The synthesis of 1,2,3,6,6a,7-hexahydro-7-methyl-5-imino-1*H*-pyrrolo[1,2-*c*]imidazolo[5,4-*b*]indole

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This paper is dedicated to Henk van der Plas who has for many years inspired heterocyclic chemists the world over with his innovative research, his impeccable standards and his charming personality

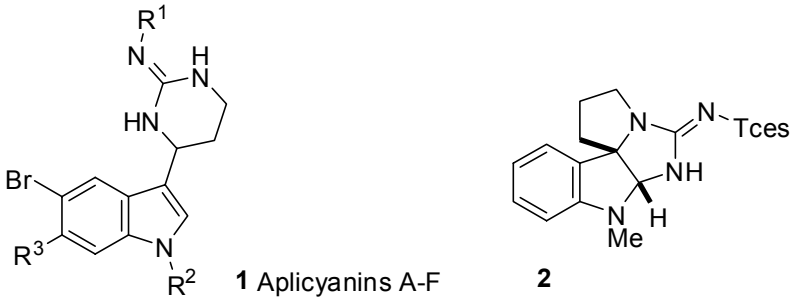
Abstract
N-3-(1-Methylindol-3-yl)propan-*N*-(2,2,2-trichloroethoxysulfonyl)guanidine was synthesized from 3-formyl-1-methylindole in six steps and subjected to conditions intended to convert the side-chain into a 2-iminotetrahydropyrimidine- containing product, of relevance to a possible synthesis of the aplicyanins. An alternative reaction course was observed, resulting in the formation of a new tetracyclic system.

Keywords: Aplicyanins, C–H amination, nitrene, aziridine, homotryptamine, guanidine

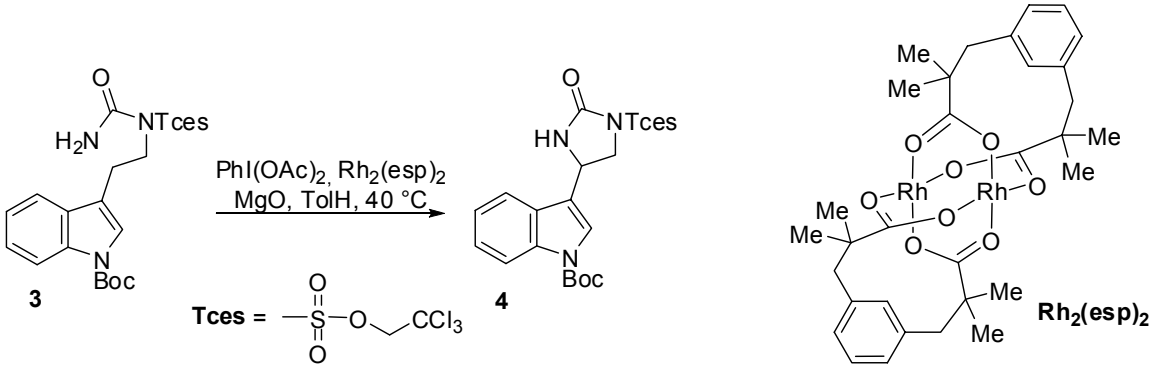
Introduction

Recently, a new family of five antitumor agents, the aplicyanins, **1**, was isolated from an Antarctic ascidian *Aplidium cyaneum*,[1] for example aplicyanin A has R^1=R^2=R^3=H, aplicyanin B has R^1=Ac, R^2=R^3=H, and the most complex, aplicyanin F has R^1=Ac, R^2=OMe, R^3=Br. Following our studies on the synthesis of a variety of heterocyclic marine natural products[2] and derivatives[3] we were attracted to the synthesis of such structures and describe here our initial model study aimed at constructing a 4-(indol-3-yl)tetrahydropyrimidine. Our plan was to construct the reduced pyrimidine unit, following the recent work by Du Bois *et al*.[4] However, an

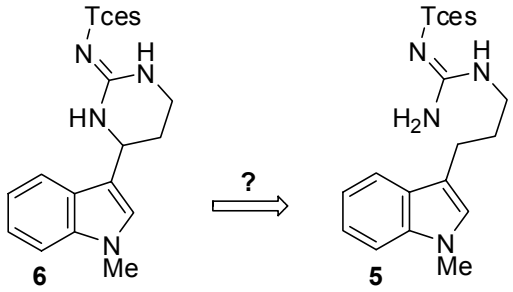
unexpected cyclization took place involving the indole unit and there was formed a fused tetracyclic structure, **2**, an example of a previously unknown heterocyclic system.



