Syntheses of Batzelline A, Batzeline B, Isobatzelline A, and Isobatzelline B

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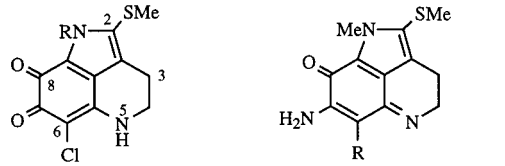
Batzellines A and B (**1a**, **b**) and isobatzellines A and B (**2a**, **b**) are 1,3,4,5-tetrahydropyrrolo[4,3,2-*de*]quinoline-containing marine alkaloids characterized by the presence of a methylthio substituent at C-2 of the tricyclic system. We describe here the total synthesis of these natural compounds following the synthetic strategy that we have used previously for the synthesis of damirones A and B, batzelline C, isobatzelline C, discorhabdin C, and makaluvamines A, B, C, and D. The introduction of the methylthio group by electrophilic substitution of a pyrrolo[4,3,2-*de*]quinoline, appropriately substituted and in a suitable oxidation state, is the key step in the success of these syntheses.

We have previously described our strategy for the synthesis of 1,3,4,5-tetrahydropyrrolo[4,3,2-*de*]quinoline-containing marine alkaloids, which is based on the elaboration of easily accessible quinoline starting compounds. Previous papers[1] have detailed the use of this route for the synthesis of damirones A and B, batzelline C, isobatzelline C, discorhabdin C, and makaluvamines A, B, C, and D, and in a preliminary communication[2] we described the first synthesis of one of the sulfur-containing members of the group, namely isobatzelline B. We present here details of our synthesis of isobatzelline B[3] **2b**, as well as of syntheses of isobatzelline A[3] **2a** and of batzellines A and B,[4] **1a** and **1b**.



1 R
a Me batzelline A
b H batzelline B

2 R
a Cl isobatzelline A
b H isobatzelline B

Figure 1. Structures of the synthesised marine alkaloids

Each of the natural products described in this paper has as a common feature, namely a methylthio substituent at the α-position of the pyrrole ring. In the design of a route to access such compounds, late reductive stages that might result in cleavage of this moiety after its introduction thus have to be avoided. The initial plan for the introduction of the methylthio group was based on previous work, in which cyclizations involving a thionium cation as an electrophile had been accomplished, with retention of sulfur in the products.[5] Thus, we set out to generate a suitable thionium cation that would allow ring-closure to the five-membered ring with retention of sulfur at the required position. The utility of dimethyl(methylthio)sulfonium tetrafluoroborate (DMTSF)[6] as a reagent for converting a dithioacetal into an electrophilic species, effectively $C{=}S^{+}Me$, has been well documented.[7] In previous studies, the thionium electrophilic entity has been trapped with an intramolecular carbon nucleophile.[5] The concept in the present work, however, is a trapping of the putative $C{=}S^{+}Me$ unit by intramolecular attack of a formamide nitrogen (Scheme 1).

Reaction of nitro aldehyde **3**[1c] with methanethiol and boron trifluoride furnished the dithioacetal **4**, but unfortunately reduction of the pyridine ring and of the nitro group also led to hydrogenolysis of the sulfurs, resulting in the formation of **5**. An alternative route to a suitable dithioacetal started from the amino acetal **6**;[1c] formylation of both nitrogen centres gave a bis(formamide), which was then converted into dithioacetal **7** by reaction with methanethiol and boron trifluoride. Treatment of **7** with DMTSF did indeed result in the formation of tricyclic product **8**, containing a methylthio group at the appropriate position, albeit only in 30% yield. The key evidence in assigning the structure of the product was a three-hydrogen singlet at δ = 2.50 attributable to the *S*-methyl group, and doublets of doublets at δ = 4.96 and 5.07 (with *J* values of 8 and 0.8 Hz) for the hydrogen at C-2, the doubling of signals resulting from restricted formamide rotation, a phenomenon which complicated many of the spectra of the compounds described in this paper. It was felt that this cyclization yield was too low to merit further investigation of this route, which would then have required dehydrogenation of the five-membered ring, perhaps by *S*-oxidation and a Polonovski-type process.

We next examined the possibility of introducing the methylthio group into an intact tricycle at the tetrahydropyrrolo[4,3,2-*de*]quinoline oxidation level, i.e. into a β-substituted indole. There were two obvious methods to be evaluated: (1) α-lithiation of an *N*-masked indole followed by reaction with dimethyl disulfide, and (2) electrophilic substitution at the unsubstituted indole α-position using

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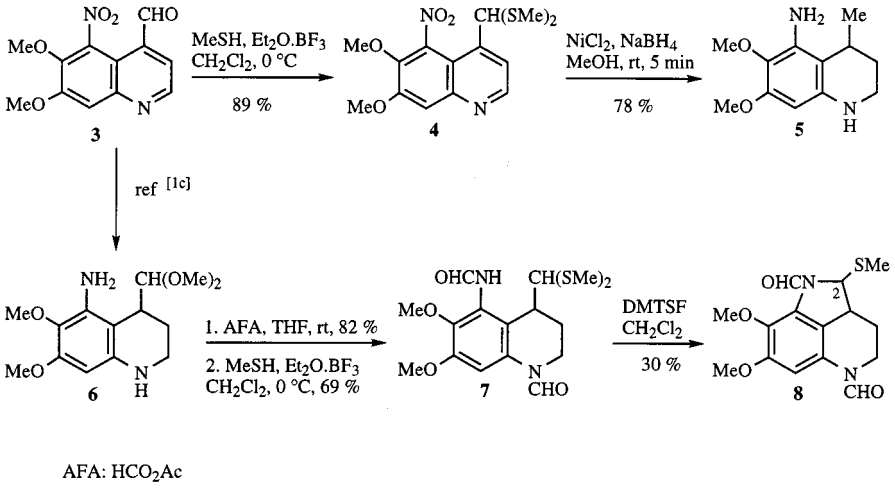
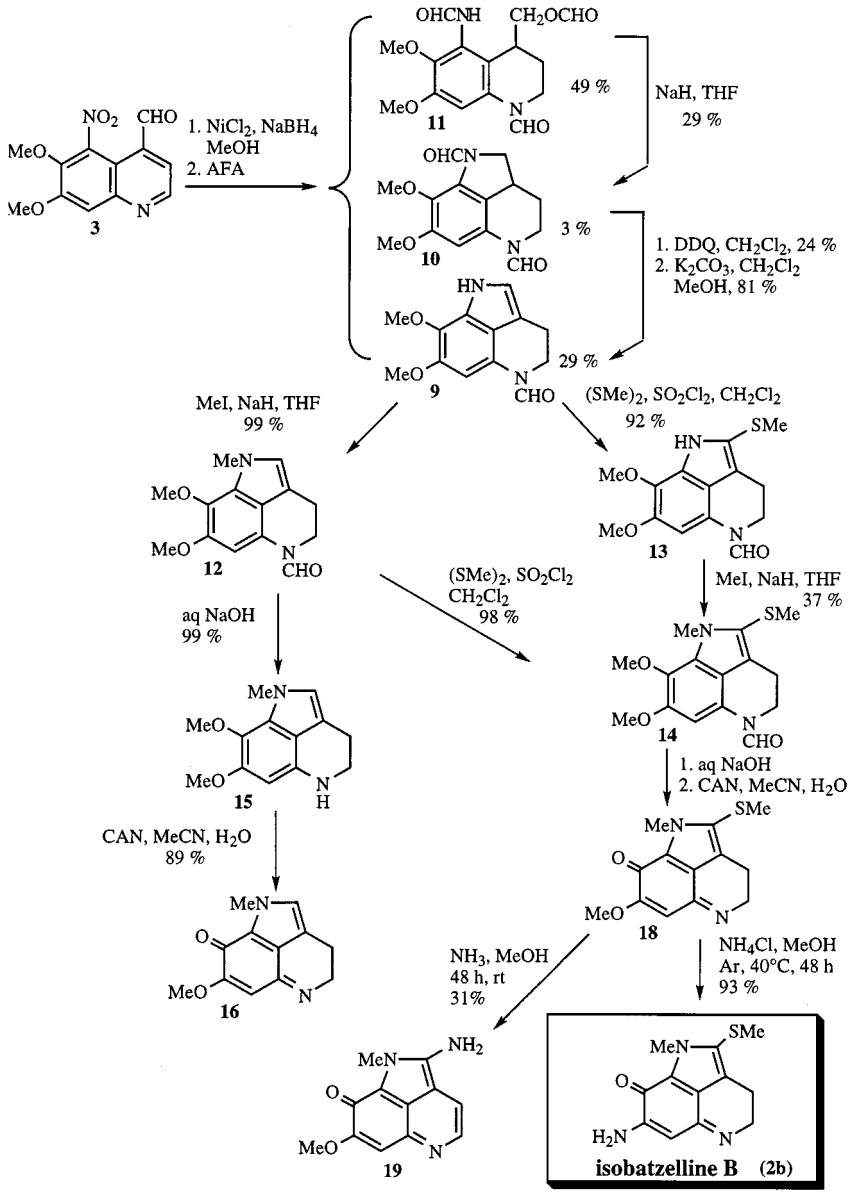


Scheme 1. Synthesis of 1,5-diformyl-1,2,2a,3,4,5-hexahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline



Scheme 2. Synthesis of isobatzelline B (**2b**)

some source of "MeS^+". Scheme 2 shows how the second strategy was employed in our synthesis of isobatzelline B.

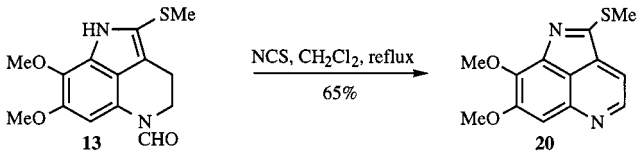
Reduction of the nitro aldehyde **3** with a large excess of nickel(II) chloride and sodium borohydride, followed by formylation with acetic formic anhydride (AFA), gave a three-component mixture of the desired tricyclic indole **9**, the indoline **10**, and the bicyclic tetrahydroquinoline **11**. Both of the side-products could be utilized; thus, the bicyclic bis(formamide)formate **11** could be converted into tricyclic **10**, using sodium hydride to generate a nitrogen nucleophile capable of displacing formate, and **10** could be dehydrogenated and selectively hydrolysed to give **9**. The *N*-methyl group required in the structure of isobatzelline B could easily be introduced by treating **9** with iodomethane and sodium hydride as a base, thereby affording **12**.

The crucial electrophilic sulfur substitution worked equally well with the *N*-hydrogen indole **9** or its *N*-methyl derivative **12**, giving **13** and **14**, respectively. However, since the *N*-methylation of **13** was not so efficient as that of **9**, it proved preferable to perform the *N*-methylation first. Methanesulfenyl chloride was generated in situ[8] by the interaction of dimethyl disulfide with sulfuryl chloride, and led to α-substitutions of indoles **9** and **12** in yields exceeding 90%. That the methylthio group had been introduced at the 2-position and not at the 6-position of the electron-rich six-membered ring was confirmed by an NMR experiment: irradiation of the one-hydrogen aromatic singlet signal of **13** resulted in a positive NOE for the methoxy group at C-7.

