prepared by recrystallization from ether: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 8.89 (bs, 1 H, NH), 7.18 (d, 1 H), 6.64 (d, 1 H), 4.60 (s, 1 H, OH), 3.7–4.1 (m, 2 H), 3.71 (s, 3 H, OCH_3), 2.5–3.1 (m, 3 H), 1.9–2.2 (m, 2 H), 1.29 (t, 3 H, CH_3), 0.83 (t, 3 H, CH_3); IR (KBr) 3420, 1735 cm^{-1}; mass spectrum, *m/e* 317, 288, 244; R_f (ether–petroleum ether) 0.57. Anal. Calcd for $C_{18}H_{23}NO_4$: C, 68.12; H, 7.30; N, 4.41. Found: C, 68.02; H, 6.98; N, 4.28.

1,8-Diethyl-7-hydroxy-1,3,4,9-tetrahydropyrano[3,4-*b*]indole-1-acetic Acid (2). A degassed solution of potassium carbonate (480 g, 3.47 mol) in water (1.7 L) and methanol (1.7 L) was added to 53.7 g (0.169 mol) of **12**. The flask was evacuated and then filled with N_2 (procedure repeated three times). The reaction mixture was heated at 50 °C. During the reaction period, the reaction flask was evacuated and fresh N_2 was introduced at 1-h intervals. After 3 h, 240 g (1.74 mol) of K_2CO_3 was added. After evacuation and N_2 introduction, the reaction mixture was heated at 50 °C for 5 h. The red solution was cooled to 0 °C and treated with degassed 4 N HCl (2.68 mL, 10.7 mol) until pH 2 was obtained. The resulting tan crystals were collected, washed thoroughly with water, and dried in vacuo at 25 °C to provide 49.3 g (96%) of analytically pure title compound as a beige solid: mp 180 °C dec; ^{1}H NMR (DMSO, 400 MHz) δ 11.1 (s, 1 H), 10.1 (s, 1 H), 6.96 (d, 1 H), 6.54 (d, 1 H), 3.8–4.0 (m, 2 H), 2.87 (d, 1 H), 2.7 (d, 1 H), 1.10 (t, 3 H), 0.59 (t, 3 H); IR (KBr) 3350, 1690 cm^{-1}; mass spectrum, *m/e* 303, 259; R_f (33% acetone–CH_2Cl_2; on 1% H_3PO_4–MeOH pretreated plates) 0.5. Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.02; H, 6.71; N, 4.87.

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Registry No. **1**, 41340-25-4; **2**, 101901-07-9; **4**, 56619-93-3; **5**, 114274-14-5; **6**, 114274-15-6; **6** (free base), 114274-16-7; **7**, 114274-17-8; **8**, 114274-18-9; **9**, 114274-19-0; **10**, 114274-20-3; **11**, 114274-21-4; **12**, 114274-22-5; CH_3CHO, 75-07-0; $Cl(CO)_2OEt$, 4755-77-5; *m*-anisidine, 536-90-3; trimethylacetyl chloride, 3282-30-2; *N*-(*tert*-butylcarbonyl)-2-ethyl-3-methoxyaniline, 114274-23-6; *tert*-butylacetate, 540-88-5; methyl 3-methoxy-2-pentenoate, 104065-67-0.

Isoquinoline Quinones. Preparation of Saframycin Intermediates and a Total Synthesis of Mimosamycin

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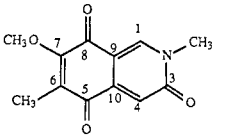
The isoquinoline quinones comprise a new structural class of naturally occurring antibiotics.[1] Mimosamycin (**1**),[2] one of the "monomeric" isoquinoline quinones, was found to have antitubercular activity.[3] Saframycin A (**2**),[4] which represents the more complex "dimeric" members of the class, exhibits antitumor activity.[5]



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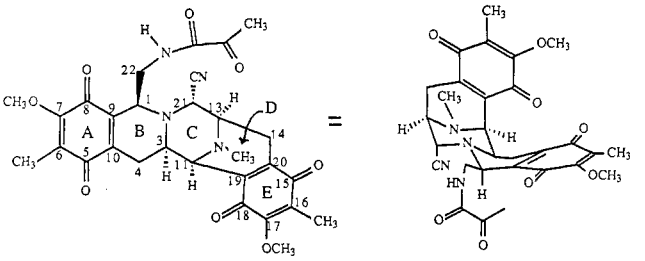

2

In earlier work directed toward the synthesis of the saframycins, the strategy of conjugate addition to quinone monoketal **3** was used to introduce functionality for the A/B ring system.[6] We imagined that this approach might also be employed to construct precursors to the functionally similar D/E ring system of saframycin A and to the natural product, mimosamycin.

