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Correlations between Carbon-13 Nuclear Magnetic Resonance Chemical Shifts and Reactivities of Siloxybutadienes and Siloxyazabutadienes in the Diels–Alder Reaction with Dimethyl Acetylenedicarboxylate

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In the reaction of silylated butadiene derivatives (1) with dimethyl acetylenedicarboxylate (DMAD), it is proposed that the reactivities of the dienes can be predicted from the carbon-13 nuclear magnetic resonance chemical shifts of the terminal methylene carbons (δ^{13}C-4) of the dienes based on the following linear relationships, a) total electron densities against δ^{13}C-4; b) ln$k$ against $1/[E_{\mathrm{LUMO(DMAD)}}-E_{\mathrm{HOMO(diene)}}]$; c) ln$k$ against δ^{13}C-4. The total electron densities and energy levels of highest occupied molecular orbitals (HOMOs) and lowest unoccupied molecular orbitals (LUMOs) of the dienes were calculated by the modified neglect of diatomic overlap (MNDO) method.

Keywords siloxybutadiene; siloxyazabutadiene; Diels–Alder reaction; frontier molecular orbital; MNDO; ^{13}C-NMR; kinetics; dimethyl acetylenedicarboxylate

The Diels–Alder reaction is one of the most important reactions in the field of organic synthesis, and consequently it has been the subject of extensive preparative,[1] theoretical,[2] and mechanistic[3] studies. The frontier molecular orbital theory[4] ((FMO) method) and the conservation of orbital symmetry theory[2b] have been found to be effective tools for theoretical studies of the Diels–Alder reaction. In particular, the rates of Diels–Alder reactions are clearly related to the magnitude of highest occupied molecular orbital (HOMO)–lowest unoccupied molecular orbital (LUMO) energy/separations of dienes and dienophiles as determined by the FMO method.[5] In the normal electron demand Diels–Alder reaction[6] (reaction of electron-rich dienes with electron-deficient dienophiles), the reactivities of dienes increase with rise of the HOMO energy levels. Therefore, when the same dienophiles are used, the reactivities of dienes can be predicted from a comparison of HOMO energy levels.

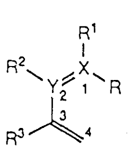
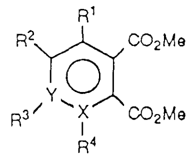
In this paper we show that the reactivities of the siloxybutadienes and siloxyazabutadienes can be predicted from the carbon-13 nuclear magnetic resonance (^{13}C-NMR) chemical shifts of the terminal methylene carbon (δ^{13}C-4) of the dienes, as well as from the HOMO energy levels. The theoretical approach to the reactivities and ^{13}C-NMR chemical shifts is performed with the help of semi-empirical molecular orbital theory (modified neglect of diatomic overlap (MNDO) method).

Results and Discussion

Several 1,3-butadienes (**1a**,[7] **1b**, **1c**,[8] **1d**,[9] and **1e**[10]), 1-azabutadienes (**1f**,[11] **1g**, **1h**,[12] **1i**, and **1j**), and 2-azabutadienes (**1k**[13] and **1l**[13]) were prepared by reported or modified methods. The reactivities of the dienes were compared by reaction with dimethyl acetylenedicarboxylate (DMAD) as a dienophile and the results are summarized in Table I. The ^{13}C-NMR chemical shifts of the dienes are also shown in Table II.

