Synthesis of the Pyrrole-Imidazole Alkaloid Sventrin from the Marine Sponge *Agelas sventres*

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The marine pyrrole-imidazole alkaloid sventrin (**1**) and the hitherto unknown dehydrooroidin (**3**) have been synthesized stereoselectively *via* alkyne intermediates. The pathways start from a 2-azido-4-alkynylimidazole which can be chemo- and stereoselectively reduced to the corresponding amino alkene using $NaAlH_2(OCH_2CH_2OMe)_2$ (Red-Al) or, alternatively, to the amino alkyne. Selective removal of simultaneously present Boc or trityl protecting groups was possible employing either *p*-TsOH or acetic *resp.* formic acid.

Key words: Alkynes, Red-Al, Marine Natural Products

Pyrrole-imidazole alkaloids are exclusively found in marine sponges of the orders Agelasida, Axinellida and Halichondrida. Various modes of cyclization and dimerization of a common precursor lead to the economic generation of structural diversity. A detailed mechanistic consideration on the biogenesis of cyclized and dimerized pyrrole-imidazole alkaloids starting from the non-cyclized precursor oroidin (**2**) [1] has been published by Al Mourabit and Potier [2]. As part of our program on the exploration of the biomimetic chemistry of the pyrrole-imidazole alkaloids [3], we report here the first synthesis of the natural product sventrin (**1**) and of the hitherto unknown dehydrooroidin (**3**). Köck *et al.* recently isolated sventrin (**1**) from *Agelas sventres* as the pyrrole-*N*-methylated analog of oroidin (**2**, Scheme 1) [4].

Since oroidin cannot be methylated regioselectively, the *N*-methylated pyrrolylcarbonyl unit had to be introduced as a preformed building block. Ideally, the bifunctional, unprotected 2-amino-4(5)-(3-amino-1-propenyl)imidazole unit present in sventrin (**1**) would have to be acylated. Reported yields for the acylation of that partial structure with 4,5-dibromo-2-trichloroacetylpyrrole (**11**) range from 13% to 65% [5,6]. Although side products were not reported, interference by the 2-aminoimidazole portion of **1** on reaction of the bifunctional "east-half" of oroidin (**2**) with the trichloromethylketones **7** *resp.* **11** appears possible. *E. g.*, treatment of oroidin (**2**) with acetic anhydride leads to acetylation of the imidazole 2-amino group [1b].

Our strategy aimed at an improvement of the low to moderate coupling yields by introducing a bulky protecting group at the imidazole portion that was to be removed in the final step. The structures of two of our synthetic intermediates (**5**, **10**) in the crystal outline the steric shielding of the imidazole 2-amino group effected by trityl protecting groups (Fig. 1).

Scheme 1 summarizes our syntheses of sventrin (**1**) and of dehydrooroidin (**3**), starting from the Boc- and trityl-protected alkynyl imidazole **4** which had been obtained *via* Sonogashira alkynylation of the corresponding iodoimidazole [7]. Lindlar hydrogenation of **4** would yield the Z-double bond which would have to be isomerized subsequently. We found that reduction of both the azide function and the triple bond of **4** with $NaAlH_2(OCH_2CH_2OMe)_2$ (Red-Al) in toluene/THF conveniently yielded stereochemically pure (*E*)-alkene **5** in a yield of 76%. To our knowledge, this example is the first reduction of alkynylated *N*-heterocycles to the corresponding alkenes employing Red-Al. The reduction of alkynes to alkenes by Red-Al has in particular been reported for propargylic alcohols [8–11] and for alkynyl ethers [12]. Mechanistic considerations on the stereo- and regioselectivity of hydroalumination reactions of internal alkynes have been published [13].

