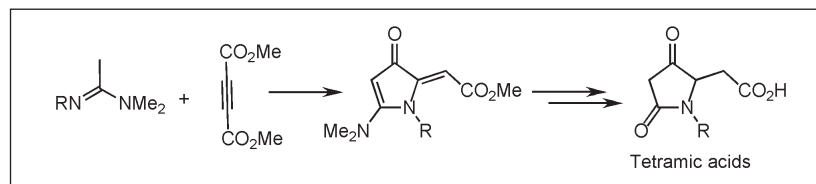


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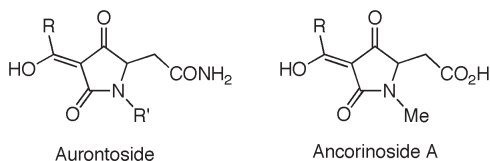
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Amidines undergo cyclocondensations with dimethyl acetylenedicarboxylate (DMAD) to give highly functionalized 5-dialkylamino-4-pyrrolin-3-ones. The products are crystalline, highly colored compounds that are uniquely functionalized and represent advanced intermediates in the construction of several other heterocycles, in particular the biologically active tetramic acids. The synthetic transformations of these compounds to tetramic acids are also described.

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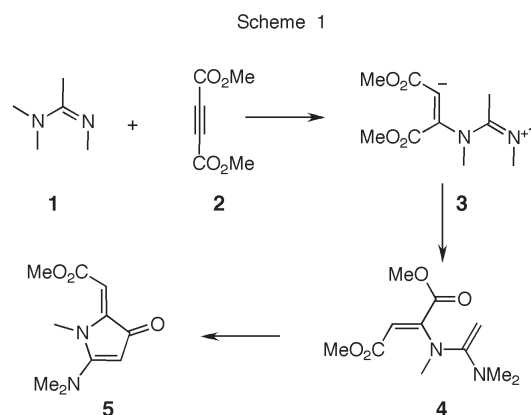
Dimethyl acetylenedicarboxylate (DMAD) combines with electron-rich alkenes to give 2+2 cycloadducts that may expand to seven membered rings; enamines, guanidines and related compounds have been reported to undergo cycloadditions with DMAD to give nitrogen heterocycles [1-8]. Diaminomethylenehydrazones have been reported to give imidazolinone and 1,6-dihydropyrimidine derivatives [9]. We report here the cyclocondensation of amidines [10] with DMAD resulting in highly functionalized five-membered nitrogen heterocycles that show excellent promise as versatile intermediates in the synthesis of tetramic acids [11]. These latter compounds, *e.g.* aurentoside and ancorinoside are of considerable interest due to their potent antibiotic, antiviral and antiulcerative properties, as well as their cytotoxicity and mycotoxicity, and inhibition of tumors.



The DMAD-amidine cyclocondensations proceed readily at low temperatures in  $\text{CH}_2\text{Cl}_2$  solution to give 5-dialkyl(or alkylaryl)amino-4-pyrrolin-3-ones as highly colored crystalline compounds in moderate to good yields (Table I) [12].

The mechanism starts with initial conjugate attack at the propargyl system, followed by proton transfer to give **4**; the subsequent intramolecular condensation delivers a five-membered ring (**5**) rather than a six-membered heterocycle (Scheme 1). The *E* or *Z* isomers were easily identi-

fied by the characteristic singlets for the olefinic hydrogen atoms on the exocyclic double bond at either *ca.* 6 ppm (*Z*), or 5 ppm (*E*), respectively, in the  $^1\text{H}$  NMR spectrum.



