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Preferential Introduction of a Pyridylmethyl Group into Sulfonamides as an Approach to an Intramolecular Transimination[1)]

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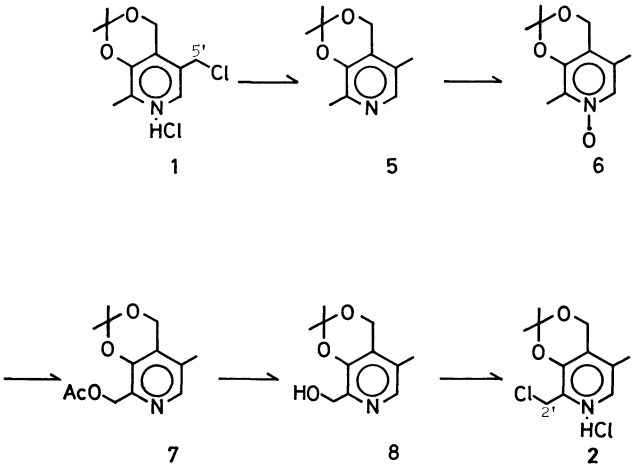
N,N'-Bis(*p*-tolylsulfonyl)-α,ω-alkanediamine disodium salts (n=3, 4, 5, 6, 7, 8, 9, 10) were subjected to monopyridylmethylation by the reaction with 5'-deoxy-5'-chloro- or 5'-deoxy-2'-chloro-3,4'-*O*-isopropylidenepyridoxine hydrochloride, accompanied by the corresponding bispyridylmethylation. Monopyridylmethylation became remarkable for longer methylene chains of the diamine. Thus, introduction of an amino group protected by a sulfonyl group at the end of either the C_2- or the C_5-side chains of pyridoxine derivatives was achieved.

Catalysis of coenzyme pyridoxal phosphate in the enzyme system has been belived to be initiated through transimination of the coenzyme originally bound to an ε-amino group of a lysine residue of the enzyme to the amino group of a substrate amino acid.[2)] The transimination of the coenzyme provides several orders faster rate acceleration of the coenzyme catalysis in the enzymic reaction, compared with the catalysis of the direct imine formation of the coenzyme with a substrate.[3)] The biologically inherent properties of the coenzyme process have become kinetically well understood[3)] and the essential part of the chemical process has been successfully applied to a solution of synthetic problem in several cases.[4)] The present work was started, expecting that if a suitable three-dimensional disposition of a primary amino group were introduced into pyridoxal molecule, then the catalytic potency would be remarkably increased through intramolecular transimination. In this context, Fisher and Metzler studied a cyclic imine derivative of pyridoxal,[5)] demonstrating that the imine is catalytically inactive, due to the formation of the stable six-membered ring; its electronic absorption spectrum is strikingly similar to those of pyridoxal phosphate-containing enzymes.

The development of a general method for the synthesis of diaza(2,5)pyridinophanes[6)] by the reaction of dichloropyridoxine derivative with *N,N'*-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine disodium salts (**4**) encouraged us to examine systematically the possibility of the molecular construction of a "intramolecular transimination model" system by the use of 2'- or 5'-position of pyridoxal where the substituent is dispensable for catalysis in the nonenzymic system.[7)] The coupling method was expected to be equally applicable to the reaction of a monochloropyridoxine derivative with the alkanediamine disodium salt, even though the reaction will be accompanied by complete alkylation on two nucleophilic sites of the disodium salt. Therefore, the syntheses of 5'-deoxy-5'-chloro- and 5'-deoxy-2'-chloro-3,4'-*O*-isopropylidenepyridoxine, **1** and **2** respectively, were first examined; these were then subjected to a coupling reaction with **4**.

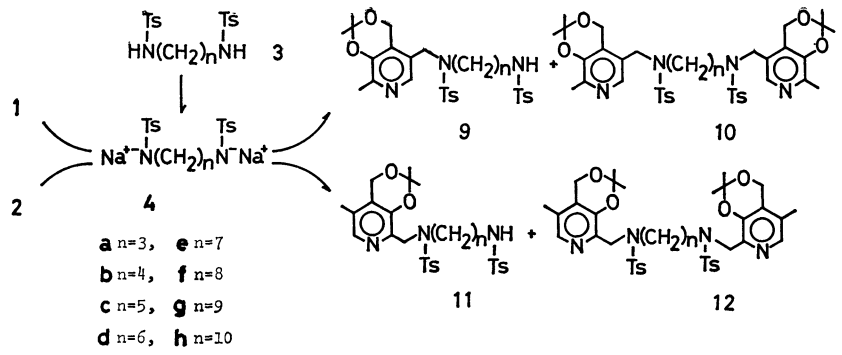
Results and Discussion

5'-Deoxy-5'-chloro-3,4'-*O*-isopropylidenepyridoxine hydrochloride (**1**) was synthesized by the known method[8)] from pyridoxine hydrochloride. For the synthesis of 5'-deoxy-2'-chloro-3,4'-*O*-isopropylidenepyridoxine hydrochloride (**2**), **1** was used as a starting material; neutralization of **1** followed by catalytic hydrogenation afforded 5'-deoxy-3,4'-*O*-isopropylidenepyridoxine (**5**) (92% yield). This was then oxidized to 5'-deoxy-3,4'-*O*-isopropylidenepyridoxine 1-oxide (**6**) with *m*-chloroperbenzoic acid (87% yield). The *N*-oxide was converted to 5'-deoxy-2'-acetoxy-3,4'-*O*-isopropylidenepyridoxine (**7**) in acetic anhydride–chloroform in 91% yield. Treatment of **7** with sodium methoxide afforded 5'-deoxy-2'-hydroxy-3,4'-*O*-isopropylidenepyridoxine (**8**) in 90% yield. This was subjected to chlorination with thionyl chloride to give **2** in 95% yield (Scheme 1).