DuBois demonstrated the use of trichloroethoxysulfonamides in intermolecular benzylic C–H insertion reactions,[4b] and further that trichloroethoxysulfonyl (Tces)- protected ureas and guanidines can be used for intramolecular insertions into benzylic and tertiary positions.[4c] The example which was of most relevance for our proposed synthesis is shown in Scheme 1 wherein a five-membered reduced imidazole **4** was constructed from precursor **3**. Our thesis was that a comparable insertion into the indolylic position of a compound **5** would lead to **6** (Scheme 2).



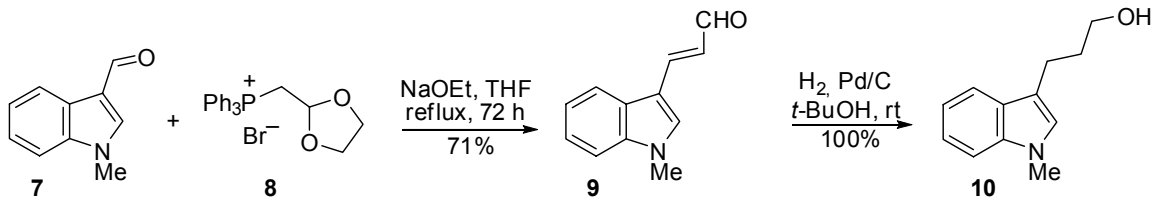
Scheme 1



Scheme 2

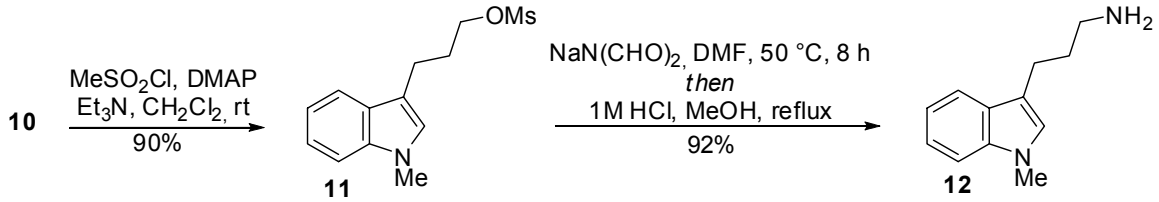
Results and Discussion

The construction of the cyclization precursor **5** began with 3-formyl-1-methylindole, **7,** which was brought into a Wittig reaction with commercially available **8**, giving the unsaturated aldehyde **9**.[5] Catalytic reduction of compound **9** saturated the double bond and also converted the aldehyde into an alcohol, producing the *N*-methyl homotryptophol **10** [6] (Scheme 3).



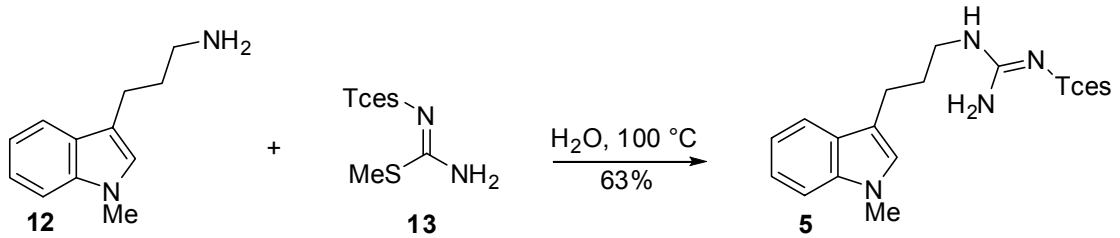
Scheme 3

Conversion of the alcoholic function into a primary amine was achieved in three steps, the last two in one pot. The alcohol was converted efficiently into a mesylate **11**, and the nitrogen introduced by displacement using the anion of diformamide, hydrolysis then liberating the *N*-methyl homotryptamine, **12**, in an overall 92% yield for the last two steps (Scheme 4).



