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SYNTHESIS OF BOSTRYCOIDIN VIA DIRECTED LITHIATION OF TERTIARY NICOTINAMIDE

M. Watanabe*, E. Shinoda, Y. Shimizu, and S. Furukawa
Faculty of Pharmaceutical Sciences, Nagasaki University

M. Iwao* and T. Kuraishi
Faculty of Liberal Arts, Nagasaki University
1-14 Bunkyo-machi, Nagasaki 852, Japan

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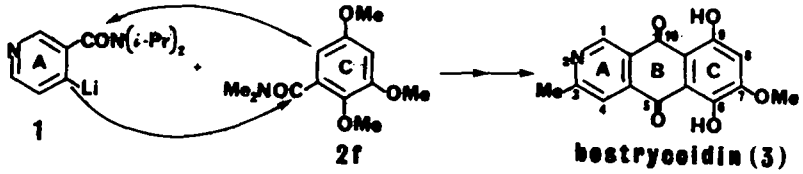
Summary: The formal total synthesis of the antibiotic bostrycoidin **3** was achieved by using 4-selective lithiation of N,N-diisopropylnicotinamide **4b** followed by condensation with N,N-dimethyl-2,3,5-trimethoxybenzamide **2f** as a key reaction.

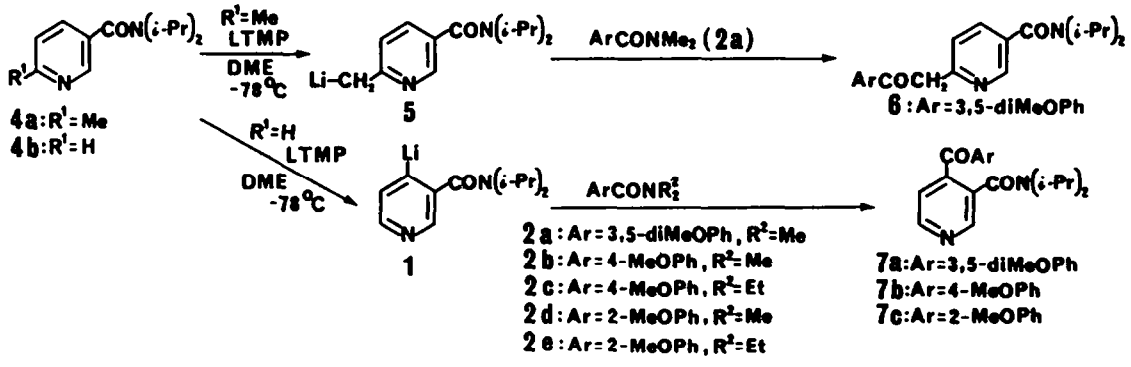
Although anthraquinones represent a large class of natural products,[1] their aza-analogues are rarely found in nature. So far, only two 2-azaanthraquinones, bostrycoidin and its 9-O-methyl derivative,[2] and two 1-azaanthraquinones, phomazarin[3] and isophomazarin,[4] have been isolated. Bostrycoidin was isolated from Fusarium bostrycoides[5] and F. solani D_2 purple,[6] and was shown to possess an antibiotic activity against the tubercle bacilus in vitro.[5] Its structure was elucidated by Arsenault[6] as 6,9-dihydroxy-7-methoxy-3-methylbenz[g]isoquinolin-5,10-dione. The first total synthesis of bostrycoidin and its 9-O-methyl derivative were achieved by Cameron and coworkers[7] in 1980 using two key reactions for the construction of the 2-azaanthraquinone skeleton,[8] i.e., reaction of 1,1-dimethoxyethene with azanaphthoquinones and radical benzoylation of a pyridine ring. However, each of these methods suffers from the disadvantages of poor regioselectivity and low yields. In this paper,[9] we describe a regiospecific synthesis of bostrycoidin **3** based on the directed lithiation strategy.[10] The advantage of the directed lithiation reaction for the synthesis of pyridine-containing natural products has been demonstrated in the total syntheses of ellipticine[11] and sesbanine.[12] For the synthesis of bostrycoidin, we have selected the lithiated nicotinamide **1** and the 2,3,5-trimethoxybenzamide **2f** as starting points (**Scheme 1**). The methyl group at 3-position of bostrycoidin **3** was planned to be introduced after the condensation of **1** and **2f** was accomplished, because highly acidic property of methyl group at α-position of the pyridine ring was anticipated to be problematical in the ring metalation.