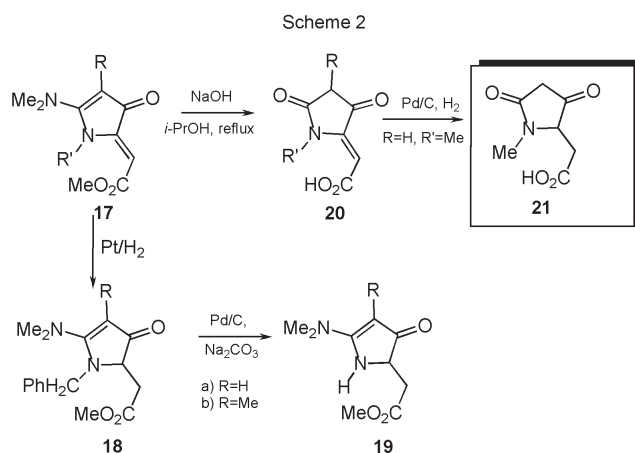
The resulting 5-dialkylamino-4-pyrrolin-3-ones were purified by chromatography on silica gel (5%  $\text{MeOH}/\text{CH}_2\text{Cl}_2$ ) followed by recrystallization. In order to gain access to the tetramic acid skeleton, the vinylogous amide moiety was hydrolytically removed by heating with  $\text{NaOH}$  in *i*-propyl alcohol. Attempts to hydrolyze the enaminoketone functionality under acidic conditions, even through initial *N*-alkylation by treatment with  $\text{MeI}$ , were unsuccessful [13]. Under basic conditions the ester group was saponified as well. The unsubstituted parent system **20** did not seem to enolize in chloroform at room temperature. Catalytic hydrogenation of **20a** on  $\text{Pd/C}$  gave the tetramic acid **21** in quantitative yield. Since various tetramic acids are not alkylated or arylated at the ring nitrogen, we took advantage of the reductive removal of the benzyl group in

Table 1  
Amidine-DMAD Cyclocondensation Products

| Entry | Amidine | Product(s) | Yield% [a] |
|-------|---------|------------|------------|
| 1     |         |            | 77         |
| 2     |         |            | 53         |
| 3     |         |            | 75         |
| 4     |         |            | 73         |
| 5     |         |            | 68         |
| 6     |         |            | 66         |

[a] Isolated yields after chromatography and/or recrystallization.

**18a** and **18b** (R=H, or Me; R'=Bn) to give **19a** and **19b**, respectively (Scheme 2).

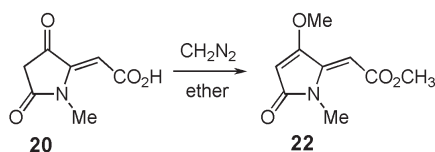


Catalytic hydrogenation of **19** using Adam's catalyst in methanol at atmospheric pressure and room temperature resulted in the selective hydrogenation of the exocyclic double bond (the vinylogous amide double bond was not touched under a variety of conditions and using different catalysts). Under the conditions the N-benzyl group was not reduced. On Pd/C, the reduction yielded an 8:1 mixture of **18** and **19**. Complete reduction of both the exocyclic double bond and the N-benzyl group was achieved upon prolonged hydrogenation (4 days at r.t.) with Pd/C in MeOH in the presence of Na<sub>2</sub>CO<sub>3</sub>.

Treatment of **20** with excess CH<sub>2</sub>N<sub>2</sub> in ether resulted in the esterification as well trapping of the 1,3-dione moiety as its enol ether, to give **22** in excellent yield.

The tetramic acids so obtained as well as the N-debenzylated vinylogous amides also represent advanced precursors of pyrrolizidine and indolizidine ring systems

Scheme 3



that should be accessible by way of  $N\text{-CH}_2\text{CO}_3$  and  $N\text{-CH}_2\text{CH}_2\text{CO}_2\text{Me}$  derivatives of **21** and subsequent Dieckmann condensations, respectively. These aspects of the 4-pyrrolin-3-one methodology, as well as the total syntheses of several naturally occurring 3-acylated tetramic acid antibiotics, in particular streptolydigin, erythroskyrine, ancorinoside, and auronthoside are underway.