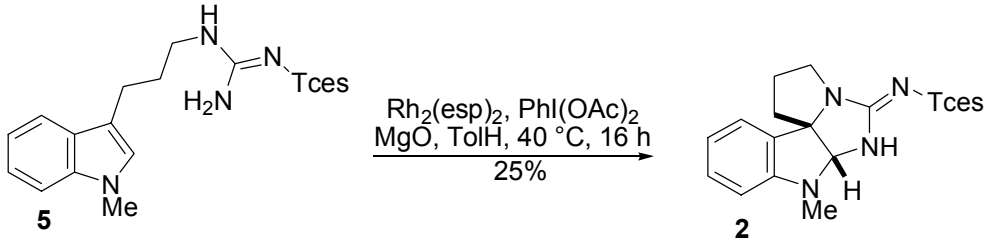
Scheme 4

Finally, the Tces- protected guanidine unit in **5** was constructed by reaction of the primary amine with the isothiourea **13**, again following the work of Du Bois[4c] (Scheme 5).

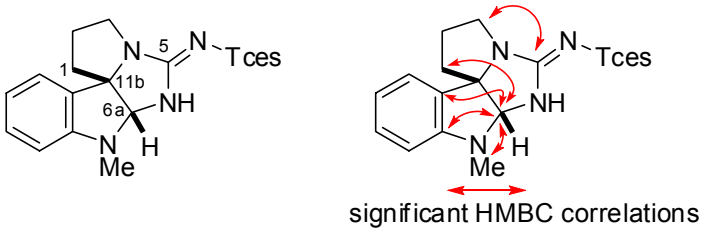


Scheme 5

We were now ready to attempt the side-chain cyclization hoping for the formation of the tetrahydropyrimidine, **6**. Exposure of **5** to the conditions described by Du Bois produced, in 25% yield, a product that we deduce has structure **2** (Scheme 6). Initially, we were surprised to observe the presence of three CH_2 groups in the product, instead of the two expected for a tetrahydropyrimidine derivative. Thus, in addition to the benzene ring signals, there were signals for the $(CH_2)_3$ unit, but there was no indole α-proton signal in the ^{1}H NMR spectrum, but instead a singlet signal at 5.34 was observed for H-6a (see Scheme 7 and Table 1). A detailed HMBC and NOESY study revealed correlations (Scheme 7) that support the proposed structure **2**. The H-6a shows HMBC long distance correlations (C1, C5, *N*-Me, C7a, and C11a), as well as NOE signals (H1, H6, and *N*-Me) with at least one atom of each ring, which was very useful for the assignment of the structure and stereochemistry of **2**. In particular, the NOE effect between H6a and one of the protons on C1 established the *cis*- relationship shown in **2**. Deprotection of **2** gave the corresponding *N*-hydrogen guanidine **14**.



Scheme 6



Scheme 7

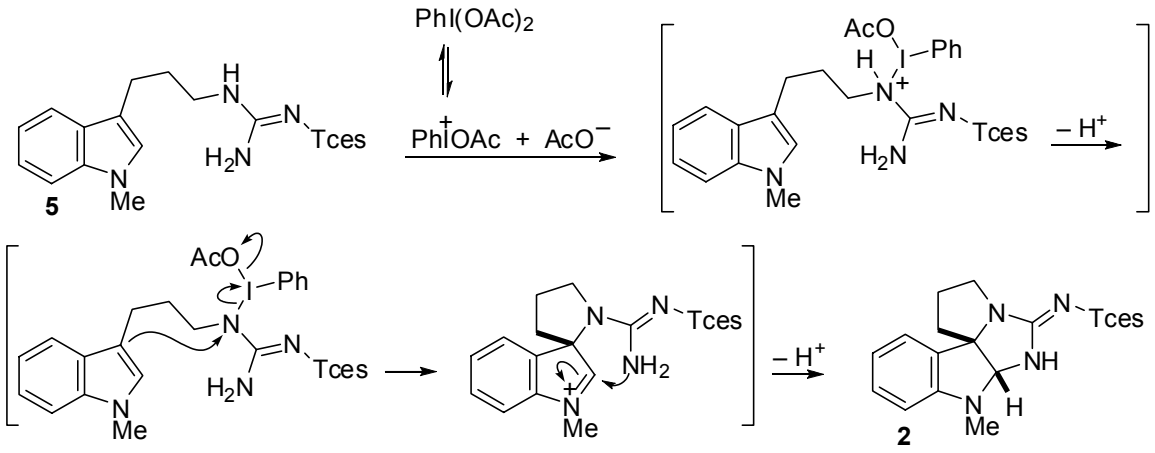
Table 1. NMR data for 1,2,3,6,6a,7-hexahydro-7-methyl-5-(*N*-(2,2,2-trichloroethoxy-sulfonyl)imino)-1*H*-pyrrolo[1,2-*c*]imidazolo[5,4-*b*]indole (**2**)

