PHOTOCHEMICAL ARYLAMINOMETHYLATION OF THE PYRAZINE DERIVATIVES HAVING ELECTRONEGATIVE SUBSTITUENTS

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Abstract - 5,6-Dichloropyrazine-2,3-dicarbonitrile (**1**), 2,3-dichloroquinoxaline (**2**), and pyrazine-2,3-dicarbonitrile (**3**) were photolyzed in acetonitrile in the presence of *N*-acyl-*N*-trimethylsilylmethylanilines (**4** or **5**). The photolysis is proposed to give an *N*-acylanilinomethyl radical by an electron transfer followed by the rupture of a trimethylsilyl cation. The anilinomethyl radical thus formed couples with the radical anion from the diazines to give the substitution products (**6~9** and **11~14**) of **1~3**.

Tetrahydrofolic acid is an important coenzyme which mediates C_1-unit *transfer - formyl, hydroxymethyl,* or methyl group - in biological systems.[1] Transfer of formyl group from ^{10}N- or ^{5}N-formyltetrahydrofolic acid is associated with the biosynthesis of purine bases[2] and formylmethionyl t-RNA.[3] Folic acid, an oxidized form of the bioactive coenzyme, has *p*-aminocarbonylanilinomethyl group at the 6-position of pteridine ring

(Figure 1).

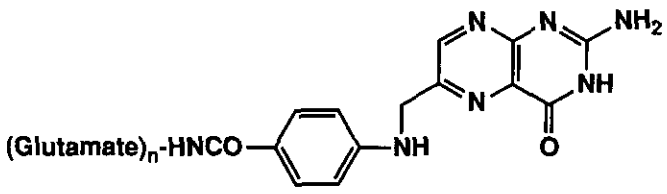
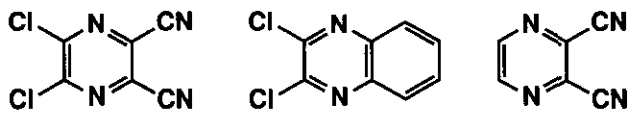


Figure 1. Folic Acid

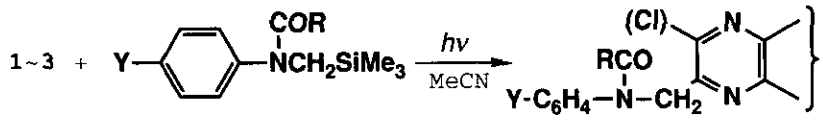
We have already tried to introduce this *N*-acylanilinomethyl group on pyrazine rings by radical substitution.[4] In these studies Minisci oxidation ($S_2O_8^{2-}/Ag^+$)[5] was applied to generate arylaminomethyl radical from 2-arylaminoacetic acid. In the present study we tried the introduction of *N*-formylanilinomethyl group or its congener *N*-acetylanilinomethyl group on pyrazine ring by the photo-induced single electron transfer reaction between *N*-acyl-*N*-trimethylsilylmethylaniline and pyrazine derivatives.

It has been established that photo-excitation of enone in the presence of trimethylsilylmethylamine derivatives causes the single electron transfer between the enone and amine to afford an ion radical pair.[6] The radical cation of trimethylsilylamine derivative, thus formed, looses easily trimethylsilyl cation to leave an aminomethyl radical. The photo-excited pyrazine having electronegative substituents is expected as an electron acceptor from trimethylsilylmethylanilines.

In this guide line we photolyzed 5,6-dichloropyrazine-2,3-dicarbonitrile (**1**), 2,3-dichloroquinoxaline (**2**), and pyrazine-2,3-dicarbonitrile (**3**) in the presence of *N*-acyl-*N*-trimethylsilylmethylaniline (**4**) or *N*-acyl-*N*-trimethylsilylmethyl-4-methoxycarbonylaniline (**5**) (Eq. 1).