Chemoselective removal of the Boc group on treatment of **5** with *p*-TsOH monohydrate in THF gave the diamine **6** which was condensed with the *N*-methylated trichloromethyl ketone **7** [14] to

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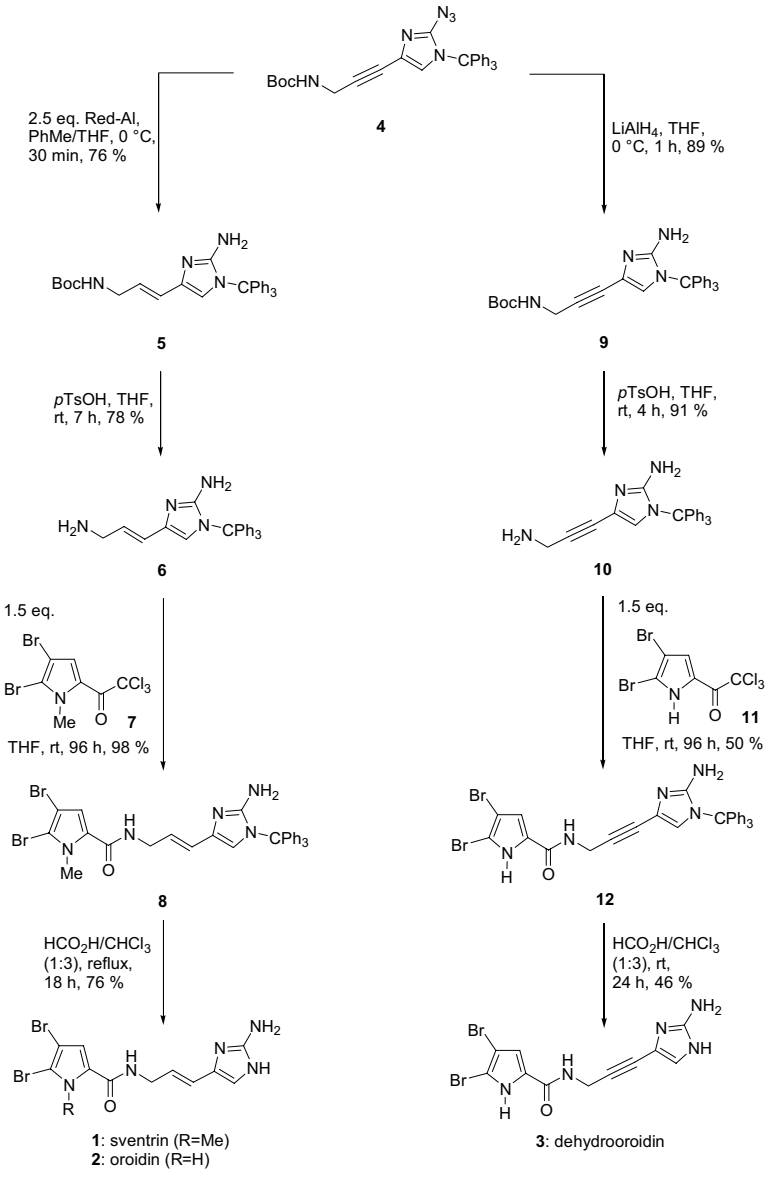

Scheme 1. Syntheses of the marine pyrrole-imidazole alkaloid sventrin (**1**) and the hitherto unknown dehydrooroidin (**3**) *via* alkyne intermediates.

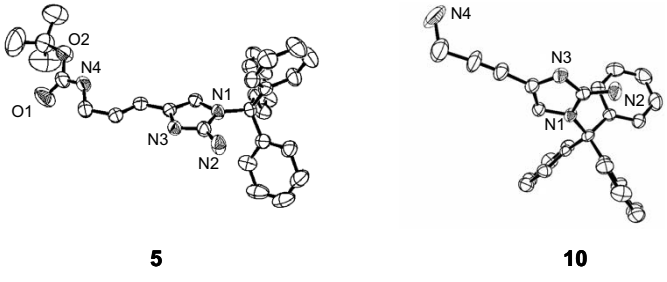

Fig. 1. Sterical shielding of the imidazole 2-amino group by the trityl protecting group alkylating the imidazole ring nitrogen (single-crystal XRD analysis, see Table 1).