C /H number	δ_H (multiplicity, number of H)	δ_C	HMBC	NOESY
1	1.99-2.07 (m, 1H); 2.31-2.41 (m, 1H)	34.8 (t)	H1-C3 H1-C6a H1-C11a	H6a
2	2.16-2.25 (m, 1H); 2.31-2.41 (m, 1H)	25.4 (t)		H3
3	3.33-3.38 (m, 1H); 3.89-3.95 (m, 1H)	45.1 (t)	H3-C1 H3-C5	H2, H3
5	-	160.9 (s)		-
6	7.55 (bs, 1H)		H6-C5 H6-C6a	H6a, Me
6a	5.34 (s, 1H)	84.7 (d)	H6a-C1 H6a-C5 H6a-Me H6a-C7a H6a-C11a	H1, H6, Me
7a	-	149.8 (s)		-
8	6.54 (d, 1H)	107.4 (d)	H8-C10 H8-C11a	H9, Me
9	7.24 (t, 1H)	130.5 (d)	H9-C7a H9-C11	H8, H10
10	6.76 (t, 1H)	118.8 (d)	H10-C8 H10-C11a	H9, H11
11	7.13 (d, 1H)	122.9 (d)	H11-C7a H11-C9	H10
11a	-	129.2 (s)		-
11b	-	29.7 (s)	-	-
N-$SO_3\mathbf{CH_2}CCl_3$	4.60 (d, 1H); 4.65 (d, 1H)	78.3 (t)	-	
-CCl_3	-	94.1 (s)		-
Me	2.94 (s, 3H)	32.7 (q)	Me-C6a Me-C7a	H6, H6a, H8

Mechanism of the cyclization

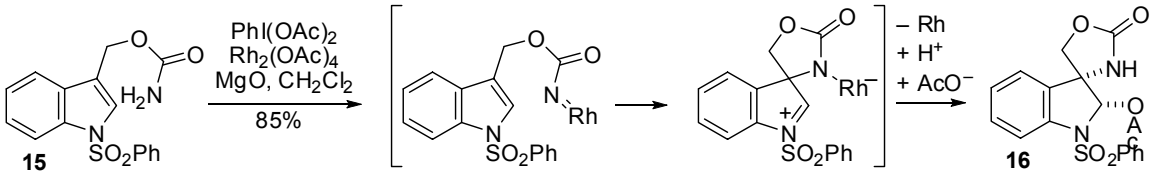
We have considered several mechanisms whereby the tetracycle **2** might be formed. One possibility, summarized in Scheme 8, is that the rhodium catalyst is not involved and that the conversion is initiated by activation of nitrogen by $PhIOAc^+$ then electrophilic attack at the indole β position. We discounted this possibility on the grounds that when compound **5** was

exposed to $PhI(OAc)_2$ and MgO *without* the rhodium catalyst, a very complex mixture was obtained, in which the tetracycle **2** could not be detected.



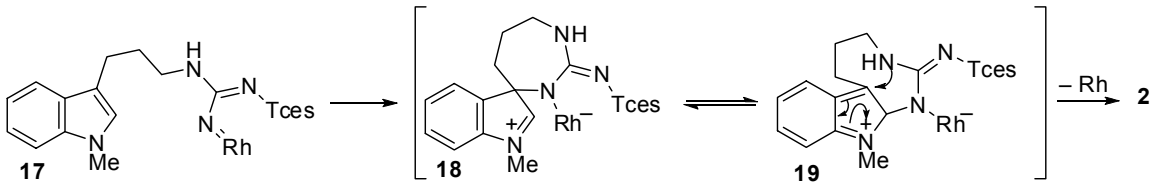
Scheme 8

We speculate that the rhodium-catalyzed oxidative cyclization of an indol-3-ylmethanol carbamate[7] (Scheme 9, **15** → **16**), which was postulated to involve nucleophilic attack of the indole on the nitrogen of a rhodium-nitrene complex, is a partial precedent for the present conversion.