1 2 3



(Eq.1)

4a: Y=H, R=H
4b: Y=H, R=Me
5a: Y=COOMe, R=H
5b: Y=COOMe, R=Me

6~9, 11~14

The equimolar mixture of a pyrazine derivative (**1**, **2**, or **3**) and *N*-acyl-*N*-trimethylsilylmethylaniline (**4**) or *N*-acyl-*N*-trimethylsilylmethyl-4-methoxycarbonylaniline (**5**) (**1**, **2** 0.02 mol/l; **3** 0.1 mol/l) in acetonitrile was irradiated through pyrex glass and the results are shown in Table 1. The irradiation was stopped when the reaction mixture became non-transparent and no further progress of the reaction was expected. Substantial amount of the starting pyrazines were recovered after work-up (**1**, 7~27%; **2**, 48~58%; **3**, 49~71%), and the product yields in the Table 1 were based on the amount of the starting materials used. Structures of the products were determined straight forward by the ^{1}H- and ^{13}C-nmr spectra, elemental analyses (crystalline product), and high resolution mass spectra (viscous oily product). In all the reactions one of the substituents, Cl or CN, was replaced by *N*-acylanilinomethyl or *N*-acyl-4-methoxycarbonyl-anilinomethyl group.

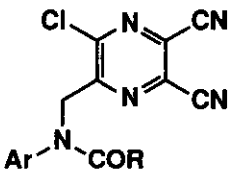
The reaction of 5,6-dichloropyrazine-2,3-dicabonitrile (**1**) with an aniline derivative (**4a**) and (**4b**) gave 6-chloro-5-(*N*-formylanilino)methylpyrazine-2,3-dicarbonitrile (**6a**) and 6-chloro-5-(*N*-acetylanilino)methylpyrazine-2,3-dicarbonitrile (**6b**), respectively. Similarly the reaction of 2,3-dichloroquinoxaline (**2**) with **4a** and **4b** gave 3-chloro-2-(*N*-

formylanilino)methylquinoxaline (**7a**) and 3-chloro-2-(*N*-acetylanilino)methylquinoxaline (**7b**), respectively. The photoreaction of pyrazine-2,3-dicarbonitrile (**3**) in the same manner gave 5-(*N*-formylanilino)methylpyrazine-2,3-dicarbonitrile (**8a**) and 5-(*N*-acetylanilino)methylpyrazine-2,3-dicarbonitrile (**8b**) as well as the cyano-substituted products (**9a**) and (**9b**) in poor yields. In the photoreactions between chlorinated pyrazine derivatives (**1** and **2**) and aniline derivatives (**4**), the latters were partly lost by the second electron transfer to give *N*-acylanilines (**10**) in 10~50% yield. The yields of products (**6a**) and (**6b**) were somewhat improved by using an excess amount of aniline derivatives (**4**) (Table 1).

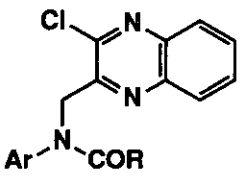
Similarly the reaction of **1**, **2**, and **3** with *N*-acyl-*N*-trimethylsilylmethyl-4-methoxycarbonylaniline (**5**) gave products (**11~14**) as shown in the Table 1. In these reactions 4-methoxycarbonylaniline derivatives (**5**) were also lost in some extent to give *N*-acyl-4-methoxycabonylanilines (**15**). Excess amount of the aniline derivatives (**5**) to compensate this loss, however, resulted in the deterioration of the reaction mixture and no improvement was seen in the yields of the substitution products (**11~14**).

Extinction coefficients of the pyrazine derivatives are much larger than those of the *N*-acyl-*N*-trimethylsilylmethylaniline in the present irradiation range(>300 nm). The reaction, therefore, can be understood by the photo-electron transfer mechanism (Scheme I) proposed by Mariano *et al.* for the photoreaction between enones and trimethylsilylmethylamines.[6] Efficiency of this reaction must be controlled by the rate of electron transfer to form **A**.

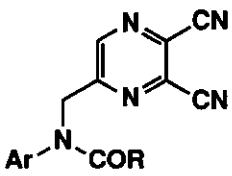
The absorption of *N*-acyl-*N*-trimethylsilylmethyl-4-methoxycarbonylaniline is comparable to those of the pyrazine derivatives and we can not define which molecule is excited for the reaction. Nonetheless, the proposed mechanism is reasonable even the excited anilines are responsible for the reaction.