give trityl-protected sventrin **8** in the high coupling yield of 98%. The clean detritylation of **8** without formation of side products turned out to be difficult, probably due to the good stabilization of the guanidinylated triphenylmethane partial structure, on protonation. Earlier, Ahond, Poupat *et al.* had reported low yields in detritylation of the corresponding oroidin precursor [15]. We performed a study on the selective deprotection of the 5-alkynyl-2-aminoimidazole **9** revealing that the trityl group can be selectively removed even in the presence of the Boc group when **9** is treated with 90% $HOAc/CH_2Cl_2/MeOH$ (2:1:1) under reflux (see also [16]). On transfer of this protocol to the problem of deprotecting the alkene synthetic intermediate **8**, surprisingly low yields (30–40%) of sventrin (**1**) were obtained. It turned out that the deprotection yield starting from **8** could be improved to 76% by alternative employment of formic acid in chloroform. The natural product sventrin (**1**) was obtained in 4 steps from **4** in an overall yield of 42%.

For the synthesis of dehydrooroidin (**3**), chemoselective reduction of the azide group of **4** was required with retention of the triple bond. Treatment of **4** with $LiAlH_4$ for a short reaction time (60 min) allowed the isolation of the alkyne **9**, again with a sterically hindered imidazole 2-amino group. The Boc protecting group was selectively removed by treatment with *p*TsOH, providing **10**. As a difference to the sventrin case, acylation of **10** with the *N*-unsubstituted trichloromethyl ketone **11** [17] gave the tritylated dehydrooroidin precursor **12** in the moderate yield of 50%. The subsequent detritylation proceeded completely, but the isolated yield (46%) was again lower than in the case of the *N*-methylated pyrrole amide **8**.

In summary, the first total syntheses of the marine natural product sventrin (**1**) and of the hitherto unknown dehydrooroidin (**3**) have been developed. Both compounds are now available for further studies on their cyclization and dimerization. The true potential of the biogenetic key building block underlying the pyrrole-imidazole

Table 1. Crystal data and structure refinement of **5** and **10**.

	5	**10**
Empirical fomula	$C_{30}H_{32}N_4O_2 \cdot ½\ C_4H_8O_2$	$C_{25}H_{22}N_4 \cdot 2\ CH_3OH$
Formula weight	524.65	442.55
Temperature [K]	295(2)	295(2)
λ (Mo-K_α) [Å]	0.71073	0.71073
Crystal system	triclinic	triclinic
Space group	$P\ \bar{1}$	$P\ \bar{1}$
a [Å], α [°]	13.073(2), 112.922(12)	9.162(2), 72.87(2)
b [Å], β [°]	15.952(3), 98.736(10)	9.893(2), 81.89(2)
c [Å], γ [°]	16.693(2), 105.612(13)	14.829(3), 70.94(2)
Volume [Å^3]	2955.8(7)	1212.5 (4)
Z	4	2
$\varrho_{calcd.}$ [Mg/m^3]	1.179	1.212
Absorption coefficient [mm^{-1}]	0.077	0.078
$F(000)$	1120	472
Crystal size [mm]	0.53 × 0.43 × 0.23	0.53 × 0.33 × 0.23
Range for data coll. Θ [°]	2.36 to 23.97	2.70 to 21.66
Index ranges *hkl*	$-14 \le h \le 0$, $-17 \le k \le 18$, $-18 \le l \le 19$	$-9 \le h \le 9$, $-10 \le k \le 9$, $15 \le l \le 0$
Reflections collected	9707	2990
Independent reflections	9238 [R(int) = 0.0178]	2854 [R(int) = 0.0332]
Absorption correction	Semi-empirical by psi-scans	None
Max., and min. transmission	0.9989 and 0.9196	
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	9238/40/714	2854/2/311
Goodness of fit on F^2	1.093	1.082
Final R indices [$I > 2\sigma$(I)]	$R1$ = 0.0676, $wR2$ = 0.1716	$R1$ = 0.0661, $wR2$ = 0.1530
R Indices (all data)	$R1$ = 0.0988, $wR2$ = 0.1980	$R1$ = 0.1019, $wR2$ = 0.1821
Largest diff. peak and hole [e/Å^3]	0.369 and – 0.295	0.283 and – 0.283

alkaloids has hardly been explored [18]. Due to its *N*-methylation, cyclizations of sventrin (**1**) would at most involve the pyrrole carbon atom, leading, *e.g.*, to analogs of *N*-methylisophakellin [19]. The triple bond of dehydrooroidin (**3**) is designed to prevent intramolecular cyclization and, instead, favor the formation of dimers.

