# Structure and Synthesis of New Cyclopentenyl Isonitriles from *Trichoderma hamatum* (Bon.) Bain. aggr. HLX 1379

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Two new cyclopentenyl isonitriles have been isolated from the fungus *Trichoderma hamatum* (Bon.) Bain. aggr. HLX 1379; their structures have been established by spectroscopic means and in one case confirmed by synthesis.

In connection with our biosynthetic studies on the family of cyclopentenyl isonitriles produced by *Trichoderma hamatum* (Bon.) Bain. aggr. HLX 1379 we have isolated† two new isonitriles (**1**) and (**2a**) which were present at lower levels in the culture filtrate than the previously reported (**3**), (**4**), and (**5**).[1]

The spirolactone (**1**) (configuration unknown), was isolated by repeated chromatography on basic alumina and its structure followed from its n.m.r. spectrum [$\delta_H$ ($C^2HCl_3$, 500 MHz) 2.25—2.45 (2H, m, $CH_2$), 2.65—2.80 (1H, m, $CH_2$), 2.85—3.00 (1H, m, $CH_2$), 5.70 (1H, t, *J* 1.8 Hz, HC=C–NC), 6.13 (1H, d, *J* 5.6 Hz, *H*C=$CHCO_2$), and 7.30 (1H, d, *J* 5.6 Hz, HC=C*H*$CO_2$); $\nu_{max.}$ ($CCl_4$) 2120s (NC) and 1783s (lactone CO) $cm^{-1}$; $\lambda_{max.}$ ($Et_2O$) 215 nm ($\varepsilon$ 22 000); *m/z* (electron impact, E.I.) 161 ($M^+$, 12%), 68 (100); ($NH_3$ chemical ionisation, C.I.) 179 (100%)].

The synthesis of (±)-(**1**) was achieved by direct addition of lithium (*Z*)-β-lithioacrylate to the ketoisonitrile (**10**), as in Scheme 1. This cyclopentenone (**10**) [$\delta_H$ ($C^2HCl_3$, 300 MHz) 2.55—2.65 (2H, m, $CH_2$), 2.85—2.90 (2H, m, $CH_2$), and 6.25 (1H, br. s, vinyl H); $\nu_{max.}$ ($CHCl_3$) 2120s (NC), 1730s (C=O), and 1610s (C=C) $cm^{-1}$; *m/z* (E.I.) 107 ($M^+$, 70%), and 52 (100); found 107.0372: $C_6H_5NO$ requires 107.0371], upon treatment with lithium β-lithioacrylate[3] gave, upon acidification and cyclisation, the spirolactone (**1**), identical ($^1H$ n.m.r., i.r., and *m/z*) to the biosynthetic sample [$\delta_C$ ($C^2HCl_3$, 125 MHz) 32.1 (t, $CH_2$), 33.0 (t, $CH_2$), 95.75 (s,C–O), 121.7 and 127.2 (2 × d, HC=), 133.0 (t, =CNC), 155.8 (d, HC=), 170.7 (br. s, NC), and 171.1 (s, $CO_2$); found 161.0476: $C_9H_7NO_2$ requires 161.0477].

The second isonitrile, isolated as its methyl ester (**2b**) was obtained by flash neutral alumina chromatography followed by h.p.l.c. (normal phase Zorbax-CN column, using diethyl ether–hexane as eluant). The structure as (**2b**) follows from its spectral data [$\delta_H$ ($C^2HCl_3$, 500 MHz) 2.96 (1H, m), 3.01 (1H, m), 3.78 (3H, s, $CO_2Me$), 4.59 (1H, m), 6.04 (1H, m, HC=CNC), 6.22 (1H, d, *J* 16 Hz, CH=C*H*$CO_2$), 7.19 (1H, d, *J* 16 Hz, C*H*=$CHCO_2$); $\delta_c$ ($C^2HCl_3$, 125 MHz), 46.2 (t, $CH_2$), 52.0 (q,$CO_2$*Me*), 81.3 (s, $R_3COH$), 83.3 (d, CHOH), 128.1 (t, =*C*NC), 121.2, 129.8, 147.9 (3 × d, CH=), and 166.8 and 169.1 (2 × s, $CO_2$, C–N*C*); $\nu_{max.}$ ($CH_2Cl_2$), 3580m (OH),