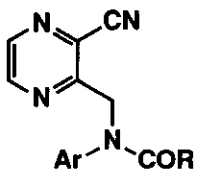
6a,b
11a,b



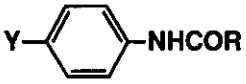
7a,b
12a,b



8a,b
13a,b



9a,b
14a,b



10: Y=H
15: Y=COOMe

Table 1. Photoreaction between pyrazine derivative (**1**~**3**) and trimethylsilylmethylaniline derivatives (**4**) and (**5**).[a]

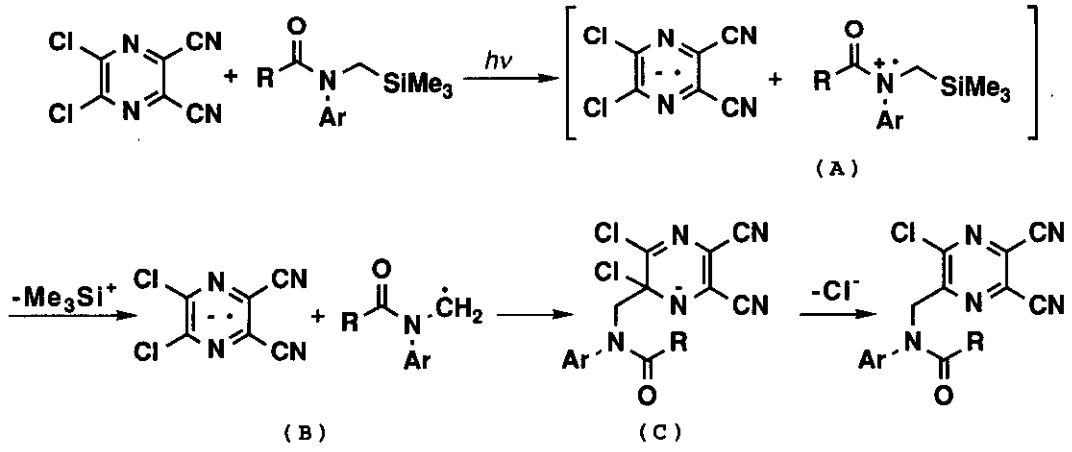
Starting pyrazines	Starting anilines	Product	Ar	R	Yield(%)
1	**4a**	**6a**	Ph	H	12(20)[b]
1	**4b**	**6b**	Ph	Me	20(24)[b]
2	**4a**	**7a**	Ph	H	17
2	**4b**	**7b**	Ph	Me	20
3	**4a**	**8a/9a**	Ph	H	7/12
3	**4b**	**8b/9b**	Ph	Me	8/15
1	**5a**	**11a**	C_6H_4COOMe	H	20(21)[b]
1	**5b**	**11b**	C_6H_4COOMe	Me	26(25)[b]
2	**5a**	**12a**	C_6H_4COOMe	H	17
2	**5b**	**12b**	C_6H_4COOMe	Me	20
3	**5a**	**13a/14a**	C_6H_4COOMe	H	3/6
3	**5b**	**13b/14b**	C_6H_4COOMe	Me	4/5

a. A mixture of i) **1** and **4** (or **5**) (0.02 mol/l), ii) **2** and **4** (or **5**) (0.02 mol/l), or iii) **3** and **4** (or **5**) (0.1 mol/l) in acetonitrile was irradiated for 6~24 h.

b. The yields in parentheses were obtained by using five equivalents of **4a**, **4b**, **5a** or **5b** (0.1 mol/l) to pyrazine derivative (**1**) (0.02 mol/l).

The dichloropyrazine derivative (**1**) is more reactive than the non-chlorinated derivative (**3**), and this must be due to the lowering of the reduction potential (E_{red}) by the chloro-substituents; E_{red} = -1.25 V (**1**) and -1.42 V (**3**) *vs* Ag/Ag^+ in acetonitrile. Reduction potentials of the excited states of pyrazine derivatives were estimated,[7] as a primary approximation, from the reduction potential (E_{red}) and emission energy (E_{0-0}) of **1** and **3** in acetonitrile; (E_{red} + E_{0-0} = 1.84 V (**1**) and 1.63 V (**3**) *vs* Ag/Ag^+ in acetonitrile).