Hydrolytic deformylation of **12** and subsequent oxidation with ammonium cerium(IV) nitrate (CAN) produced **15** and quinone-imine **16**, respectively. The latter quinone-imine proved to be totally resistant to the electrophilic sulfur reagent. The desired quinone-imine **18** was obtained by hydrolysis followed by CAN oxidation of **14**, such that only replacement of the 7-methoxy group with an amino group remained to complete the synthesis of isobatzelline B (**2b**).

A first attempt at carrying out the desired displacement yielded **19**, in which the methylthio, not the methoxy group, had been replaced and in which oxidation had also occurred. We speculate that the oxidation preceded the sulfur displacement as this reaction pathway was completely suppressed when the ammonolysis was conducted under argon in a tightly sealed flask. Under the latter conditions, isobatzelline B (**2b**) was produced in almost quantitative yield from **18**.

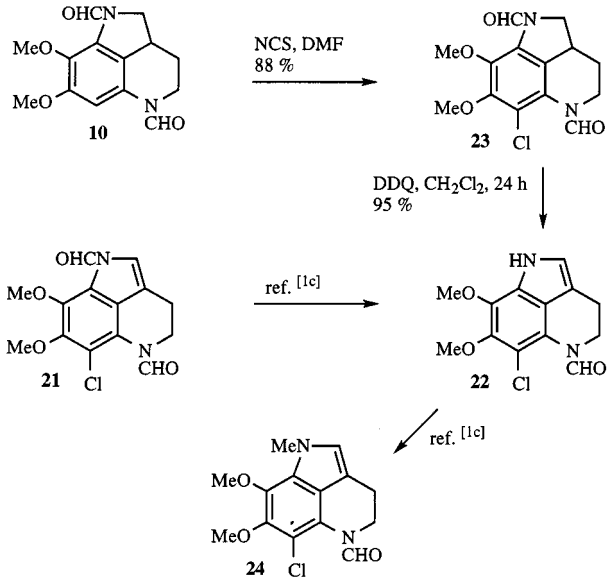
Besides each having a 2-methylthio group, batzellines A and B, and isobatzelline A also have in common a chloro substituent at C-6. As discussed in relation to the introduction of the sulfur substituent, the stage at which the reductively sensitive 6-chloro could be introduced was of central importance in planning the synthetic sequences leading to these three natural products. Hence, an attempt was made to introduce the chlorine into one of the later intermediates described above. Reaction of **13** with *N*-chlorosuccinimide, however, led only to aromatization and the formation of **20**, not to chlorination of the benzene ring (Scheme 3). Schemes 4 and 5 show how we were able to introduce the chlorine at an early stage and retain it throughout the sequence, thereby furnishing batzelline A (**1a**) and isobatzelline A (**2a**).



Scheme 3. Attempted 6-chlorination of 5-formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (**13**)

In a previous paper, we described the synthesis of the chlorobis(formamide) **21** as well as its efficient and selective hydrolysis to chloroformamide **22** and *N*-methylation of the latter to give **24**.[1c] As an alternative route to that used previously, the chloroformamide **22** could also be obtained from **10** in two efficient steps. Reaction of **10** with *N*-chlorosuccinimide gave **23** and subsequent dehydrogenation using 2,3-dichloro-5,6-dicyanobenzo-1,4-quinone (DDQ) gave **22**. Products **22** and **24** form the basis of our syntheses of batzellines A and B, and of isobatzelline A.

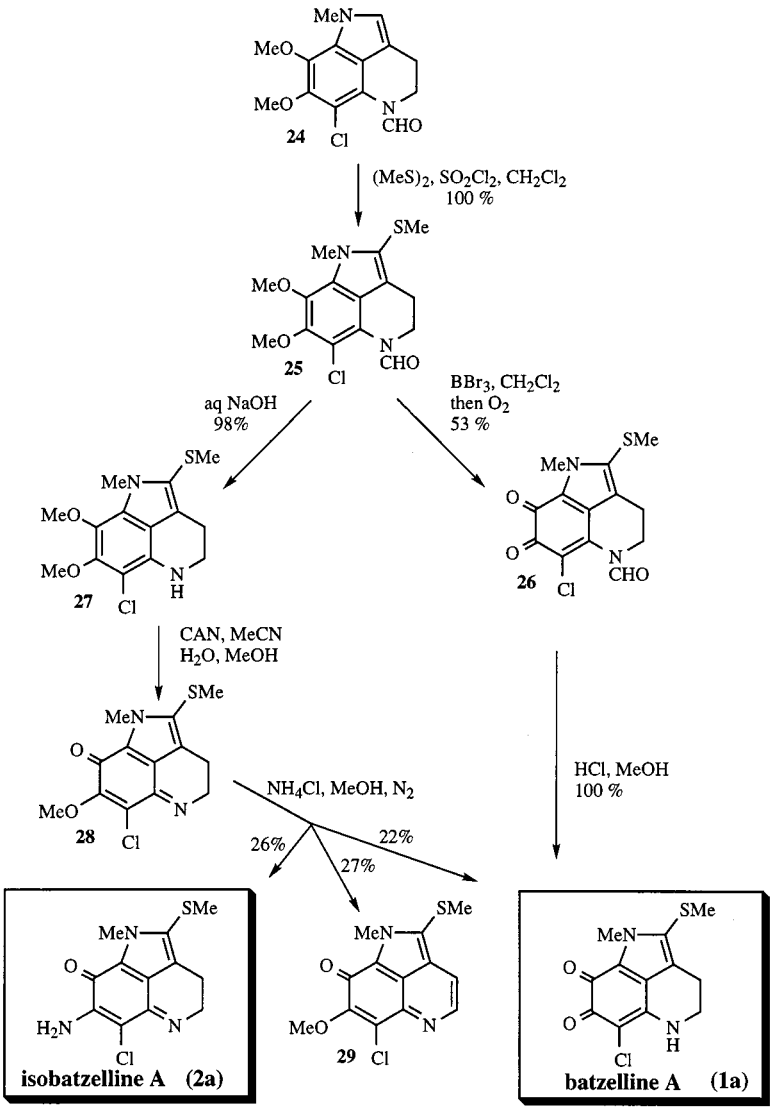
Compounds **13**, **15**, **23** and **25** were subjected to proton−carbon hetero-multibond correlation (HMBC) NMR experiments, the results of which allowed us to assign unambiguously all of the carbon signals of these and related compounds described in this paper (see Experimental Section).



Scheme 4. Synthesis of 6-chloro-5-formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-1-methylpyrrolo[4,3,2-*de*]quinoline (**24**)

Introduction of the methylthio group into **24** using the aforementioned electrophilic substitution protocol gave **25**, again in high yield. Subsequent double de-*O*-methylation using boron tribromide and aerial oxidation gave the *ortho*-quinone **26**, which was simply and quantitatively hydrolysed in aqueous acid to give batzelline A (**1a**) (Scheme 5).

Isobatzelline A (**2a**) was also prepared from the formamide **25**. Base-catalysed hydrolytic removal of the formyl protection gave **27**, and subsequent oxidation with CAN and replacement of the 6-methoxy group by reaction with am-



Scheme 5. Syntheses of batzelline A (**1a**) and isobatzelline A (**2a**)

monium chloride in methanol with exclusion of air in a tightly sealed flask gave **2a**, together with approximately equal yields of the oxidized derivative **29** and batzelline A (**1a**). The formation of the latter must involve attack by water, either on **2a**, or rather, as we believe, on the quinone-imine **28**, as indicated in Scheme 5.

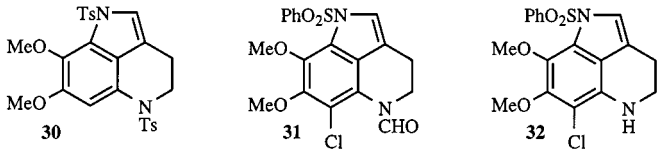
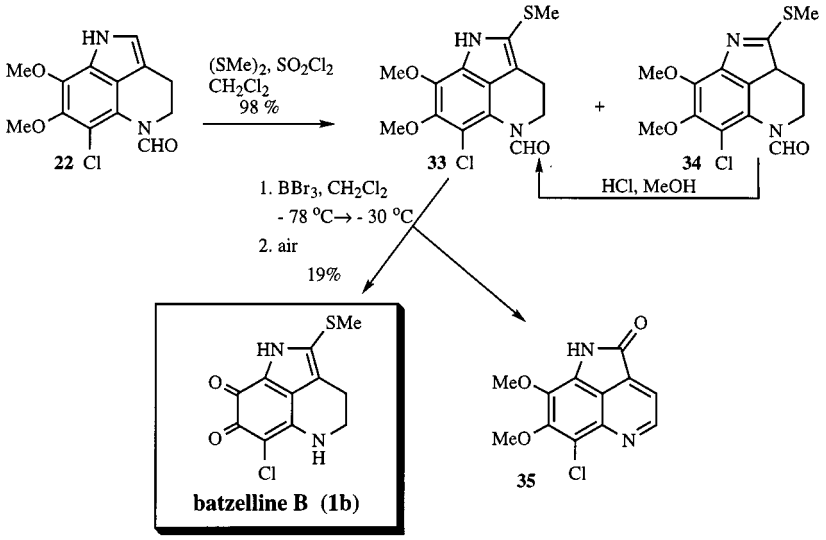


Figure 2. Structures of the *N*-arylsulfonyl derivatives **30**, **31** and **32**

We next examined the possibility of introducing the methylthio group through α-lithiation of the indole subunit. Experiments were conducted using the bis-*p*-toluenesulfonyl derivative **30**[1c] as well as the *N*-phenylsulfonylindole **31**, obtained from **22** by a catalysed phase-transfer reaction with benzenesulfonyl chloride. Treatment of **30** with *n*-butyllithium at −78°C produced a deep-red solution, from which the starting material could be recovered in high yield by the addition of water. However, quenching of the red solution with CD_3OD led to the incorporation (61% by ^{1}H-NMR analysis) of deuterium at C-6 and not at the desired C-2 position. With the 6-blocked 1-phenylsulfonylindole **31**, no evidence for any lithiation could be detected; the only changed product obtained upon treatment of **31** with lithium diisopropylamide (LDA) (then with dimethyl disulfide) under conditions that routinely bring about α-lithiation of 1-phenylsulfonylindoles,[9][10] was the deformylated compound **32**. It may be significant that, although lithiation of 3-substituted 1-phenylsulfonylindoles, e.g. of 3-methyl-1-phenylsulfonylindole,[11] proceeds normally, there are no reported examples of 7-methoxy-1-phenylsulfonylindoles undergoing C-2 lithiation.