We considered that δ^{13}C-4 might reflect the relative reactivities of the dienes on the basis of the following observations. Namely, the dienes (**1d**, **1e**, **1k**, and **1l**), in which δ^{13}C-4 appeared at high magnetic field (more than

TABLE I. Diels–Alder Reactions of Dienes (**1**) with DMAD

	Diene						Product							Reaction	Conditions	Yield (%)
	R	R^1	R^2	R^3	X	Y		R^1	R^2	R^3	R^4	X	Y			
1a	TMSO	Me	MeS	TMSO	C	C	**2a**	Me	MeS	HO	H	C	C	Toluene	Reflux 17 h	59[7]
1b	TMSO	Me	MeS	AcO	C	C	**2a**							Toluene	Reflux 48 h	10
1c	AcO	Me	MeS	AcO	C	C								Toluene	Reflux 48 h	—[8]
1d	TMSO	Me	H	TMSO	C	C	**2b**	Me	H	HO	H	C	C	Benzene	Reflux 12 h	70[9]
1e	MeO	H	H	TMSO	C	C	**2c**	H	H	HO	H	C	C	Benzene	Reflux 4 h	79[10]
1f	TMSO	—	H	TMSO	N	C	**2d**	H	HO	H	—	N	C	Toluene	Reflux 12 h	25
1g	TMSO	—	H	Me	N	C								Toluene	Reflux 48 h	—
1h	OH	—	H	Me	N	C								Toluene	Reflux 48 h	—
1i	TMSO	—	Me	TMSO	N	C	**2e**	H	HO	Me	—	N	C	Benzene	Reflux 8 h	60
1j	TMSO	—	CO_2Me	TMSO	N	C	**2f**	H	HO	CO_2Me	—	N	C	Benzene	Reflux 8 h	62
1k	TBDMSO	H	—	TBDMSO	C	N	**2g**	H	HO	—	H	C	N	Chloroform	Reflux 12 h	71[13]
1l	TBDMSO	Me	—	TBDMSO	C	N	**2h**	H	HO	—	Me	C	N	Chloroform	Reflux 12 h	83[13]

TMSO: trimethylsiloxy. TBDMSO: *tert*-butyldimethylsiloxy.

Table II. MNDO Eigenvalues and Eigenvectors for HOMO π Orbitals and ^{13}C-NMR Chemical Shifts of Dienes (**1**)

	Chemical shifts (ppm)				Total electron density				HOMO energy levels (eV)
	X-1	Y-2	C-3	C-4	X-1	Y-2	C-3	C-4	
1a	149.2	114.8	153.2	97.3	3.901	4.169	3.897	4.160	−8.945
1b	149.9	110.4	155.3	105.7	3.899	4.149	3.930	4.123	−9.161
1c	148.1	120.6	150.0	108.8	3.880	4.109	3.890	4.075	−9.313
1d	150.5	107.1	154.4	93.2	3.951	4.122	3.913	4.185	−8.812
1e	150.4	103.2	154.0	91.0	3.906	4.124	3.792	4.198	−8.561
1f	—	152.0	151.1	103.3	4.084	4.019	3.875	4.092	−8.634
1g	—	156.2	139.5	121.4	4.105	3.975	4.137	3.996	−9.207
1h	—	153.0	138.5	122.3	3.869	3.955	4.144	3.986	−9.457
1i	—	153.4	157.5	97.2	4.098	4.007	3.832	4.177	−8.728
1j	—	154.6	148.5	100.8	4.042	4.007	3.809	4.187	−8.812
1k	157.0	—	153.7	84.2	3.647	4.406	3.794	4.192	−8.430
1l	160.2	—	151.9	88.8	3.653	4.414	3.782	4.193	−8.502

Table III. Kinetic Data for Cycloadditions of Dienes (**1**) with DMAD at 100±0.5 °C

Diene	**1a**	**1b**	**1d**	**1e**	**1f**	**1i**	**1j**	**1k**	**1l**
k [$\text{M}^{-1}\,\text{s}^{-1}$]	7.20×10^{2}	0	8.70×10^{3}	1.04×10^{5}	1.75×10^{2}	5.72×10^{2}	91.1	1.71×10^{4}	1.29×10^{4}