Scheme I



Another factor influencing the reactivity is the efficiency in the aromatization process from the anion **C** in Scheme I. Poor reactivity of pyrazine-2,3-dicarbonitrile (**3**) can be accounted for also by this factor. This aromatization process involves the loss of chloride anion in the cases of chlorinated pyrazines, whereas it requires oxidation in the case of the non-chlorinated **3** for the loss of hydrogen atom or proton. Efficiency of the present reaction, therefore, must be controlled by the photochemical single electron transfer and the aromatization process.

Hydride reduction of the products (**6**) and (**11**), which retain chloro-

substituent, can lead to tetrahydropyrazine derivatives,[8] active forms of folic acid, with the elimination of the persisting chloro-substituent.

The present photochemical procedure open a new strategy for the introduction of an *N*-acyl-*N*-arylaminomethyl group on the pyrazine rings and provides the method of syntheses of folic acid models by the conversion of the pyrazine-2,3-dicarbonitrile system into pteridines as reported by us,[9] though a practical use may require improvement of the yield.

ACKNOWLEDGEMENT

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EXPERIMENTAL

Ir spectra were measured by a Perkin-Elmer 1640 spectrophotometer. 60 MHz ^{1}H-Nmr, 90 MHz ^{1}H-nmr, and 100 MHz ^{13}C-nmr spectra were recorded on a JEOL PMX-60SI, a Hitachi R-90, and a JEOL GSX-400 spectrometers, respectively. Chemical shifts were given in δ (ppm) relative to the internal tetramethylsilane or dichloromethane (high field) standard, and coupling constants were recorded in Hz. Mass spectra and high resolution mass spectra were measured by a Shimadzu GCMS QP-1000 and JEOL JMS-DX300 spectrometers. Uv spectra were measured by a Shimadzu UV-3101PC spectrophotometer in ethanol. Melting points were recorded on a Büchi apparatus and are uncorrected. Microanalyses were performed at the Materials Characterization Central Laboratory in Waseda University.

Starting Materials

i) 5,6-Dichloropyrazine-2,3-dicarbonitrile (**1**),[10] 2,3-dichloroquinoxaline (**2**),[11] and pyrazine-2,3-dicarbonitrile (**3**)[12] were prepared by the reported method.

ii) Methyl *p*-*N*-formylaminobenzoate[13] and methyl *p*-*N*-acetylanimobenzoate[14] were prepared by the reported method. *N*-acyl-*N*-trimethylsilylmethylanilines (**4a** and **4b**) and *N*-acyl-*N*-trimethylsilylmethyl-4-methoxycarbonylanilines (**5a** and **5b**) were prepared by the general procedure exemplified by the synthesis of **4a**.

Formanilide (0.67 g, 5 mmol) in 10 ml of dry THF was treated under nitrogen with sodium hydride (60% mineral oil dispersion, 200 mg, 5 mmol) which was washed with haxane twice. After refluxing for 1 h the mixture was treated with tris[2-(2-methoxyethoxy)ethyl]amine (0.3 ml, 1 mmol), sodium iodide (80 mg, 0.5 mmol), and (chloromethyl)trimethylsilane (0.69 ml, 5 mmol). The mixture was then refluxed for 24 h, added with 25 ml of 0.2N HCl, and then extracted with chloroform (30 ml X 3). Evaporation of the extract after drying over sodium sulfate gave the crude product, which was subjected to silica gel chromatography to remove polar materials (hexane-ethyl acetate 7:1), and distilled under reduced pressure.

Other aniline derivatives (**4b**, **5a**, and **5b**) were prepared by the same procedure as recorded above except for the solvent systems for chromatography (hexane-ethyl acetate 4:1 for **4b**, chloroform for **5a** and **5b**).

4a, bp 92°C/1.2 mmHg; ^{1}H-nmr(60 MHz, CCl_4) δ 0.03(9H, s), 3.36(2H, s), 7.01~7.59(5H, m), 8.82(1H, s); ir(neat) 3064, 1673, 1595 cm^{-1}; ms(70 eV) m/z 207(M^+, 14%), 73(100%); uv(λmax, log ε) 203.5(4.23), 242.5 nm(3.96). *Anal. Calcd for* $C_{11}H_{17}NOSi$: C, 63.72; H, 8.27; N, 6.76. *Found*: C, 63.51; H, 8.46; N, 6.73.