For example, conjugate addition of a one-carbon nucleophile to the readily available quinone monoketal **3**[6] would append a functionalized carbon-11 to the latent E ring of saframycin. In the same fashion, we might add a functionalized carbon-1 to the latent quinone of mimosamycin. Then allylation (Scheme I) would provide the basis for the elaboration of the side chains required (C-14, C-13, and C-21 of saframycin and C-4 and C-3 of mimosamycin). In this paper, we report the preparation of allylbenzonitriles **6**, regarded as potential intermediates in a total synthesis of saframycin A,[7] and the elaboration of nitrile **6c** (X = H) to the antibiotic mimosamycin (**1**).

Cyanide addition to a naphthoquinone monoketal (KCN, methanol, reflux) has been demonstrated by Semmelhack and co-workers.[9] In our hands, the conversion of quinone ketal **3** to benzonitrile **4** was improved (60% yield) when potassium cyanide (slightly more than 1 equiv) was added in the presence of 1 equiv of 18-crown-6 in THF.

Our first attempts to introduce the acetic acid side chain of mimosamycin were based on oxidative cleavage of a haloallyl substituent.[10,11] Both bromo and chloro substitution were examined in this application.

The haloallyl side chain was to be introduced into the sixth position on the aromatic nucleus by Claisen rearrangement. Alkylation of phenol **4** with the appropriate

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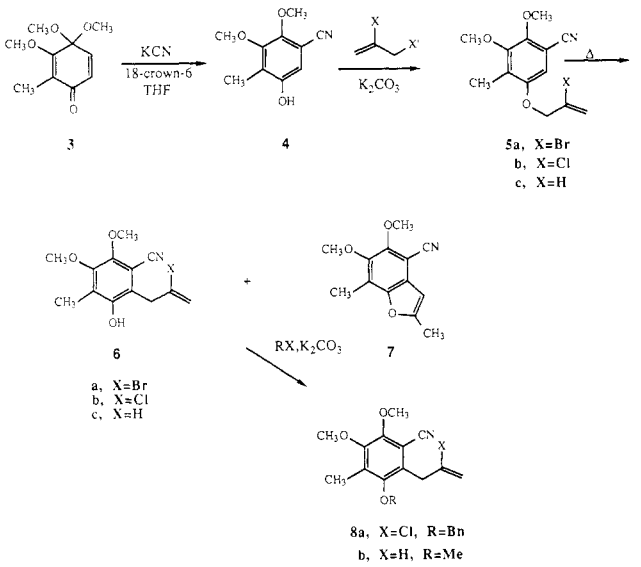
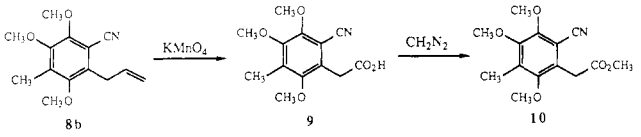
0022-3263/88/1953-2847$01.50/0

Scheme I



Scheme II



allyl halide yielded the allyl phenyl ethers **5a** and **5b**. Heating bromoallyl compound **5a** in dimethylaniline for 5.5 h produced a mixture of **5a**, **6a**, and **7**; compound **7** presumably results from cyclization of **6a**.[11]

Rearrangement of the chloroallyl side chain in **5b** was much cleaner. Chloroallylphenol **6b** was produced in 81% yield with no contaminating benzofuran. The free phenol was protected as its benzyl ether **8a**.