Scheme 1

The directed lithiation of pyridine derivatives[13] has been studied by several groups. Epsztajn et al.[13a] achieved 4-selective lithiation of N,N-diisopropylnicotinamide using LDA(2 eq.)/ether system at -78 °C and reported 60% deuterium incorporation by MeOD quenching. On the other hand, Iwao and Kuraishi[12] used LTMP(1.2 eq.)/DME system for metalation of the same amide in the total synthesis of sesbanine. By deuteration experiment, we have found that the LTMP/DME system is quite efficient and 75% deuterium incorporation was observed after 15 min at -78 °C by a MeOD quench experiment. Therefore, we employed the LTMP/DME metalation conditions in the present study.

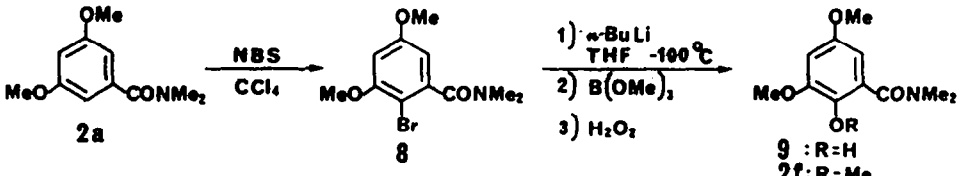
The condensation of N,N-diisopropyl-6-methylnicotinamide **4a** and N,N-diisopropylnicotinamide **4b** with various methoxy-substituted benzamides **2a-e** was examined as a preliminary study to model the A-C ring connection reaction needed for bostrycoidin (**Scheme 2**). A DME solution of the 6-methylnicotinamide **4a** was treated with 1.5 eq. LTMP, prepared from 1.5 eq. n-BuLi and 1.5 eq. 2,2,6,6-tetramethylpiperidine at -78 °C, to give orange-red lithio species **5**. After 15 min, 1.0 eq. of N,N-dimethyl-3,5-dimethoxybenzamide **2a** was added to the reaction mixture. Following standard workup, only N,N-diisopropyl-6-(3,5-dimethoxybenzoyl)methylnicotinamide **6** was obtained in a quantitative yield. This result indicates, as expected, that the lithiation of α-methyl group of the pyridine ring is much faster than ring metalation. On the other hand, when N,N-diisopropylnicotinamide **4b** was lithiated under the same conditions and then reacted with **2a**, only N,N-diisopropyl-4-(3,5-dimethoxybenzoyl)nicotinamide **7a** was obtained in a quantitative yield. Next, we checked the difference in the reactivity of N,N-dimethylamide and N,N-diethylamide groups towards the lithio species **1**. When **1** was treated with N,N-dimethy-4-methoxybenzamide **2b** and N,N-diethyl-4-methoxybenzamide **2c**, N,N-diisopropyl-4-(4-methoxybenzoyl)nicotinamide **7b** was obtained in 98% and 53% yields, respectively. These results show the advantage of the N,N-dimethylamide group over the N,N-diethyl group for the introduction of benzoyl groups into the pyridine ring which may be rationalized by the steric effects in the respective amide carbonyls. This tendency is even more remarkable in the case of ortho substituted benzamides. Thus, when N,N-dimethyl-2-methoxybenzamide **2d** was treated with **1**, the condensation product **7c** was obtained in 71% yield. On the other hand, by using the corresponding N,N-diethylamide **2e** the same product **7c** was obtained in only 6% yield. Therefore, for the preparation of N,N-diisopropyl-4-(2,3,5-trimethoxybenzoyl)nicotinamide **10**, N,N-dimethyl-2,3,5-trimethoxybenzamide **2f** should be used as a benzoylating agent.