4b, bp 100°C/0.6 mmHg; ^{1}H-nmr(60 MHz, CCl_4) δ 0.16(9H, s), 1.90(3H, s), 3.21(2H, s), 6.98~7.51(5H, m); ir(neat) 3064, 1658, 1598 cm^{-1}; ms(20 eV) m/z 221(M^+, 25%), 73(100%); uv(λmax, log ε) 203.0(4.23), 237.5 nm(3.72). *Anal. Calcd for* $C_{12}H_{19}NOSi$: C, 65.11; H, 8.65; N, 6.33. Found: C, 64.84; H, 8.80; N, 6.34.

5a, bp 147°C/0.53 mmHg; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 0.04(9H, s), 3.51(2H, s), 3.98(3H, s), 7.29(2H, d, J=9.0), 8.12(2H, d, J=9.0), 8.57(1H, s); ir(neat) 3067, 1721, 1674, 1603 cm^{-1}; ms(20 eV) m/z 265(M^+, 35%), 250(100%); uv(λmax, log ε) 215.4(4.09), 276.6 nm(4.19). *Anal. Calcd for* $C_{13}H_{19}NO_3Si$: C, 58.84; H, 7.22; N, 5.28. *Found*: C, 59.00; H, 7.28; N, 5.26.

5b, bp 137°C/0.37 mmHg; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 0.03(9H, s), 1.96(3H, s),

3.38(2H, s), 3.99(3H, s), 7.32(2H, d, J=8.6), 8.13(2H, d, J=8.6); ir(neat) 3064, 1724, 1658, 1603 cm^{-1}; ms(20 eV) m/z 279(M^+, 35%), 264(100%); uv(λmax, log ε) 217.0(4.07), 275.4 nm(3.92). *Anal. Calcd for* $C_{14}H_{21}NO_3Si$: C, 60.18; H, 7.58; N, 5.01. *Found*: C, 59.92; H, 7.71; N, 5.05.

*Photoreactions between pyrazine derivatives (**1**~**3**) and N-acylaniline derivatives (**4**) and (**5**).*

An equimolar mixture of one of the pyrazine derivatives (**1** and **2**, 0.02 mol/l; **3**, 0.1 mol/l) and *N*-acylaniline derivatives (**4**) or (**5**) in acetonitrile (10 ml) was placed in a tube type reaction vessel of Pyrex (diameter, 14 mm) which was capped with a rubber septum. The reaction vessel was dipped in an ultrasonic bath and the solution was bubbled with argon through a syringe needle to purge dissolved air. The solution was then irradiated with a 450 w high pressure mercury lamp mounted on a rotary type irradiation apparatus (Rikoh RH-400, the distance between the lamp and the reaction vessel: 5 cm). After the irradiation the solution was concentrated and the product was isolated by preparative tlc on silica gel plate (20X20 cm, 2 mm thickness) using the following solvent systems; hexane-ethyl acetate (3:1) for **6b**, **8a**, **8b**, **9a**, **9b**, and **11b**; haxane-ethyl acetate (1:1) for **6a** and **11a**; chloroform-ethyl acetate (6:1) for **7a**, **7b**, **12a**, and **12b**; repeated developments first with hexane-ethyl acetate (3:1) and then ethyl ether-chloroform (1:1) for **13a** and **14a**; first with hexane-ethyl acetate (3:1) and then ethyl acetate for **13b** and **14b**.

Product (**8a**) and (**8b**) were reported earlier and identified by the comparison of spectral data.[4]

6a, viscous oil; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 5.18(2H, s),7.11~7.90(5H, m), 8.55(1H, s); ^{13}C-nmr(100 MHz, $CDCl_3$) δ 48.7, 111.6, 112.2, 124.2, 127.8, 130.0, 130.7, 140.1, 150.7, 155.4, 162.4; ir($CHCl_3$) 3026, 2234, 1678, 1596 cm^{-1}; ms(70 eV) m/z 299(M^++2, 3%), 297(M^+, 10%), 106(100%); High resolution ms *Calcd for* $C_{14}H_8N_5OCl$: m/z=297.0419. *Found*: m/z=297.0395.

6b, mp 148.5~149.2°C (EtOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 1.98(3H, s), 5.15(2H, s), 7.19~7.78(5H, m); ir($CHCl_3$) 3022, 2266, 1663, 1596 cm^{-1}; ms(70 eV) m/z 313(M^++2, 2%), 311(M^+, 6%), 43(100%). *Anal. Calcd for* $C_{15}H_{10}N_5OCl$: C, 57.80; H, 3.23; N, 22.47. *Found*: 57.73; H, 3.23; N, 22.35.