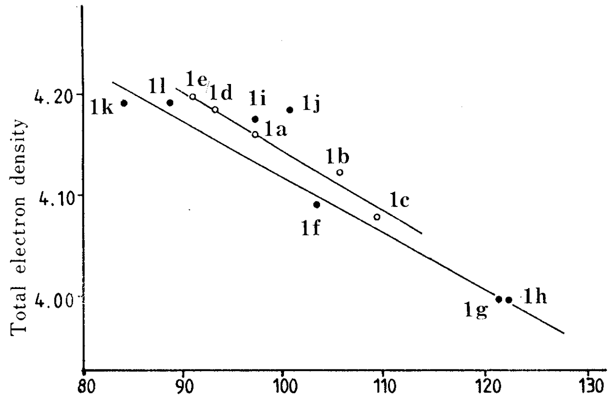


Fig. 1. Plots of Total Electron Density against δ^{13}C-4
Siloxybutadienes (○); siloxyazabutadienes (●).

95 ppm) reacted in chloroform or benzene under reflux to give the corresponding cycloadducts in moderate yields. When δ^{13}C-4 appeared in the 97—106 ppm region, the dienes (**1a**, **1b**, **1f**, **1i**, and **1j**) reacted in benzene or toluene under reflux in poor to moderate yields. The dienes (**1c**, **1g**, and **1h**) for which δ^{13}C-4 appeared at lower magnetic field than 108 ppm gave no cycloadduct.

The main contribution to ^{13}C chemical shifts is the paramagnetic shielding constant (σ_p) of the nuclei and σ_p depends on the following factors[14]: a) total electron density of the nuclei; b) excitation energy of the molecule; c) bond order of the nuclei. In the case of analogous molecules, the influence of b) and c) can be ignored. Indeed, dependence of ^{13}C chemical shifts on total electron densities was observed at corresponding carbon atoms in 1,3-butadiene derivatives[15] and other homologous series.[16] Therefore, we considered that the relationship of total electron density to δ^{13}C-4 could be validly employed. The total electron densities were calculated by the MNDO method,[17] and the results are shown in Table II. In the case of siloxybutadienes, a good relationship was observed between the total electron densities and δ^{13}C-4 (Fig. 1). There is a similar tendency for the aza-compounds, though 1-aza compounds possessing a substituent at the 2-position deviated from the straight line.

In order to obtain quatitative reactivities of the butadiene derivatives (**1**), we measured the reaction rate of dienes (**1**) with DMAD at 100 °C and followed the time course of DMAD amount by gas-liquid chromatography (GLC). All of the reactions were second-order, because plots of time against 1/[DMAD] (concentration of DMAD) showed good linearity. The reaction rate constants (k) were calculated and the results are shown in Table III.

Generally, the perturbation theory is used as a theoretical basis to discuss reactivities. Mok and Nye[18] have considered the relationship between the perturbation equation (ΔE FMO) and the rate constant of cycloaddition reactions. They connected the Eyring equation and rate constant, and obtained Eq. 1.

$$\ln k = C - \frac{2\gamma^2}{RT} \times W \tag{1}$$

where

$$W = \left[\frac{(C_{A1H}C_{B1L} + C_{A2H}C_{B2L})^2}{|E_{AH} - E_{BL}|} + \frac{(C_{A1L}C_{B1H} + C_{A2L}C_{B2H})^2}{|E_{BH} - E_{AL}|} \right]$$

They plotted $\ln k$ against W for the reaction between cyclopentadiene and a series of dienophiles. Unfortunately, the points were widely scattered and they judged that Eq. 1 was not applicable. However, they suggested that $\ln k$ would be linearly related to $1/(E_{\text{HOMO}} - E_{\text{LUMO}})$, where E_{HOMO} and E_{LUMO} are the eigenvalues of the more closely lying pair of HOMOs and LUMOs, on the basis of Eq. 2.

$$\ln k = C + \frac{2\gamma^2\delta}{RT}\left[\frac{1}{E_H - E_L}\right] \tag{2}$$