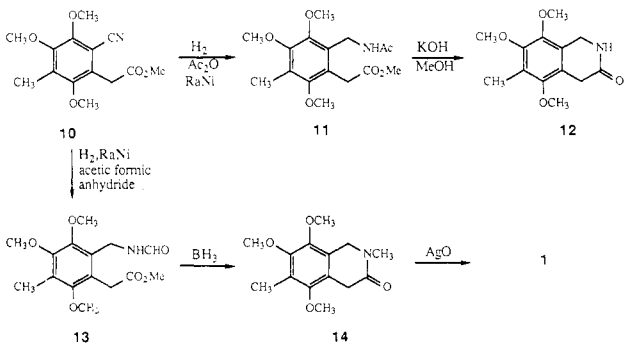
The halogenated olefin of **8a** was unreactive toward osmium tetraoxide under catalytic reaction conditions;[12] the starting material was recovered unchanged. Under conditions using stoichiometric osmium tetraoxide,[13] the olefin **8a** was consumed but no product could be isolated. However, potassium permanganate in a phase-transfer system[14] converted **8a** to a mixture of products containing the desired acid **9**.

Because of difficulties in cleaving the chloroallyl side chain, we decided to test the oxidation of allylbenzene **8b**. Thus phenol **5** was allylated with allyl bromide to give ether **5c**; rearrangement provided the allylphenol **6c**. The overall yield of **6c** from quinone ketal **3** is 33%. Phenol **6c** may, therefore, be considered readily available for incorporation in a saframycin synthesis.

Protection of **6c** as its methyl ether (**8b**) and oxidation with $KMnO_4$ yielded acid **9**, which was then treated with diazomethane to give methyl ester **10**. The overall yield from **6c** to **10** was 70% without isolation of intermediates.

Nitrile ester **10** was converted to tetrahydroisoquinoline **12** in two steps. Hydrogenation of **10** over Raney nickel in acetic anhydride[15] afforded the *N*-acetyl ester (**11**). Treatment of **11** with methanolic KOH yielded lactam **12**.

Scheme III



All attempts at N-methylation of **12** failed. Standard phase-transfer conditions or sodium hydride/methyl iodide in either THF or DMF[16] was not effective and a multitude of products was observed.

As an alternative, the preparation of the *N*-methylamine prior to ring closure was explored. Although the hydrogenation of **10** over Raney nickel in acetic formic anhydride[17] was more capricious than hydrogenation of **10** in acetic anhydride, careful catalyst preparation, use of large quantities of catalyst, and long reaction times provided useful quantities of *N*-formyl ester **13**. Diborane reduction of **13** then gave the *N*-methyl lactam **14** directly.[18]

On oxidative demethylation of lactam **14** with AgO in dioxane/nitric acid,[19] a mixture rich in mimosamycin (**1**) was produced. Although it appeared that decomposition occurred during attempts to purify the product by chromatography, a sample of mimosamycin that showed the same major NMR features as an authentic sample[20] was obtained in 18% yield.

Experimental Section

^1H NMR spectra were recorded on either a 250- or a 400-MHz Bruker FT spectrometer in $CDCl_3$ with tetramethylsilane as internal standard and are reported in parts per million. Infrared spectra were recorded in $CHCl_3$ or as neat films on a Perkin-Elmer 681 spectrophotometer. Mass spectra, both low- and high-resolution (peak matching), were obtained on a Kratos MS-80 at 70 eV under electron impact conditions. Melting points were determined on a Thomas-Hoover capillary melting apparatus and are uncorrected. Chromatography was performed either on a Harrison Research Corp. Chromatotron or on Analtech 1000-μm preparative TLC plates with fluorescent indicator. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratories, Woodside, NY.

2,3-Dimethoxy-5-hydroxy-4-methylbenzonitrile (4). Quinone monoketal **3** (422 mg, 2.13 mmol) was heated at reflux in 20 mL of dry THF containing 174 mg of KCN (2.7 mmol) and 564 mg of 18-crown-6 for 5.5 h. After cooling, the reaction mixture was diluted with 15 mL of Et_2O and stirred over 10 mL of 1% aqueous H_2SO_4 for 30 min. Separation of the layers, washing of the Et_2O layer with H_2O, and drying over $MgSO_4$ followed by Chromatotron separation (2 mm, 20% EtOAc/hexanes) of the crude product mixture provided 248 mg (60%) of nitrile **4**, which could be further purified by crystallization from Et_2O/hexanes: mp 114.5–115.5 °C; ^1H NMR (250 MHz) δ 2.19 (s, 3 H, CH_3), 3.85 (2 s, 3 H each, OCH_3), 6.75 (s, 1 H, ArH); IR 2223 cm^{-1} (CN); MS

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m/z 193 (M^+, 100); HRMS, exact mass obsd: 193.0732 ($C_{10}H_{11}NO_3$ requires 193.0739).

