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SYNTHESIS OF (±)-RUTACRIDONE[1]

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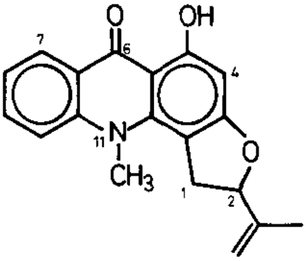
Abstract --- (±)-Rutacridone (**1**) was synthesized by condensation of 1,3-dihydroxy-10-methylacridone (**3**) with isoprene dibromide. As by-product the linear isomer (±)-isorutacridone (**2**) was also obtained.

The alkaloid (−)-rutacridone was isolated[2] some time ago as the first member of a series of dihydrofuroacridone derivatives from the roots of Ruta graveolens L. (Rutaceae). Its structure as **1** was established[2-4] on the basis of spectroscopic evidences. Recently Gonzales et al.[5] have isolated the same alkaloid from Ruta chalepensis L. and proposed the alternative linear structure **2** for it.

As a further contribution to the synthesis of acridone alkaloids[6], we report here a simple one-step synthesis of (±)-rutacridone (**1**) by condensation of 1,3-dihydroxy-10-methylacridone (**3**) with 1,4-dibromo-2-methyl-but-2-ene (isoprene dibromide), using the procedure of Nickl[7,8] to obtain isopropenyldihydrobenzofuran derivatives. Two isomeric products ($C_{19}H_{17}NO_3$, M^+ 307) were obtained. Comparison of their ^{1}H-NMR, and especially their ^{13}C-NMR spectra showed that in one of the isomers the resonance of the N-methyl and furan-methylene groups are shifted to lower fields. Earlier, we have demonstrated, that such a shift of N-methyl signal is caused by substitution in position 4 of a 10-methylacridone molecule[6,9]. Thus this isomer must have an angular anellation. As the latter showed identical IR, ^{1}H-NMR, ^{13}C-NMR, and mass spectra with the naturally occurring (−)-rutacridone, the angular structure of the naturally alkaloid is thus determined beyond any doubt.

The other isomeric product, consequently, should have a linear anellation corresponding to structure 2, for which the name (±)-isorutacridone is proposed.

A solution of 1,3-dihydroxy-10-methylacridone (3) (600 mg) in methanol (10 ml) containing sodium (114.5 mg) was treated with 1,4-dibromo-2-methyl-but-2-ene (568 mg). After standing 4 days at room temperature, the mixture was diluted with water (50 ml) and extracted with ethyl acetate.



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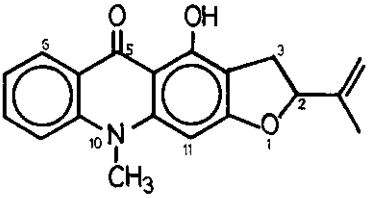

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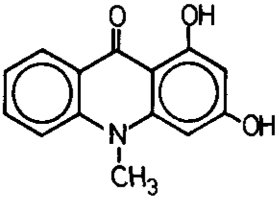

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Concentration of the ethyl acetate solution gave a gum (452 mg), that was resolved by tlc (silica gel, eluent toluene-ethyl acetate 4:1) into (±)-isorutacridone (2) (highest R_f, 40 mg, yield 5.2 %), (±)-rutacridone (1) (middle R_f, 118 mg, yield 15.4 %), and unreacted 1,3-dihydroxy-10-methylacridone (3) (lowest R_f, 49 mg).

(±)-Rutacridone (1) has mp. 145-147°C; IR (KBr): 3420 (broad, OH), 3082 (=CH_2), 1635 cm^{-1} (CO); ^{1}H-NMR ($CDCl_3$): δ=1.78 (3H, s, CH_3), 3.59 (2H, m, furan CH_2), 3.80 (3H, s, NCH_3), 4.95 and 5.10 (2H, m, exocyclic CH_2), 5.11 (1H, m, H-2), 6.09 (1H,s,H-4), 7.13 (1H, m, H-8), 7.23 (1H, bd, J=8.4 Hz, H-10), 7.58 (1H, m, H-9), 8.21 (1H, ddd, J=8.0, 1.2 and 0.6 Hz, H-7), 15.20 (1H, s, OH); ^{13}C-NMR ($CDCl_3$): δ=17.11 (CH_3), 37.16 (C-1), 37.71 (NCH_3), 86.07 (C-2), 92.40 (C-4), 99.68 (C-11b), 105.95 (C-5a), 112.74 (CH_2), 114.53 (C-10), 120.87 (C-6a), 121.39 (C-8), 126.04 (C-7), 133.74 (C-9), 143.16 (C-10a, C-11a, H_3C-$\underline{C}$=CH_2), 166.07 (C-5), 167.27 (C-3a), 180.63 (C-6); MS (80 eV): m/e (% rel. int.)= 307 (M^+, 100), 292 (38), 278 (22), 264 (22), 250 (13), 239 (17),236 (15), 211 (12), 180 (7), 146 (9), 107 (12), 89 (8), 77 (24).

(±)-Isorutacridone (2) has mp. 168-170°C; IR (KBr): 3440(broad, OH), 1660 cm^{-1} (CO);

^{1}H-NMR ($CDCl_3$): δ=1.78 (3H, t, J=0.6 Hz, CH_3), 3.18 (2H, m, furan CH_2), 3.72 (3H, s, NCH_3), 4.94 and 5.1i (2H, m, exocyclic CH_2), 5.31 (1H, t, J=9.6 Hz, H-2), 6.27 (1H, s, H-11), 7.23 (1H, m, H-7), 7.41 (1H, bd, J=8.0 Hz, H-9), 7.67 (1H, m, H-8), 8.39 (1H, ddd, J=7.8, 1.8 and 0.6 Hz, H-6), 15.07 (1H, s, OH); ^{13}C-NMR ($CDCl_3$): δ=17.09 (CH_3), 30.71 (C-3), 34.25 (NCH_3), 85.20 (C-2), 88.00 (C-11), 105.06 (C-3a), 105.61 (C-4a), 112.43 (CH_2), 114.45 (C-9), 120.91 (C-5a), 121.34 (C-7), 126.54 (C-6), 133.62 (C-8), 141.97 (C-9a), 143.53 (C-10a, $H_3C\text{-}\underline{C}{=}CH_2$), 160.07 (C-4), 167.32 (C-11a), 180.35 (C-5); MS (80 eV): m/e (% rel. int.)= 307 (M^+, 64), 292 (100), 290 (9), 277 (7), 266 (8), 264 (9), 254 (7), 236 (3), 180 (3), 154 (7), 146 (8), 115 (5), 89 (5), 77 (15).

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