Scheme 9

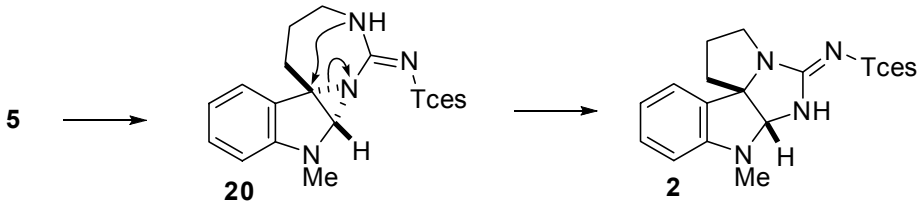
The analogy is not exact, as in the present case the nitrene nitrogen becomes attached to C2 of the indole. However, it is possible that a similar mechanism could operate, perhaps by initial direct attack at indole C3 (→ **18**), followed by migration (or equilibration) to C2 (Scheme 10, **18** → **19**).



Scheme 10

A variant on this would involve attack of the indole on the metal, followed by reductive elimination. Such processes may be related to the palladium- and rhodium-catalyzed direct intermolecular arylations of indoles, which proceed *via* electrophilic metallation and involve C2/C3 equilibration.[8,9]

Finally, the mechanism could involve a nitrene formed from the primary amino group engaging in a cycloaddition with the indole double bond forming an aziridine **20**. Intramolecular nucleophilic ring opening, as indicated in Scheme 11 would complete the process. This step would have to involve considerable S_N1 character in the breaking of the C–N bond, to allow formation of the observed stereochemical outcome.



Scheme 11

Experimental Section

General Procedures. Reagents and solvents were purified according to *Purification of Laboratory Chemicals,* Armarego, W. and Chai C., Elsevier (2003). Melting points (mp) were determined in a Büchi Melting Point B540 in open capillaries and are uncorrected. Automatic flash chromatography was carried out in an Isco Combiflash medium pressure liquid chromatograph with Redisep silica gel columns (47-60 μm), and C-18 reverse phase columns. A Branson ultrasound bath was used to perform sonication. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Mercury 400 MHz spectrometer and a Gemini 200 MHz spectrometer. Multiplicity of the carbons was assigned with DEPT and gHSQC experiments, although the usual abbreviations according to off-resonance decoupling are used: (s) singlet, (d) doublet, (t) triplet, and (q) quartet. The same abbreviations are used for the multiplicity of signals in H-NMR and also: (m) multiplet, (bs) broad singlet, (bt) broad triplet. Spectra were referenced to appropriate residual solvent peaks (d_6-DMSO, or $CDCl_3$). IR spectra were obtained on a Thermo Nicolet FT-IR spectrometer. HRMS were performed on a Bruker Autoflex high-resolution mass spectrometer by Unidad de Espectrometría de Masas (Universidad de Santiago de Compostela) and by Servei d'Espectrometria de Masses (Universitat de Barcelona). Microwave-assisted reactions were carried out in a CEM Discover microwave apparatus. An automatic syringe pump was used as specified for controlled addition of some reactants. Reversed phase analytical HPLC was performed on a Waters Alliance separation module 2695 using a Waters Xterra MS C_{18} column (150 x 4.6 mm, 5 μm) and a Waters 996 PDA detector at 254 nm.

(*E*)-3-(1-Methylindol-3-yl)propenal (9). NaOEt (1.35 g, 18.8 mmol) was added to a suspension of 2-(1,3-dioxolan-2-yl)ethyltriphenylphosphonium bromide **8** (4.40 g, 10.1 mmol) in THF-EtOH (99:1, 100 mL). The mixture was stirred at r.t. for 1 h during which time it turned yellow. Then, 3-formyl-1-methylindole **7** (1.0 g, 6.3 mmol) was added, and the mixture was stirred for 72 h at reflux. The solvent was removed and the residue was dissolved in EtOAc, and washed with sat. NH_4Cl then brine. The organic solution was dried over $MgSO_4$ and solvent removed. The residue was digested with hexane. The hexane solution was collected and evaporated. The residue was purified by SiO_2 flash chromatography. Elution with CH_2Cl_2 gave **9** (1.02 g, 71%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.85 (s, 3H); 6.74 (dd, *J* = 15.7, 7.9 Hz, 1H); 7.26-7.37 (m, 3H); 7.38 (s, 1H); 7.65 (d, *J* = 15.7, 1H); 7.90 (dd, *J* = 7.9 and 2.3 Hz, 1H); 9.60 (d, *J* = 7.9 Hz, 1H). MS (ESI) 186 (M+1, 100).