General Method for Preparing Allyl Phenyl Ethers. The phenol **4** was heated at reflux in acetone containing excess K_2CO_3 and the desired allyl halide overnight. The reaction mixture was cooled, diluted with Et_2O, filtered, and evaporated. Purification by Chromatotron (10–20% EtOAc/hexanes) yielded the product.

5-((2-Bromoallyl)oxy)-2,3-dimethoxy-4-methylbenzonitrile (5a). **4** (329 mg) in 15 mL of acetone containing 0.25 mL of dibromopropene yielded 223 mg of **5a** (42%) after purification: mp 80–82 °C; ^1H NMR (250 MHz) δ 2.23 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 4.60 (t, 2 H, CH_2, J = 1.3 Hz), 5.71 (dt, 1 H, vinyl, J = 2.1, 1.1 Hz), 5.99 (m, 1 H, vinyl), 6.68 (s, 1 H, ArH); IR 2225 cm^{-1} (CN); MS m/z 311, 313 (M^+, 9, 8), 192 (100); HRMS, exact mass obsd: 311.0133 ($C_{13}H_{14}NO_3Br$ requires 311.0156).

5-((2-Chloroallyl)oxy)-2,3-dimethoxy-4-methylbenzonitrile (5b). **4** (259 mg) in 20 mL of acetone containing 0.5 mL of dichloropropene yielded 336 mg (93%) of crude **5b**, which was crystallized from Et_2O/hexanes: mp 84–86 °C; ^1H NMR (250 MHz) δ 2.22 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 4.55 (t, 2 H, CH_2), 5.47 (m, 1 H, vinyl), 5.55 (m, 1 H, vinyl), 6.69 (s, 1 H, ArH); IR 2222 cm^{-1} (CN); MS m/z 267 (M^+, 14), 192 (100). Anal. Calcd for $C_{13}H_{14}NO_3Cl$: C, 58.33; H, 5.27; N, 5.23; Cl, 13.24. Found: C, 58.23; H, 5.17; N, 5.06; Cl, 13.03.

5-(Allyloxy)-2,3-dimethoxy-4-methylbenzonitrile (5c). **4** (280 mg) 28 mL of acetone containing 0.55 mL of allyl bromide yielded 327 mg (97%) of **5c** after chromatography. An analytical sample was prepared by crystallization from MeOH/H_2O: mp 59.5–61 °C, 93% recovery; ^1H NMR (400 MHz) δ 2.21 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 3.96 (s, 3 H, OCH_3), 4.51 (dt, 2 H, CH_2, J = 5, 1.5 Hz), 5.31 (dq, 1 H, vinyl, J = 10.6, 1.4 Hz), 5.42 (dq, 1 H, vinyl, J = 17.3, 1.6 Hz), 6.03 (ddq, 1 H, vinyl, J = 17.3, 10.6, 5 Hz), 6.71 (s, 1 H, ArH); IR 2222 cm^{-1} (CN); MS m/z 233 (M^+, 48), 192 (100). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.82; H, 6.46; N, 5.90.

6-(2-Bromoallyl)-2,3-dimethoxy-5-hydroxy-4-methylbenzonitrile (6a) and 5,6-Dimethoxy-2,7-dimethyl-4-cyanobenzofuran (7). Allyl phenyl ether **5a** (120 mg) was heated at reflux in 10 mL of dimethylaniline for 5.5 h. The reaction mixture was diluted with Et_2O and thoroughly extracted with 1 N HCl. The organic layer was dried ($MgSO_4$), evaporated, and separated on the Chromatotron (10–20% EtOAc/hexanes) to yield three bands: unreacted **5a** (67 mg, 56%), benzofuran **7** (13 mg, 11%), and **6a** (34 mg, 28%). Longer reaction times produced **7** exclusively.

6a: mp 114.5–115.5 °C; ^1H NMR (250 MHz) δ 2.22 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 3.94 (t, 2 H, CH_2, J = 1 Hz), 3.95 (s, 3 H, OCH_3), 4.98 (s, 1 H, ArOH), 5.57 (m, 1 H, vinyl), 5.69 (m, 1 H, vinyl); IR 2225 cm^{-1} (CN); MS m/z 311, 313 (M^+, 49, 47), 232 (100); HRMS, exact mass obsd: 311.0183 ($C_{13}H_{14}NO_3Br$ requires 311.0156).

7. The solid was recrystallized from Et_2O/hexanes: mp 85–87 °C; ^1H NMR (250 MHz) δ 2.44 (s, 3 H, CH_3), 2.47 (s, 3 H, CH_3), 3.85 (s, 3 H, OCH_3), 4.03 (s, 3 H, OCH_3), 6.46 (s, 1 H, ArH); IR 2220 cm^{-1} (CN); MS m/z 231 (M^+, 100). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.46; H, 5.66; N, 5.95.

6-(2-Chloroallyl)-2,3-dimethoxy-5-hydroxy-4-methylbenzonitrile (6b). Allyl ether **5b** (90 mg) was heated at reflux in 10 mL of dimethylaniline for 7.5 h. After dilution with Et_2O, the reaction mixture was thoroughly extracted with 1 N HCl. The organic layer was dried ($MgSO_4$), evaporated, and separated on the Chromatotron in 50% EtOAc/hexanes to give 73 mg (81%) of **6b**: mp 103–104.5 °C; ^1H NMR (250 MHz) δ 2.22 (s, 3 H, CH_3), 3.82 (m, 2 H, CH_2), 3.85 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 5.26 (m, 1 H, vinyl), 5.31 (m, 1 H, vinyl); IR 2217 cm^{-1} (CN); MS m/z 267 (M^+, 77), 233 (100); HRMS, exact mass obsd: 267.0646 ($C_{13}H_{14}NO_3Cl$ requires 267.0662).

5-(Benzyloxy)-6-(2-chloroallyl)-2,3-dimethoxy-4-methylbenzonitrile (8a). Allylphenol **6b** (108 mg, 0.402 mmol) was heated at reflux with 134 mg of K_2CO_3 and 100 μL of benzyl bromide in 7 mL of acetone overnight. The reaction mixture was diluted with Et_2O, filtered, evaporated, and separated by Chromatotron in 20% EtOAc/hexanes to give 124 mg (86%) of **8a**: ^1H NMR (250 MHz) δ 2.29 (s, 3 H, CH_3), 3.79 (s, 2 H, allyl CH_2), 3.87 (s, 3 H, OCH_3), 4.00 (s, 3 H, OCH_3), 4.81 (s, 2 H, benzyl), 5.00 (m, 1 H, vinyl), 5.29 (m, 1 H, vinyl), 7.30–7.44 (m, 5 H, ArH); IR 2219 cm^{-1} (CN); MS m/z 357 (M^+, 21), 91 (100); HRMS, exact mass obsd: 357.1119 ($C_{20}H_{20}ClNO_3$ requires 357.1131).

6-Allyl-2,3-dimethoxy-5-hydroxy-4-methylbenzonitrile (6c). Allyl ether **5c** (33 mg) was heated at reflux in 1.5 mL of dimethylaniline for 8 h. After dilution with Et_2O and thorough extraction with 1 N HCl, the organic layer was dried ($MgSO_4$), evaporated, and separated on the Chromatotron in 20% EtOAc/hexanes to provide 23 mg (74%) of **6c**. An analytical sample was prepared by crystallization from Et_2O/hexanes: mp 106–107 °C, 81% recovery; ^1H NMR (250 MHz) δ 2.20 (s, 3 H, CH_3), 3.58 (dt, 2 H, CH_2), 3.83 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 5.18 (m, 1 H, vinyl), 5.24 (m, 1 H, vinyl), 5.96 (m, 1 H, vinyl); IR 2222 cm^{-1} (CN); MS m/z 233 (M^+, 100). Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.93; H, 6.44; N, 5.90.

6-Allyl-4-methyl-2,3,5-trimethoxybenzonitrile (8b). Allylphenol **6c** (36.9 mg) was heated at reflux with excess K_2CO_3 and 50 μL of methyl iodide in 5 mL of acetone overnight. The reaction mixture was diluted with an equal volume of Et_2O, filtered, and evaporated. The residue was purified on a prep plate in 20% EtOAc/hexanes to give 34.4 (88%) of a pale oil, **8b**: ^1H NMR (250 MHz) δ 2.25 (s, 3 H, CH_3), 3.52 (dt, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 3.97 (s, 3 H, OCH_3), 5.06 (dq, 1 H, vinyl), 5.11 (t, 1 H, vinyl), 5.96 (m, 1 H, vinyl); IR 2225 cm^{-1} (CN); MS m/z 247 (M^+, 100); HRMS, exact mass obsd: 247.1210 ($C_{14}H_{17}NO_3$ requires 247.1208).

2-Cyano-5-methyl-3,4,6-trimethoxyphenylacetic Acid (9). Allyl nitrile **8b** (109.1 mg, crude) was stirred at room temperature in 3 mL of CH_2Cl_2, 3 mL of H_2O, 1 mL of glacial AcOH, and a catalytic amount of Bu_4NBr. Solid $KMnO_4$ (267.7 mg) was added in portions over 5 h, and the reaction mixture was stirred overnight. Solid sodium bisulfite was added to dissolve the precipitated MnO_2, and the mixture was poured into a separatory funnel. The organic layer was washed well with H_2O and then extracted with aqueous Na_2CO_3. The organic layer contained unreacted **8b** (43.6 mg). Upon acidification of the basic solution with HCl, the product was extracted into CH_2Cl_2. The organic layer was dried ($MgSO_4$) and evaporated to give crude acid **9**: ^1H NMR (250 MHz) δ 2.25 (s, 3 H, CH_3), 3.71 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.86 (s, 2 H, CH_2), 3.98 (s, 3 H, OCH_3); IR 2225 cm^{-1} (CN); MS m/z 265 (M^+, 100); HRMS, exact mass obsd: 265.0930 ($C_{13}H_{15}NO_5$ requires 265.0950).

Methyl 2-Cyano-5-methyl-3,4,6-trimethoxyphenylacetate (10). Crude acid **9** (from the previous reaction) in CH_2Cl_2 was esterified by the addition of ethereal diazomethane generated from Diazald. Excess diazomethane was destroyed by addition of glacial AcOH. The solution was evaporated and chromatographed (Chromatotron, 1 mm, 20% EtOAc/hexanes) to give 60.6 mg of purified **10**. Yields of up to 70% could be realized for the three steps from **6c** without chromatography of the intermediates. ^1H NMR (400 MHz) δ 2.25 (s, 3 H, $ArCH_3$), 3.68 (s, 3 H, $ArOCH_3$), 3.75 (s, 3 H, CO_2CH_3), 3.82 (s, 2 H, CH_2), 3.85 (s, 3 H, $ArOCH_3$), 3.98 (s, 3 H, $ArOCH_3$); IR 2217, (CN), 1742 cm^{-1} (ester); MS 279 (M^+, 88), 220 (100); HRMS, exact mass obsd: 279.1122 ($C_{14}H_{17}NO_5$ requires 279.1106).

Methyl 2-((Acetylamino)methyl)-5-methyl-3,4,6-trimethoxyphenylacetate (11). A portion of RaNi in H_2O was washed thoroughly with absolute EtOH and then with Ac_2O. The catalyst thus prepared was washed into a hydrogenation vessel with additional Ac_2O. Nitrile ester **10** (60.1 mg) was taken up in Ac_2O and added to the catalyst, and the reaction mixture was hydrogenated on a Parr apparatus at an initial pressure of 40 psi overnight. The reaction mixture was filtered, and the catalyst was washed with acetone. The combined filtrate was evaporated. Chromatography on a prep plate in 50% EtOAc/hexanes provided 58.6 mg (84%) of **11**: ^1H NMR (250 MHz) δ 1.93 (s, 3 H, Ac), 2.20 (s, 3 H, $ArCH_3$), 3.66 (s, 3 H, $ArOCH_3$), 3.73 (s, 3 H, CO_2CH_3), 3.80 (s, 2 H, CH_2CO_2), 3.84 (s, 3 H, $ArOCH_3$), 4.41 (d, 2 H, CH_2N); IR 3300 (NH), 1739 (ester), 1649 cm^{-1} (amide); MS m/z 325 (M^+, 17), 251 (100); HRMS, exact mass obsd: 325.1493 ($C_{16}H_{23}NO_6$ requires 325.1525).

6-Methyl-5,7,8-trimethoxy-1,4-dihydroisoquinolin-3-(2*H*)-one (12). Amido ester **11** (22.9 mg) was stirred at room temperature in 4 mL of MeOH containing 1 pellet of KOH for 3 days. The solution was partitioned between EtOAc and H_2O.

The organic layer was washed with brine, dried ($MgSO_4$), and evaporated to give 15.7 mg (89%) of pure **12**: ^1H NMR (250 MHz) δ 2.20 (s, 3 H, CH_3), 3.55 (s, 2 H, CH_2CO), 3.70 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 4.51 (s, 2 H, CH_2N); IR 1682 cm^{-1} (amide); m/z 251 (M^+, 100); HRMS, exact mass obsd: 251.142 ($C_{13}H_{17}NO_4$ requires 251.1157).

Methyl 2-((Formylamino)methyl)-5-methyl-3,4,6-trimethoxyphenylacetate (13). A large portion of RaNi in H_2O (approximately 1 mL of settled solid) was thoroughly washed with absolute EtOH, Ac_2O, and then distilled acetic formic anhydride. The catalyst was washed into a hydrogenation vessel with additional mixed anhydride. Nitrile ester **10** (18.6 mg, 0.067 mmol) was taken up in mixed anhydride and added to the catalyst. The reaction mixture was hydrogenated in a Parr apparatus at an initial pressure of 40 psi for 5 days. The mixture was filtered, and the catalyst was washed with acetone. The combined filtrate was concentrated, and the residue was chromatographed on a prep plate in 50% EtOAc/hexanes to give 17 mg (82%) of crystalline **13**: mp 117.5–118.5 °C; ^1H NMR (250 MHz) δ 2.20 (s, 3 H, CH_3), 3.66 (s, 3 H, OCH_3), 3.73 (s, 3 H, CO_2CH_3), 3.82 (s, 5 H, OCH_3 and CH_2CO_2), 3.87 (s, 3 H, OCH_3), 4.46 (d, 2 H, CH_2N), 8.12 (s, 1 H, CHO); IR 3300 (NH), 1732 (ester), 1645 cm^{-1} (amide); MS m/z 311 (M^+, 54), 251 (100); HRMS, exact mass obsd: 311.1348 ($C_{15}H_{21}NO_6$ requires 311.1369). Anal. Calcd: C, 57.87; H, 6.80; N, 4.50. Found: C, 57.80; H, 6.57; N, 4.38.

***N*,6-Dimethyl-5,7,8-trimethoxy-1,4-dihydroisoquinolin-3-(2*H*)-one (14).** *N*-Formyl compound **13** (69.4 mg) was dissolved in 25 mL of dry THF and cooled in an ice/H_2O bath under N_2. BH_3 in THF (1 M, 1.90 mL) was added to the cold solution. The ice bath was removed, and the reaction mixture was heated at reflux for 1 h and then stirred overnight. After quenching with 1 M HCl, the THF was removed by evaporation and the remaining aqueous solution was made strongly basic by addition of solid KOH. The product was extracted into EtOAc and dried ($MgSO_4$). The solution was evaporated and chromatographed on a prep plate to give 32.7 mg of **14** (55%): ^1H NMR (400 MHz) δ 2.20 (s, 3 H, CH_3), 3.12 (s, 3 H, NCH_3), 3.57 (s, 2 H, CH_2CO), 3.68 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.48 (s, 2 H, CH_2N); IR 1630 cm^{-1} (amide); MS m/z 265 (M^+, 100); HRMS, exact mass obsd: 265.1306 ($C_{14}H_{19}NO_4$ requires 265.1314).

Mimosamycin (1). Compound **14** (12.3 mg) was dissolved in 2 mL of dry dioxane containing 55 mg of AgO. The mixture was sonicated, and a solution of 10 drops of 6 M HNO_3 in 1 mL of dioxane was added dropwise over 45 min. During the addition, the reaction mixture was repeatedly frozen and thawed. The yellow solution was partitioned between H_2O and CH_2Cl_2 and extracted until all the yellow color was in the organic layer. The CH_2Cl_2 solution was dried ($MgSO_4$), filtered through neutral alumina, and concentrated to yield 9.3 mg of a yellow residue. Chromatography over alumina in 50% EtOAc/hexanes provided purified **1**: ^1H NMR (400 MHz) δ 2.07 (s, 3 H, CH_3), 3.67 (s, 3 H, NCH_3), 4.17 (s, 3 H, OCH_3), 7.11 (s, 1 H, CHCO), 8.26 (s, 1 H, CHN); MS m/z 233 (M^+, 60), 44 (100); HRMS exact mass obsd: 233.0677 ($C_{12}H_{11}NO_4$ requires 233.0688).

In another experiment, an 18% yield of mimosamycin was obtained from a silica prep plate eluted with 50% EtOAc/hexanes. The NMR spectrum of this material exhibited several peaks in addition to those reported for mimosamycin.

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Electron Spin Resonance Spectroscopic Study of Cyclic Thiocarboxamidyl Radicals, 3-Oxo-1,2-benzisothiazolin-2-yls: Complete Evaluation of ESR Parameters by Measuring ^{17}O and ^{33}S Hyperfine Splittings and Comparison of the ESR Parameters with Acyclic Analogues[1]

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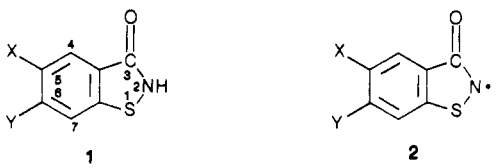
In two earlier papers,[2,3] we reported ESR studies of ArCONSAr′ radicals **3**. From the high $a_{^{33}S}$ value for **3** the unpaired electron was found to delocalize extensively onto the sulfur. On the other hand, the low $a_{^{17}O}$ value revealed that the unpaired electron delocalization onto the oxygen was not important. In the extension of these ESR studies, 3-oxo-1,2-benzisothiazolin-2-yls (**2**), cyclic analogues of **3**, have been studied by ESR spectroscopy. In this report the ESR spectral data for **2** are presented and these are compared with those for **3**. Comparison of the ESR parameters between cyclic and acyclic carboxamidyl (amidyl) radicals is the recent subject of interest.[4–6]

Results and Discussion

Radicals **2a–c** were generated by photolysis of 1,2-benzisothiazolin-3-ones **1a–c** in carefully degassed benzene or toluene solution containing di-*tert*-butyl peroxide. The ESR parameters for **2** are summarized in Table I.



1 **2**

a, X = Y = H; **b**, X = Cl, Y = H; **c**, X = H, Y = Cl

Upon UV irradiation at room temperature (18 °C), precursor **1a** in benzene gave a relatively intense ESR spectrum consisting of a 1:1:1 triplet of 1:2:1 triplets. When being recorded with a low modulation amplitude (<0.4 G), each line of the spectrum was incompletely further split into a 1:1 doublet with the interval of 0.4 G. Although the ESR signal intensity was increased with the time of UV irradiation, a prolonged irradiation yielded undesired impure radicals. On the other hand, interruption of the UV irradiation led to immediate disappearance of the ESR signal due to **2a** and the impure radicals. In the cases of **2b** and **2c** the ESR spectra were much weaker because of the poor solubilities of precursors **1b** and **1c** in benzene.

In previous ESR studies of radicals **3**,[2,3] it was shown that the phenylthio benzene ring protons of **3** gave splittings with the interval of 1.68–1.97 G. On the other hand, the benzoyl benzene ring protons of **3** afforded no splitting. On the basis of these ESR results the two protons giving the 1:2:1 triplet splitting in the spectrum of **2a** were assigned to those on C-5 and C-7. This assignment was

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