Short Communications

Hermidin, a chromogen from *Mercurialis perennis* L.

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3 October 1983

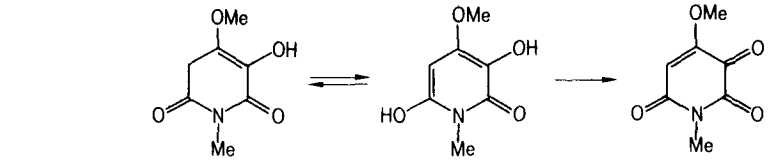
Summary. Aqueous extracts of *Mercurialis perennis* L. contain a chromogen (hermidin) shown to be 3,6-dihydroxy-4-methoxy-1-methyl-2-pyridinone (**2**). The transient blue color formed by atmospheric oxidation of these extracts is due to a radical-anion and the final yellow-brown color is due to dimeric oxidation products.

The green plant *Mercurialis perennis* L. (belonging to the Euphorbiaceae) contains a chromogen which is a powerful reducing agent and which is most abundant in the young and vigorously growing plant. Colorless underground stems when cut or bruised develop a transient blue or yellow color[2]. The plant is said to be poisonous and to have diuretic activity; and animals fed on it produce red urine and excreta[3].

Fresh plant material collected in spring when extracted under nitrogen with water at 45 °C for 1 h yields an almost colorless solution which when shaken with air rapidly turns deep blue, then green, and finally yellow-brown. Haas and Hill[2] named the colorless chromogen hermidin, the transient blue compound cyanohermidin, and the yellow-brown compound chrysohermidin, and showed that the color changes were independent of enzyme action.

By extraction of the aqueous solution with chloroform in the presence of sodium dithionite it was possible to isolate a colorless, crystalline compound (*A*), which sublimes at 110 °C/0.01 mm (Found: C, 49.18; H, 5.18; N, 8.25% $C_7H_9NO_4$ requires C, 49.12; H, 5.30; N, 8.18%); M^{+}171.0534, $C_7H_9NO_4$ requires 171.0532; δ ($CDCl_3$) 3.2 (3H, s, NMe), 3.5 (2H, s, CH_2), 4.05 (3H, s, O–Me), 5.75 (1H, broad s, OH); δ (CF_3CO_2H), 3.9 (3H, s, N–Me), 4.1 (3H, s, O–Me), 6.5 (1H, s, –CH=). As proved by synthesis (below) this crystalline compound is 5-hydroxy-4-methoxy-l-methylpyridine-2,6 (1*H*, 3*H*)-dione (**1**), although in water or CF_3CO_2H it exists as the tautomeric form 3,6-dihydroxy-4-methoxy-l-methyl-2-pyridinone (**2**).

Dimethyl 3-methoxypent-2-enedioate reacted with methylamine to afford 4-methoxy-1-methylpyridine-2,6(1*H*,3*H*)-dione [as (**1**) with H in place of OH] m.p. 114–115 °C; M^{+}155.0587, $C_7H_9NO_3$ requires 155.0582; δ ($CDCl_3$) 3.2 (3H, s, N–Me), 3.4 (2H, s, CH_2), 4.2 (3H, s, O–Me), 5.4 (1H, s, –CH=). The latter underwent Elbs peroxydisulphate oxidation[4] to give a product identical spectroscopically (IR, MS,



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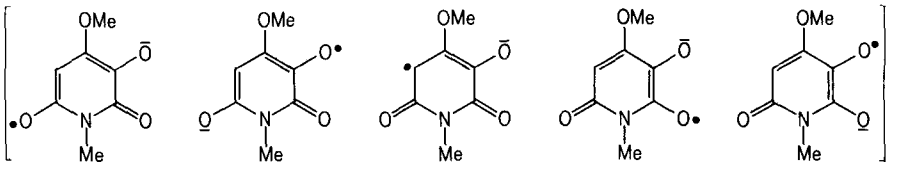

