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An 3-Indolyl-imidazol-4-one from the Tunicate *Dendrodoa grossularia*.

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Abstract: *A new compound, possessing an unusual 4H-imidazole ring was isolated; structure elucidation was performed using spectral analysis and confirmed by synthesis.*

Only few representatives of unsubstituted 4*H*-imidazoles are known (1) and to our best knowledge this paper is the first report of an 4*H*-imidazol-4-one as a natural as well as a synthetic product.

3-Indolyl-4*H*-imidazol-4-one was isolated from *Dendrodoa grossularia*, a Tunicate collected in Brittany, which already provided some interesting indole derivatives (2-4). The dichloromethane extract of *D.grossularia* obtained either from lyophilized or wet animals (5) subjected to chromatography on a silica gel column ($CHCl_3$ with 0 to 100 % acetone) furnished a fraction eluted with $CHCl_3$-acetone, 2:8 which contained a yellow pigment. Further purification on silica gel ($CHCl_3$-MeOH, 9:1), then LH 20 (MeOH-$CHCl_3$, 5:4) afforded 1 as an orange powder which cristallized in MeOH as orange needles, yield 0.03 % dry weight, m.p. 356-358°C, u.v. (EtOH) λ_{max}: 213 (15250), 261 (7140), 284 (6010), 343 (5120), 430 (5360) nm, i.r.: 1640, 1610, 1580 cm^{-1}.

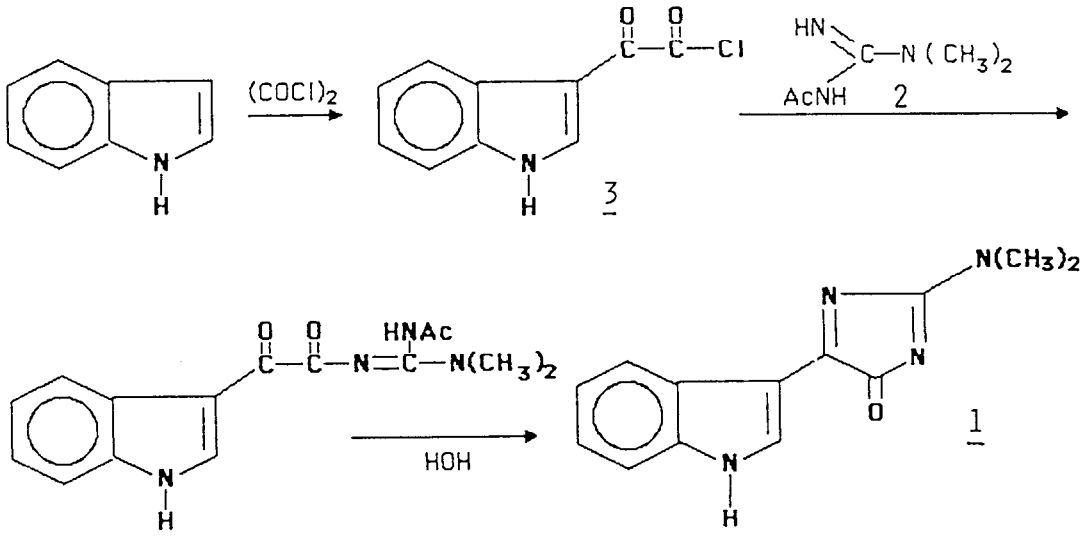
The empirical formula found by h.r.m.s. was $C_{13}H_{12}N_4O$: M^+ 240.101 (calcd. 240.1011). The ^1H n.m.r. spectrum (DMSO-d_6): δ 8.83 (d,1H), 8.24 (m,1H), 7.50 (m,1H), 7.24 (m,2H), 3.54 (s, 3H), 3.33 (s,3H) was indicative of a 3-substituted indole and of a $N(CH_3)_2$ group. More structural information was gained by ^{13}C n.m.r. (DMSO-d_6): δ 182.26 (s,C-11), 180.89 (s,C-13), 167.79 (s,C-10), 138.14 (s,C-8), 137.01 (d,C-2), 125.09 (s,C-9), 123.66 (d,C-6), 122.40 (d, C-4), 122.00 (d,C-5), 112.40 (d,C-7), 104.48 (s,C-3), 37.16 (q,$N(CH_3)_2$). These data confirmed the presence of an indole moiety and of 3 (C=N or C=O).

Although a carbonyl was detected in the ^{13}C n.m.r. spectrum, the parent ion observed in mass spectrometry: *m/e* 142, $C_9H_6N_2$ (h.m.r.s.) (6) indicates that the indole was substituted at the 3-position by a C=N group. Therefore the sole possible structure was 1.

A synthetic approach of 1 seemed rather easy, and in fact, the most delicate step was the obtention of the suitably protected dimethylguanidine 2. For this purpose, free dimethylguanidine, obtained from the chlorhydrate by elution with ethanol through an Amberlite IRA 400 column (7) was acetylated by ethyl acetate (7), M^+ 129, ^1H n.m.r.: 1 $COCH_3$ and 1 $N(CH_3)_2$.

The indolyl-oxalyl chloride 3 was prepared according to (8), dissolved in acetonitrile solution and added to a suspension of 2 in acetonitrile; the mixture was stirred 1 h at room temperature. After evaporation of acetonitrile,the crude product,when hydrolysed by addition of H_2O, spontaneously cyclise into 1,which was extracted by ethyl acetate. After purification on a silica gel column, synthetic 1 was identical to the natural sample in all respects: m.p.,

^{1}H n.m.r., ^{13}C n.m.r. Yield: 64 % from indole (Scheme 1).



SCHEME 1

This indolyl-imidazol-4-one in solution is sensitive to light, and the rearrangement product(s) will be described later.

It is noteworthy that 1 is related to the sponge metabolites aplysinopsin and methylaplysinopsin (9-11), this latter being a potential antidepressant (12).

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5 - Wet animals were extracted by $CHCl_3$-MeOH (1/1), the organic layer was decanted and the solvent distilled off in vacuo, and the aqueous suspension obtained extracted with dichloromethane. This method provides a better yield for polar products as 1.

6 - HRMS: Found 142.0528, calcd. for $C_9H_5N_2$: 142.0530; found 98.0476, calcd. for $C_4H_6N_2O$: 98.0480.

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