

Synthesis of
4-Hydroxy-3-methylene-2,2,10-trimethyl-2,3-dihydrofuro[3,2-*b*]-
acridin-5(10*H*)-one, a New Synthetic Analog of Noracronycine

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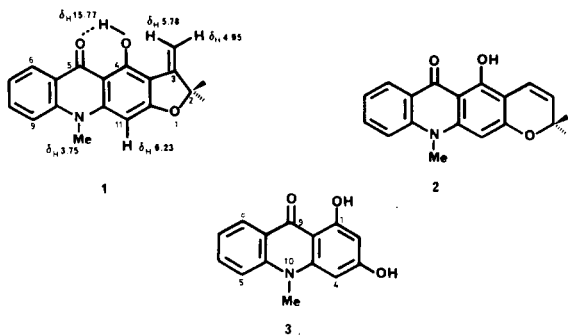
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A new tetracyclic acridinone, 4-hydroxy-3-methylene-2,2,10-trimethyl-2,3-dihydrofuro[3,2-*b*]acridin-5(10*H*)-one (**1**), has been synthesized. The linear orientation of the furan ring was confirmed by an nOe experiment.

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Compounds belonging to the class of acridinones, show an array of biological activities and has been the subject of various pharmacological/biological investigations [1-7]. Continuing our synthetic studies on bioactive acridinones, we have now performed the synthesis of hitherto unknown **1**, an isomeric compound of isonoracronycine (**2**) [8], by a single step.

The major product, isolated by column chromatography, of the reaction between 1,3-dihydroxy-10-methyl-9(10*H*)-acridinone (**3**) and 3-bromo-3-methyl-2-butanone, showed in its ¹H nmr spectrum a singlet at δ 6.23 for one proton, indicating that C-2 or C-4 of the acridinone nucleus has been substituted. The molecular formula, C₁₉H₁₇NO₃, and the presence of two 1H singlets in the vinylic region (δ 5.78 and 4.95) and 6H singlet at δ 1.55 in the ¹H nmr spectrum together with the above information, suggested the proposed structure **1** or the structure with angular orientation of the five membered ring. Confirmation of the structure, of this new synthetic analog, as **1** and assignment of all the ¹H nmr signals to respective protons were achieved by nOe experiments. The nOe difference spectrum at 300 MHz showed enhancements for *H*-9 and *H*-11 signals upon irradiation of *N*-Me signal at δ 3.75, confirming the linear orientation of the furan ring. Furthermore, irradiation of one of the vinylic proton signals (δ 5.78) showed enhancements for signals due to *O*-*H* and the other vinylic *H* (δ 4.95), while enhancement of the signal at δ 5.78 was observed when irradiation was carried out at δ 4.95. Assignments of the ¹³C nmr signals were possible, by comparison of reported data for acridinones [9,10].



EXPERIMENTAL

General Procedures.

Melting points were determined on a Kofler hot stage apparatus and are uncorrected. Ir spectra were recorded for potassium bromide discs on a Pye Unicam SP 3-200 ir spectrophotometer. ¹H nmr and ¹³C nmr spectra were recorded in deuteriochloroform with TMS as internal reference on Bruker WM 300 spectrometer. Mass spectra were obtained on a Varian MAT 44S instrument at 70 eV. Silica gel 60 GF₂₅₄ (Merck 7730) was used for column chromatography under medium pressure. Light petroleum had bp 30-40°.

4-Hydroxy-3-methylene-2,2,10-trimethyl-2,3-dihydrofuro[3,2-*b*]acridin-5(10*H*)-one (**1**).

A solution of 1,3-dihydroxy-10-methyl-9(10*H*)-acridinone (**3**, 0.10 g) in anhydrous acetone (10 ml) was refluxed with 3-bromo-3-methyl-2-butanone (0.3 ml) and anhydrous potassium carbonate (0.10 g) for 2 hours. Reaction mixture was filtered, solids were washed with anhydrous acetone and dichloromethane. The combined organic solutions were evaporated and chromatographed over column of silica gel under medium pressure, with dichloromethane as the eluant, to obtain **1** as crystalline yellow solid (0.075 g, 59%), golden-yellow needles from dichloromethane/light petroleum, mp 214-215°; ir: ν 3600-3200 br, 3000, 2960, 1645, 1625, 1605, 1570, 1555, 1505, 1455, 1445, 1365, 1325, 1270, 1210, 1140, 1075, 1030, 1005, 955, 930, 880, 860, 820, 740, 640 cm⁻¹; ¹H nmr: δ (300 MHz) 15.77 (1H, s, *OH*), 8.41 (1H, dd, *J* = 8 and 1.5 Hz, 6-*H*), 7.68 (1H, ddd, *J* = 8.5, 7.0 and 1.5 Hz, 8-*H*), 7.45 (1H, brd, *J* = 8.6 Hz, 9-*H*), 7.26 (1H brt, *J* = 8.4 Hz, 7-*H*), 6.23 (1H, s, 11-*H*), 5.78 (1H, s, =*CH*), 4.95 (1H, s, =*CH*), 3.75 (3H, s, *N*-*CH*₃), 1.55 (6H, s, 2 × *CH*₃); ¹³C nmr: δ (75.46 MHz), 180.31 (C-5), 166.98 (C-11a), 161.61 (C-4), 148.92 (C-3), 145.87 (C-10a), 141.59 (C-9a), 133.62 (C-8), 126.14 (C-6), 121.40 (C-7), 120.52 (C-5a), 114.40 (C-9), 105.38 (= *CH*₂), 105.11 (C-4a), 101.96 (C-3a), 91.35 (C-11), 85.23 (C-2), 34.10 (*N*-*Me*), 28.30 (2 × *Me*); ms: *m/z* (relative intensity) 307 (*M*⁺, 90%), 292 (100), 277 (8), 264 (14), 254 (12), 249 (10), 236 (5), 225 (8), 191 (8), 178 (5), 167 (5), 154 (10), 150 (8), 146 (18), 140 (13), 132 (10), 115 (10), 102 (11), 96 (8), 89 (14), 77 (41), 75 (32), 63 (28), 51 (36).

Anal. Calcd. for C₁₉H₁₇NO₃: C, 74.24; H, 5.58; N, 4.56. Found: C, 74.02; H, 5.50; N, 4.51.

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