SYNTHESIS OF DUTADRUPINE

François Tillequin, Geneviève Baudouin and Michel Koch
Laboratoire de Pharmacognosie, Faculté des Sciences Pharmaceutiques et
Biologiques de l'Université René Descartes, 4 Avenue de l'Observatoire
F - 75006 PARIS (France)

Abstract --- Dutadrupine (3) was synthetized by Claisen rearrangement of
7-(1,1-dimethylpropyn-1-oxy)-4-methoxyfuro[2,3b]quinoline (2) obtained
by condensation of 7-hydroxy-4-methoxyfuro[2,3b]quinoline (1) with 3-
chloro-3-methylbutyne.

In a previous paper¹, we reported the isolation from Dutaillyea drupacea (Rutaceae)
and the structure determination of a novel alkaloid, dutadrupine (3). As a further
contribution to the chemistry of new caledonian plants, we report here a simple
synthesis of this compound by condensation of 7-hydroxy-4-methoxyfuro[2,3b]-quino-
line (1)² with 3-chloro-3-methylbutyne³,⁴ followed by Claisen rearrangement of the
obtained propargyl ether (2)⁵-¹⁰.
To a solution of 7-hydroxy-4-methoxyfuro[2,3b]quinoline (1) (0.86 g) in dry acetone (25 ml) containing potassium carbonate (2 g) and potassium iodide (2 g) was added 3-chloro-3-methylbutyne (5 g). The reaction mixture was refluxed for 72 h and then evaporated. The solid residue was extracted with chloroform. Concentration of the chloroform solution gave a gum, the tlc analysis of which showed two major products, easily isolated by column chromatography (silica gel, eluent: benzene-ethyl acetate 9:1). The first one was the expected propargyl ether (2) (0.39 g, yield: 35%). The second was identified to dutadrupine (3) (0.31 g, yield: 28%), identical with the natural product, the Claisen rearrangement having surprisingly occurred at relatively low temperature.

7-(1,1-dimethylpropyn-1-oxy)-4-methoxyfuro[2,3b]quinoline (2): mp 144-145°C; UV (EtOH): 247, 308, 320, 332 (sh) nm; IR (KBr): 3240, 2995, 2950, 1625, 1590, 1460, 1380, 1295, 1150, 1090, 980, 865, 755, 725 cm⁻¹; MS m/z (%): 281 (M⁺) (18), 280 (6), 266 (39), 251 (9), 215 (100), 200 (20), 172 (10); "H-NMR (CDCl₃): δ = 8.03 (1H, d, J = 9Hz, H-5), 7.42 (1H, d, J = 2.5Hz, H-6), 5.67 (1H, d, J = 10Hz, H-3'), 4.40 (3H, s, O-Me), 2.57 (1H, s, -C=CH₂), 1.72 (6H, s, CMe₂).

Dutadrupine (3): mp 139-140°C; UV (EtOH): 249 (sh), 257, 279 (sh), 293 (sh), 315, 331, 350, 359 nm; IR (KBr): 2980, 2870, 1635, 1595, 1375, 1280, 1130, 1100, 990, 825, 780, 750 cm⁻¹; MS m/z (%): 281 (M⁺) (20), 267 (18), 266 (100), 251 (28); "H-NMR (CDCl₃): δ = 8.00 (1H, d, J = 9Hz, H-5), 7.51 (1H, d, J = 3Hz, H-4), 6.98 (1H, d, J = 3Hz, H-6), 6.93 (1H, d, J = 9Hz, H-6), 5.67 (1H, d, J = 10Hz, H-3'), 4.40 (3H, s, O-Me), 2.51 (6H, s, CMe₂).

References and Notes
2. For synthesis and/or natural sources of this compound, see: