

# Electronic Spectra of Cycl[3.3.2]azine and Related Compounds: Solvent Effect on Vibronic Couplings

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The CASSCF and MS-CASPT2 computational details for cycl[3.2.2]azine (**1a**)

The Atomic Natural Orbitals large sets (ANO-L: C,N,O[4s3p2d]/H[3s2p]) were employed augmented with an optimized set of 1s1p1d Rydberg-type functions placed on the center nitrogen atom. The five near-frontier occupied MOs (HOMO-4(2b<sub>1</sub>), HOMO-3(1a<sub>2</sub>), HOMO-2(3b<sub>1</sub>), HOMO-1(2a<sub>2</sub>), HOMO(4b<sub>1</sub>)) constitute the 10π-peripheral aromatic system. The energy gap between HOMO-4 and HOMO-5(1b<sub>1</sub>) are sufficiently large 0.17 a.u., which separate the π-MOs and the inner MOs. On the other hand, the LUMO has π-character (3a<sub>2</sub>), followed by σ-LUMO+1(19a<sub>1</sub>), π-LUMO+2(5b<sub>1</sub>), with σ- and π-orbitals being mixed in low-lying virtual MOs. The b<sub>1</sub>->b<sub>1</sub> and a<sub>2</sub>->a<sub>2</sub> excitation afford the A<sub>1</sub> excited state and b<sub>1</sub>->a<sub>2</sub> and a<sub>2</sub>->b<sub>1</sub> excitation give the B<sub>2</sub> excited state, respectively. Other forbidden modes such as <sup>1</sup>A<sub>1</sub>-><sup>1</sup>A<sub>2</sub> and <sup>1</sup>A<sub>1</sub>-><sup>1</sup>B<sub>1</sub> (Rydberg excitations σ->π\* or π->σ\*) are not expected to contribute to the UV-vis intense peaks. The 10 electrons and 12 orbitals CASSCF (0048:a<sub>1</sub>b<sub>2</sub>a<sub>2</sub>b<sub>1</sub>) includes LUMO+7(6b<sub>1</sub>), LUMO+8 (7b<sub>1</sub>: Rydberg orbital) in consideration of the valence-Rydberg mixing to obtain the balanced description of the electronic structure. The CASSCF calculations were carried first by the A<sub>1</sub> and B<sub>2</sub> state-specific four state averaged CASSCF with the core 1s orbitals of the carbon and nitrogen atoms being fixed. Subsequently, the state-specific single state (SS)-CASPT2 calculations were performed, followed by four state averaged MS-CASPT2 calculations through diagonalization of the interactions of SS-CASPT2 wavefunctions in order to remove the intruder states. A real level-shift parameter of 0.3 was employed. The transition dipole moments and oscillator strength were computed using PMCAS-CI module of the MOLCAS ver.7.4 software.

## Experimental

All melting points were determined in a capillary tube and are uncollected. Infrared (ir) spectra were recorded in potassium bromide pellets on JASCO S10 spectrometer and ultraviolet (uv) absorption spectra were determined in 95% ethanol on a Shimadzu UV3100pc spectrometer. Nuclear magnetic

resonance (nmr) spectra were obtained on Gemini 300NMR(300 MHz) and JEOL-GX-400 (400 MHz) spectrometers with tetramethylsilane as an internal standard. Mass (ms) spectra were recorded on JEOL MA-DX303 mass spectrometer. Elemental analyses were performed at the Microanalytical Laboratory of the Center for Instrumental Analysis in Nagasaki University.

#### 4-([2.2.3]cyclazin-1-yl)-2,5-dioxo-1H-pyrrole-3-carbonitrile (**3a**)

A solution of dimethyl[2.2.3]cyclazine-1,2-dicarboxylate (0.26g, 1.0 mmol) 10 ml of 2N sodium hydroxide solution in 15 ml of methanol was refluxed for 30 minutes. After removal of the methanol, the residual solid was dissolved in water. The aqueous solution was acidified with 10% hydrochloric acid. The solid that appeared was collected by filtration to give diacid. This acid must be used after drying by the vacuum pump. A solution of this crude diacid, copper chromite (0.93 g, 3.0 mmol), 0.32 g of copper (powder), and 3 ml of quinoline was refluxed for 1hour. After cooling, this mixture was chromatographed on silicagel column using hexane as an eluent to give 50 ml of hexane solution of cycl[3.2.2]azine. A mixture of this hexane solution and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (54mg, 0.30 mmol) was refluxed for 3hours. The color of this reaction mixture changed from yellow to orange, and then red. After 3 hours, the solvent of the mixture was removed by distillation using hot plates. A mixture of this residue and 6 ml of acetic acid was refluxed for 8 hours. After cooling, the precipitate that appeared was collected by filtration and recrystallized from a mixture of methanol and toluene to give the target compound (**2a**) (58 mg, 0.21 mmol) as dark red needles, mp 219-255°C, in 71% yield. Ir(KBr):  $\nu$  max 2205(CN), 1768(C=O), 1705(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 513(4.52), 342(3.72), 256(4.79); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  3.20(3H, s, NMe), 7.46(1H, d, J=4.9Hz, 4-H), 7.67(1H, d, J=4.9Hz, 3-H), 7.99(1H, dd, J=7.8, 1.6Hz, 5-H), 8.01(1H, dd, J=7.8, 7.4Hz, 6-H), 8.66(1H, s, 2-H), 8.98(1H, dd, J=7.4, 1.6 Hz, 7-H); MS(EI) m/z: 276(M<sup>++1</sup>, 20), 275(M<sup>+</sup>, 100), 191(17), 190(89), 97(10). Anal Calcd. for C<sub>16</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>(275.0694): Found: 275.0682.