#### EXPERIMENTAL

Melting points were determined in open class capillary tubes and are uncorrected. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a General Electric QE-Plus 300 MHz and Bruker Avance DRX 300 MHz spectrometers, using  $\text{CDCl}_3$  as solvent and TMS as internal standard, unless specified otherwise. IR spectra were obtained on a Nicolet Avanta 370 DTGS FT-IR spectrometer. Column chromatographic separations were carried out with Davison 6-200 Mesh silica gel. For preparative TLC, Merck silica gel (grade 60  $\text{PF}_{254}$ ) was used. All reactions were conducted under an atmosphere of dry nitrogen or argon. Non-deuterated solvents were dried and distilled prior to use. Amidines **1**, **6** and **10** were prepared according to the procedure reported by Haug and Kantlehner [12a], whereas amidines **8**, **13** and **15** were synthesized using Weintraub et al.'s method [12b].

General Procedure for the Cyclocondensation of Amidines with DMAD.

To a solution of  $N,N$ -dimethyl- $N'$ -methylacetamidine (1 g, 10 mmol) in 10 mL of dry  $\text{CH}_2\text{Cl}_2$  that was cooled to  $-20^\circ\text{C}$ , a solution of DMAD (1.42 g, 10 mmol) in 5 mL of dry  $\text{CH}_2\text{Cl}_2$  was added dropwise with stirring. The mixture was allowed to warm up and was stirred for two hours after having removed the cold bath. The solvent was then removed *in vacuo* (rotovapped), and the residue purified by preparative TLC on silica gel, eluting with 5%  $\text{MeOH}/\text{CH}_2\text{Cl}_2$ . It was then crystallized from  $\text{CH}_2\text{Cl}_2/\text{ether}$ .

(Z)-Methyl 2-(5-(dimethylamino)-1-methyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**5**).

Bright yellow crystals, mp:  $136\text{--}7^\circ\text{C}$ , yield: 77%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  5.96 (1H, s), 4.84 (1H, s), 3.76 (3H, s,  $\text{OCH}_3$ ), 3.19 (3H, s,  $\text{N-CH}_3$ ), 3.09 (6H, s,  $\text{N-CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  182.8, 177.5, 166.2, 153.2, 97.5, 86.4, 51.8, 40.9, 40.2 ppm; IR (KBr):  $\nu$  3128, 3108, 2950, 2926, 2910, 2891, 2847, 1716, 1705, 1667, 1616, 1591, 1463, 1429, 1416, 1396, 1354, 1338, 1276, 1230, 1205, 1172, 1159, 1063, 1036, 972, 901, 880  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3$ : C, 57.13; H, 6.71; N, 13.33. Found: C, 57.09; H, 6.70; N, 13.36.

(Z)-Methyl 2-(5-(dimethylamino)-1-benzyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**7**).

Dark yellow crystal, mp:  $130\text{--}131^\circ\text{C}$ , yield: 53%.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.28–6.95 (m, 5H, ArH), 5.98 (s, 1H), 4.99 (s, 2H,  $\text{CH}_2$ ), 4.94 (s, 1H), 3.75 (s, 3H,  $\text{OCH}_3$ ), 3.08 (s, 6H,  $\text{N-CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  183.2, 176.7, 166.3, 150.4, 135.5, 128.6, 127.7, 127.6, 99.6, 89.2, 53.0, 51.8, 40.9 ppm; IR (KBr):  $\nu$  3062, 3027, 2965, 2934, 2832, 2806, 1695, 1673, 1651, 1598, 1571, 1494, 1450, 1434, 1408, 1366, 1348, 1326, 1273, 1200, 1162, 1089, 1953, 1029, 1009, 936, 896  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$ : C, 67.12; H, 6.34; N, 9.78. Found: C, 67.09; H, 6.31; N, 9.80.

(Z)-Methyl 2-(5-(dimethylamino)-3-methyl-1-phenyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**9**).