7a, viscous oil; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 5.44(2H, s), 6.98~7.61(5H, m),

7.61~7.94(2H, m), 7.94~8.23(2H, m), 8.73(1H, s); ir($CHCl_3$) 3069, 1675, 1597 cm^{-1}; ms(20 eV) m/z 299(M^++2, 34%), 297(M^+, 100%). High resolution ms *Calcd for* $C_{16}H_{12}N_3OCl$: m/z=297.0669. Found: m/z=297.0671.

7b, mp 117.5~118.2°C (from EtOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 2.06(3H, s), 5.33(2H, s), 7.04~7.66(5H, m), 7.66~7.92(2H, m), 7.92~8.29(2H, m); ir($CHCl_3$) 3068, 1654, 1596 cm^{-1}; ms(20 eV) m/z 313(M^++2, 9%), 311(M^+,25%), 276(100%). *Anal. Calcd for* $C_{17}H_{14}N_3OCl$: C, 65.49; H, 4.53; N, 13.48. *Found*: C, 65.76; H, 4.54; N, 13.49.

9a, viscous oil; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 5.32(2H, s), 6.93~7.72(5H, m), 8.57(1H, d, J=2.4), 8.57(1H, s) 8.71(1H, d, J=2.4); ir($CHCl_3$) 3022, 2239, 1678, 1597 cm^{-1}; ms(70 eV) m/z 238(M^+, 8%), 106(100%). High resolution ms *Calcd for* $C_{13}H_{10}N_4O$: m/z=238.0854. Found: m/z=238.0850.

9b, viscous oil, ^{1}H-nmr(90 MHz, $CDCl_3$) δ 1.96(3H, s), 5.24(2H, s), 7.16~7.70(5H, m), 8.57(1H, d, J=2.4), 8.75(1H, d, J=2.4); ir($CHCl_3$) 3010, 2238, 1659, 1596 cm^{-1}; ms(70 eV) m/z 252(M^+, 16%), 43(100%). High resolution ms *Calcd for* $C_{14}H_{12}N_4O$: 252.1012. *Found*: 252.1015.

11a, mp 146.0~147.1°C (MeOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 3.93(3H, s), 5.32(2H, s), 7.31(2H, d, J=8.8), 8.10(2H, d, J=8.8), 8.67(1H, s); ir($CHCl_3$) 3123, 2243, 1721, 1685, 1607 cm^{-1}; ms(20 eV) m/z 357(M^++2, 9%), 355(M^+, 27%), 164(100%); *Anal. Calcd for* $C_{16}H_{10}N_5O_3Cl$: C, 54.02; H, 2.83; N, 19.69. *Found*: C, 54.05; H, 2.85; N, 19.45.

11b, mp 150.8~151.5°C (MeOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 2.01(3H, s), 3.94(3H, s), 5.16(2H, s), 7.47(2H, d, J=8.6), 8.12(2H, d, J=8.6); ir($CHCl_3$) 3024, 2243, 1721, 1666, 1606 cm^{-1}; ms(20 eV) m/z 371(M^++2, 2%), 369(M, 6%), 327(100%). *Anal. Calcd for* $C_{17}H_{12}N_5O_3Cl$: C, 55.22, H, 3.27; N, 18.94. *Found*: C, 55.30; H, 3.21; N, 18.79.

12a, mp 152.4~153.6°C (MeOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 3.90(3H, s), 5.44(2H, s), 7.37(2H, d, J=8.8), 7.62~7.86(2H, m), 7.86~8.08(2H, m), 8.05(2H, d, J=8.8), 8.82(1H, s); ir($CHCl_3$) 3022, 1717, 1684, 1606 cm^{-1}; ms(20 eV) m/z 357(M^++2, 1%), 355(M^+, 3%), 164(100%). *Anal. Calcd for* $C_{18}H_{14}N_3O_3Cl$: C, 60.77; H, 3.97; N, 11.81. *Found*: C, 60.71; H, 3.94; N, 11.72.