Experimental Section

General

Unless otherwise noted, reagents were purchased from commercial suppliers and used without further purification. Reactions were controlled by thin-layer chromatography (precoated silica gel plate Merck F_{254}). Flash chromatography was carried out on silica gel (Merck, silica gel 60 (40–63 μm)). Melting points are uncorrected. NMR spectra were recorded on Varian 200 or 400 MHz spectrometers. Chemical shifts refer to residual solvent signals based on $\delta_{TMS} = 0$. Mass spectra were taken in EI, FAB (nitrobenzyl alcohol as matrix), or ESI modes. Yields refer to purified compounds.

*[3-(2-Amino-1-trityl-1*H*-imidazol-4-yl)-allyl]-carbamic acid tert-butyl ester* (**5**)

To a solution of the azidoalkynylimidazole **4** ([7], 1.10 g, 2.2 mmol) in dry THF (50 ml) at 0 °C was added Red-Al (2.5 equiv., 65% wt in toluene) under an argon atmosphere. After 30 min the reaction mixture was quenched with saturated Na_2CO_3 (5 ml), followed by addition of brine (5 ml). The mixture was extracted with EtOAc (3 × 20 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting residue was purified by flash chromatography (silica gel, EtOAc) to yield **5** (809 mg, 76%) as a pale yellow solid. Crystallization from EtOAc afforded colorless crystals: M.p. 160 °C (decomp.). – UV/vis ($CHCl_3$): λ_{max} (lg ε) = 269 nm (4.17). – IR (KBr): $\tilde{\nu}$ = 3444, 3059, 2976, 1713, 1617, 1534, 1493, 1447, 1365, 1248, 1170, 962, 747, 702 cm^{-1}. – ^{1}H NMR (199.98 MHz, $CDCl_3$): δ = 7.50–7.25 (m, 9H, phenyl-C*H*), 7.26–7.15 (m, 6H, phenyl-C*H*), 6.28 (s, 1H, NCC*H*N), 6.15 (d, ^3J = 15.4 Hz, 1H, CH_2CHCH), 5.98 (dt, ^3J = 15.4, 5.5 Hz, 1H, CH_2CH), 4.58 (br. s, 1H, N*H*), 3.76 (dd, ^3J = 5.5, 5.1 Hz, 2H, NHCH_2C), 3.60 (s, 2H, NH_2), 1.42 (s, 9H, C(CH_3)$_3$). – ^{13}C NMR (100.57, $CDCl_3$): δ = 155.70 (C = O), 149.57 (*C*NH_2), 141.45 (3C, phenyl-*C*), 133.24 (N*C*CHN), 129.99 (6C, phenyl-*o*-*C*H), 128.17 (6C, phenyl-*m*-*C*H), 128.07 (3C, phenyl-*p*-*C*H), 123.46 (CH_2CH), 122.87 (CH_2CHCH), 115.68 (NC*C*HN), 79.50 (*C*(CH_3)$_3$), 74.26 (*C*Ph_3), 42.70 (NCH_2), 28.44 (3C, *C*(CH_3)$_3$). – MS (ESI): *m/z* (%) = 481 (100) [M$^+$]. – HRESIMS $C_{30}H_{33}N_4O_2$ [M + H$^+$]: calcd. 481.2603; found 481.2576. – $C_{30}H_{32}N_4O_2$ (480.6): calcd. C 74.97, H 6.71, N 11.66; found C 74.69, H 6.60, N 11.61.