Yellow crystals, mp:  $162\text{--}3^\circ\text{C}$ , yield: 75%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.28 (5H, m, ArH), 5.99 (1H, s), 3.42 (3H, s,  $\text{OCH}_3$ ), 2.90 (6H, s,  $\text{N-CH}_3$ ), 1.99 (3H, s,  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  184.8, 174.2, 166.3, 150.0, 143.5, 129.8, 129.4, 128.6, 100.9, 98.4, 51.9, 41.7, 9.3 ppm; IR (KBr):  $\nu$  3044, 3025, 3002, 2946, 2865, 2806, 1723, 1679, 1655, 1583, 1486, 1441, 1414, 1371, 1351, 1318, 1269, 1211, 1174, 1095, 1045, 992, 936, 917  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$ : C, 67.12; H, 6.34; N, 9.78. Found: C, 67.31; H, 6.32; N, 9.80.

(Z)-Methyl 2-(5-(dimethylamino)-1-benzyl-3-methyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**11**).

Light yellow crystals, mp:  $120\text{--}1^\circ\text{C}$ , yield: 55%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.2 (3H, m, ArH), 6.95 (2H, m, ArH), 6.0 (1H, s), 4.89 (2H, s), 3.76 (3H, s,  $\text{OCH}_3$ ), 3.08 (6H, s,  $\text{N-CH}_3$ ), 1.84 (3H, s,  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  185.3, 174.1, 167.0, 150.4, 136.4, 128.9, 128.4, 127.9, 99.4, 99.3, 53.2, 52.3, 41.4, 8.8 ppm; IR (KBr):  $\nu$  3036, 2948, 2923, 2899, 2864, 2803, 1720, 1697, 1666, 1573, 1488, 1452, 1413, 1357, 1319, 1263, 1241, 1215, 1202, 1176, 1162, 1123, 1100, 1080, 1055, 1017, 953, 914  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$ : C, 67.98; H, 6.71; N, 9.33. Found: C, 67.94; H, 6.68; N, 9.35.

(E)-Methyl 2-(5-(dimethylamino)-1-benzyl-3-methyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**12**).

Brown crystals, mp:  $93\text{--}4^\circ\text{C}$ , yield: 18%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.29–7.19 (5H, m, ArH), 5.20 (1H, s), 4.48 (2H, s), 3.71 (3H, s,  $\text{OCH}_3$ ), 2.95 (6H, s,  $\text{N-CH}_3$ ), 1.80 (3H, s,  $\text{CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  181.7, 171.05, 167.2, 147.4, 136.5, 129.0, 127.5, 125.7, 101.5, 97.1, 52.2, 51.4, 41.4, 8.0 ppm; IR (KBr):  $\nu$  3060, 3032, 2940, 2886, 2802, 1694, 1671, 1579, 1484, 1442, 1410, 1351, 1320, 1246, 1215, 1201, 1163, 1100, 1073, 1009, 957, 883  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_3$ : C, 67.98; H, 6.71; N, 9.33. Found: C, 67.96; H, 6.69; N, 9.37.

(E)-Methyl 2-(5-Dimethylamino-1-benzyl-3-phenyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**14**).

Dark yellow crystals, mp:  $138\text{--}140^\circ\text{C}$ , yield: 68%;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta$  7.45–7.20 (10H, m, ArH), 5.39 (1H, s), 4.67 (2H, s), 3.78 (3H, s,  $\text{OCH}_3$ ), 2.79 (6H, s,  $\text{N-CH}_3$ ) ppm;  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta$  180.9, 170.4, 167.6, 147.1, 136.9, 132.5, 130.2, 129.7, 128.4, 128.2, 126.6, 126.3, 103.6, 103.0, 52.9, 52.0, 42.7 ppm. IR (KBr):  $\nu$  3432, 3054, 3020, 2945, 2917, 2796, 1727, 1667, 1641, 1576, 1560, 1507, 1456, 1404, 1359, 1327, 1277, 1249, 1209, 1167, 1082, 1026, 1003, 964  $\text{cm}^{-1}$ .