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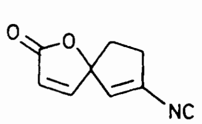
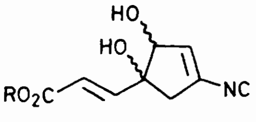
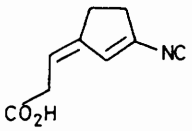
† In a typical procedure, the crude culture fluid was filtered, acidified to pH 4.2, extracted with ethyl acetate, dried, concentrated, and treated with an excess of diazomethane (20 °C, 30 min). Evaporation gave a crude derivatised mixture which was subsequently purified.



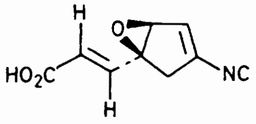
**(1)**



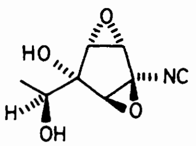
**(2)**
**a**; R = H
**b**; R = Me



**(3)**

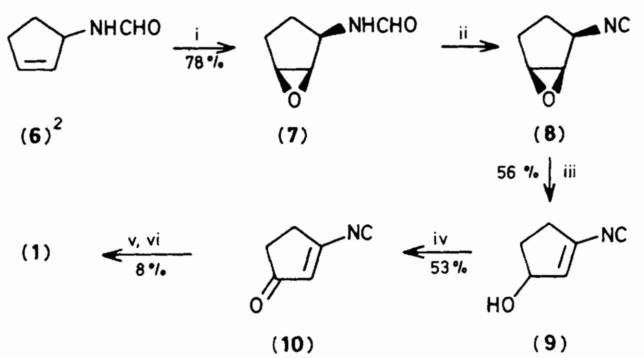


**(4)**



**(5)**

3450m (OH), 2120s (NC), 1730s ($CO_2$), and 1660m (C=C) $cm^{-1}$, the peak at 3450 $cm^{-1}$ disappears on dilution; $m/z$ ($NH_3$ C.I.) 227 ($MNH_4^+$, 100%), 210 (20, $MH^+$), and 194 (20): (E.I.) 209 ($M^+$, 1%), 194 ($M^+$ − Me, 86),[4] and 176 (29); found 194.0454 : $C_9H_8NO_4$ requires 194.0453]. Proton nuclear Overhauser enhancements showed that the diol (**2b**) had a similar regiochemistry to the methyl ester of dermadin (**4**), while a 2D Jeener spectra showed that the ring protons were all coupled. The possibility that this diol is an artefact, arising from ring opening of dermadin's epoxy group was eliminated as follows. The methyl ester of dermadin (**4**) was hydrolysed (aqueous LiOH–tetrahydrofuan, 15 °C, 1 h), extracted with ethyl acetate, acidified to pH 4 (dilute hydrochloric acid), then left at 15 °C for 15 minutes. Extraction into ethyl acetate and reaction with an excess of a diethyl ether solution of diazomethane gave the methyl ester of dermadin (**4**) with no trace of (**2b**) (500 MHz n.m.r.).



**Scheme 1.** *Reagents:* i, $MeCO_3H$, $CHCl_3$, 20 °C; ii, $COCl_2$, $NMe_3$, 0 °C; iii, $KOBu^t$, tetrahydrofuran, −78 °C; iv, pyridinium chlorochromate, $CH_2Cl_2$, 0 °C; v, (*Z*)-CHLi=$CHCO_2Li$, $Et_2O$, −78 °C then $H_3O^+$; vi, dicyclohexylcarbodiimide, EtOAc, 20 °C.

Interestingly, the spirolactone (**1**) has an oxidation state one unit above that of (**3**), which is the most abundant isonitrile in the culture filtrate. Biosynthetic studies to determine whether a monoepoxide of (**3**) could be an intermediate between (**1**) and (**3**) are in progress.

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## References

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3 D. Caine and A. S. Frobese, *Tetrahedron Lett.*, 1978, 5167.
4 A similar ion due to loss of methyl radical was reported as the major fragmentation of the methyl ester of (**4**), R. T. Aplin, Dyson Perrins Laboratory, University of Oxford, personal communication.