3-(1-Methylindol-3-yl)propan-1-ol (10). Pd/C (10%) was added to a solution of **9** (2.2 g, 12.0 mmol) in *t*-BuOH (100 mL). The suspension was purged with H_2 and stirred for 16 h. The reaction mixture was filtered through a Celite pad, which was then washed with CH_2Cl_2. The solvent was removed under vacuum to provide compound **10** (quant. yield). ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.42 (bs, 1H); 1.97 (m, 2H); 2.85 (t, *J* = 7.5 Hz, 2H); 3.72 (t, *J* = 6.5 Hz, 2H); 3.74 (s, 3H, Me); 6.85 (s, 1H); 7.10 (t, *J* = 7.6 Hz, 1H); 7.18-7.27 (m, 2H); 7.60 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.3 (t); 32.6 (q); 33.2 (t); 62.7 (t); 109.1 (d); 114.3 (s); 118.5 (d); 118.9 (d); 121.4 (d); 126.1 (d); 127.9 (s); 137.0 (s). MS (ESI) 190 (M+1, 100), 191 (M+2, 16).

3-(1-Methylindol-3-yl)prop-1-yl methanesulfonate (11). Mesyl chloride (299 μL, 3.9 mmol) was added to a solution of **10** (609.5 mg, 3.2 mmol), DMAP (39.3 mg, 0.3 mmol) and Et_3N (449 μL, 3.54 mmol) in CH_2Cl_2 (30 mL). The reaction mixture was stirred for 1 h at r.t. After this time, the solution was washed with sat. NH_4Cl then brine. The organic solution was dried and evaporated to give **11** as a yellow oil (770 mg, 90%) which was used without further purification. ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.14 (m, 2H); 2.90 (t, *J* = 7.2 Hz, 2H); 2.98 (s, 3H, Me); 3.75 (s, 3H, Me); 4.27 (t, *J* = 6.3 Hz, 2H); 6.88 (s, 1H); 7.10 (dd, *J* = 6.7 and 1.5 Hz, 1H); 7.19-7.32 (m, 3H); 7.56 (d, *J* = 7.8 Hz, 1H).

3-(1-Methylindol-3-yl)propan-1-amine (12). A mixture of **11** (1.07 g, 4.0 mmol) and sodium diformylamide (0.57 g, 6.0 mmol) in dry DMF (30 mL) were stirred for 8 h at 50 ºC. The solvent was removed under reduced pressure. The crude material was dissolved in MeOH (30 mL) and heated at reflux for 2 h. After this time 1M HCl·MeOH (45 mL) was added and the solution was heated at reflux temperature for 3 h. Elimination of the solvent under vacuum afforded **12** (693 mg, 92%) pure, as a yellow solid. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.86-1.92 (m, 4H); 2.81-2.86 (m, 4H); 3.73 (s, 3H, Me); 6.85 (s, 1H); 7.16 (t, *J* = 7.9 Hz, 1H); 7.27 (t, *J* = 7.9 Hz, 1H); 7.32 (d, *J* = 7.9 Hz, 1H); 7.65 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.2 (t); 32.3 (q); 33.9 (t); 41.7 (t); 108.9 (d); 114.5 (s); 118.3 (d); 118.8 (d); 121.2 (d); 125.8 (d); 127.7 (s); 136.8 (s). MS (ESI) 189 (M+1, 100), 190 (M+2, 15).