For the synthesis of batzelline B, formamide **22** was reacted with the dimethyl disulfide/sulfuryl chloride reagent. Once again, introduction of the methylthio group at the in-



Scheme 6. Synthesis of batzelline B (**1b**)

dole 2-position proceeded smoothly and efficiently, but interestingly, a mixture of the 1*H*- and 3*H*-indole tautomers **33** and **34** was obtained. In some runs, *only* the 3*H*-tautomer **34** was isolated. Transformation of the unexpected tautomer into the 1*H*-tautomer was easily achieved by heating in methanol containing a trace of acid. There do not seem to be any previous examples of the isolation of the 3*H*-tautomer of a 2-alkylthioindole such as **34**.

The conversion of **33** into batzelline B (**1b**) by treatment with boron tribromide and subsequent exposure to air was accompanied by the formation of some of the aromatized lactam **35**, which was isolated following column chromatographic work-up. The formation of **35** may involve oxidation of the 3*H*-indole tautomer **34**, since no such lactam was obtained in the corresponding conversion of the *N*-1-methyl analogue **25** into **26**.

Experimental Section

General: Melting points were determined in capillary tubes and are uncorrected. − TLC was carried out on SiO_2 (Merck silica gel 60 F_{254}, 0.063−0.200 mm) and spots were located with UV light. − Column chromatography was carried out on SiO_2 (SDS silica gel 60, 0.060−0.2 mm). − Flash chromatography was carried out on SiO_2 (Merck silica gel 60 A CC). − Organic extracts were dried with anhydrous Na_2SO_4; solvents were evaporated under reduced pressure in a rotary evaporator. − IR spectra were recorded on a Nicolet 205 FT-IR spectrometer. − NMR spectra were measured with Varian Gemini 200 (200 MHz), Varian Gemini 300 (300 MHz), and Varian VXR-500 (500 MHz) spectrometers; data are given in δ referenced to TMS. − Mass spectra were measured in electron impact (EI) mode with a Hewlett-Packard model 5989A. High-resolution mass spectra were obtained with an Autospec/VG by the Departament de Química Orgànica Biològica (C.S.I.C.), Barcelona. − Elemental analyses were performed with a C. E. Instruments EA-1108 analyser at the Serveis Científico-Tècnics de la Universitat de Barcelona.

4-Bis(methylthio)methyl-6,7-dimethoxy-5-nitroquinoline (4): A solution of the quinoline **3**[1c] (0.5 g, 1.9 mmol), $BF_3{\cdot}Et_2O$ (2.3 mL, 18.7 mmol), and an excess of methanethiol in dry CH_2Cl_2 (27 mL) was stirred at 0°C for 16 h in a tightly stoppered flask. The solution was then poured onto ice, basified with 12 N NaOH, and extracted with CH_2Cl_2. The organic extract was dried and the solvent was evaporated to give the dithioacetal **4** (565 mg, 89%) as an oil. − IR (film): $\tilde{\nu}$ = 1534 cm^{-1} (s, NO_2), 1286 (s, NO_2). − ^1H NMR (200 MHz, $CDCl_3$): δ_H = 2.14 (s, 6 H, SCH_3), 4.06 (s, 3 H, OCH_3), 4.09 (s, 3 H, OCH_3), 5.06 (s, 1 H, CH), 7.80 (s, 1 H, 8-H), 7.99 (d, *J* = 5.2 Hz, 1 H, 3-H), 8.88 (d, *J* = 5.2 Hz, 1 H, 2-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 15.7 (q, SCH_3), 49.6 (d, CH), 56.8 (q, OCH_3), 62.8 (q, OCH_3), 108.6 (s, C-4a), 110.3 (d, C-8), 112.4 (s, C-5), 120.8 (d, C-3), 122.2 (s, C-6), 143.8 (s, C-8a), 145.9 (s, C-4), 148.3 (d, C-2), 154.8 (s, C-7). − MS (EI); *m/z* (%) = 341 [M + 1] (0.3), 294 (100), 293 (17), 246 (4). − HRMS: calcd. for $C_{13}H_{13}N_2O_4S$ [(M + 1 − SMe)$^+$] 294.0674; found 294.0675.

5-Amino-1,2,3,4-tetrahydro-6,7-dimethoxy-4-methylquinoline (5): To a solution of **4** (100 mg, 0.3 mmol) in MeOH (10 mL) was added $NiCl_2{\cdot}6H_2O$ (909 mg, 3.8 mmol). After stirring for 5 min. at room temp., $NaBH_4$ (890 mg, 23.5 mmol) was added in small portions. Following the addition, stirring was continued for a further 5 min. The reaction mixture was then diluted with H_2O and extracted with CH_2Cl_2. The organic extract was dried and the solvent was evaporated, giving 4-methyltetrahydroquinoline **5** (71 mg, 78%) as an oil. − IR (film): ν = 3360 cm^{-1} (s, NH_2), 3350 (s, NH_2). − ^1H NMR (200 MHz, $CDCl_3$): δ_H =1.19 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.70 (ddd, *J* = 13.0, 7.5 and 2.0 Hz, 1 H, 3-Hax), 1.87−1.95 (m, 1 H, 3-Heq), 2.67−2.82 (m, 1 H, 4-H), 3.20 (dt, *J* = 11.3 and 8.1 Hz, 1 H, 2-Hax), 3.33 (ddd, *J* = 13.0, 11.3 and 2.8 Hz, 1 H, 2-Heq), 3.75 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 5.59 (s, 1 H, 8-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C =20.5 (q, CH_3), 25.1 (d, C-4), 28.7 (t, C-3), 36.2 (t, C-2), 55.3 (q, OCH_3), 60.1 (q, OCH_3), 88.9 (d, C-8), 104.6 (s, C-4a), 128.1 (s, C-6), 138.4 (s, C-5), 139.9 (s, C-8a), 151.3 (s, C-7). − MS (EI); *m/z* (%) = 222 [M^+] (35), 207 (100). − HRMS: calcd. for $C_{12}H_{18}N_2O_2$ 222.1368; found 222.1375.

4-Dimethoxymethyl-5-formamido-1-formyl-1,2,3,4-tetrahydro-6,7-dimethoxyquinoline: To a solution of **6**[1c] (270 mg, 1.0 mmol) in dry THF (3 mL) was added acetic formic anhydride (AFA) [prepared from HCO_2H (0.2 mL, 4.5 mmol) and Ac_2O (0.4 mL, 4.5 mmol)] and the resulting mixture was stirred at room temp. under nitrogen for 16 h. The solvent was then evaporated under reduced pressure, the residue was redissolved in CH_2Cl_2, and the resulting

solution was washed with satd. aq. $NaHCO_3$. The organic phase was dried and the solvent was evaporated to give a crude product, which was purified by column chromatography. Elution with CH_2Cl_2/MeOH (99:1 to 98:2) gave the bis(formamide) of **6** (266 mg, 82%) as an oil. − IR (film): $\tilde{\nu}$ = 3317 cm^{-1} (s, NH), 1688 (s, CO), 1673 (s, CO), 1671 (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.62−1.80 (m, 1 H, 3-Hax), 2.29 (dm, *J* = 12.8 Hz, 1 H, 3-Heq), 3.20−3.80 (m, 3 H, 2-Hax, 2-Heq and 4-H), 3.35 (s, 3 H, OCH_3), 3.44 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 4.36 (d, *J* = 8.4 Hz, 1 H, CH), 6.67 and 6.68 (2 s, 1 H, 8-H), 8.07 (d, *J* = 11.5 Hz, 1 H, NH), 8.44 (d, *J* = 11.5 Hz, 1 H, 1-NCHO), 8.84 (s, 1 H, 5-NCHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 22.7 (t, C-3), 35.2 (d, C-4), 38.5 (t, C-2), 51.6 (q, OCH_3), 56.0 (q, OCH_3), 56.7 (q, OCH_3), 60.3 (q, OCH_3), 99.8 (d, CH), 105.1 (d, C-8), 115.0 and 116.9 (2 s, C-4a), 128.5 and 130.0 (2 s, C-5), 132.5 and 133.1 (2 s, C-6), 139.6 (s, C-8a), 152.5 and 152.7 (2 s, C-7), 159.5 and 161.4 (2 d, CHO), 164.9 and 165.3 (2 d, CHO). — MS (EI); *m/z* (%) = 338 [M^+] (3), 307 (2), 276 (2), 294 (4). − HRMS: calcd. for $C_{16}H_{22}N_2O_6$ 338.1478; found 338.1469.

4-Bis(methylthio)methyl-5-formamido-1-formyl-1,2,3,4-tetrahydro-6,7-dimethoxyquinoline (7): A solution of 4-dimethoxymethyl-5-formamido-1-formyl-1,2,3,4-tetrahydro-6,7-dimethoxyquinoline (362 mg, 1.1 mmol) and $BF_3{\cdot}Et_2O$ (1.24 mL, 10.1 mmol) in dry CH_2Cl_2 (7 mL) was stirred at 0°C under nitrogen. After 20 min., excess MeSH was added and the mixture was stirred at 0°C in a tightly closed vessel for 48 h. The reaction mixture was then poured onto ice, basified with 12 N NaOH, and extracted with CH_2Cl_2. Elution with CH_2Cl_2/MeOH (98:2) gave the dithioacetal **7** (269 mg, 69%) as an oil. − IR (film): $\tilde{\nu}$ = 3310 cm^{-1} (s, NH), 1668 (s, CO), 746 (m, CS). − ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.66−1.82 (m, 1 H, 3-Hax), 1.92 and 1.96 (2 s, 3 H, SCH_3), 2.17 and 2.22 (2 s, 3 H, SCH_3), 2.62−2.74 (m, 1 H, 3-Heq), 3.18−3.40 (m, 1 H, 2-Hax), 3.54−3.68 (m, 2 H, 2-Heq and 4-H), 3.78 and 3.85 (2 s, 3 H, OCH_3), 3.87 (d, 1 H, CH), 3.90 and 3.92 (2 s, 3 H, OCH_3), 6.62 and 6.68 (2 s, 1 H, 8-H), 7.39 and 7.65 (br s, d, *J* = 11.7 Hz, 1 H, NH), 8.32 and 8.46 (d, br s, *J* = 11.7 Hz, 1 H, CHO), 8.78 (s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 11.5 and 12.2 (2 q, SCH_3), 15.0 and 15.3 (2 q, SCH_3), 25.2 and 25.8 (2 t, C-3), 36.5 and 36.6 (2 d, C-4), 38.0 (t, C-2), 56.0 (d, CH), 56.1 and 56.2 (2 q, OCH_3), 60.6 and 60.9 (2 q, OCH_3), 102.2 and 103.2 (2 d, C-8), 119.8 (s, C-4a), 121.9 (s, C-5), 127.9 and 129.1 (2 s, C-6), 132.3 and 132.6 (2 s, C-8a), 152.6 and 153.0 (2 s, C-7), 160.0 and 161.3 (2 d, CHO), 165.0 (d, CHO). − MS (EI); *m/z* (%) = 370 [M^+] (2), 322 (8), 263 (100). − HRMS: calcd. for $C_{16}H_{22}N_2O_4S_2$ 370.1021; found 370.1018.