*Anal.* Calcd. for  $C_{22}H_{22}N_2O_3$ : C, 72.91; H, 6.12; N, 7.73. Found: C, 72.89; H, 6.14; N, 7.76.

(Z)-Methyl 2-(5-Dimethylamino-1-benzyl-3-phenyl-3-oxo-1H-pyrrol-2(3H)-ylidene)acetate (**16**).

Yellow crystals, m.p. 138–140 °C, yield: 66%;  $^1H$ -NMR ( $CDCl_3$ , 300 MHz):  $\delta$  7.30 (5H, m, ArH), 5.98 (1H, s), 5.04 (1H, s), 3.38 (3H, s,  $OCH_3$ ), 2.84 (6H, s, N- $CH_3$ ) ppm;

$^{13}C$ -NMR ( $CDCl_3$ , 75 MHz):  $\delta$  182.8, 174.8, 166.2, 150.1, 132.3, 130.0, 129.6, 129.0, 101.0, 88.4, 52.0, 41.6 ppm; IR (KBr):  $\nu$  2995, 2883, 2811, 1719, 1680, 1654, 1604, 1575, 1493, 1454, 1418, 1403, 1334, 1269, 1198, 1179, 1168, 1156, 1086, 1067, 1039, 1000, 940, 919  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{15}H_{16}N_2O_3$ : C, 66.16; H, 5.92; N, 10.29. Found: C, 66.13; H, 5.94; N, 10.26.

#### General Procedure for the Hydrogenation of **7** and **11**.

A solution of 0.47 mmol of **7** (or **11**) was dissolved in 10 mL of methanol, 20 mg of  $PtO_2$  was added and the mixture was hydrogenated at atmospheric pressure for 1.5 h (or until  $H_2$  uptake ceased). The catalyst was filtered off, the solvent removed *in vacuo*, leaving behind a quantitative yield of **18a** (or **18b**).

Methyl 2-(1-Benzyl-5-(dimethylamino-4-methyl-3-oxo-2,3-dihydro-1H-pyrrol-2-yl) acetate (**18a**).

Yellow oil:  $^1H$ -NMR ( $CDCl_3$ , 300 MHz):  $\delta$  7.35–7.20 (5H, m, ArH), 4.75 (1H, s), 4.50 (1H, d,  $J=16$  Hz, B part of AB system), 4.40 (1H, d,  $J=16$  Hz, A part of AB system), 3.89 (1H, dd,  $J=8.8$  and 3.3 Hz, X part of ABX system), 3.58 (3H, s,  $OCH_3$ ), 3.0 (6H, s, N- $CH_3$ ), 2.90 (1H, dd,  $J=16.6$  and 3.3 Hz, A part of ABX system), 2.48 (1H, dd,  $J=16.6$  and 8.8 Hz, B part of ABX system) ppm;  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  195.8, 179.6, 172.7, 136.9, 129.2, 128.3, 128.1, 89.9, 66.5, 54.4, 52.1, 41.2, 38.0 ppm; IR ( $CDCl_3$ ):  $\nu$  3062, 3026, 2947, 2925, 2909, 2808, 1768, 1733, 1654, 1572, 1493, 1453, 1431, 1409, 1357, 1257, 1221, 1161, 1061, 1031, 990  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{16}H_{20}N_2O_3$ : C, 66.65; H, 6.99; N, 9.72. Found: C, 66.62; H, 7.02; N, 9.70.

Methyl 2-(1-Benzyl-5-(dimethylamino-3-oxo-2,3-dihydro-1H-pyrrol-2-yl)acetate (**18b**).