We plotted $\ln k$ against $1/[E_{\text{LUMO(DMAD)}} - E_{\text{HOMO(diene)}}]$, and obtained a linear plot of positive slope, as shown in Fig. 2. The energy levels of LUMOs and HOMOs were obtained

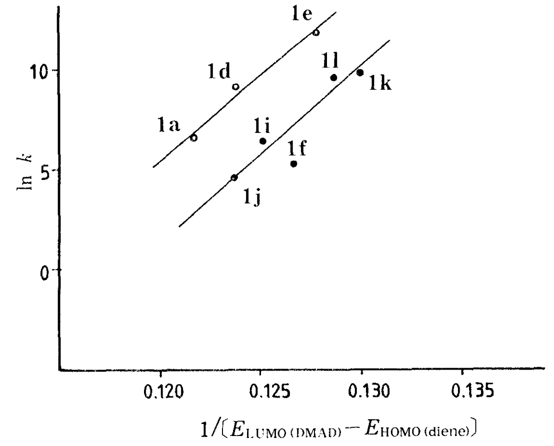


Fig. 2. Plots of $\ln k$ against $1/[E_{\mathrm{LUMO(DMAD)}}-E_{\mathrm{HOMO(diene)}}]$ for the Reactions of Siloxybutadienes (○) and Siloxyazabutadienes (●) with DMAD

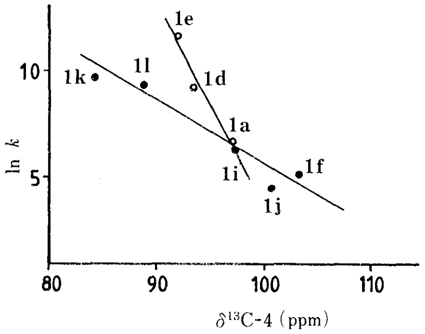


Fig. 3. Plots of $\ln k$ against δ^{13}C-4 for the Reactions of Siloxybutadienes (○) and Siloxyazabutadienes (●) with DMAD

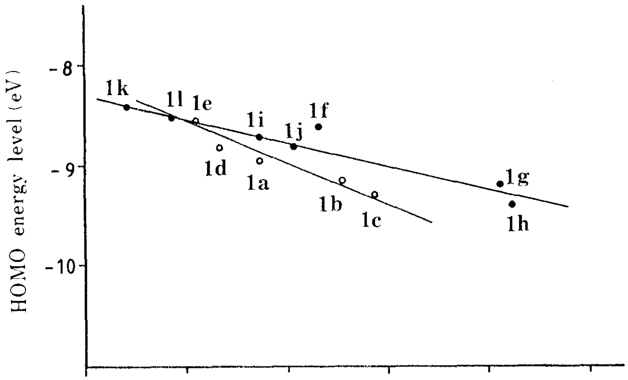


Fig. 4. Plots of HOMO Energy Level against δ^{13}C-4
Siloxybutadienes (○); siloxyazabutadienes (●).

by the MNDO method.[17)] Similarly, a relation between $\ln k$ and δ^{13}C-4 was observed (Fig. 3). Thus, it was clear that the reactivities of the dienes (**1**) could be predicted from δ^{13}C-4. Moreover, correlations were observed between HOMO energy levels and δ^{13}C-4 as shown in Fig. 4. Therefore, δ^{13}C-4 of the dienes could be used for prediction of reactivity in Diels–Alder reactions.

Conclusion

In the reaction of 4-π electron system compounds with DMAD, four linear relationships were obtained: a) total electron density against δ^{13}C-4 (Fig. 1); b) $\ln k$ against $1/[E_{\mathrm{LUMO(DMAD)}}-E_{\mathrm{HOMO(diene)}}]$ (Fig. 2); c) $\ln k$ against δ^{13}C-4 (Fig. 3); d) HOMO energy level against δ^{13}C-4 (Fig. 4). By using these correlations, the relative reactivities of the dienes could be predicted easily from their δ^{13}C-4.