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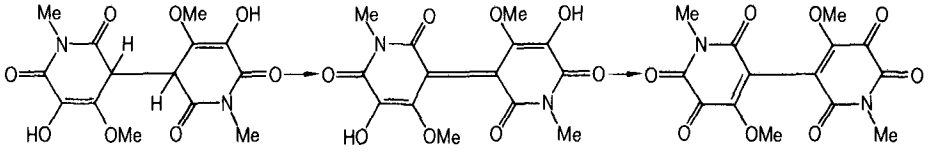
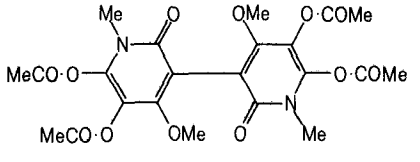


5 **6** **7**



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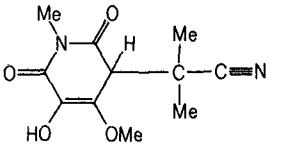

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NMR) with *A*; and both could be oxidized by air in aqueous solution around neutrality with color changes as observed with extracts of *Mercurialis perennis*.

Compound *A* was oxidized by nitric acid to 4-methoxy-1-methylpyridine-2,3,6-(1*H*)-trione (**3**), m.p. 132 °C; M^+169, $C_7H_7NO_4$ requires 169; δ ($CDCl_3$) 3.35 (3H, s, N–Me), 3.9 (3H, s, O–Me), 6.25 (1H, s, –CH=); δ (CF_3CO_2H), 3.45 (3H, s, N–Me), 4.0 (3H, s, O–Me), 6.5 (1H, s, –CH=). When equimolecular amounts of this and *A* were mixed at pH 7.1 an immediate deep blue color was produced. Compounds *A* and (**3**) can be regarded as analogous to a quinol and a quinone, respectively, and the blue compound might then be a semiquinone-like radical-anion (**4**). ESR spectroscopic evidence consistent with the latter structure is presented in the following communication by A.R. Forrester[6].

When a solution of *A* in methanol was warmed in the presence of air rapid oxidation occurred with the formation of a very sparingly soluble, colorless, crystalline compound (*B*), 5,5′-dihydroxy-4,4′-dimethoxy-1,1′-dimethyl[3,3′-bipyridine]-2,6,2′,6′(1*H*,3*H*,1′*H*,3′*H*)-tetrone (**5**), which on acetylation afforded a crystalline product formulated as either 5,6,5′,6′-tetra-acetoxy-4,4′-dimethoxy-1,1′-dimethyl [3,3′-bipyridine]-2,2′-dione (**8**) or 2,5,2′,5′-tetraacetoxy-4,4′dimethoxy-1,1′-dimethyl[3,3′-bipyridine]-6,6′-dione, and which had m.p. 174–175 °C (decomp.); M^+508.1313, $C_{22}H_{24}N_2O_{12}$ requires 508.1329; δ ($CDCl_3$) 2.15 (6H, s, 2OCOCH_3), 2.3 (6H, s, 2OCOCH_3), 3.35 (6H, s, 2 N–Me), 3.8 (6H, s, 2OMe). In CF_3CO_2H *B* disproportionates to give *A* and (**3**). The symmetrical homolysis of *B* on heating was demonstrated by trapping the resulting radical with 2,2′-azobis(2-methylpropionitrile) to yield 3-[2′-(2′-cyanopropyl)]-5-hydroxy-4-methoxy-1-methylpyridine-2,6-(1*H*,3*H*)-dione (**9**), m.p. 152 °C, M^+238.0953, $C_{11}H_{14}N_2O_4$ requires 238.0953.

When a solution of either *A* or *B* in pyridine was exposed to air it afforded a yellow compound 4,4′-dimethoxy-1,1′-dimethyl[3,3′-bipyridine]-2,2′,-5,5′,6,6′(1*H*,1′*H*)-hexone (**7**); *m/e* 336, *321*; δ ($CDCl_3$) 3.35 (N–Me) and 4.15 (O–Me) equal in area.