Yellow oil:  $^1H$ -NMR ( $CDCl_3$ , 300 MHz):  $\delta$  7.31–7.14 (5H, m, ArH), 4.40 (1H, d,  $J=15.7$  Hz, B part of AB system), 4.30 (1H, d,  $J=15.7$  Hz, A part of AB system), 3.85 (1H, dd,  $J=8.6$  and 3.6 Hz, X part of ABX system), 3.62 (3H, s,  $OCH_3$ ), 3.08 (6H, s, N- $CH_3$ ), 2.85 (1H, dd,  $J=16.5$  and 3.6 Hz, A part of ABX system), 2.40 (1H, dd,  $J=16.5$  and 8.6 Hz, B part of ABX system), 1.79 (3H, s,  $CH_3$ ) ppm;  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  196.7, 177.0, 172.8, 136.9, 129.2, 128.3, 128.2, 98.5, 64.5, 54.0, 52.2, 41.3, 38.2, 9.1 ppm; IR ( $CDCl_3$ ):  $\nu$  2949, 2923, 1731, 1646, 1555, 1492, 1454, 1436, 1408, 1359, 1230, 1165  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{17}H_{22}N_2O_3$ : C, 67.53; H, 7.33; N, 9.26. Found: C, 67.50; H, 7.34; N, 9.22.

For the reduction of **18a** and **18b**, the same procedure was used except  $Pd/C$  was used in the presence of 200 mg of  $Na_2CO_3$  instead of  $PtO_2$ , and the hydrogenation was carried out for 4 days.

**19a**:  $^1H$ -NMR ( $CDCl_3$ , 300 MHz):  $\delta$  5.98 (1H, s, NH), 4.53 (1H, s), 4.05 (1H, dd,  $J=10.9$  and 2.5 Hz, X part of ABX system), 3.71 (3H, s,  $OCH_3$ ), 3.1 (1H, dd,  $J=17.1$  and 2.5 Hz, A part of ABX system), 3.0 (6H, s, N- $CH_3$ ), 2.32 (1H, dd,  $J=17.1$  and 10.9

Hz, B part of ABX system) ppm;  $^{13}C$ -NMR ( $CDCl_3$ , 75 MHz):  $\delta$  194.4, 713.5, 172.6, 81.9, 60.4, 52.3, 51.0, 37.6 ppm; IR ( $CDCl_3$ ):  $\nu$  2950, 2922, 2855, 1734, 1635, 1588, 1437, 1401, 1358, 1263, 1235, 1203, 1168, 1065, 986  $cm^{-1}$ .

*Anal.* Calcd. for  $C_9H_{14}N_2O_3$ : C, 54.53; H, 7.12; N, 14.13. Found: C, 54.54; H, 7.12; N, 14.10.

**19b**:  $^1H$ -NMR ( $CDCl_3$ , 300 MHz):  $\delta$  5.5 (1H, s, NH), 4.0 (1H, dd,  $J=11$  and 2.6 Hz, X part of ABX system), 3.71 (3H, s,  $OCH_3$ ), 3.1 (6H, s, N- $CH_3$ ), 3.0 (1H, dd,  $J=17.2$  and 2.6 Hz, A part of ABX system), 2.26 (1H, dd,  $J=17.2$  and 11.0 Hz, B part of ABX system), 1.87 (3H, s,  $CH_3$ ) ppm;  $^{13}C$ -NMR ( $CDCl_3$ , 75 MHz):  $\delta$  193.9, 173.2, 171.2, 90.1, 63.6, 51.9, 39.2, 37.2, 8.9 ppm; IR ( $CDCl_3$ ):  $\nu$  2989, 2953, 2927, 1802, 1730, 1681, 1596, 1440, 1407, 1374, 1198, 1165, 1073, 957, 919  $cm^{-1}$ .

*Anal.* Calcd. for  $C_{10}H_{16}N_2O_3$ : C, 56.59; H, 7.60; N, 13.20. Found: C, 56.55; H, 7.59; N, 13.16.