Scheme 2

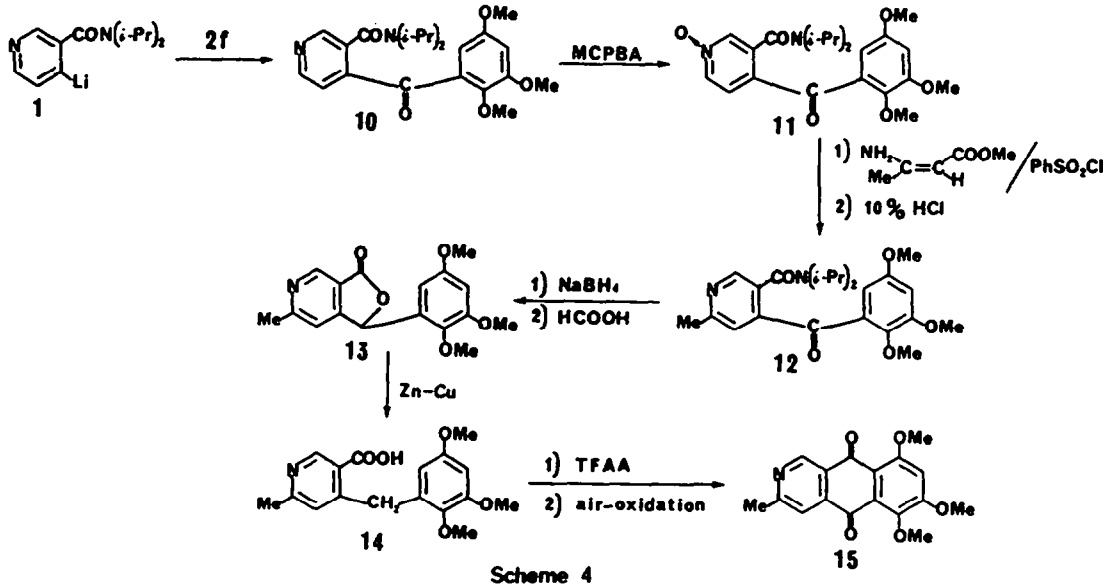
The synthesis of N,N-dimethyl-2,3,5-trimethoxybenzamide **2f**, the C-ring part of bostrycoidin, is shown in **Scheme 3**. N,N-Dimethyl-3,5-dimethoxybenzamide **2a** was brominated[14] by NBS in CCl_4 to give N,N-dimethyl-2-bromo-3,5-dimethoxybenzamide **8** in 89% yield. Bromine-lithium exchange reaction of **8** using n-BuLi at -100 °C and subsequent hydroxylation[15] using trimethyl borate and hydrogen peroxide afforded N,N-dimethyl-2-hydroxy-3,5-dimethoxybenzamide **9** in 86% yield. Methylation of **8** by MeI/K_2CO_3 furnished the requisit C-ring part

2f of bostrycoidin in 77% yield. The overall yield of 2f from 2a was 60%. An attempted direct ortho-lithiation of 2a using the standard conditions (sec-BuLi/TMEDA/-78 °C) was failed due to the rapid attack of sec-BuLi at the amide carbonyl.



Scheme 3

N,N-Dimethyl-2,3,5-trimethoxybenzamide 2f thus obtained was then treated with 1 to give N,N-diisopropyl-4-(2,3,5-trimethoxybenzoyl)nicotinamide 10 in 58% yield (Scheme 4). For the introduction of the methyl group to 6-position of the pyridine ring of 10, we employed a method developed by Iwao and Kuraishi.[16] Thus, the keto-amide 10 was treated with m-chloroperbenzoic acid (MCPBA) in dichloromethane at room temperature to give the N-oxide 11 in 56% yield. The N-oxide 11 was treated with methyl 3-aminocrotonate in acetonitrile in the presence of benzenesulfonyl chloride and then the crude adduct was hydrolysed with 10% HCl to give the desired 6-methylated compound 12 in 60% yield. In this reaction, none of the regioisomer (2-methylated compound) was detected, probably because the nucleophilic attack of methyl 3-aminocrotonate at the 2-position of the O-benzenesulfonylated N-oxide is prohibited by the adjacent bulky N,N-diisopropylamide group. The keto-amide 12 was reduced by $NaBH_4$ to give the amide-alcohol which, without isolation, was converted by treatment with formic acid into the lactone 13 in quantitative yield. The use of other acid catalysts, such as TsOH or trifluoroacetic acid, decreased the yield of this transformation. The lactone 13 was reductively cleaved by zinc-copper couple[17] to give the acid 14 which was cyclized with trifluoroacetic anhydride (TFAA) and then air-oxidized to afford bostrycoidin dimethylether 15 in 50% overall yield. The synthetic bostrycoidin dimethylether 15 thus obtained was shown to be identical with an authentic sample by spectroscopic and TLC comparisons. Since the conversion of bostrycoidin dimethylether to bostrycoidin has been already achieved,[7] our work completes a formal total synthesis of bostrycoidin.