*4-(3-Amino-propenyl)-1-trityl-1*H*-imidazol-2-ylamine* (**6**)

To a solution of the alkenylaminoimidazole **5** (100 mg, 0.2 mmol) in THF (7 ml) was added *p*-toluenesulfonic acid monohydrate (2.5 g) in small portions over a period of 7 h. After addition of saturated Na_2CO_3 (5 ml) and brine (5 ml) the reaction mixture was extracted with THF (3 × 5 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (silica gel, $CHCl_3$-MeOH-aq. NH_3 (70:10:1)) afforded **6** (61 mg, 78%) as a pale yellow solid: M.p. 170 °C (decomp.) – UV/vis (MeOH): λ_{max} (lg ε) = 276 nm (4.03). – IR (KBr): $\tilde{\nu}$ = 3439, 3058, 1968, 1621, 1535, 1446, 1326, 965, 748, 702 cm^{-1}. – ^{1}H NMR (399.92 MHz, CD_3OD): δ = 7.41–7.29 (m, 9H, phenyl-C*H*), 7.26–7.12 (m, 6H, phenyl-C*H*), 6.37 (s, 1H, NCC*H*N), 6.15 (d, ^3J = 15.7 Hz, 1H, CH_2CHCH), 6.10 (dt, ^3J = 15.7, 4.5 Hz, 1H, CH_2CH), 3.28 (d, ^3J = 4.5 Hz, 2H, NHCH_2C). – ^{13}C NMR (100.57, CD_3OD): δ = 150.40 (N*C*NH_2N), 141.45 (3C, phenyl-*C*), 133.31 (N*C*CHN), 129.68 (6C, phenyl-*o*-*C*H), 127.89 (6C, phenyl-*m*-*C*H), 127.81 (3C, phenyl-*p*-*C*H), 126.52 (CH_2CH), 121.51 (CH_2CHCH), 114.60 (NC*C*HN), 74.20 (*C*Ph_3), 43.04 (NH*C*H_2). – MS (FAB+): *m/z* (%) = 381 (2) [M + H$^+$], 243 (100) [CPh_3^+]. – HRFABMS $C_{25}H_{25}N_4$ [M + H$^+$]: calcd. 381.2058; found 381.2079.

*4,5-Dibromo-1-methyl-1*H*-pyrrole-2-carboxylic acid [3-(2-amino-1-trityl-1*H*-imidazol-4-yl)-allyl]-amide* ***(8)***

(4,5-Dibromo-1-methyl-1*H*-pyrrole-2-yl)-tri-chloromethylketone **7** ([14], 227 mg, 0.60 mmol) was added to a solution of **6** (150 mg, 0.40 mmol) in dry THF (15 ml). After 96 h the mixture was concentrated *in vacuo* and purified by flash chromatography (silica gel, $CHCl_3$-MeOH (10:1)) to yield **8** as a pale yellow solid (254 mg, 99%). M.p. 140 °C (decomp.) – UV/vis ($CHCl_3$): λ_{max} (lg ε) = 281 nm (4.34). – IR (KBr): $\tilde{\nu}$ = 3436, 1639, 1533, 1492, 1447, 1254, 957, 747, 701 cm^{-1}. – ^{1}H NMR (399.92 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 9H, phenyl-C*H*), 7.21–7.14 (m, 6H, phenyl-C*H*), 6.57 (s, 1H, BrCC*H*), 6.33 (s, 1H, NCC*H*N), 6.27 (d, ^3J = 15.4 Hz, 1H, CH_2CHCH), 6.16 (dt, ^3J = 15.4 Hz, ^3J = 6.3 Hz, 1H, CH_2CH), 5.95 (t, ^3J = 5.2 Hz, 1H,

N*H*CH_2), 4.04 (dd, ^3J = 6.3 Hz, ^3J = 5.2 Hz, 2H, NHCH_2), 3.94 (s, 3H, NCH_3), 3.55 (s, 2H, CNH_2). – ^{13}C NMR (100.57, $CDCl_3$): δ = 160.10 (*C* = O), 149.63 (N*C*NH_2N), 141.41 (3C, phenyl-*C*), 133.11 (N*C*CHN), 129.98 (6C, phenyl-*o*-*C*H), 128.19 (6C, phenyl-*m*-*C*H), 128.10 (3C, phenyl-*p*-*C*H), 127.74 (CH*C*CO), 124.71 (CH_2CH*C*H), 121.42 (CH_2*C*H), 116.08 (NC*C*HN), 113.36 (BrC*C*H), 111.42 (Br*C*NCH_3), 97.88 (Br*C*CH), 74.30 (*C*Ph_3), 41.50 (NHCH_2CH), 35.69 (N*C*H_3). – MS (FAB+): *m/z* (%) = 644/646/648 (6/12/6) [M + H^+], 243 (100) [CPh_3^+]. – HRFABMS $C_{31}H_{28}Br_2N_5O$ [M + H^+]: calcd. 644.0644; found 644.0661.