Experimental

All melting points were measured with a Yanaco micro melting point apparatus, and are uncorrected. Infrared (IR) spectra were measured with a JASCO IR-810 spectrophotometer. Ultraviolet (UV) spectra were recorded in ethanol on a Hitachi 323 spectrophotometer. ^{1}H-NMR spectral measurements were carried out with a JEOL JNM FX-90Q Fourier-transform spectrometer (90 MHz), ^{13}C-NMR spectra were measured with a JEOL JNM GX-400 Fourier-transform spectrometer (100 MHz). Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) as an internal standard. Mass spectra (MS) were taken with a JEOL JMS-DX-303 spectrometer and a JEOL JMA-DA-5000 data processor by the electron impact (EI) ionization method. Gas chromatographic analyses were performed on a Shimadzu GC-8APF chromatograph equipped with a flame ionization detector and a Shimadzu C-R6A Chromatopac.

Reaction Rate Determination of the Dienes (1) with DMAD A solution of a diene (**1**, 3 mmol) and DMAD (3 mmol) in 10 ml of purified xylene was placed in a flask, which was immersed in a thermostated oil bath (Riko-Kagaku MH-10A and Riko MINI-HEATER) controlled at 100±0.5 °C. One microliter of the reaction mixture was subjected to GLC at regular intervals, and the reaction rate was estimated from the decrease of DMAD. A linear relation passing through the origin was obtained between the area ratio of [DMAD/ethylbenzene (internal standard)] and amount of DMAD in the range of 0.01—0.4 mmol/ml ($y=29.7x$, $r=0.999$). GLC conditions: glass column (3 m × 2.6 mm i.d.); 5% Silicon GE SE-30 supported on Shimalite W; injection temperature 130 °C; oven temperature 100 °C; pressure of carrier gas (N_2) 0.5 kg/cm^2.

2-Acetyl-3-methylthio-4-trimethylsiloxy-1,3-pentadiene (1b) Trimethylchlorosilane (TMSCl) (6.52 g, 60 mmol) was added portionwise to a solution of 2-acetoxy-3-methylthio-2-penten-4-one (5.71 g, 30 mmol), triethylamine (6.07 g, 60 mmol) and $ZnCl_2$ (0.15 g) in dry benzene (50 ml). The mixture was stirred at room temperature for 30 min then stirred overnight under N_2 at 40 °C. After removal of the solvent, dry ether (50 ml) was added to the residue. The resulting precipitate was filtered off. The filtrate was concentrated to give a brown oil. Distillation of the oil gave 6.64 g (85%) of a pale yellow oil, bp 110—113 °C (5 mmHg). *Anal.* Calcd for $C_{11}H_{20}O_3SSi$: C, 50.73; H, 7.74. Found: C, 50.94; H, 7.68. IR (neat): 1765 (C=O) cm^{-1} MS *m/z*: 260 (M$^+$). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.22 and 0.24 (each, 9H, s, SiMe$_3$), 2.14 (9H, br s, Me × 3), 5.02 and 5.12 (each 1H, s, C=CH$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 0.76 (SiMe), 15.55 (SMe), 17.34 (O–CO–$\underline{\text{Me}}$), 20.91 (C–$\underline{\text{Me}}$), 105.65 (C=$\underline{\text{C}}$H$_2$), 110.42 ($\underline{\text{C}}$=C–SMe), 149.87 (C=$\underline{\text{C}}$–SMe), 155.30 ($\underline{\text{C}}$–C–SMe), 168.72 (O–$\underline{\text{C}}$O–Me).