1,5-Diformyl-1,2,2a,3,4,5-hexahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (8): A solution of **7** (0.5 g, 1.4 mmol) in dry CH_2Cl_2 (100 mL) in a Schlenk system was cooled to −78°C and Ar was bubbled through the solution for 5 min. DMTSF (0.4 mg, 2.7 mmol) was then added and the temperature was allowed to rise to 0°C. After stirring for 3 h at this temperature, the mixture was washed with satd. aq. $NaHCO_3$. The organic phase was dried and the solvent was evaporated, affording a mixture which was purified by column chromatography. Elution with hexane/ethyl acetate (30:70) gave the tricyclic compound **8** (130 mg, 30%) as an oil. − IR (film): $\tilde{\nu}$ = 1679 cm^{-1} (s, CO), 1615 (s, CO), 800 (m, CS). − ^1H NMR (200 MHz, $CDCl_3$): δ_H =1.50−1.86 (m, 2 H, 3-H), 2.47 and 2.50 (2 s, 3 H, SCH_3), 3.06−3.17 (m, 1 H, 2a-H), 3.42 (td, *J* = 13.0 and 5.0 Hz, 1 H, 4-Hax), 3.84 (s, 3 H, OCH_3), 3.89 and 3.90 (2 s, 3 H, OCH_3), 4.20 (dd, *J* = 13.0 and 5.4 Hz, 1 H, 4-Heq), 4.96 and 5.07 (2 dd, *J* = 8.0 and 0.8 Hz, 1 H, 2-H), 6.47 and 6.75 (2 s, 1 H, 6-H), 8.88 and 8.97 (2 s, 1 H, CHO), 9.48 and 9.70 (2 s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 16.1 (q, SCH_3), 25.3 and 26.0 (2 t, C-3), 39.7 and 41.7 (2 t, C-4), 43.6 and 44.1 (2 d, C-2a), 56.7 (q, OCH_3), 60.7 (q, OCH_3), 71.0 and 71.9 (2 d, C-2), 94.1 (d, C-6), 113.5 (s, C-8a), 114.5 (s, C-5a), 130.0 (s, C-8b), 132.5 (s, C-8), 155.3 (s, C-7), 159.7 (d, CHO), 161.8 (d, CHO). − MS (EI); *m/z* (%) = 323 [M + 1] (16), 322 [M^+] (80), 275 (92), 247 (41), 216 (100). − HRMS: calcd. for $C_{15}H_{18}N_2O_4S$ 322.0987; found 322.0977.

5-Formyl-1,3,4,5-tetrahydro-7,8-dimethoxypyrrolo[4,3,2-*de*]quinoline (9), 1,5-Diformyl-1,2,2a,3,4,5-hexahydro-7,8-dimethoxypyrrolo[4,3,2-*de*]quinoline (10), and 1-Formyl-5-formylamino-4-formyloxymethyl-1,2,3,4-tetrahydro-6,7-dimethoxyquinoline (11): To a solution of **3** (0.4 g, 1.5 mmol) in CH_3OH (40 mL) was added $NiCl_2{\cdot}6H_2O$ (4.7 g, 19.8 mmol). After 5 min., $NaBH_4$ (4.6 g, 122.1 mmol) was added in very small portions such that the temperature did not increase significantly, and then the mixture was stirred for a further 5 min. Thereafter, H_2O was added and the mixture was extracted with CH_2Cl_2. The organic extract was dried and concentrated. The resulting residue was redissolved in AFA (3 mL) and this solution was stirred at room temp. for 2 h. The excess reagent was then evaporated in vacuo, the residue was redissolved in CH_2Cl_2, and the resulting solution was washed with satd. aq. $NaHCO_3$. The organic extract was dried and concentrated to leave a solid residue, which was purified by column chromatography (hexane/CH_2Cl_2, 3:7 to 1:9) to give **9** (373 mg, 29%) as a white solid; m.p. 97−98°C (hexane). − IR (KBr): $\tilde{\nu}$ = 3500 cm^{-1} (s, NH), 1666 (s, CO), 1642 (s, CO). − ^1H NMR (200 MHz, $CDCl_3$): δ_H =2.95 and 3.10 (2 t, *J* = 5.8 Hz, 2 H, 3-H), 3.89 and 4.06 (2 t, *J* = 5.8 Hz, 2 H, 4-H), 3.93 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 6.64 (s, 1 H, 6-H), 6.82 (s, 1 H, 2-H), 8.46 and 8.94 (2 s, 1 H, CHO), 8.49 and 8.62 (br s, 1 H, NH). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 22.1 and 23.2 (2 t, C-3), 40.4 and 47.4 (2 t, C-4), 57.6 and 58.2 (2 q, OCH_3), 60.9 (q, OCH_3), 94.1 (d, C-6), 99.7 (s, C-2a), 108.8 and 109.3 (2 s, C-8b), 116.8 and 117.5 (2 d, C-2), 125.8 and 126.8 (2 s, C-5a), 127.8 and 128.3 (2 s, C-8a), 131.7 and 132.4 (2 s, C-8), 147.9 and 148.5 (2 s, C-7), 160.2 and 161.7 (2 d, CHO). − MS (EI); *m/z* (%) = 247 [M + 1] (16), 246 [M^+] (100), 231 (93). − HRMS: calcd. for $C_{13}H_{14}N_2O_3$ 246.1001; found 246.1004. − $C_{13}H_{14}N_2O_3$ (246.10): calcd. C 63.40, H 5.73, N 11.38; found C 63.43, H 5.67, N 11.48.

Elution with CH_2Cl_2/CH_3OH (99:1) gave **10** (14 mg, 3%) as an oil. − IR (film): $\tilde{\nu}$ = 1674 cm^{-1} (s, CO), 1612 (s, CO). − ^1H NMR (200 MHz, $CDCl_3$): δ_H =1.45 (m, 1 H, 3-Hax), 2.36 (m, 1 H, 3-Heq), 3.23−3.32 (m, 2 H, 2-Hax and 2a-H), 3.42 (ddd, *J* = 12.0, 10.0 and 1.0 Hz, 1 H, 4-Hax), 3.79 and 3.83 (2 s, 3 H, OCH_3), 3.90 and 3.92 (2 s, 3 H, OCH_3), 4.31 (ddm, *J* = 15.0 and 5.0 Hz, 1 H, 2-Heq), 4.56 (ddd, *J* = 12.0, 9.5 and 1.0 Hz, 1 H, 4-Heq), 6.50 (s, 1 H, 6-H), 8.02 and 9.00 (2 s, 1 H, CHO), 8.42 and 9.25 (2 s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 25.8 and 26.2 (2 t, C-3), 34.2 and 35.3 (2 d, C-2a), 41.5 and 46.7 (2 t, C-2), 52.6 and 52.7 (2 t, C-4), 56.7 (q, OCH_3), 60.5 (q, OCH_3), 93.6 and 100.1 (2 d, C-6), 116.6 (s, C-8a), 130.4 (s, C-5a), 132.8 (s, C-8b), 133.6 (s, C-8), 154.9 (s, C-7), 159.6 (d, CHO), 160.9 and 162.1 (d, CHO). − MS (EI); *m/z* (%) = 277 [M + 1] (13), 276 [M^+] (76), 233 (100). − HRMS: calcd. for $C_{14}H_{16}N_2O_4$ 276.1110; found 276.1112.

Elution with CH_2Cl_2/CH_3OH (98:2) gave **11** (489 mg, 49%) as an oil. − IR (film): $\tilde{\nu}$ = 3250 cm^{-1} (s, NH), 1720 (s, CO), 1671 (s, CO), 1608 (m). − ^1H NMR (200 MHz, $CDCl_3$): δ_H = 1.80−1.96 (m, 1 H, 3-Hax), 2.00−2.25 (m, 1 H, 3-Heq), 3.31−3.40 (m, 1 H, 2-Hax), 3.46−3.60 (m, 1 H, 2-Heq), 3.78 and 3.82 (2 s, 3 H, OCH_3), 3.90 and 3.91 (2 s, 3 H, OCH_3), 3.75−4.28 (m, 3 H, 4-H and CH_2), 6.67 (br d, *J* = 7.2 Hz, 1 H, 8-H), 7.41 and 7.72 (br s, br d, *J* = 8.0 Hz, 1 H, NH), 8.06 (br s, 1 H, CHO), 8.42 and 8.47 (2 s, 1 H,

CHO), 8.77 (br s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 23.2 and 23.4 (t, C-3), 31.0 and 31.7 (d, C-4), 36.4 and 36.9 (t, C-2), 56.0 (q, OCH_3), 60.5 and 60.9 (q, OCH_3), 63.9 and 64.2 (t, CH_2), 100.6 and 102.0 (d, C-8), 115.1 and 117.4 (s, C-4a), 128.4 and 129.3 (s, C-5), 133.5 (s, C-6), 140.6 and 142.0 (s, C-8), 152.4 and 152.9 (s, C-7), 160.8 (d, CHO), 161.2 (d, CHO), 165.5 (d, CHO). − MS (EI); *m/z* (%) = 322 [M^+] (11), 276 (100), 261 (52), 233 (68). − HRMS: calcd. for $C_{15}H_{18}N_2O_6$ 322.1165; found 322.1164.

1,5-Diformyl-1,2,2a,3,4,5-hexahydro-7,8-dimethoxypyrrolo[4,3,2-*de*]-quinoline (10): A solution of **11** (900 mg, 2.8 mmol) in dry THF (14 mL) was added to a suspension of NaH (224 mg, 5.6 mmol) in dry THF (14 mL) and the mixture was refluxed for 12 h. After cooling, H_2O was added, the solvent was evaporated under reduced pressure, and the residue was extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated to leave a crude product, which was purified by flash column chromatography. Elution with CH_2Cl_2 gave **10** (224 mg, 29%), spectroscopically identical with the material described above, and 5-amino-1-formyl-1,2,3,4-tetrahydro-4-hydroxymethyl-6,7-dimethoxyquinoline (237 mg, 32%). − IR (film): $\tilde{\nu}$ = 3364 cm^{-1} (s, NH, OH), 1658 (s, CO), 1620 (s). − ^{1}H NMR (300 MHz, $CDCl_3$): δ_H =1.78−1.90 (m, 1 H, 3-Hax), 2.15 (dm, *J* = 13.9 Hz, 1 H, 3-Heq), 3.05−3.20 (m, 1 H, 4-H), 3.46 (td, *J* = 13.0 and 4.9 Hz, 1 H, 2-Hax), 3.66−3.77 (m, 2 H, CH_2), 3.80 (s, 3 H, OCH_3), 3.84 (s, 3 H, OCH_3), 3.95 (ddd, *J* = 13.0, 5.9 and 2.6 Hz, 1 H, 2-Heq), 6.14 (s, 1 H, 8-H), 8.70 (s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 23.6 (t, C-3), 34.2 (d, C-4), 36.9 (t, C-2), 55.6 (q, OCH_3), 59.9 (q, OCH_3), 63.8 (t, CH_2OH), 92.2 (d, C-8), 108.5 (s, C-4a), 132.8 (s, C-8a), 133.1 (s, C-6), 139.6 (s, C-5), 151.4 (s, C-7), 161.5 (d, CHO). − MS (EI); *m/z* (%) = 266 [M^+] (48), 235 (100). − HRMS: calcd. for $C_{13}H_{18}N_2O_4$ 266.1267; found 266.1260.