***N*-3-(1-Methylindol-3-yl)propan-*N*-(2,2,2-trichloroethoxysulfonyl)guanidine (5).** A thick-walled tube was charged with *S*-methyl-*N*-(2,2,2-trichloroethoxysulfonyl)isothiourea **13** (267.7

mg, 0.9 mmol), **12** (167.1 mg, 0.9 mmol), 2.0 mL of H_2O, and a magnetic stir bar. The vessel was sealed with a Teflon screw-cap and heated at 100 ºC for 4 h. After this time, the reaction mixture was cooled to r.t. and 5 mL of CH_2Cl_2 were added. The biphasic mixture was transferred to a separatory funnel, and partitioned between 10 mL CH_2Cl_2 and 10 mL H_2O. The aqueous solution was extracted with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by SiO_2 chromatography with hexane-EtOAc (80:20 to 40:60) afforded the product **5** (247 mg, 63%) as a yellow oil. IR (film) ν 3460, 3358, 2942, 2250, 1628, 1588, 1551, 1318, 1180, 1131, 1021, 742 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.95 (bs, 2H, CH_2); 2.80 (bt, 2H, CH_2); 3.12 and 3.30 (2x bs, 2H, CH_2); 3.72 (s, 3H, Me); 4.59 (s, 2H); 5.90 (bs, 1H); 6.26 (bs, 1H); 6.53 (bs, 1H); 6.88 (s, 1H); 7.11 (t, *J* = 7.9 Hz, 1H); 7.26 (t, *J* = 7.9 Hz, 1H); 7.30 (d, *J* = 7.9 Hz, 1H); 7.57 (d, *J* = 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.0 (t); 29.1 (t); 32.5 (q); 41.2 (t); 78.0 (t); 94.0 (s); 109.2 (d); 118.6 (2d); 121.5 (d); 126.4 (d); 127.4 (s); 136.9 (s); 156.8 (s). MS (ESI) 441 (M+1, 96), 443 (M+3, 100), 444 (M+4, 12). HRMS *m/z* calcd. for $C_{15}H_{20}Cl_3N_4O_3S$ 441.0316, found 441.0316.

1,2,3,6,6a,7-Hexahydro-7-methyl-5-(*N*-(2,2,2-trichloroethoxysulfonyl)imino)-1*H*-pyrrolo[1,2-*c*]imidazolo[5,4-*b*]indole (2). A flame-dried 25 mL Schlenk flask was charged with **5** (96.6 mg, 0.22 mmol), $Rh_2(esp)_2$ (3.3 mg, 4.4 μmol), $PhI(OAc)_2$ (116.4 mg, 0.35 mmol), and MgO (22.5 mg, 0.55 mmol). The reaction vessel was closed with a rubber septum, the contents placed briefly under vacuum, and the flask then backfilled with Ar. This process was repeated two additional times prior to the addition of 2 mL of deoxygenated toluene. The resulting deep green suspension was heated at 40 °C and stirred for 16 h. After this time, the mixture was cooled to r.t., and the residue was purified by column chromatography over silica gel. Elution with hexane-EtOAc (from 75:25 to 65:35), afforded **2** (23 mg, 23%) as a yellow oil. IR (film) ν 3367, 2925, 1786, 1584, 1498, 1179, 852 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.99-2.07 (m, 1H); 2.16-2.25 (m, 1H); 2.31-2.41 (m, 2H); 2.94 (s, 3H); 3.33-3.38 (m, 1H); 3.89-3.95 (m, 1H); 4.60 (d, *J* = 11.0 Hz, 1H); 4.65 (d, *J* = 11.0 Hz, 1H); 5.34 (s, 1H, CH); 6.54 (d, *J* = 7.5 Hz, 1H); 6.76 (t, *J* = 7.5 Hz, 1H); 7.13 (d, *J* = 7.5 Hz, 1H); 7.24 (t, *J* = 7.5 Hz, 1H); 7.55 (bs, 1H, NH). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.4 (t); 29.7 (s); 32.7 (q); 34.8 (t); 45.1 (t); 78.3 (t); 84.7 (d); 94.1 (s); 107.4 (d); 118.8 (d); 122.9 (d); 129.2 (s); 130.5 (d); 149.8 (s); 160.9 (s). MS (ESI-TOF) 439 (M+1, 84), 441 (M+3, 100). HRMS *m/z* calcd. for $C_{15}H_{18}Cl_3N_4O_3S$ 439.0165, found 439.0159.