4-(Benzo[a][2.2.3]cyclazin-2-yl)-1-methyl-2,5-dioxo-1H-pyrrole-3-carbonitrile (**3b**)

A mixture of benzo[a]cycl[3.2.2]azine (7 mg, 0.04 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (7 mg, 0.04 mmol) was refluxed in acetic acid (4 ml) for 9 hours. The color of the reaction mixture changed from yellow to red, and then dark purple red. After cooling, the precipitate that appeared was collected by filtration to give the target compound in dark brown needles (10mg, 0.03 mmol), mp310-315 °C, in 82% yield. Ir(KBr):  $\nu$  max 2230(CN), 1765(C=O), 1718(C=O)  $\text{cm}^{-1}$ ; UV(Ethanol)  $\lambda$  max nm(insufficient solubility): 541, 400;  $^1\text{H-nmr}(\text{CDCl}_3)$ :  $\delta$  3.21(3H, s, NMe), 7.67(1H, m, 7-H), 7.79(1H, m, 8-H), 8.06(1H, dd, J=8.5, 7.3Hz, 4-H), 8.12(1H, d, J=7.3 Hz, 5-H), 8.24(1H, m, 9-H), 8.34(1H, m, 6-H), 8.68(1H, s, 1-H), 9.11(1H, d, J=8.5 Hz, 3-H); MS(EI) m/z: 326( $\text{M}^+ + 1$ , 24), 325( $\text{M}^+$ , 100), 240(24), 120(12). Anal Calcd. for  $\text{C}_{20}\text{H}_{11}\text{N}_3\text{O}_2$ (325.0851): Found: 325.0858.

4-(Benzo[g][2.2.3]cyclazin-2-yl)-1-methyl-2,5-dioxo-1H-pyrrole-3-carbonitrile (**3c**)

A mixture of benzo[g]cycl[3.2.2]azine (57 mg, 0.30 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (54 mg, 0.30 mmol) was refluxed in acetic acid (6 ml) for 5 hours. The color of the reaction mixture changed from yellow to red, and then dark purple red. After cooling, the precipitate that appeared was collected by filtration to give the target compound in dark brown needles, mp237-245 °C, in 78 % yield. Ir(KBr):  $\nu$  max 2200(CN), 1763(C=O), 1700(C=O)  $\text{cm}^{-1}$ ; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 562(4.33), 399(3.56);  $^1\text{H-nmr}(\text{CDCl}_3)$ :  $\delta$  3.20(3H, s, NMe), 7.64(1H, d, J=8.24 Hz, 2-H), 7.78(1H, dd, J=7.0, 8.24 Hz, 7-H), 7.81(1H, d, J=4.6 Hz, 1-H), 7.84(1H, dd, J=7.0, 8.0 Hz, 8-H), 8.34(1H, d, J=8.2 Hz, 6-H), 8.53(1H, d, J=8.0 Hz, 9-H), 8.89(1H, s, 3-H), 9.30(1H, s, 5-H); MS(EI)

m/z: 326(M<sup>+</sup>+1, 8), 325(M<sup>+</sup>, 44), 240(24), 79(100), 52(63), 43(58). Anal Calcd. for C<sub>20</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub>(325.0851): Found: 325.0855.