5-Formyl-1,3,4,5-tetrahydro-7,8-dimethoxypyrrolo[4,3,2-*de*]-quinoline (9): A solution of **10** (125 mg, 0.4 mmol) in dry CH_2Cl_2 (5 mL) containing DDQ (142 mg, 0.6 mmol) was stirred at room temp. under nitrogen for 12 h. It was then filtered, the solvent was evaporated under reduced pressure, and the residue was purified by column chromatography. Elution with hexane/CH_2Cl_2 (4:6 to 2:8) afforded 1,5-diformyl-1,3,4,5-tetrahydro-7,8-dimethoxypyrrolo-[4,3,2-*de*]quinoline (30 mg, 24%). − IR (film): $\tilde{\nu}$ = 1694 cm^{-1} (s, CO), 1681 (s). − ^{1}H NMR (300 MHz, $CDCl_3$): δ_H =2.97 and 3.05 (2 td, *J* = 6.0 Hz and 1.4 Hz, 2 H, 3-H), 3.98 (s, 6 H, OCH_3), 3.90 and 4.08 (2 t, *J* = 6.0 Hz, 2 H, 4-H), 6.76 and 7.87 (2 s, 1 H, 6-H), 7.42 and 7.44 (2 d, *J* = 1.4 Hz, 1 H, 2-H), 8.47 and 8.91 (2 s, 1 H, CHO), 9.71 (s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 21.9 and 22.9 (2 t, C-3), 39.7 and 46.5 (2 t, C-4), 57.1 and 57.4 (2 q, OCH_3), 60.7 (q, OCH_3), 96.5 and 102.1 (2 d, C-6), 114.2 and 114.8 (2 d, C-2), 116.3 and 116.7 (2 s, C-2a), 117.8 (s, C-8b), 126.5 and 127.8 (2 s, C-8a), 133.9 and 134.2 (2 s, C-5a), 151.9 and 152.3 (2 s, C-8), 155.9 (s, C-7), 159.2 and 159.4 (2 d, CHO), 159.8 and 161.5 (2 d, CHO). − MS (EI); *m/z* (%) = 274 [M^+] (67), 231 (100). − Elution with CH_2Cl_2 and then with CH_2Cl_2/MeOH (99:1) gave the starting material **10** (25 mg, 20%).

A solution of the diformyl-tetrahydroquinoline (30 mg, 0.1 mmol) in CH_2Cl_2/MeOH (1:1) (1 mL) and 10% aq. K_2CO_3 (0.5 mL) was stirred for 5 h at room temp. The solvent was then evaporated, the residue was redissolved in CH_2Cl_2, and the resulting solution was washed with H_2O. The organic phase was dried and the solvent was evaporated to give the mono(formamide) **9** (22 mg, 81%).

5-Formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-1-methylpyrrolo[4,3,2-*de*]-quinoline (12): A solution of **9** (30 mg, 0.1 mmol) in dry THF (0.5 mL) was added to a suspension of NaH (9 mg, 0.2 mmol) in dry THF (0.5 mL) at room temp. under nitrogen. The mixture was stirred for 30 min. at room temp. and then refluxed for 15 min. After cooling to room temp. once more, MeI (0.1 mL, 1.4 mmol) was added and the resulting mixture was stirred for 1 h. Thereafter, H_2O was added, the organic solvent was removed under reduced pressure, and the resulting solution was extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated to give **12** (30 mg, 99%). − IR (film): $\tilde{\nu}$ = 1677 cm^{-1} (s, CO). − ^{1}H NMR (300 MHz, $CDCl_3$): δ_H =2.95 and 3.02 (2 t, *J* = 5.7 Hz, 2 H, 3-H), 3.93 (s, 3 H, CH_3), 3.94 (s, 3 H, CH_3), 3.95 (s, 3 H, CH_3), 3.87 and 4.06 (2 t, *J* = 5.7 Hz, 2 H, 4-H), 6.59 (s, 2 H, 2-H and 6-H), 8.41 and 8.90 (2 s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 21.7 and 22.8 (2 t, C-3), 34.3 (q, NCH_3), 39.9 and 46.9 (2 t, C-4), 57.3 and 57.9 (2 q, OCH_3), 61.6 (q, OCH_3), 93.7 and 99.2 (2 d, C-6), 106.5 and 107.7 (2 s, C-2a), 117.1 (s, C-8b), 122.2 and 122.8 (2 d, C-2), 125.9 and 126.6 (2 s, C-8a), 127.9 and 128.1 (2 s, C-5a), 132.9 and 133.1 (2 s, C-8), 148.1 and 148.7 (2 s, C-7), 159.8 and 161.3 (2 d, CHO). — MS (CI); *m/z* (%) = 262 [M + 2] (17), 261 [M + 1] (100), 260 [M^+] (42). − HRMS: calcd. for $C_{14}H_{16}N_2O_3$ 260.1161; found 260.1167.

5-Formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (13): A solution of SO_2Cl_2 (11 mg, 0.08 mmol) in dry CH_2Cl_2 (0.04 mL) was added to a solution of $(MeS)_2$ (7 mg, 0.08 mmol) in dry CH_2Cl_2 (0.08 mL) at 0°C under nitrogen. After stirring for 30 min., a solution of **9** (30 mg, 0.1 mmol) in dry CH_2Cl_2 (0.3 mL) was added at this temperature, still under nitrogen. The reaction mixture was allowed to warm to room temp. and was stirred for 2 h, then basified with ammonium hydroxide, and extracted with CH_2Cl_2. The organic solution was dried and the solvent was evaporated to give **13** (32 mg, 92%). − IR (film): $\tilde{\nu}$ = 3350 cm^{-1} (m, NH), 1671 (s, CO), 1370 (s, CS), 1215 (m, SC), 755 (s, CS). − ^{1}H NMR (300 MHz, $CDCl_3$): δ_H =2.40 and 2.43 (2 s, 3 H, SCH_3), 2.96 and 3.03 (2 t, *J* = 5.9 Hz, 2 H, 3-H), 3.93 (s, 3 H, 7-OCH_3), 3.97 (s, 3 H, 8-OCH_3), 3.91 and 4.10 (2 t, *J* = 5.9 Hz, 2 H, 4-H), 6.61 and 6.65 (2 s, 1 H, 6-H), 8.15 and 8.20 (br s, 1 H, NH), 8.90 and 8.92 (2 s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 19.9 (q, SCH_3), 39.9 and 40.2 (2 t, C-3), 46.8 and 47.2 (2 t, C-4), 57.6 and 58.0 (2 q, OCH_3), 60.9 (q, OCH_3), 94.3 and 94.8 (2 d, C-6), 99.8 and 100.3 (2 s, C-8b), 114.6 (s, C-2a), 116.5 (s, C-8a), 122.7 (s, C-2), 126.5 and 126.9 (2 s, C-5a), 132.0 (s, C-8), 149.2 (s, C-7), 160.1 and 161.6 (d, CHO). − MS (EI); *m/z* (%) = 294 [M + 2] (8), 293 [M + 1] (18), 292 [M^+] (100), 277 (93), 265 (30). − HRMS: calcd. for $C_{14}H_{16}N_2O_3S$ 292.0882; found 292.0876.

5-Formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-1-methyl-2-methylthiopyrrolo[4,3,2-*de*]quinoline (14): A solution of SO_2Cl_2 (11 mg, 0.08 mmol) in dry CH_2Cl_2 (0.04 mL) was added to a solution of $(MeS)_2$ (7 mg, 0.08 mmol) in dry CH_2Cl_2 (0.08 mL) at 0°C under nitrogen. The mixture was stirred for 30 min. and then added to a cooled solution (0°C) of **12** (30 mg, 0.1 mmol) in dry CH_2Cl_2 (0.3 mL). When the addition was complete, the temperature was allowed to rise to ambient and the mixture was stirred for 2 h. Thereafter, the solution was basified with ammonium hydroxide and extracted with CH_2Cl_2. The organic extracts were dried and the solvent was evaporated affording **14** (36 mg, 98%). − IR (film): $\tilde{\nu}$ = 1679 cm^{-1} (s, CO). − ^{1}H NMR (200 MHz, $CDCl_3$): δ_H =2.28 (s, 3 H, SCH_3), 2.88 and 2.99 (2 t, *J* = 5.8 Hz, 2 H, 3-H), 3.91 (s, 3 H, CH_3), 3.93 (s, 3 H, CH_3), 4.01 (s, 3 H, CH_3), 4.08 (t, *J* = 5.8 Hz, 2 H, 4-H), 6.58 and 6.60 (2 s, 6-H), 8.87 and 8.89 (2 s, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 20.0 (q, SCH_3), 31.4 (q, NCH_3), 39.8 and 40.2 (2 t, C-3), 46.6 and 47.2 (2 t, C-4), 57.6 and 58.2 (2 q, OCH_3), 61.9 and 62.0 (2 q, OCH_3), 94.1 and 94.6 (2 d, C-6), 114.4 and 115.1 (2 s, C-8b), 116.2 and 117.0 (2 s, C-2a), 125.5 and 126.0 (2 s,

C-8a), 126.9 (s, C-2), 129.8 (s, C-5a), 133.1 (s, C-8), 149.9 (s, C-7), 160.1 and 161.6 (2 d, CHO). − MS (EI); *m/z* (%) = 308 [M + 2] (8), 307 [M + 1] (20), 306 [M^+] (100). − HRMS: calcd. for $C_{15}H_{18}N_2O_3S$ 306.1038; found 306.1040.

1,3,4,5-Tetrahydro-7,8-dimethoxy-1-methylpyrrolo[4,3,2-*de*]-quinoline (15): A solution of **12** (100 mg, 0.4 mmol) in 2.5 N NaOH (6 mL) was stirred under reflux for 12 h. The solvent was then evaporated, the residue was redissolved in CH_2Cl_2, and the resulting solution was washed with H_2O. The organic phase was dried and the solvent was evaporated giving **15** (87 mg, 99%) as a solid; m.p. 190°C (CH_2Cl_2). − IR (film): $\tilde{\nu}$ = 3364 cm^{-1} (s, NH). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =2.93 (t, *J* = 5.7 Hz, 2 H, 3-H), 3.42 (t, *J* = 5.7 Hz, 2 H, 4-H), 3.86 (s, 3 H, CH_3), 3.87 (s, 3 H, CH_3), 3.90 (s, 3 H, CH_3), 5.98 (s, 1 H, 6-H), 6.43 (s, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 22.8 (t, C-3), 34.4 (q, NCH_3), 43.6 (t, C-4), 57.9 (q, OCH_3), 62.0 (q, OCH_3), 89.9 (d, C-6), 109.4 (s, C-2a), 114.7 (s, C-8b), 120.5 (d, C-2), 128.3 (s, C-8a), 128.7 (s, C-5a), 136.7 (s, C-8), 149.6 (s, C-7). − MS (EI); *m/z* (%) = 234 [M + 2] (3), 233 [M + 1] (16), 232 [M^+] (58), 217 (100). − HRMS: calcd. for $C_{13}H_{16}N_2O_2$ 232.1212; found 232.1213.