12b, viscous oil, ^{1}H-nmr(90 MHz, $CDCl_3$) δ 2.08(3H, s), 3.91(3H, s), 5.33(2H, s), 7.58(2H, d, J=8.6), 7.68~7.88(2H, m), 7.88~8.34(4H, m); ^{13}C-nmr(100 MHz, $CDCl_3$) δ 22.5, 52.3, 52.4, 128.1, 128.2, 129.0, 129.7, 130.2,

130.6, 131.0, 140.6, 141.3, 145.9, 147.4, 149.2, 166.1, 170.3; ir($CHCl_3$) 3022, 1721, 1661, 1606 cm^{-1}; ms(20 eV) m/z 371(M^++2, 2%), 369(M^+, 5%), 334(100%). High resolution ms *Calcd for* $C_{19}H_{16}N_3O_3Cl$: m/z=369.0881. *Found*: m/z=369.0883.

13a, viscous oil; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 3.93(3H, s) 5.24(2H, s), 7.34(2H, d, J=8.6), 8.12(2H, d, J=8.6), 8.66(1H, s), 8.97(1H, s); ir($CHCl_3$) 3020, 2244, 1723, 1681, 1607 cm^{-1}; ms(20 eV) m/z 321(M^+, 16%), 293(100%). High resolution ms *Calcd for* $C_{16}H_{11}N_5O_3$: m/z=321.0863. *Found*: m/z=321.0849.

13b, mp 111.7~112.1°C (MeOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 1.97(3H, s), 3.95(3H, s), 5.05(2H, s), 7.39(2H, d, J=8.6), 8.13(2H, d, J=8.6), 8.99(1H, s); ir($CHCl_3$) 3023, 2244, 1724, 1662, cm^{-1}; ms(20 eV) m/z 335(M^+, 6%), 293(100%). *Anal. Calcd for* $C_{17}H_{13}N_5O_3$: C, 60.89; H, 3.91; N, 20.89. *Found*: C, 60.61; H, 3.90; N, 20.83.

14a, mp 88.4~89.5°C (MeOH); ^{1}H-nmr(90 MHz, $CDCl_3$) δ 3.92(3H, s), 5.39(2H, s), 7.35(2H, d, J=8.8), 8.07(2H, d, J=8.8), 8.60(1H, d, J=2.4), 8.69(1H, s), 8.69(1H, d, J=2.4); ir($CHCl_3$) 3031, 2239, 1720, 1684, 1607 cm^{-1}; ms(20 eV) m/z 296(M^+, 11%), 268(199%). *Anal. Calcd for* $C_{15}H_{12}N_4O_3$: C, 60.81; H, 4.08; N, 18.91. *Found*: C, 60.87; H, 4.02; N, 18.70.

14b, viscous oil; ^{1}H-nmr(90 MHz, $CDCl_3$) δ 1.99(3H, s), 3.93(3H, s), 5.24(2H, s), 7.47(2H, d, J=8.6), 8.08(2H, d, J=8.6), 8.58(1H, d, J=2.2), 8.73(1H, d, J=2.2); ^{13}C-nmr(100 MHz, $CDCl_3$) δ 22.2, 51.7, 52.3, 114.5, 127.9, 129.6, 129.9, 131.1, 143.5, 146.4, 147.0, 156.1, 165.9, 170.3; ir($CHCl_3$) 3020, 2239, 1721, 1665, 1606 cm^{-1}; ms(20 eV) m/z 310(M^+, 14%), 268(100%). High resolution ms *Calcd for* $C_{16}H_{14}N_4O_3$: m/z=310.1067. *Found*: m/z=310.1089.

*Cyclic voltammetry of pyrazine derivatives (**1**) and (**3**).*

Reduction potential of pyrazine derivatives (**1**) and (**3**) was determined by a CV-27 voltammetry controller (BAS Co.) using a platinum electrode. An acetonitrile solution (7 ml) of the pyrazine derivative (0.1 mol/l) and tetrabutylammonium perchlorate (8.5 mmol/l) was deaerated by bubbling nitrogen through the solution for 10 min. Scanning started from 0.0 V toward -1.8 V and returned 0.0 V at a rate of 0.1 V/sec. Pyrazine derivatives showed irreversible reduction waves at -1.25 (**1**) and -1.42 V (**3**) vs Ag / AgCl.

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