Scheme 4

Acknowledgment: We are grateful to Professor D.W. Cameron, University of Melbourne, for providing an authentic sample of bostrycoidin dimethylether.

EXPERIMENTAL

General. All melting points are uncorrected. Mass spectra (MS) were determined on JEOL JMS-01SG spectrometer. IR spectra were obtained in KBr disk using JASCO IRA-2 spectrometer. UV spectra were recorded in 95% ethanol on Hitachi 323 spectrometer. ^{1}H NMR spectra obtained with JEOL FX 90Q or JEOL JNM-PMX 60 spectrometer using $CDCl_3$ as a solvent and TMS as an internal standard. Elemental analyses were performed at microanalytical laboratory in Nagasaki University. All solvents used for lithiation reactions were freshly distilled from sodium benzophenone ketyl before use. For column chromatography, Silica gel 60 (230-400 mesh, Merck Art 9385) was employed.

N,N-Diisopropyl-6-(3,5-dimethoxybenzoylmethyl)nicotinamide (6): Under nitrogen atmosphere, a solution of n-BuLi in hexane (1.0 M, 4.5 ml, 4.5 mmol) was injected to a stirred solution of 2,2,6,6-tetramethylpiperidine (0.75 ml, 4.5 mmol) in 60 ml of dimethoxyethane (DME) at -78 °C, and the mixture was stirred for 1 h. A solution of N,N-diisopropyl-6-methylnicotinamide (**4a**) (0.66 g, 3 mmol) in DME (5 ml) was added to this solution. After being stirred for 15 min, a solution of N,N-dimethyl-3,5-dimethoxybenzamide (**2a**) (0.63 g, 3 mmol) in DME was injected to the resulting orange-red solution of 5. Dry Ice-acetone bath was removed, and the mixture was stirred for 10 h. The mixture was quenched with saturated NH_4Cl and evaporated. The residue was extracted with CH_2Cl_2, washed with water, and dried over Na_2SO_4. The extract was evaporated and the residue was chromatographed over silica gel using ethyl acetate as an eluent giving 1.13 g (98%) of **6** as a viscous oil. An analytical sample was obtained by distillation, bp 210 °C/0.5 mm Hg. MS: m/e=384 (M^+). IR: 1680 and 1615 cm^{-1}. UV: 275 (logε 3.90), 353 (4.18), and 435 nm sh (3.30). ^{1}H NMR: δ=1.36 (d, 12H, J=7 Hz), 3.50-3.80 (m, 2H), 3.80 (s, 6H), 4.47 (s, 2H), 6.50-7.57 (m, 5H), and 8.37-8.56(m, 1H). Anal. Calcd for $C_{22}H_{28}N_2O_4$: C, 68.72; H, 7.34; N, 7.29%. Found: C, 68.92; H, 7.37; N, 7.09%.

N,N-Diisopropyl-4-(3,5-dimethoxybenzoyl)nicotinamide (7a): The following procedures for the synthesis of **7a** are representative for the syntheses of other keto-amides **7b**, **7c**, and **10**. A solution of N,N-diisopropylnicotinamide (**4b**) (1.03 g, 5 mmol) in DME (10 ml) was added to a solution of LTMP in DME (100 ml), which was prepared in a similar manner as described above from n-BuLi in hexane (1.05 M, 7.21 ml, 7.5 mmol) and 2,2,6,6-tetramethylpiperidine (1.26 ml, 7.5 mmol), at -78 °C under nitrogen atmosphere. The resulting reddish-brown solution of **1** was stirred for 15 min and then a solution of **2a** (1.09 g, 5 mmol) in DME (10 ml) was injected. After stirring for 30 min at -78 °C and then for 8 h at room temperature, the reaction mixture was quenched with saturated NH_4Cl and worked up in a similar manner as described for **6** giving 1.08 g (98%) of **7a**. An analytical sample was recrystallized from methanol, mp 116-118 °C. MS: m/e=370 (M^+). IR: 1680 and 1640 cm^{-1}. UV: 283 (logε 3.36) and 340 nm sh (2.74). ^{1}H NMR: δ=1.05-1.50 (m, 12H), 3.30-3.82 (m, 2H), 3.76(s, 6H), 6.60 (d, 1H, J=2 Hz), 6.89 (d, 2H, J=2 Hz), 7.33 (d, 1H, J=7 Hz), 8.63 (br s, 1H), and 8.66 (d, 1H, J=7 Hz). Anal. Calcd for $C_{21}H_{26}N_2O_4$: C, 68.09; H, 7.07; N, 7.56%. Found: C, 67.94; H, 7.26; N, 7.64%.