1,3,4,8-Tetrahydro-7-methoxy-1-methyl-8-oxopyrrolo[4,3,2-*de*]-quinoline (16): To a solution of **15** (100 mg, 0.4 mmol) in MeCN (6 mL) was added a solution of CAN (486 mg, 0.9 mmol) in H_2O (4 mL) and the mixture was stirred for 10 min. The solution was then diluted with H_2O and extracted with CH_2Cl_2. The organic extracts were dried and the solvent was evaporated affording **16** (77 mg, 89%). − IR (film): $\tilde{\nu}$ = 1671 cm^{-1} (s, CO), 1640 (s, CN). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =3.05 (t, *J* = 8.1 Hz, 2 H, 3-H), 3.99 (s, 3 H, CH_3), 4.00 (s, 3 H, CH_3), 4.14 (t, *J* = 8.1 Hz, 2 H, 4-H), 6.60 (s, 1 H, 6-H), 6.85 (s, 1 H, 2-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 18.4 (t, C-3), 36.5 (q, NCH_3), 44.1 (t, C-4), 58.7 (q, OCH_3), 97.6 (d, C-6), 117.4 (s, C-2a), 119.7 (s, C-8b), 125.1 (s, C-8a), 128.7 (d, C-2), 159.6 (s, C-7), 162.9 (s, C-5a), 168.6 (s, C-8). − MS (CI); *m/z* (%) = 218 [M + 2] (19), 217 [M + 1] (16), 216 [M^+] (45), 69 (100). − HRMS: calcd. for $C_{12}H_{12}N_2O_2$ 216.0899; found 216.0905.

1,3,4,5-Tetrahydro-7,8-dimethoxy-1-methyl-2-methylthiopyrrolo-[4,3,2-*de*]quinoline (17): A mixture of **14** (350 mg, 1.1 mmol) and 2.5 N NaOH (18 mL) was refluxed for 6 h. After cooling, the solution was extracted with CH_2Cl_2 and the organic layer was washed with H_2O. The organic phase was dried and the solvent was evaporated affording **17** (308 mg, 97%) as a green gum; m.p. 120°C (Et_2O). − IR (film): $\tilde{\nu}$ = 3364 cm^{-1} (s, NH). − ^1H NMR (200 MHz, $CDCl_3$): δ_H =2.22 (s, 3 H, SCH_3), 2.95 (t, *J* = 5.9 Hz, 2 H, 3-H), 3.39 (t, *J* = 5.9 Hz, 2 H, 4-H), 3.84 (s, 3 H, CH_3), 3.85 (s, 3 H, CH_3), 4.00 (s, 3 H, CH_3), 5.94 (s, 1 H, 6-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 20.3 (q, SCH_3), 22.9 (t, C-3), 31.1 (q, NCH_3), 43.4 (t, C-4), 57.6 (q, OCH_3), 62.1 (q, OCH_3), 89.7 (d, C-6), 109.4 (s, C-8b), 113.4 (s, C-2a), 116.7 (s, C-8a), 120.5 (s, C-5a), 129.7 (s, C-2), 136.7 (s, C-8), 150.7 (s, C-7). − MS (EI); *m/z* (%) = 278 [M^+] (57), 263 (100). − HRMS: calcd. for $C_{14}H_{18}N_2O_2S$ 278.1089; found 278.1092. − $C_{14}H_{18}N_2O_2S$ (278.11): calcd. C 60.41, H 6.52, N 10.06, S 11.52; found C 60.24, H 6.62, N 9.88, S 11.50.

1,3,4,8-Tetrahydro-7-methoxy-1-methyl-2-methylthio-8-oxopyrrolo-[4,3,2-*de*]quinoline (18): A solution of CAN (197 mg, 0.4 mmol) in H_2O (2 mL) was added to a solution of **17** (100 mg, 0.4 mmol) in MeCN (5 mL) at 0°C. After stirring for 10 min., H_2O was added and the mixture was extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated, giving a mixture that was purified by flash column chromatography. Elution with CH_2Cl_2 gave **18** (28 mg, 30%). − IR (film): $\tilde{\nu}$ = 1674 cm^{-1} (s, CO), 1644 (s, CN). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =2.39 (s, 3 H, SCH_3), 3.10 (t, *J* = 8.0 Hz, 2 H, H-3), 4.00 (s, 3 H, CH_3), 4.00 (s, 3 H, CH_3), 4.19 (t, *J* = 8.0 Hz, 2 H, 4-H), 6.61 (s, 1 H, 6-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 17.4 (t, C-3), 17.7 (q, SCH_3), 32.5 (q, NCH_3), 43.4 (t, C-4), 57.5 (q, OCH_3), 96.7 (d, C-6), 104.5 (s, C-2a), 110.8 (s, C-8b), 121.6 (s, C-8a), 141.3 (s, C-2), 159.2 (s, C-7), 163.5 (s, C-5a), 169.4 (s, C-8). − MS (EI); *m/z* (%) = 264 [M + 2] (12), 263 [M + 1] (2), 262 [M^+] (15). − HRMS: calcd. for $C_{13}H_{14}N_2O_2S$ 262.0776; found 262.0765.

2-Amino-1,8-dihydro-7-methoxy-1-methyl-8-oxopyrrolo[4,3,2-*de*]-quinoline (19): A solution of **18** (45 mg, 0.2 mmol) in satd. NH_3/CH_3OH (4 mL) was stirred at room temp. under argon for 48 h. The solvent was then removed under reduced pressure and the residue was purified by flash column chromatography. Elution with CH_2Cl_2 gave **19** (12 mg, 31%). − IR (film): $\tilde{\nu}$ = 3432 cm^{-1} (s, NH_2), 3097 (s, NH_2), 1655 (s, CO). − ^1H NMR (300 MHz, CD_3OD): δ_H = 4.04 (s, 3 H, CH_3), 4.10 (s, 3 H, CH_3), 6.98 (s, 1 H, 6-H), 7.91 (d, *J* = 5.1 Hz, 1 H, 3-H), 8.68 (br s, 1 H, 4-H). − ^{13}C NMR (75 MHz, CD_3OD): δ_C = 32.4 (q, NCH_3), 57.2 (q, OCH_3), 102.1 (d, C-6), 112.2 (s, C-2a), 114.5 (s, C-8b), 116.4 (d, C-3), 129.9 (s, C-8a), 143.1 (s, C-7), 145.7 (d, C-4), 150.2 (s, C-2), 154.1 (s, C-5a), 157.4 (s, C-8). − MS (EI); *m/z* (%) = 229 [M^+] (54), 213 (14). − HRMS: calcd. for $C_{12}H_{11}N_3O_2$ 229.0851; found 229.0845.

7-Amino-1,3,4,8-tetrahydro-1-methyl-2-methylthio-8-oxopyrrolo-[4,3,2-*de*]quinoline (Isobatzelline B) (2b): A solution of **18** (15 mg, 0.06 mmol) and NH_4Cl (33 mg, 0.6 mmol) in CH_3OH (5 mL) was deoxygenated by bubbling argon through it. The mixture was then warmed at 40°C for 48 h in a tightly sealed vessel. The solvent was subsequently evaporated under reduced pressure and the residue was purified by flash column chromatography. Elution with CH_2Cl_2/MeOH (9:1) gave isobatzelline B (13 mg, 93%). − IR (film): $\tilde{\nu}$ = 3365 cm^{-1} (s, NH_2), 1611 (s, CO), 1599 (s, C=N). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =2.37 (s, 3 H, SCH_3), 2.94 (t, *J* = 7.4 Hz, 2 H, 3-H), 3.89 (t, *J* = 7.4 Hz, 2 H, 4-H), 3.99 (s, 3 H, NCH_3), 6.12 (br s, 1 H, 6-H). − ^{13}C NMR (75 MHz, $CDCl_3$ + CD_3OD): δ_C = 18.6 (q, SCH_3), 18.8 (t, C-3), 33.3 (q, NCH_3), 42.4 (t, C-4), 88.6 (d, C-6), 121.5 (s, C-2a), 122.9 (s, C-8b), 125.5 (s, C-8a), 128.9 (s, C-2), 154.3 (s, C-7), 157.3 (s, C-5a), 168.3 (s, C-8). − MS (EI); *m/z* (%) = 249 [M + 2] (8), 248 [M + 1] (20), 247 [M^+] (100).

7,8-Dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (20): A solution of **13** (30 mg, 0.1 mmol) and NCS (16 mg, 0.1 mmol) in CH_2Cl_2 (2 mL) was refluxed for 3 h. Further CH_2Cl_2 was then added and the solution was washed with H_2O. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography. Elution with CH_2Cl_2 gave the aromatic compound **21** (17 mg, 65%). − IR (KBr): $\tilde{\nu}$ = 1670 cm^{-1} (s, S−C=N), 1251 (m, SC). − ^1H NMR (200 MHz, $CDCl_3$): δ_H = 2.82 (s, 3 H, SCH_3), 4.04 (s, 3 H, 7-OCH_3), 4.63 (s, 3 H, 8-OCH_3), 7.10 (s, 1 H, 6-H), 7.55 (d, *J* = 4.8 Hz, 1 H, 3-H), 8.89 (d, *J* = 4.8 Hz, 1 H, 4-H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 13.6 (q, SCH_3), 56.9 (q, OCH_3), 61.8 (q, OCH_3), 103.6 (d, C-6), 113.3 (d, C-3), 123.5 (s, C-8b), 133.9 (s, C-2a), 138.7 (s, C-8a), 142.4 (s, C-8), 143.8 (s, C-7), 148.7 (d, C-4), 157.1 (s, C-5a), 166.5 (s, C-2). − MS (CI); *m/z* (%) = 262 [M + 2] (18), 261 [M + 1] (100), 260 [M^+] (17). − HRMS: calcd. for $C_{13}H_{12}N_2O_2S$ 260.0620; found 260.0624.