Methyl 4-(4-cyano-1-methyl-2,5-dioxo-1H-pyrrol-3yl)-6-dimethylamino[2.2.3]cyclazine-1-carboxylate (**4a**)

A mixture of 6-dimethylamino[2.2.3]cyclazine-1-carboxylate (0.48 g, 2.0 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (0.36 g, 2.0 mmol) was refluxed in acetic acid (8 ml) for 1 hour. The color of the reaction mixture changed readily from yellow to dark red. After cooling, the precipitate that appeared was collected by filtration to give the target compound in black needles, mp 315-318 °C, in 42 % yield. Ir(KBr):  $\nu$  max 2200(CN), 1768(C=O), 1702(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 614(4.33), 427(3.81); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  3.23(3H, s, NMe), 3.62(6H, s, NMe), 4.12(3H, s, OMe), 8.43(1H, s, 3-H), 8.76(1H, brs, 5-H), 8.94(1H, s, 2-H), 9.27(1H, brs, 7-H); MS(EI) m/z: 377(M<sup>+</sup>+1, 23), 376(M<sup>+</sup>, 100), 345(11), 129(10), 79(15), 52(10), 44(14). Anal Calcd. for C<sub>20</sub>H<sub>16</sub>N<sub>4</sub>O<sub>4</sub>(376.374): Found: 376.392.

Methyl 4-(4-cyano-1-methyl-2,5-dioxo-1H-pyrrol-3yl)-6-dimethylamino-3-methylthio[2.2.3]cyclazine-1-carboxylate (**4b**)

A mixture of methylthio-6-dimethylamino[2.2.3]cyclazine-1-carboxylate (0.14 g, 0.50 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (0.09 g, 0.5 mmol) was refluxed in acetic acid (7 ml) for 6 hours. The color of the reaction mixture changed readily from yellow to dark green. After cooling, the precipitate that appeared was collected by filtration to give the target compound in black needles, mp 243-245 °C, in 86 % yield. Ir(KBr):  $\nu$  max 2201(CN), 1761(C=O), 1701(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 590(4.18), 439(3.95), 346(4.12), 289(4.53); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  2.96(3H, s, SMe), 3.20(6H, s, NMe), 3.25(6H, s, NMe<sub>2</sub>), 4.00(3H, s, OMe), 7.31(1H, d, J=1.9 Hz, 5-H),

7.45(1H, d, J=1.9 Hz, 7-H), 7.97(1H, s, 2-H); MS(EI) m/z: 423(M<sup>+</sup>+1, 26), 422(M<sup>+</sup>, 16), 421(100), 322(21), 304(10), 69(13), 57(14), 55(13), 44(26), 43(15), 41(16). Anal Calcd. for C<sub>21</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S(422.462): Found: 422.481.

Methyl 4-(4-cyano-1-methyl-2,5-dioxo-1H-pyrrol-3yl)-6-dimethylamino[2.2.3]cyclazine-1,2-dicarboxylate (**4c**)

A mixture of 6-dimethylamino[2.2.3]cyclazine-1,2-dicarboxylate (0.15 g, 0.50 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (0.09 g, 0.5 mmol) was refluxed in acetic acid (6 ml) for 6 hours. The color of the reaction mixture changed readily from yellow to dark red. After cooling, the precipitate that appeared was collected by filtration to give the target compound in black needles, mp 320-324°C, in 54 % yield. Ir(KBr):  $\nu$  max 2202(CN), 1740(C=O), 1708(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 624(4.37), 428(3.91); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  3.18(3H, s, NMe), 3.30(6H, s, NMe<sub>2</sub>), 4.02(3H, s, OMe), 4.07(3H, s, OMe), 7.56(1H, s, 3-H), 8.23(1H, s, 5-H), 8.61(1H, s, 7-H); MS(EI) m/z: 435(M<sup>+</sup>+1, 28), 434(M<sup>+</sup>, 100), 317(13), 44(34). Anal Calcd. for C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>6</sub>S(434.411): Found: 434.429.

Methyl 4-(4-cyano-1-methyl-2,5-dioxo-1H-pyrrol-3yl)-6-dimethylamino[2.2.3]cyclazine-1,2-dicarboxylate (**4c**)

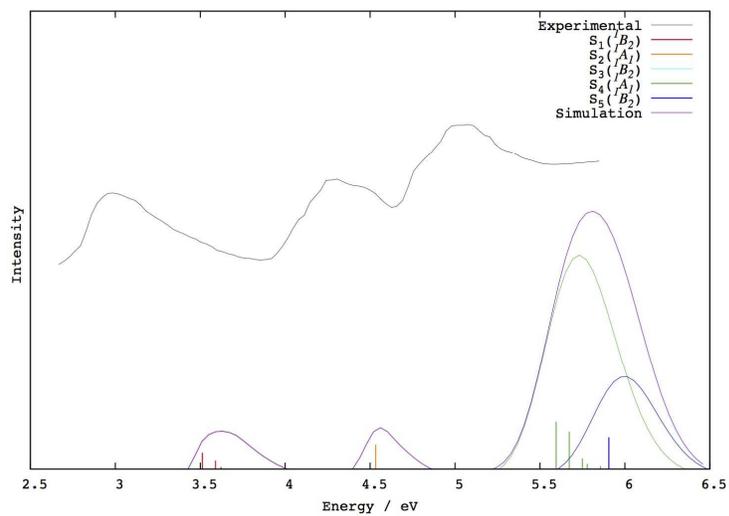
A mixture of 6-dimethylamino[2.2.3]cyclazine-1,2-dicarboxylate (0.15 g, 0.50 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (0.09 g, 0.5 mmol) was refluxed in acetic acid (6 ml) for 6 hours. The color of the reaction mixture changed readily from yellow to dark red. After cooling, the precipitate that appeared was collected by filtration to give the target compound in black needles, mp 320-324°C, in 54 % yield. Ir(KBr):  $\nu$  max 2202(CN), 1740(C=O), 1708(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 624(4.37), 428(3.91); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  3.18(3H, s, NMe), 3.30(6H, s, NMe<sub>2</sub>),