N,N-Diisopropyl-4-(4-methoxybenzoyl)nicotinamide (7b): This compound was prepared in 98% yield from **4b** and **2b**, or in 53% yield from **4b** and **2c**, according to the procedure described for **7a**, mp 146-147 °C (ether). MS: m/e=340 (M^+). IR: 1660 and 1620 cm^{-1}. UV: 233 sh (logε 4.16) and 300 nm (4.24). ^{1}H NMR: δ=1.10-1.43 (m, 12H), 3.33-3.80 (m, 2H), 3.83 (s, 3H), 6.83 (d, 2H, J=9 Hz), 7.23 (d, 1H, J=7 Hz), 7.69 (d, 2H, J=9 Hz), 8.50 (br s, 1H), and 8.56 (d, 1H, J=7 Hz). Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.56; H, 7.11; N, 8.23%. Found: C, 70.49; H, 7.21; N, 8.22%.

N,N-Diisopropyl-4-(2-methoxybenzoyl)nicotinamide (7c): This compound was obtained in 71% yield from **4b** and **2d**, or in 6% yield from **4b** and **2e**, by the procedures described for **7a**, mp 112-113 °C (ether). MS: m/e=340 (M^+). IR: 1670 and 1630 cm^{-1}. UV: 269 sh (logε 3.73) and 320 nm (3.48). ^{1}H NMR: δ=1.13 (d, 6H, J=7 Hz), 1.46 (d, 6H, J=7 Hz), 3.30-3.60 (m, 2H), 3.56 (s, 3H), 6.83-7.60 (m, 5H), 8.51 (s, 1H), and 8.56 (d, 1H, J=6 Hz). Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.56; H, 7.11; N, 8.23%. Found: C, 70.53; H, 7.22; N, 8.31%.

N,N-Dimethyl-2-bromo-3,5-dimethoxybenzamide (8): A solution of N,N-dimethyl-3,5-dimethoxybenzamide (**2a**) (1.05 g, 5 mmol) and NBS (0.9 g, 5 mmol) in CCl_4 (60 ml) was refluxed for 2 h. After the solution was allowed to cool, the precipitated solid was filtered off and the filtrate was evaporated to dryness to afford crude **8**, which was distilled by bulb to bulb distillation apparatus to give pure **8** (1.28 g, 89%), bp 150 °C/0.5 mmHg. MS: m/e=288 (M^+). IR: 1625 cm^{-1}. UV: 292 nm (logε 3.00). ^{1}H NMR: δ=2.83 (s, 3H), 3.07 (s, 3H), 3.73 (s, 3H), 3.83 (s, 3H), 6.30 (d, 1H, J=2Hz), and 6.40 (d, 1H, J=2Hz). Anal. Calcd for $C_{11}H_{14}NO_3Br$: C, 45.85; H, 4.89; N, 4.89%. Found: C, 45.69; H, 4.99; N, 4.79%.

N,N-Dimethyl-2-hydroxy-3,5-dimethoxybenzamide (9): To a stirred solution **8** (2.16 g, 7.5 mmol) in THF (120 ml) was added n-BuLi (9 ml, 9 mmol, 1.0 M hexane solution) dropwise over 5 min at -100 °C (liquid nitrogen-methanol bath) under nitrogen atmosphere. After the addition was completed, a solution of trimethyl borate (1.05 ml, 9.2 mmol) in THF (2 ml) was injected immediately and then the cooling bath was removed. After stirring for 1 h at

room temperature, glacial acetic acid (0.6 ml, 10.5 mmol) was added, followed immediately by the addition of 30% H_2O_2 (1.5 ml). The reaction mixture was stirred overnight at room temperature, quenched with saturated NH_4Cl and 10% HCl, and evaporated. The residue was extracted with $CHCl_3$, washed with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed over silica gel using chloroform as an eluent giving 1.44 g (86%) of **9**, mp 102-104 °C (hexane). MS: m/e=225 (M^+). IR: 1610 cm^{-1}. UV: 300 nm (log ε 3.78). ^1H NMR: δ=3.04 (s, 6H), 3.73 (s, 3H), 3.81 (s, 3H), 6.35 (d, 1H, J=3 Hz), and 6.48 (d, 1H, J=3 Hz). Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.65; H, 6.71; N, 6.22%. Found: C, 58.84; H, 6.85; N, 6.17%.