6-Chloro-1,5-diformyl-1,2,2a,3,4,5-hexahydro-7,8-dimethoxy-pyrrolo[4,3,2-*de*]quinoline (23): A solution of **10** (525 mg, 1.9 mmol) in DMF (6 mL) was heated at 60°C, whereupon NCS (285 mg, 2.1 mmol) was added in three portions at intervals of 20 min. After 2 h, a final portion of NCS (67 mg, 0.5 mmol) was added and the mixture was stirred at 60°C for a further 45 min. CH_2Cl_2 (30 mL)

was then added and the organic solution was washed several times with H_2O. The organic phase was dried and the solvent was evaporated giving the monochloro derivative **23** (519 mg, 88%). − IR (KBr): $\tilde{\nu}$ = 1678 cm^{-1} (s, CO), 1663 (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =1.54−1.70 (m, 1 H, 3-Hax), 2.48−2.56 (m, 1 H, 3-Heq), 3.17−3.30 (m, 1 H, 2a-H), 3.59 (ddd, *J* = 12.6, 8.6, and 0.9 Hz, 1 H, 2-Hax), 3.76−3.91 (m, 2 H, 4-H), 3.93 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 4.59 (ddd, *J* = 12.6, 9.5 and 0.7 Hz, 1 H, 2-Heq), 9.06 (s, 1 H, CHO), 9.24 (s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 28.8 (t, C-3), 34.1 (d, C-2a), 41.7 (t, C-2), 52.2 (t, C-4), 60.7 (q, OCH_3), 60.9 (q, OCH_3), 114.2 (s, C-6), 124.5 (s, C-5a), 128.4 (s, C-8a), 130.9 (s, C-8b), 139.1 (s, C-8), 151.4 (s, C-7), 160.4 (d, CHO), 162.7 (d, CHO). − MS (EI); *m/z* (%) = 312 [M + 2] (34), 311 [M + 1] (16), 310 [M^+] (93), 275 (54), 267 (64), 239 (100). − HRMS: calcd. for $C_{14}H_{15}ClN_2O_4$ 310.0720; found 310.0725.

6-Chloro-5-formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-1-methyl-2-methylthiopyrrolo[4,3,2-*de*]quinoline (25): A solution of SO_2Cl_2 (19 μL, 0.2 mmol) in dry CH_2Cl_2 (0.14 mL) was added to a solution of $(MeS)_2$ (21 μL, 0.2 mmol) in dry CH_2Cl_2 (0.35 mL) at 0°C under nitrogen. After stirring for 30 min., the solution was added to a cooled (0°C) solution of **24** (111 mg, 0.4 mmol) in dry CH_2Cl_2 (1 mL). The cooling bath was removed and the reaction mixture was stirred at room temperature for 1 h. The solution was then basified with NH_4OH and extracted with CH_2Cl_2. The organic phase was dried and concentrated giving **25** (128 mg, 95%); m.p. 106−108°C (hexane). − IR (KBr): $\tilde{\nu}$ = 1679 cm^{-1} (s, CO), 800 (w, CS). − ^1H NMR ($CDCl_3$, 300 MHz): δ_H =2.30 (s, 3 H, SCH_3), 2.95 (t, *J* = 5.7 Hz, 2 H, 3-H), 3.94 (s, 3 H, CH_3), 4.01 (s, 3 H, CH_3), 4.02 (s, 3 H, CH_3), 4.10 (t, *J* = 5.7 Hz, 2 H, 4-H), 9.05 (s, 1 H, CHO). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ_C = 19.9 (q, SCH_3), 22.7 (t, C-3), 31.6 (q, NCH_3), 40.5 (t, C-4), 61.5 (q, OCH_3), 62.0 (q, OCH_3), 109.3 (s, C-6), 115.5 (s, C-2a), 118.9 (s, C-8b), 124.1 (s, C-5a), 127.0 (s, C-8a), 127.6 and 127.9 (2 s, C-2), 138.0 (s, C-8), 146.1 (s, C-7), 162.6 (d, CHO). − MS (EI); *m/z* (%) = 342 [M + 2] (39), 341 [M + 1] (19), 340 [M^+] (100), 325 (65). − HRMS: calcd. for $C_{15}H_{17}ClN_2O_3S$ 340.0648; found 340.0660. − $C_{15}H_{17}ClN_2O_3S$ (340.06): calcd. C 52.56, H 5.02, N 8.21, S 9.41; found C 52.70, H 5.03, N 8.18, S 9.22.

6-Chloro-5-formyl-1,3,4,5-tetrahydro-1-methyl-2-methylthio-7,8-dioxopyrrolo[4,3,2-*de*]quinoline (26): A solution of BBr_3 in CH_2Cl_2 (1 M, 1.6 mL, 1.6 mmol) was added to a cold (−78°C) solution of **25** (107 mg, 0.31 mmol) in dry CH_2Cl_2 (12 mL) under nitrogen. The reaction mixture was allowed to warm to −30°C over a period of 90 min. and was maintained at this temperature for a further 30 min. A satd. solution of $NaHCO_3$ was then added and the mixture was extracted with CH_2Cl_2. The organic phase was dried and concentrated giving a crude material which was purified by flash column chromatography. Elution with hexane/EtOAc (7:3) afforded the starting material (34 mg, 32%) and a brown solid identified as **26** (52 mg, 53%); m.p. 187−189°C (hexane). − IR (KBr): $\tilde{\nu}$ = 1694 cm^{-1} (s, CO), 1655 (s, CO). − ^1H NMR ($CDCl_3$, 200 MHz): δ_C = 2.38 (s, 3 H, SCH_3), 2.78 (t, *J* = 6.1 Hz, 2 H, 3-H), 4.00 (s, 3 H, NCH_3), 4.18 (t, *J* = 6.1 Hz, 2 H, 4-H), 9.19 (s, 1 H, CHO). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ_C =18.5 (q, SCH_3), 21.0 (t, C-3), 33.6 (q, NCH_3), 40.9 (t, C-4), 111.2 (s, C-6), 124.2 (s, C-2a and C-8b), 124.9 (s, C-8a), 135.7 (s, C-2), 142.2 (s, C-5a), 161.2 (d, CHO), 164.6 (s, C-7), 176.3 (s, C-8). − MS (EI); *m/z* (%) = 312 [M + 2] (14), 311 [M + 1] (6), 310 [M^+] (41), 275 (100). − HRMS: calcd. for $C_{13}H_{11}ClN_2O_3S$ 310.0179; found 310.0165. − $C_{13}H_{11}ClN_2O_3S{\cdot}1/3\ H_2O$ (316.01): calcd. C 49.29, H 3.71, N 8.84; found C 49.68, H 3.73, N 8.51.

6-Chloro-1,3,4,5-tetrahydro-1-methyl-2-methylthio-7,8-dioxopyrrolo[4,3,2-*de*]quinoline (Batzelline A, 1a): A solution of **26** (17.8 mg, 0.57 mmol) in MeOH (2 mL) containing a catalytic amount of 1 N HCl was refluxed for 2.5 h. The solvent was then removed under reduced pressure, affording batzelline A (16 mg, 100%). − IR (KBr): $\tilde{\nu}$ = 3400 cm^{-1} (s, NH), 3200 (s), 1670 (s, CO), 1590 (m, CO). − ^1H NMR ($CDCl_3$, 300 MHz): δ_H =2.35 (s, 3 H, SCH_3), 2.90 (t, *J* = 6.9 Hz, 2 H, 3-H), 3.75 (td, *J* = 6.9 Hz and 2.3 Hz, 2 H, 4-H), 3.98 (s, 3 H, NCH_3), 5.70 (br s, 1 H, NH). − ^{13}C NMR ([D_6]DMSO, 50 MHz): δ_C = 18.3 (q, SCH_3), 19.3 (t, C-3), 33.0 (q, NCH_3), 41.6 (t, C-4), 97.4 (s, C-6), 122.2 (s, C-2a), 124.1 (s, C-8b), 125.0 (s, C-8a), 132.6 (s, C-2), 148.7 (s, C-5a), 169.0 (s, C-7), 171.2 (s, C-8).

6-Chloro-1,3,4,5-tetrahydro-7,8-dimethoxy-1-methyl-2-methylthiopyrrolo[4,3,2-*de*]quinoline (27): A mixture of **25** (250 mg, 0.7 mmol) and 2.5 N NaOH (13 mL) was refluxed for 20 h. After cooling, the reaction mixture was extracted with CH_2Cl_2, the organic phase was dried, and the solvent was evaporated to give **27** (180 mg, 98%) as an oil. − IR (film): $\tilde{\nu}$ = 3400 cm^{-1} (s, NH). − ^1H NMR ($CDCl_3$, 200 MHz): δ_H =2.25 (s, 3 H, SCH_3), 2.98 (t, *J* = 6.0 Hz, 2 H, 3-H), 3.49 (t, *J* = 6.0 Hz, 2 H, 4-H), 3.91 (s, 3 H, OCH_3), 3.92 (s, 3 H, CH_3), 3.97 (s, 3 H, CH_3), 4.30 (br s, 1 H, NH). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ_C = 20.1 (q, SCH_3), 22.8 (t, C-3), 31.2 (q, NCH_3), 42.9 (t, C-4), 61.4 (q, OCH_3), 62.2 (q, OCH_3), 98.8 (s, C-6), 114.4 (s, C-2a), 116.1 (s, C-8b), 124.0 (s, C-5a), 127.7 (s, C-8a), 132.3 (s, C-2), 133.3 (s, C-8), 146.3 (s, C-7). − MS (EI); *m/z* (%) = 312 [M^+] (57), 314 (21), 297 (100). − HRMS: calcd. for $C_{14}H_{17}ClN_2O_2S$ 312.0699; found 312.0691.

7-Amino-6-chloro-1,3,4,8-tetrahydro-1-methyl-2-methylthio-8-oxopyrrolo[4,3,2-*de*]quinoline (Isobatzelline A, 2a): To a solution of **27** (20 mg, 0.06 mmol) in MeCN (0.9 mL) at 0°C was added a solution of CAN (35 mg, 0.06 mmol) in H_2O (0.4 mL). The reaction mixture was stirred at this temperature for 20 min., and then extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated to give a crude product, which was redissolved in MeOH (4.5 mL). NH_4Cl (31 mg, 0.6 mmol) was added to the resulting solution and the mixture was kept at 40°C in a tightly sealed flask for 15 h. The solvent was then removed and the residue was purified by column chromatography. Elution with CH_2Cl_2/MeOH (95:5) afforded **29** (5 mg, 27%). − IR (film): ν = 1723 cm^{-1} (s, CO), 1650 (s, C=N). − ^1H NMR ($CDCl_3$, 200 MHz): δ_H =2.69 (s, 3 H, SCH_3), 4.13 (s, 3 H, CH_3), 4.38 (s, 3 H, CH_3), 7.72 (d, *J* = 5.8 Hz, 1 H, 3-H), 8.65 (d, *J* = 5.8 Hz, 1 H, 4-H). − MS (EI); *m/z* (%) = 296 [M + 2] (24), 295 [M + 1] (12), 294 [M^+] (56), 86 (66). − HRMS: calcd. for $C_{13}H_{11}ClN_2O_2S$ 294.0230; found 294.0221.

Subsequent fractions gave batzelline A (**1a**) (4 mg, 22%) and finally elution with CH_2Cl_2/MeOH (90:10) gave isobatzelline A (4.5 mg, 26%). − ^1H NMR ($CDCl_3$/CD_3OD, 1:1, 300 MHz): δ_H =2.43 (s, 3 H, SCH_3), 3.03 (t, *J* = 7.7 Hz, 2 H, 3-H), 3.96 (t, *J* = 7.7 Hz, 2 H, 4-H), 4.02 (s, 3 H, NCH_3). − ^{13}C NMR ($CDCl_3$/CD_3OD, 1:1, 75 MHz): δ_C = 17.3 (q, SCH_3), 18.1 (t, C-3), 32.6 (q, NCH_3), 42.9 (t, C-4), 93.2 (s, C-6), 120.5 (s, C-2a), 123.2 (s, C-8b), 123.5 (s, C-8a), 135.7 (s, C-2), 151.3 (s, C-7), 152.9 (s, C-5a), 164.9 (s, C-8). − MS (EI); *m/z* (%) = 283 [M + 2] (4), 282 [M + 1] (1), 281 [M^+] (7), 85 (62), 83 (100).