*4,5-Dibromo-1-methyl-1*H*-pyrrole-2-carboxylic acid [3-(2-amino-1*H*-imidazol-4-yl)-allyl]-amide (sventrin)* (**1**)

The coupling product **8** (139 mg, 0.22 mmol) was dissolved in $CHCl_3$ (10 ml) and treated with HCO_2H (3 ml). The mixture was refluxed for 18 h and concentrated *in vacuo*. Flash chromatography (silica gel, $CHCl_3$:MeOH:NH_3 = 40:10:1) yield sventrin (**1**) as a pale yellow solid (66 mg, 76%). M. p. 100 °C (decomp.) – UV/vis ($CHCl_3$): λ_{max} (lg ε) = 279 nm (4.31). – IR (KBr): $\tilde{\nu}$ = 3308, 2928, 1632, 1578, 1540, 1499, 1449, 1414, 1329, 1262, 1164, 1092, 956, 805, 752 cm^{-1}. – ^{1}H NMR (399.92 MHz, CD_3OD): δ = 6.87 (s, 1H, BrCC*H*), 6.49 (s, 1H, NCC*H*N), 6.28 (dt, ^3J = 15.9 Hz, ^4J = 1.4 Hz, 1H, CH_2CHC*H*), 5.89 (dt, ^3J = 15.9, 6.2 Hz, 1H, CH_2C*H*), 3.97 (dd, ^3J = 6.2 Hz, ^4J = 1.4 Hz, 2H, NHCH_2), 3.94 (s, 3H, NCH_3). – ^{13}C NMR (100.57, CD_3OD): δ = 162.72 (*C* = O), 151.93 (N*C*NH_2N), 131.26 (N*C*CHN), 129.44 (CH*C*CO), 122.52 (CH_2CH*C*H), 122.48 (CH_2*C*H), 117.13 (NC*C*HN), 115.91 (BrC*C*H), 112.49 (Br*C*NCH_3), 99.18 (Br*C*CH), 42.48 (N*C*H_2CH), 36.41 (N*C*H_3). – MS (ESI+): *m/z* (%) = 402/404/406 (47/94/42) [M + H^+]. – HRESIMS $C_{12}H_{14}{}^{79}Br^{81}BrN_5O$ [M + H^+]: calcd. 403.9545; found 403.9503.

*[3-(2-Amino-1-trityl-1*H*-imidazol-4-yl)-prop-2-ynyl]-carbamic acid tert-butyl ester* (**9**)