N,N-Dimethyl-2,3,5-trimethoxybenzamide (2f): A mixture of **9** (2.1 g, 9.3 mmol), powdered K_2CO_3 (10 g), and methyl iodide (3.9 g, 28 mmol) was refluxed with stirring for 4 h. After cooling, the reaction mixture was filtered and the filtrate was evaporated to dryness. An aqueous 5% Na_2CO_3 solution was added to the residue and the mixture was extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated to give an oil which was distilled under reduced pressure to give 1.7 g (77%) of **2f**, bp 150 °C/0.5 mmHg. MS: m/e=239 (M^+). IR: 1620 cm^{-1}. UV: 289 nm (log ε 2.91). ^1H NMR: δ=2.79 (s, 3H), 3.03 (s, 3H), 3.68 (s, 6H), 3.76 (s, 3H), 6.22 (d, 1H, J=3 Hz), and 6.41 (d, 1H, J=3 Hz). Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85%. Found: C, 59.81; H, 7.19; N, 5.81%.

N,N-Diisopropyl-4-(2,3,5-trimethoxybenzoyl)nicotinamide (10): This compound was synthesized in 58% yield by the reaction of the lithiated nicotinamide **1** with N,N-dimethyl-2,3,5-trimethoxybenzamide (**2f**) in the same manner as described for the preparation of **7**. Bp 185 °C/0.5 mmHg. MS: m/e=400 (M^+). IR: 1625 cm^{-1}. UV: 282 (log ε 3.91), 345 sh (3.29). ^1H NMR: δ=1.22 (d, 6H, J=7 Hz), 1.49 (d, 6H, J=7 Hz), 3.50-3.90 (m, 2H), 3.57 (s, 3H), 3.79 (s, 3H), 3.84 (s, 3H), 6.63 (d, 1H, J=3 Hz), 6.68 (d, 1H, J=3 Hz), 7.34 (d, 1H, J=5 Hz), 8.57 (s, 1H), and 8.65 (d, 1H, J=5 Hz),. Anal. Calcd for $C_{22}H_{28}N_2O_5$: C, 65.98; H,7.05; N, 7.00%. Found: C, 66.30; H, 7.28; N, 7.06%.

N,N-Diisopropyl-6-methyl-4-(2,3,5-trimethoxybenzoyl)nicotinamide (12): To a stirred solution of **10** (2.2 g, 5.5 mmol) in CH_2Cl_2 (50 ml) was added m-chloroperbenzoic acid (70%, 2.9 g, 12 mmol) at room temperature and the mixture was stirred for 4 h. An aqueous solution of 5% K_2CO_3 (20 ml) was added and the organic layer was separated, dried over Na_2SO_4, and evaporated. The residual viscous oil was chromatographed using chloroform-acetone (4:1) as an eluent to give 1.3 g (56%) of the N-oxide **11**. ^1H NMR: δ=1.26 (d, 6H, J=8 Hz), 1.58 (d, 6H, J=8 Hz), 3.50-3.85 (m, 2H), 3.58 (s, 3H), 3.71 (s, 3H), 3.81 (s, 3H), 6.45 (d, 1H, J=4 Hz), 6.58 (d, 1H, J=4 Hz), 7.31 (d, 1H, J=5 Hz), 7.97 (s, 1H), and 8.03 (d, 1H, J=5 Hz). Without further purification, the N-oxide **11** was used for the next reaction. Under ice-cooling, a solution of benzenesulfonyl chloride (0.85 g, 4.8 mmol) in acetonitrile (10 ml) was added dropwise to a stirred solution of **11** (1 g, 2.4 mmol) and methyl 3-aminocrotonate (1.1 g, 9.6 mmol)in acetonitrile (30 ml). The reaction mixture was stirred for 4 h and evaporated. Water was added to the residue and the mixture was extracted with chloroform. The extract was evaporated and the residue was dissolved in 10% HCl (20 ml). The mixture was heated at 90 °C for 2 h. After cooling, the mixture was neutralized with 15% NaOH solution and extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated to dryness. The residual solid was purified by chromatography using ethyl acetate as an eluent giving 0.6 g (60%) of **12**. An analytical sample was obtained by recrystallization from ether, mp 162-163 °C. MS: m/e=414 (M^+). IR: 1670 and 1630 cm^{-1}. UV: 284 (log ε 4.77) and 335 nm sh (4.23). ^1H NMR: δ=1.21 (d, 6H, J=8 Hz), 1.48 (d, 6H, J=8 Hz), 2.58 (s, 3H), 3.58 (s, 3H), 3.60-3.95 (m, 2H), 3.80 (s, 3H), 3.85 (s, 3H), 6.63 (d, 1H, J=3 Hz), 6.68 (d, 1H, J=3 Hz), 7.18 (s, 1H) and 8.44 (s, 1H). Anal. Calcd for $C_{23}H_{30}N_2O_5$: C, 66.64; H, 7.30; N, 6.76%. Found: C, 67.06; H, 7.31; N, 7.10%.