6-Chloro-5-formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-1-phenylsulfonylpyrrolo[4,3,2-*de*]quinoline (31): A mixture of **22** (163 mg, 0.6 mmol), Bu_4NHSO_4 (3 mg, 0.01 mmol), C_6H_6 (2 mL), and 50% NaOH (0.6 mL) was stirred at room temp. for 5 min., and then a solution of benzenesulfonyl chloride (0.1 mL, 0.8 mmol) in C_6H_6 (0.9 mL) was added. The resulting mixture was stirred for 7 h. The two phases were subsequently separated and the organic phase was

washed with H_2O, dried, and the solvent was evaporated to give **31** (207 mg, 87%) as a solid; m.p. 118−119°C (hexane). − IR (KBr): $\tilde{\nu}$ = 1686 cm^{-1} (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =2.91 (t, *J* = 5.8 Hz, 2 H, 3-H), 3.85 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.07 (t, *J* = 5.8 Hz, 2 H, 4-H), 7.49−7.64 (m, 4 H, 2-H, 3′-H, 4′-H, and 5′-H), 7.97 (dd, *J* = 8.2 and 0.6 Hz, 2 H, 2′-H and 6′-H), 8.98 (s, 1 H, CHO). − ^{13}C NMR (50 MHz, $CDCl_3$): δ_C = 22.1 (t, C-3), 39.9 (t, C-4), 61.1 (q, OCH_3), 61.2 (q, OCH_3), 113.9 (s, C-6), 114.1 (s, C-8b), 122.3 (s, C-2a), 122.9 (d, C-2), 124.8 (s, C-8a), 124.9 (s, C-5a), 127.4 (d, C-2′ and C-6′), 129.0 (d, C-3′ and C-5′), 133.7 (d, C-4′), 138.7 (s, C-8), 139.5 (s, C-1′), 148.3 (s, C-7), 162.2 (d, CHO). − MS (EI); *m/z* (%) = 422 [M + 2] (9), 421 [M + 1] (5), 420 [M^+] (22), 280 (21), 278 (100). − HRMS: calcd. for $C_{19}H_{17}ClN_2O_5S$ 420.0547; found 420.0541.

6-Chloro-1,3,4,5-tetrahydro-7,8-dimethoxy-1-phenylsulfonylpyrrolo[4,3,2-*de*]quinoline (32): A solution of **31** (50 mg, 0.1 mmol) in CH_3OH (5 mL) containing a catalytic amount of conc. HCl was refluxed for 7 h. The solvent was then removed under reduced pressure, the residue was redissolved in CH_2Cl_2, and the resulting solution was washed with satd. aq. $NaHCO_3$. The organic phase was dried and the solvent was evaporated to give the amine **32** (48 mg, 94%). − IR (film): $\tilde{\nu}$ = 3405 cm^{-1} (s, NH). − ^1H NMR (200 MHz, $CDCl_3$): δ_H = 2.91 (td, *J* = 6.0 and 1.8 Hz, 2 H, 3-H), 3.43 (t, *J* = 6.0 Hz, 2 H, 4-H), 3.75 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 4.29 (br s, 1 H, NH), 7.29 (t, *J* = 1.8 Hz, 1 H, 2-H), 7.40−7.62 (m, 3 H, 3′-H, 4′-H, 5′-H), 7.94 (dd, *J* = 6.6 and 1.8 Hz, 2 H, 2′-H and 6′-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 19.4 (t, C-3), 45.0 (t, C-4), 61.2 (q, OCH_3), 61.3 (q, OCH_3), 111.1 (s, C-6), 116.2 (s, C-8b), 119.9 (s, C-2a), 122.2 (s, C-5a), 123.7 (d, C-2), 125.0 (s, C-8a), 127.4 (d, C-2′ and C-6′), 129.1 (d, C-3′ and C-5′), 133.8 (d, C-4′), 138.5 (s, C-8), 141.0 (s, C-1′), 148.0 (s, C-7). − MS (EI); *m/z* (%) 394 [M + 2] (6), 393 [M + 1] (3), 392 [M^+] (15), 253 (32), 251 (100). − HRMS: calcd. for $C_{18}H_{17}ClN_2O_4S$ 392.0597; found 392.0591.

6-Chloro-5-formyl-1,3,4,5-tetrahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (33): A solution of SO_2Cl_2 (24 µL, 0.28 mmol) in dry CH_2Cl_2 (0.1 mL) was added to a solution of $(MeS)_2$ (26 µL, 0.28 mmol) in dry CH_2Cl_2 (0.2 mL) at 0°C under nitrogen, and the resulting mixture was stirred at this temperature for 30 min. The solution was then added to a cold (0°C) solution of **22** (42 mg, 0.14 mmol) in dry CH_2Cl_2 (0.4 mL). When the addition was complete, the cooling bath was removed and the reaction mixture was stirred for 2.5 h. It was then made basic with NH_4OH and extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated, giving a mixture of tautomers **33** and **34**. The mixture was redissolved in MeOH (2 mL), a catalytic quantity of HCl was added, and the solution was refluxed for 1 h. Subsequent removal of the solvent gave **33** (46 mg, 98%) as a gum. − IR (film): $\tilde{\nu}$ = 3300 cm^{-1} (s, NH), 1654 (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H = 2.20 and 2.41 (2 s, 3 H, SCH_3), 2.84 and 2.92 (2 t, *J* = 5.7 Hz, 2 H, 3-H), 3.92 (s, 3 H, OCH_3), 4.04 (s, 3 H, OCH_3), 3.92 and 4.10 (2 t, *J* = 5.7 Hz, 2 H, 4-H), 8.15 (br s, 1 H, NH), 9.06 (s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 19.9 (q, SCH_3), 21.8 and 22.3 (t, C-3), 40.2 and 40.6 (t, C-4), 61.1 (q, OCH_3), 61.6 (q, OCH_3), 115.2 (s, C-6), 118.6 (s, C-8b), 119.8 (s, C-2a), 123.9 (s, C-5a), 124.6 (s, C-2), 126.8 (s, C-8a), 136.1 (s, C-8), 136.8 (s, C-7), 162.6 (d, CHO). − MS (EI); *m/z* (%) = 328 [M + 2] (3), 326 [M^+] (8). − HRMS: calcd. for $C_{14}H_{15}ClN_2O_3S$ 326.0492; found 326.0491.

6-Chloro-5-formyl-2a,3,4,5-tetrahydro-7,8-dimethoxy-2-methylthiopyrrolo[4,3,2-*de*]quinoline (34): When the reaction between **22** and the combination of SO_2Cl_2 and $(MeS)_2$ was carried out with larger quantities (200 mg of **22**), only tautomer **34** was isolated, again in virtually quantitative yield. − IR (film): $\tilde{\nu}$ = 1679 cm^{-1} (s, C=N), 1656 (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H = 1.59−1.70 (m, 1 H, 3-Hax), 2.42−2.67 (m, 1 H, 3-Heq), 3.65 (dd, *J* = 13.4 and 7.7 Hz, 1 H, 4-Hax), 3.92 (s, 3 H, OCH_3), 4.00−4.32 (m, 2 H, 2a-H, 4-Heq), 4.34 (s, 3 H, OCH_3), 9.13 (s, 1 H, CHO). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 13.7 (q, SCH_3), 32.6 (t, C-3), 38.4 (t, C-4), 61.0 (q, OCH_3), 61.4 (q, OCH_3), 67.6 (d, C-2a), 117.8 (s, C-6), 125.0 (s, C-8b), 127.2 (s, C-5a), 139.4 (s, C-8a), 142.8 (s, C-8), 151.1 (s, C-7), 162.5 (d, CHO), 181.0 (s, C-2). − MS (EI); *m/z* (%) = 328 [M + 2] (38), 327 [M + 1] (18), 326 [M^+] (100), 311 (60). − HRMS: calcd. for $C_{14}H_{15}ClN_2O_3S$ 326.0492; found 326.0488.

6-Chloro-1,3,4,5-tetrahydro-2-methylthio-7,8-dioxopyrrolo[4,3,2-*de*]-quinoline (Batzelline B) (1b) and 6-Chloro-1,2-dihydro-7,8-dimethoxy-2-oxopyrrolo[4,3,2-*de*]quinoline (35): To a solution of **33** (50 mg, 0.15 mmol) in dry CH_2Cl_2 (1 mL) at −78°C under Ar, a solution of BBr_3 (1 M in CH_2Cl_2, 0.76 mL) was added dropwise. The mixture was allowed to warm to −30°C over a period of 1.5 h and was stirred at this temperature for 0.5 h. Satd. aq. $NaHCO_3$ was then added and the aqueous layer was extracted with CH_2Cl_2. The organic phase was dried and the solvent was evaporated, leaving a dark-green gum, which was purified by column chromatography. Elution with CH_2Cl_2/MeOH (99:1) afforded **35** (9 mg, 23%) as a brown solid; m.p. 243−245°C (CH_2Cl_2/Et_2O). − IR (film): $\tilde{\nu}$ = 1698 (s, CO) cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ_H = 4.04 (s, 3 H, OMe), 4.14 (s, 3 H, OMe), 7.88 (d, *J* = 4.6 Hz, 1 H, 3-H), 8.58 (br s, 1 H, NH), 9.22 (d, *J* = 4.6 Hz, 1 H, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$ + CD_3OD): δ_C = 60.6 (q, OCH_3), 61.3 (q, OCH_3), 117.2 (s, C-6), 117.3 (d, C-3), 122.8 (s, C-8b), 128.6 (s, C-8a), 133.7 (s, C-2a), 137.9 (s, C-4a), 140.2 (s, C-8), 151.3 (d, C-4), 154.4 (s, C-7), 168.3 (s, CO). − MS (EI); *m/z* (%) = 266 [M + 2] (35), 265 [M + 1] (16), 264 [M^+] (100), 249 (28). Elution with CH_2Cl_2/MeOH (98:2) gave batzelline B (8 mg, 19%). − IR (film): $\tilde{\nu}$ = 3166 (m, NH) cm^{-1}, 1682 (s, CO), 1648 (s, CO). − ^1H NMR (300 MHz, $CDCl_3$): δ_H =2.50 (s, 3 H, SMe), 2.83 (t, *J* = 7.0 Hz, 2 H, 3-H), 3.74 (t, *J* = 7.0 Hz, 2 H, 4-H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ_C = 18.9 (q, SMe), 19.7 (t, C-3), 42.4 (t, C-4). − MS (EI); *m/z* (%) = 270 [M + 2] (25), 269 [M + 1] (17), 268 [M^+] (91), 225 (100).

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