When *B* was oxidized with ceric ammonium nitrate in acetic acid it yielded an orange-yellow product, apparently a quinhydrone-like compound formed from equimolecular amounts of (**6**) and (**7**), *m/e* 338, 336, *321*, 169. From n.m.r. spectra it appeared that in either $CDCl_3$ or in CF_3CO_2H this decomposed to give a mixture of 1 mol of (**7**) and 2 mol of (**3**). Extraction with chloroform of an aqueous extract of *Mercurialis perennis* after it had been oxidized by air afforded the same material; M^+338.0746, $C_{14}H_{14}N_2O_8$ requires 338.0750; M^+336.0604, $C_{14}H_{12}N_2O_8$ requires 336.0594.

Potentiometric titration of *A* at pH 4 gave a curve with only 1 step after the addition of 2 equivalents of $K_3Fe(CN)_6$ per mol of *A*, corresponding to oxidation to (**3**). However at pH 7.6 the first step [oxidation to (**3**)] occurred after the addition of rather less than 2 equivalents, but was followed by a second step circa 0.5 equivalent later, representing the oxidation of *B*, formed by reaction of *A* with (**3**). The curve obtained by titrating the *Mercurialis perennis* extract at pH 7.6 resembled the latter curve[5].

To summarize, an extract of *Mercurialis perennis* prepared as described by Haas and Hill contains *A* (hermidin), which on oxidation by air or $K_3Fe(CN)_6$ gives first a radical-anion (cyanohermidin) (**4**), then (**3**) which by reaction with *A* and further oxidation gives a complex of compounds (**6**) and (**7**) (chrysohermidin).

Compound *A* was also obtained by homogenizing the fresh plant in cold sodium acetate-sodium dithionite solution for 1 min, followed immediately by extraction with chloroform.

1 Acknowledgment. I thank Professor R.H. Thomson for his interest.
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Autoxidation of hermidin: an ESR study

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Summary. Aqueous solutions of hermidin readily give rise to a blue transient radical-anion on exposure to air, the identity of which has been established by ESR spectroscopy.

The preceding paper by Swan[2] describes the chemical changes which occur when the colorless chromogen hermidin (**1**), isolated from the plant *Mercurialis perennis* L. is oxidized. Aqueous solutions of hermidin (**1**) on autoxidation rapidly turn blue, then green and finally yellow-brown which suggests that radicals may be implicated. This has now been confirmed by ESR spectroscopy, the results providing supporting evidence for the previously proposed reaction scheme[2].

Hermidin (**1**) dissolved slowly in degassed aqueous buffer (pH 7.17) to give a pale blue solution which in an ESR cavity gave a complex and unsymmetrical spectrum. Over a period of a few hours the spectrum almost disappeared and was replaced by a secondary spectrum composed simply of a triplet of quarters [a_N = 1.5 and a_H = 0.5 G(3H)]. Lack of symmetry in the original spectrum made analysis difficult but repetition of the experiment using deuterated solvent (D_2O) provided a spectrum which was symmetrical and lasting. Analysis gave a_H = 0.4(3H), a_H = 0.6(3H), a_N = 1.5 and a_D = 0.5 G. Simulation using a_H = 3.45 ($a_H = a_D \times 6.5$), a_H = 0.6(3H), a_H = 0.4(3H) and a_N = 1.45 G produced a spectrum which matched well these parts of the original spectrum which were symmetrical. Hence this spectrum is attributed to the radical-anion (**2**) which exchanges H-5 for D-5 in deuterated solvent. Confirmation of this assignment was achieved by measuring a solution containing approximately equal amounts of hermidin (**1**) and the trione (**4**). This blue solution gave an unperturbed spectrum which was a good overall match for the simulated spectrum (fig.).

The secondary spectrum (triplet of quartets) had relatively broad lines (0.4 G) and did not show a large splitting due to a ring proton. Therefore, the radical giving rise to this spectrum must be substituted at C-5. The two most likely possibilities are (**5**) and (**7**) the latter arising from dimerization of (**2**) and subsequent oxidation and the former by hydroxylation of her-