1,3-Bis(trimethylsiloxy)-1-aza-1,3-butadiene (1f) This compound was prepared from isonitrosoacetone by the same method as described above. Yield 75%. bp 97 °C (20 mmHg). *Anal.* Calcd for $C_9H_{21}NO_2Si_2$: C, 46.71; H, 9.15; N, 6.05. Found: C, 46.51; H, 9.18; N, 6.00. IR (neat): 2960, 1620, 1580, 1360, 1250, 1040, 980, 950 cm^{-1}. MS *m/z*: 231 (M$^+$). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.22 (9H, s, SiMe$_3$), 0.23 (9H, s, SiMe$_3$), 4.62 (1H, d, $J=0.9$ Hz, =CH$_2$), 4.75 (1H, d, $J=0.9$ Hz, =CH$_2$), 7.67 (1H, s, CH=N). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: −0.69 (SiMe$_3$), 0.13 (SiMe$_3$), 103.5 (C=$\underline{\text{C}}$H$_3$), 151.11 ($\underline{\text{C}}$=CH$_2$), 152.00 ($\underline{\text{C}}$H=N).

3-Methyl-1-trimethylsiloxy-1-aza-1,3-butadiene (1g) This compound was prepared from methacroleinoxime[12)] by the same method as described above. Yield 59%. bp 48—51 °C (20 mmHg). *Anal.* Calcd for $C_7H_{15}NOSi$: C, 53.45; H, 9.61; N, 8.91. Found: C, 53.55; H, 9.70; N, 8.90. IR (neat): 2960, 1450, 1250, 1020, 990 cm^{-1}. MS *m/z*: 157 (M$^+$). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.23 (9H, s, SiMe$_3$), 1.91 (3H, s, Me), 5.19 (1H, s, =CH$_2$), 5.32 (1H, s, =CH$_2$), 7.83 (1H, s, CH=N). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: −0.87 (SiMe$_3$), 17.24 (Me), 121.35 (C=$\underline{\text{C}}$H$_2$), 139.49 ($\underline{\text{C}}$=CH$_2$), 156.23 ($\underline{\text{C}}$H=N).

2-Methyl-1,3-bis(trimethylsiloxy)-1-aza-1,3-butadiene (1i) TMSCl (39.11 g, 0.36 mol) was added dropwise to a solution of 2-(trimethylsiloxyimino)-3-butanone (31.20 g, 0.18 mol) (this compound was prepared from 2,3-butanedione monoxime as described above), triethylamine (36.42 g, 0.36 mol) and NaI (13.49 g, 0.09 mol) in dry acetonitrile (400 ml). The mixture was stirred at room temperature for 12 h under N_2. After removal of the solvent, ether (100 ml) was added to the residue. The resulting precipitate was filtered off. The filtrate was concentrated to give a brown oil, which was distilled to give 33.98 g (81%) of a colorless oil, bp 95 °C (18 mmHg). *Anal.* Calcd for $C_{10}H_{23}NO_2Si$: C, 48.93; H, 9.44; N, 5.71. Found: C, 48.68; H, 9.10; N, 6.10. IR (neat): 2960, 2900, 1620, 1580, 1340, 1250, 1170, 1030, 940 cm^{-1}. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 233 (4.07). MS *m/z*: 245 (M^+). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.22 (18H, s, SiMe$_3$ × 2), 1.95 (3H, s, N=C–Me), 4.52 (1H, d, *J* = 2.0 Hz, one of =CH$_2$), 4.80 (1H, d, *J* = 2.0 Hz, one of =CH$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: −0.58 (SiMe$_3$), 11.09 (N–C–$\underline{\text{Me}}$), 97.18 (C=$\underline{\text{C}}$H$_2$), 153.43 (N=$\underline{\text{C}}$–Me), 157.47 ($\underline{\text{C}}$=CH$_2$).

