.87. Calcd: C, 71.72; H, 6.57; O, 21.71

The PMR spectrum showed four methyl resonances at 1.02, 1.05, 1.24 and 1.40 ppm, a sharp one-proton singlet at 7.0 which was invariant to concentration, five phenyl protons as a broad singlet at 7.44 ppm and two three-proton ABX patterns. The ABX patterns were interpreted through use of spin decoupling and computer simulation techniques and are described below. A suitable molecular structure could not be assigned on the basis of the chemical and physical data.

A very poor quality single crystal was used to collect data on a Syntex $P2_1$ X-ray diffractometer (a = 10.248(4), b = 27.02(1), c = 6.902(2) Å. Space group $P2_12_12_1$.). The structure was solved by direct methods[4]; however, the poor data set refined only to an R factor of 13%. The X-ray determined structure, Figure 1[5], is consistent with all physical and chemical data. The hydroxyl proton is intramolecularly hydrogen bonded to the C(4) carbonyl oxygen atom which is consistent with the invariant proton signal at 7.0 ppm. The two ABX patterns are consistent with the assignment of $\delta H_{3\alpha}$ 2.95, $\delta H_{3\beta}$ 2.79 and $\delta H_{2\beta}$ 5.45 with $J_{3\alpha,3\beta}$ -17.1 Hz, $J_{2\beta,3\alpha}$ 13.5 Hz and $J_{2\beta,3\beta}$ 3.5 Hz and δH_5 2.04, $\delta H_{6\beta}$ 4.22 and $\delta H_{6\beta}$ 3.89 with $J_{6\alpha,6\beta}$ -9.0 Hz, $J_{5,6\alpha}$ 4.0 Hz and $J_{5,6\beta}$ 0.5 Hz. The magnitudes of the coupling interactions are compatible with H(2β)C(2)C(3)-

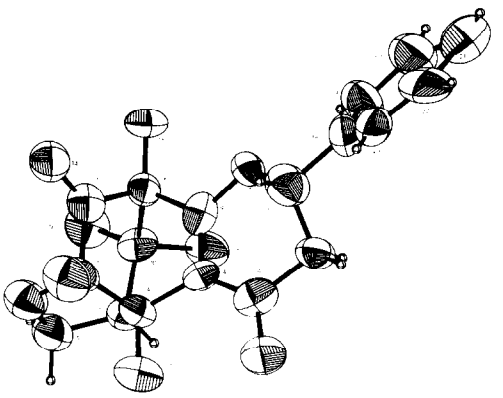


Figure 1. ORTEP drawing of louisfieserone.[5]

$H(3_\alpha)$ and H(2β)C(2)C(3)H(3β) torsion angles of 179° and -66° and H(5)C(5)C(6)-H(6α) and H(5)C(5)C(6)H(6β) torsion angles of -68° and 41°. A comparison of the simulated and experimental spectra for the ABX portion of the spectrum is presented in Figure 2.

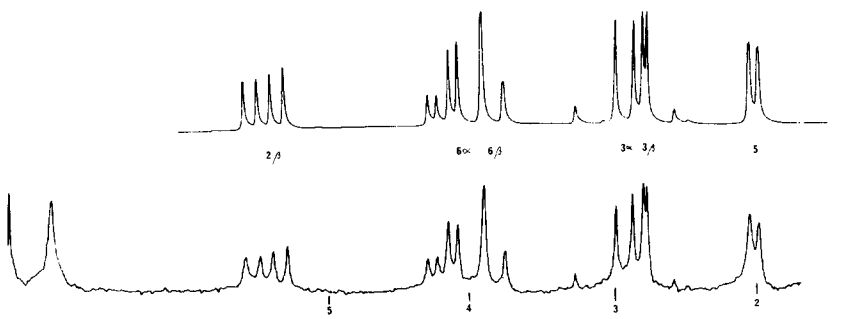


Figure 2. Simulated and experimental spectra for the ABX patterns in louisfieserone.

The C-13 magnetic resonance spectrum was determined at 15 MHz and assigned by off-resonance decoupling and by partially relaxed spectra: 203.4(8), 192.4 (4), 171.9(9a), 136.6, 129.0 and 126.1 (phenyl), 106.8(4a), 82.0(2), 81.2(4b or 7a), 80.7(4b or 7a), 68.3(6), 58.7(10), 55.6(5), 42.2(3), 37.9(9), 25.8(13),

21.6(15), 13.6(16), 6.5(17). The two upfield methyl carbon atoms relax more slowly than the two down-field methyl carbon atoms and are assigned as C(16) and C(17) on the basis of steric hinderance.

The formation of louisfieserone can be visualized as the addition of an isoprene unit to the para positions of an appropriately oxidized 6,8 dimethyl flavanone. This is a very unusual pattern of isoprene addition, particularly with the resultant loss of conjugation and the subsequent development of ring strain. Louisfieserone has shown antibiotic activity against gram positive and gram negative bacteria and inhibits the sprouting and growth of seeds of dicotyledons.[6]

Acknowledgements

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