$LiAlH_4$ (72 mg, 1.9 mmol) was suspended in dry THF (5 ml) under argon at 0 °C. To this mixture a solution of **4** (346 mg, 0.7 mmol) in dry THF (10 ml) was added. After 1 h the reaction was quenched with H_2O (5 ml). The mixture was treated with saturated Na_2CO_3 (5 ml) and extracted with EtOAc (4 × 10 ml). The combined organic layer was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (silica gel, EtOAc) afforded **9** (292 mg, 89%) as a pale yellow solid. M. p. 180 °C (decomp.) – UV/vis (MeOH): λ_{max} (lg ε) = 250 nm (4.05). – IR (KBr): $\tilde{\nu}$ = 3378, 2973, 1622, 1534, 1493, 1446, 1392, 1366, 1308, 1250, 1167, 1036, 907, 754, 740, 702, 674, 642 cm^{-1}. – ^{1}H NMR (199.98 MHz, $CDCl_3$): δ = 7.36–7.32 (m, 9H, phenyl-C*H*), 7.20–7.17 (m, 6H, phenyl-C*H*), 6.60 (s, 1H, CC*H*N), 5.20 (br. S, 1H, N*H*), 4.08 (d, ^3J = 5.3 Hz, 2H, NHCH_2C), 3.55 (s, 2H, NH_2), 1.41 (s, 9H, C(CH_3)$_3$). – ^{13}C NMR (100.57 MHz, $CDCl_3$): δ = 155.33 (*C* = O), 148.84 (N*C*NH_2N), 141.07 (3C, phenyl-*C*), 129.95 (6C, phenyl-*o*-*C*H), 128.23 (6C, phenyl-*m*-*C*H), 128.18 (3C, phenyl-*p*-*C*H), 121.85 (C*C*HN), 117.36 (CH*C*N), 85.29 (CH_2*C*C), 79.63 (*C*CH_3)$_3$), 77.36 (CH_2C*C*), 74.52 (N*C*Ph_3), 31.13 (NH*C*H_2), 28.37 (3C, C(*C*H_3)$_3$). – MS (ESI): *m/z* (%) = 481 (100) [M + H]$^+$. – HRESIMS $C_{30}H_{31}N_4O_2$ [M + H^+]: calcd. 479.2447; found 479.2422. – $C_{30}H_{30}N_4O_2$ (478.6): calcd. C 75.29, H 6.32, N 11.71; found C 74.91 H 6.25, N 11.61.

*4-(3-Amino-prop-1-ynyl)-1-trityl-1*H*-imidazol-2-ylamine* (**10**)

p-TsOH monohydrate in THF (30 ml, 1.9 M) was added to the alkynylaminoimidazole **9** (478 mg, 1 mmol). After stirring for 4 h the mixture was treated with saturated Na_2CO_3 (100 ml) and brine (50 ml), extracted with EtOAc (3 × 100 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Flash chromatography (silica gel, $CHCl_3$-MeOH-aq. NH_3 (40:10:1)) afforded **10** (286 mg, 91%) as a colorless solid. M. p. 155 °C (decomp.) – UV/vis (MeOH): λ_{max} (lg ε) = 254 nm (4.12). – IR (KBr): $\tilde{\nu}$ = 3438, 2231, 1618, 1532, 1446, 1308, 1034, 701 cm^{-1}. – ^{1}H NMR (399.9 MHz, CD_3OD): δ = 7.40–7.30 (m, 9H, phenyl-C*H*), 7.22–7.12 (m, 6H, phenyl-C*H*), 6.49 (s, 1H, NCC*H*N), 3.48 (s, 2H, NH_2CH_2). – ^{13}C NMR (100.57 MHz, CD_3OD): δ = 151.07 (N*C*NH_2N), 142.39 (3C, phenyl-*C*), 131.03 (6C, phenyl-*o*-*C*H), 129.36 (9C, phenyl-*m*-*C*H and phenyl-*p*-*C*H), 121.85 (NC*C*HN), 118.62 (N*C*CHN), 89.98 (CH_2*C*C), 77.34 (CH_2C*C*), 75.88 (N*C*Ph_3), 32.04 (NH_2*C*H_2). – MS (FAB+): *m/z* (%) = 379 (8) [M + H]$^+$, 243 (100) [CPh_3^+]. – HRFABMS $C_{25}H_{23}N_4$ [M + H^+]: calcd. 379.1875; found 379.1861.

*4,5-Dibromo-1*H*-pyrrole-2-carboxylic acid [3-(2-amino-1-trityl-1*H*-imidazol-4-yl)-prop-2-ynyl]-amide* (**12**)