(Z)-2-(1-Methyl-3,5-dioxopyrrolidin-2-ylidene)acetic acid (**20**).

A solution of 0.4 g of **5** (0.19 mmol) and 1 mL of a 2 M aqueous solution of NaOH in 1 mL of isopropyl alcohol was heated at reflux for 24 h. The reaction mixture was cooled to room temperature, and partitioned between 2 M HCl (5 mL) and ethyl acetate (5 mL). The aqueous layer was extracted with 5 mL of EtOAc and the combined organic extracts washed with 7 mL of brine. After drying over  $MgSO_4$ , the solvent was evaporated *in vacuo* to give 300 mg (93%) of white crystals, mp 153–4 °C (from ethyl acetate-hexane).  $^1H$  NMR (acetone- $d_6$ , 300 MHz):  $\delta$  3.2 (s, 2H), 3.4 (s, 3H), 5.6 (s, 1H), 11.0 (br s, 1H) ppm;  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  206.8, 171.3, 166.2, 145.8, 93.9, 38.2, 29.9 ppm.

*Anal.* Calcd. for  $C_7H_7NO_4$ : C, 49.71; H, 4.17; N, 8.28. Found: C, 49.74; H, 4.16; N, 8.24.

2-(1-Methyl-3,5-dioxopyrrolidin-2-yl)acetic Acid (**21**).

To a 170 mg (10 mmol) solution of **20** in 50 mL of methanol, 100 mg of  $Pd/C$  was added, and the mixture was stirred under hydrogen atmosphere until hydrogen uptake stopped. The solution was filtered, the solvent was removed *in vacuo*, and the oily residue dried overnight to give 168 mg (98%) of **21**.  $^1H$  NMR ( $CD_3OD$ , 300 MHz):  $\delta$  4.1 (m, 1H); 3.05 (d, A part of an AB system,  $^2J=21.3$  Hz, 1H), 2.9 (d, B part, 1H); 2.8 (m, 2H), 2.7 (s, 3H);  $^{13}C$  NMR ( $CD_3OD$ , 75 MHz):  $\delta$  207.2, 171.4, 169.4, 64.2, 40.8, 33.65, 26.6 ppm.

*Anal.* Calcd. for  $C_7H_9NO_4$ : C, 49.12; H, 5.30; N, 8.18. Found: C, 49.10; H, 5.31; N, 8.17.

(Z)-Methyl 2-(3-methoxy-1-methyl-5-oxo-1H-pyrrol-2-(5H)-ylidene)acetate (**22**).

To a solution of 0.5 g (3 mmol) in 10 mL of methanol was added dropwise at 0 °C an ether solution of a 10 fold excess of diazomethane, previously generated from diazald with KOH [14], and the mixture was stirred at room temperature for 3 h. The solvent was removed *in vacuo* to give a yellow oil, which was purified by preparative TLC (2% MeOH/ $CH_2Cl_2$ ) to give 0.4 g (80% yield) of **22**.  $^1H$  NMR ( $CDCl_3$ , 300 MHz):  $\delta$  5.1 (s, 1H), 4.4 (dd,  $J=5.4$ , 5.7 Hz, 1H), 3.8 (s, 3H), 3.7 (s, 3H), 2.9 (s, 3H), 2.9 (dd, A part of an AB system,  $^3J=5.4$  Hz,  $^2J=21.3$  Hz, 1H), 2.8 (dd, B part,  $^3J=5.7$  Hz, 1H);  $^{13}C$  NMR ( $CDCl_3$ , 75 MHz):  $\delta$  171.1, 166.9, 165.2, 144.2, 94.4, 92.4, 58.5, 51.7, 29.1 ppm.

*Anal.* Calcd. for  $C_9H_{11}NO_4$ : C, 54.82; H, 5.62; N, 7.10. Found: C, 54.81; H, 5.60; N, 7.13.

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