2-Methoxycarbonyl-1,3-bis(trimethylsiloxy)-1-aza-1,3-butadiene (1j) This compound was prepared from methyl oximinoacetoacetate[19)] by the same method as described above. Yield 89%. bp 74 °C (0.6 mmHg). *Anal.* Calcd for $C_{11}H_{23}NO_4Si_2$: C, 45.64; H, 8.01; N, 4.84. Found: C, 45.44; H, 7.74; N, 4.96. IR (neat): 2960, 2900, 1750, 1620, 1440, 1360, 1320, 1260, 1100, 1010 cm^{-1}. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 232 (4.04), 270 (3.07). MS *m/z*: 289 (M^+). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 0.23 (18H, s, SiMe$_3$ × 2), 3.84 (3H, s, COOMe), 4.67 (1H, d, *J* = 2.0 Hz, one of =CH$_2$), 4.72 (1H, d, *J* = 2.0 Hz, one of =CH$_2$). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: −0.93 (SiMe$_3$), 52.12 (COO$\underline{\text{Me}}$), 100.88 (C=$\underline{\text{C}}$H$_2$), 148.52 ($\underline{\text{C}}$=CH$_2$), 154.63 ($\underline{\text{C}}$–COOMe), 161.99 ($\underline{\text{C}}$OOMe).

Dimethyl 5-Hydroxy-2,3-pyridinedicarboxylate (2d) A solution of dimethyl acetylenedicarboxylate (1.28 g, 9 mmol) and 1,3-bis(trimethylsiloxy)-1-aza-1,3-butadiene (**1f**, 2.31 g, 10 mmol) in dry toluene (10 ml) was refluxed for 12 h under N_2. After removal of the solvent, the residue was chromatographed on a silica gel column using benzene–ethyl acetate as an eluent to give colorless needles (0.48 g, 25%), mp 129—131 °C (ether–*n*-hexane). *Anal.* Calcd for $C_9H_9NO_5$: C, 51.19; H, 4.30; N, 6.63. Found: C, 51.10; H, 4.33; N, 6.60. IR (KBr): 2950, 1750, 1730, 1600, 1570, 1430, 1340, 1300, 1250 cm^{-1}. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 252 (3.80), 285 (3.78). MS *m/z*: 211 (M^+). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.91 (3H, s, COOMe), 3.92 (3H, s, COOMe), 7.75 (1H, d, *J* = 2.6 Hz, Ar), 8.28 (1H, d, *J* = 2.6 Hz, Ar).

Dimethyl 5-Hydroxy-6-methyl-2,3-pyridinedicarboxylate (2e) The same procedure as described above was applied to **1i** and DMAD. Yield 60%. mp 157—159 °C (benzene–*n*-hexane). *Anal.* Calcd for $C_{10}H_{11}NO_5$: C, 53.33; H, 4.92; N, 6.22. Found: C, 53.34, H, 4.88; N, 6.17. IR (KBr): 3000, 2700, 1730, 1590, 1440, 1420, 1340, 1270, 1250 cm^{-1}. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 256 (3.98), 295 (3.85). MS *m/z*: 225 (M^+). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 2.52 (3H, s, C–Me), 3.89 (3H, s, COOMe), 3.91 (3H, s, COOMe), 7.39 (1H, s, Ar), 8.30 (1H, s, OH).

Trimethyl 5-Hydroxy-2,3,6-pyridinetricarboxylate (2f) The same procedure as described above applied to **1j** and DMAD. Yield 62%. mp 118—119 °C (benzene–*n*-hexane). *Anal.* Calcd for $C_{11}H_{11}NO_7$: C, 49.08; H, 4.12; N, 5.20. Found: C, 49.05; H, 4.17; N, 5.11. IR (KBr): 3150, 2950, 1720, 1680, 1560, 1460, 1430, 1370, 1320 cm^{-1}. UV $\lambda_{\max}^{\text{EtOH}}$ nm (log ε): 340 (3.92). MS *m/z*: 269 (M^+). ^{1}H-NMR (90 MHz, $CDCl_3$) δ: 3.95 (3H, s, COOMe), 3.97 (3H, s, COOMe), 4.08 (3H, s, COOMe), 7.67 (1H, s, Ar), 11.02 (1H, s, OH).

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