4.02(3H, s, OMe), 4.07(3H, s, OMe), 7.56(1H, s, 3-H), 8.23(1H, s, 5-H), 8.61(1H, s, 7-H); MS(EI) m/z: 435(M<sup>+</sup>+1, 28), 434(M<sup>+</sup>, 100), 317(13), 44(34). Anal Calcd. for C<sub>22</sub>H<sub>18</sub>N<sub>4</sub>O<sub>6</sub>S(434.411): Found: 434.429.

Methyl 4-(4-cyano-1-methyl-2,5-dioxo-1H-pyrrol-3yl)-6-dimethylamino-3-methylthio[2.2.3]cyclazine-1,2-dicarboxylate (**4d**)

A mixture of methylthio-6-dimethylamino[2.2.3]cyclazine-1,2-dicarboxylate (0.10 g, 0.30 mmol) and 1-methyl-4-methylthio-2,5-dioxo-1H-pyrrole-3-carbonitrile (0.08 g, 0.42 mmol) was refluxed in acetic acid (5 ml) for 15 hours. The color of the reaction mixture changed readily from yellow to dark yellow. After evaporation of the solvent, the residue was chromatographed on silica gel column using a mixture of toluene and ethyl acetate as an eluent to give the target compound in black crystals in 29 % yield. An analytical sample was recrystallized to give black needles, mp 234-235°C. Ir(KBr):  $\nu$  max 2205(CN), 1738(C=O), 1708(C=O) cm<sup>-1</sup>; UV(Ethanol)  $\lambda$  max nm(log  $\epsilon$ ): 592(4.19), 444(3.88), 343(4.00), 292(4.47); <sup>1</sup>H-nmr(CDCl<sub>3</sub>):  $\delta$  2.67(3H, s, SMe), 3.22(3H, s, NMe), 3.25(6H, s, NMe<sub>2</sub>), 3.99(3H, s, OMe), 4.09(3H, s, OMe), 7.38(1H, d, J=2.0 Hz, 5-H), 7.55(1H, d, J=2.0 Hz, 7-H); MS(EI) m/z: 480(M<sup>+</sup>, 18), 347(21), 346(100), 315(21), 83(12), 79(14), 69(14), 57(17), 55(18), 44(20), 43(22). Anal Calcd. for C<sub>23</sub>H<sub>20</sub>N<sub>4</sub>O<sub>6</sub>S(480.499): Found: 434.510.

**(a)**



**(b)**

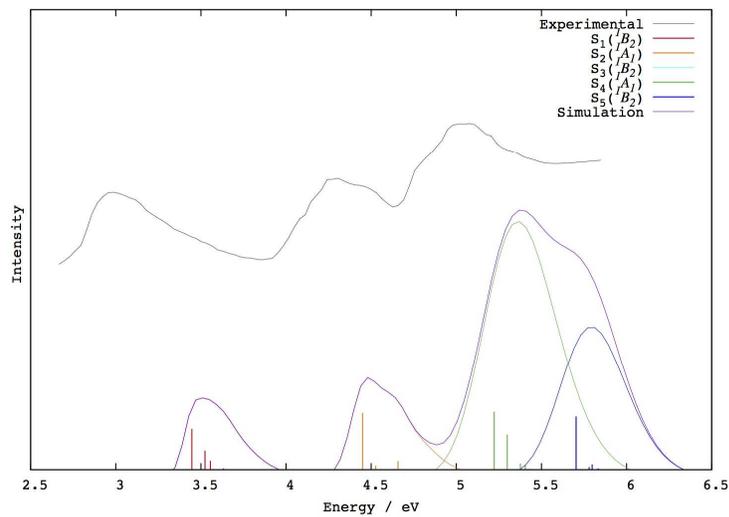


Figure S1: Absorption spectra of **1a** (a) in vacuo and (b) in ethanol using the PBE0 functional.