1-(2,3,5-Trimethoxyphenyl)-6-methylfuro[3,4-c]pyridin-3(1H)-one (13): To a solution of **12** (0.1 g, 0.24 mmol) in ethanol (50 ml) was added $NaBH_4$ (0.1 g, 2.7 mmol). The mixture was stirred for 12 h at room temperature and then quenched with ethyl acetate (1 ml). The solution was evaporated to leave an oil which was neutralized with 30% acetic acid. The mixture was extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated to give the intermediate amide-alcohol which, without isolation, used for next reaction. A solution of this material in formic acid (20 ml) was refluxed for 7 h under nitrogen atmosphere. The cooled mixture was evaporated and the residue was treated with 5% Na_2CO_3 solution. The mixture was extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated. The residue was purified by distillation giving 0.07 g (98%) of **13**, bp 190 °C/0.5 mmHg. MS: m/e=315 (M^+). IR: 1765 cm^{-1}. UV: 230 sh (log ε 4.30), 270 sh (3.46), and 292 nm (3.49). ^1H NMR: δ=2.59 (s, 3H), 3.66 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 6.10 (d, 1H, J=2 Hz), 6.46 (d, 1H, J=2 Hz), 6.59 (s, 1H), 7.26 (s, 1H), and 8.96 (s, 1H). Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44%. Found: C, 64.81; H, 5.74; N, 4.37%.

6,7,9-Trimethoxy-3-methylbenzo[g]isoquinonlin-5,10-dione (Bostrycoidin Dimethylether) (15): A mixture of **13** (0.43 g, 1.36 mmol), zinc-copper couple[17] (14 g), pyridine (7 ml), and 10% KOH solution (70 ml) was refluxed for 72 h. After cooling, the mixture was filtered and the filtrate was evaporated to dryness. The residue was acidified with 10% HCl and then neutralized with aqueous ammonia. The solution was extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated to give **14** (0.26 g, 63%) as white powder which was used for the next cyclization reaction without further purification. The acid **14** (0.26 g, 0.82 mmol) thus obtained was dissolved in dichloromethane (80 ml). Trifluoroacetic anhydride (0.3 ml, 2.25 mmol) was added to the solution and the mixture was stirred for 12 h at room temperature. The reaction mixture was evaporated to dryness. The resulting viscous residue was triturated with methanol and neutralized with 5% Na_2CO_3 solution. The

mixture was extracted with chloroform. The extract was dried over Na_2SO_4 and evaporated. The gummy residue was dissolved in methanol (30 ml) and oxygen was bubbled through this solution for 1h at room temperature. Methanol was evaporated to leave crystalline material, which was purified by chromatography using chloroform-acetone (1:1) as an eluent giving 0.2 g (80%) of **15**, mp 209-211 °C (MeOH) (lit 7. mp 210-211 C). MS: m/e=313 (M^+). IR: 1680 and 1660 cm^{-1}. UV: 240 (logε 5.56), 298 (5.19), and 420 nm (4.97). ^1H NMR: δ=2.72 (s, 3H), 3.94 (s, 3H), 4.01 (s, 3H), 4.04 (s, 3H), 6.85 (s, 1H), 7.74 (s, 1H), and 9.33 (s, 1H).

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