1,2,3,6,6a,7-Hexahydro-7-methyl-5-imino-1*H*-pyrrolo[1,2-*c*]imidazolo[5,4-*b*]indole (14). Compound **2** (22.6 mg, 0.05 mmol) was added to a suspension of powdered Zn (17.7 mg, 0.26 mmol) in 1.5 mL of a 50:50 MeOH/AcOH solution. The mixture was stirred vigorously at 40 ºC for 16 h. The reaction was then cooled to r.t. and diluted with 1 mL of MeOH, and the contents filtered through a small pad of Celite with additional elution with MeOH. The combined filtrates were concentrated under reduced pressure and the residue was purified by reverse phase chromatography. Elution with H_2O/MeCN (60:40 to 40:60) gave **14** as a white solid (3.4 mg, 29%). ^1H NMR (d_6-DMSO, 400 MHz) δ 1.85-1.96 (m, 2H, CH_2); 2.09-2.18 (m, 2H, CH_2); 2.83 (s, 3H, Me); 3.03-3.07 (m, 1H); 3.55-3.61 (m, 1H); 5.17 (s, 1H, CH); 5.74 (s, 1H); 6.48 (d, *J* =

7.9 Hz, 1H); 6.62 (t, *J* = 7.4 Hz, 1H); 7.08-7.15 (m, 2H); 8.14 (bs, 1H). MS (ESI-TOF) 229 (M+1, 100). HRMS *m/z* calcd. for $C_{13}H_{17}N_4$ 229.1453, found 229.1455.

Acknowledgements

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References

1. Reyes, F.; Fernández, R.; Rodríguez, A.; Francesch, A.; Taboada, S.; Ávila, C.; Cuevas, C. *Tetrahedron* **2008**, *64*, 5119.
2. (a) Ayats, C.; Soley, R.; Albericio, F.; Álvarez, M. *Org. Biomol. Chem.*, **2009**, *7*, 860; (b) Hernández, D.; Vilar, G.; Riego, E.; Cañedo, L. M.; Cuevas, C.; Albericio, F.; Álvarez, M. *Org. Lett.* **2007**, *9*, 809; (c) Tulla-Puche, J.; Bayó-Puxan, N.; Moreno, J. A.; Francesch, A. M.; Cuevas, C.; Álvarez, M.; Albericio, F. *J. Am. Chem. Soc.* **2007**, *129*, 5322; (d) Pla, D.; Marchal, A.; Olsen, C. A.; Albericio, F.; Álvarez, M. *J. Org. Chem.* **2005**, *70*, 8231.
3. (a) Hernández, D.; Riego, E.; Albericio, F.; Álvarez, M. *Eur. J. Org. Chem.* **2008**, 3389; (b) Hernández, D.; Altuna, M.; Cuevas, C.; Aligué, R.; Albericio, F.; Álvarez, M. *J. Med. Chem.* **2008,** *51,* 5722; (c) Hernández, D.; Riego, E.; Francesch, A.; Cuevas, C.; Albericio, F.; Álvarez, M. *Tetrahedron*, **2007**, *63*, 9862; (d) Pla, D.; Marchal, A.; Olsen, C. A.; Francesch, A.; Cuevas, C.; Albericio, F.; Álvarez, M. *J. Med. Chem.* **2006,** *49,* 3257.
4. (a) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378; (b) Fiori, K. W.; Du Bois, J. *J. Am. Chem. Soc.* **2007**, *129*, 562; (c) Kim, M.; Mulcahy, J. V.; Espino, C. G.; Du Bois, J. *Org. Lett.* **2006**, *8*, 1073.
5. For an alternative synthesis see López, S.; Rodríguez, V.; Montenegro, J.; Saa, C.; Álvarez, R.; López, C. S.; de Lera, A. R.; Simon, R.; Lazarova, T.; Padros, E. *ChemBioChem* **2005**, *6*, 2078.
6. For an alternative synthesis see Steinhoff, J.; López-Alvarado, P.; Miranda, S.; Avendano, C.; Menéndez, J. C. *International Electronic Conferences on Synthetic Organic Chemistry*, 5th, 6th, Sept. 1-30, 2001 and 2002 and 7th, 8th, Nov. 1-30, 2003 and 2004, **2004**, 1444.
7. Padwa, A.; Stengel, T. *Org. Lett*. **2002**, *4*, 2137.
8. Wang, X.; Lane, B. S.; Sames, D. *J. Am. Chem. Soc*. **2005**, *127*, 4996.
9. Campeau, L.-C.; Stuart, D. R.; Fagnou, K. *Aldrichimica Acta* **2007**, *40*, 35.