(4,5-Dibromo-1*H*-pyrrole-2-yl)-trichloromethyl-ketone **11** ([17], 76 mg, 0.20 mmol) was added to a solution of **10** (50 mg, 0.13 mmol) in dry THF (5 ml). After 7 d the mixture was concentrated

in vacuo and purified by flash chromatography (silica gel, $CHCl_3$-MeOH (20:1)) to yield **12** as a pale yellow solid (42 mg, 50%). M.p. 135 °C (decomp.) – UV/vis (CH_2Cl_2): λ_{max} (lg ε) = 273 nm (4.21). – IR (KBr): $\tilde{\nu}$ = 3429, 3059, 2928, 2236, 1639, 1560, 1530, 1493, 1447, 1314, 1212, 1034, 753, 701 cm^{-1}. – ^1H NMR (399.92 MHz, $CDCl_3$): δ = 7.34–7.30 (m, 9H, phenyl-C*H*), 7.18–7.12 (m, 6H, phenyl-C*H*), 7.10 (br. s, 1H, CONH), 6.67 (s, 1H, BrCC*H*), 6.60 (s, 1H, NCC*H*N), 4.29 (d, ^3J = 4.0 Hz, 2H, $NHCH_2$), 3.70 (br. s, 2H, CNH_2). – ^{13}C NMR (100.57, $CDCl_3$): δ = 159.34 (*C* = O), 148.95 (N*C*NH_2N), 140.74 (3C, phenyl-*C*), 129.86 (6C, phenyl-*o*-*C*H), 128.33 (6C, phenyl-*m*-*C*H), 128.30 (3C, phenyl-*p*-*C*H), 126.80 (CH*C*CO), 121.83 (NC*C*HN), 116.39 (N*C*CHN), 113.51 (BrC*C*H), 105.62 (Br*C*NCH_3), 99.61 (Br*C*CH), 85.33 (CH_2CC), 77.20 (CH_2C*C*), 74.80 (*C*Ph_3), 30.14 ($NHCH_2$). – MS (FAB+): *m/z* (%) = 628/630/632 (0.5/1.0/0.5) [M + H^+], 243 (100) [CPh_3^+]. – HRFABMS $C_{30}H_{24}{}^{81}Br_2N_5O$ [M + H^+]: calcd. 632.0316; found 632.0320.

*4,5-Dibromo-1*H*-pyrrole-2-carboxylic acid [3-(2-amino-1*H*-imidazol-4-yl)-prop-2-ynyl]-amide (dehydrooroidin)* (**3**)

Coupling product **12** (28 mg, 0.04 mmol) was dissolved in $CHCl_3$ (5 ml) and treated with HCO_2H (1 ml). The mixture was stirred for 24 h and then concentrated *in vacuo*. Flash chromatography (silica gel, $CHCl_3$-MeOH-NH_3 (40:10:1)) yielded dehydrooroidin (**3**) as a pale yellow solid (8 mg, 46%). UV/vis (MeOH): λ_{max} (lg ε) = 275 nm (3.98), 377 (2.92). – IR (KBr): $\tilde{\nu}$ = 3413, 2929, 1680, 1640, 1560, 1515, 1420, 1394, 1316, 1237, 978, 811, 754, 537 cm^{-1}. – ^1H NMR (399.92 MHz, CD_3OD): δ = 6.83 (s, 1H, NCC*H*N), 6.82 (s, 1H, BrCC*H*), 6.60 (s, 1H, NCC*H*N), 4.28 (s, 2H, $NHCH_2$). – ^{13}C NMR (100.57, CD_3OD): δ = 159.85 (*C*=O), 148.49 (N*C*NH_2N), 127.00 (CH*C*CO), 119.55 (NC*C*HN), 113.13 (BrC*C*H), 112.80 (N*C*CHN), 105.62 (Br*C*NCH_3), 98.59 (Br*C*CH), 87.51 (CH_2CC), 72.32 (CH_2C*C*), 28.66 ($NHCH_2$). – MS (FAB+): *m/z* (%) = 386/388/390 (6/11/5) [M + $H]^+$. – HRFABMS $C_{11}H_9{}^{81}Br_2N_5O$ [M + H^+]: calcd. 389.9213; found 389.9224.

Crystal structure determination

Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 204005 (**5**), CCDC 204006 (**10**)). Copies may be obtained free of charge on application to the director, CCDC 12 Union Road, Cambrige, CB2 1E2, UK (fax: int. code +(44)01223/3 36-033, E-mail: deposit@chemcrys.cam.ac.uk).

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