Scheme 1.

Utilizing a newly developed method,[6)] normalized reaction conditions were set up for the coupling reaction of monochloropyridoxine derivative hydrochloride with **4**, using *N,N'*-bis(*p*-tolylsulfonyl)-1,6-hexanediamine disodium salt (**4d**) as a representative counterpart; to a stirred suspension of **4d** in *N,N*-dimethylformaminde (DMF), which was prepared by the reaction of **3d** with sodium ethoxide, a solution of **1** or **2** in DMF[9)] was added dropwise (Scheme 2). Two products were detected on TLC; these were chromatographed to give *N*-[2,2,8-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-5-ylmethyl]-*N,N'*-bis(*p*-tolylsulfonyl)-1,6-hexanediamine (**9d**) and *N,N'*-bis[2,2,8-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-5-ylmethyl]-*N,N'*-bis(*p*-tolylsulfonyl)-1,6-hexanediamine (**10d**), when **1** was used. On the other hand, when **2** was used, detected and isolated products were *N*-[2,2,5-trimethyl-4*H*-[1,3]-dioxino[4,5-*c*]pyridin-8-ylmethyl]-*N,N'*-bis(*p*-tolylsul-



Scheme 2.

Table 1. Reaction of 5′-deoxy-5′-chloro-3,4′-*O*-isopropylidenepyridoxine hydrochloride (**1**) with *N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine disodium salt (**4**) in equivalent molar ratio

4	*n*	Product yield/%			Ratio **9**/**10**
		9	**10**	Total	
a	3	33	30	63	1.1
b	4	39	30	69	1.3
c	5	49	28	77	1.8
d	6	39	27	66	1.4
e	7	43	27	70	1.6
f	8	44	18	62	2.4
g	9	48	17	65	2.8
h	10	44	18	62	2.4

Table 2. Reaction of 5′-deoxy-2′-chloro-3,4′-*O*-isopropylidenepyridoxine hydrochloride (**2**) with *N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine disodium salt (**4**) in equivalent molar ratio

4	*n*	Product yield/%			Ratio **11**/**12**
		11	**12**	Total	
a	3	41	22	63	1.9
b	4	36	20	56	1.8
c	5	36	20	56	1.8
d	6	41	18	59	2.3
e	7	46	19	65	2.4
f	8	35	12	47	2.9
g	9	51	13	64	3.9
h	10	51	15	66	3.4

fonyl)-1,6-hexanediamine (**11d**) and *N*,*N*′-bis[2,2,5-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-8-ylmethyl]-*N*,*N*′-bis(*p*-tolylsulfonyl)-1,6-hexanediamine (**12d**). All other series of reactions were carried out as similarly as possible to those of **4d**. The results obtained are summarized in Tables 1 and 2. They demonstrate several features of the pyridylmethylation reaction; total yield of products lies in the range from 62 to 72% for **1**, and from 47 to 60% for **2**. It is quite interesting, however, to note that the ratio of the yield of **9** to that of **10** clearly increases as the methylene chain becomes longer (Table 1). A similar trend is obvious for the ratio of the yield of **11** to that of **12** as well (Table 2).

Table 3. ^{1}H NMR spectra of pyridoxine derivatives **6**, **7**, and **8**[a]

	R	X	$H^{2'}$	$H^{4'}$	$H^{5'}$	H^{6}	$C(\underline{CH}_3)_2$
6	H	O	2.40	4.74	2.11	7.82	1.59
7	OAc	—	5.18	4.74	2.14	7.97	1.58
8	OH	—	4.71	4.79	2.18	7.97	1.60

a) Chemical shift in δ, in $CDCl_3$.

The ratio was not linearly correlated with the methylene chain length. The qualitative change in the ratios is interpreted as follows: in the shorter methylene chains (n=3—5), one pyridylmethyl group bound to one end of the diamine brings another pyridylmethyl group toward the other end of the diamine through an inductive effect such as stacking between the two aromatic rings. When the methylene chain becomes longer (more than seven), it is difficult for such an inductive effect to occur and, thus, the reaction favors monopyridylmethylation over bispyridylmethylation. Decreases in yields of **10** or **12** compared to increases in those of **9** or **11** without reduction in total yield as the chain length becomes longer, support the interpretation as well. Furthermore, a comparison of both ratios suggests that such a definite interactive distance between the aromatic rings will be longer in 5′-chloro derivatives (**1**) than in 2′-chloro derivatives (**2**) at the reactive points, probably due to spatial substituent interaction. In other words, monopyridylmethylation is more likely to occur in 2′-chloro derivatives (**2**) than in 5′-chloro derivatives (**1**).

^{1}H NMR spectral data are summarized in Table 3 for **6**, **7**, and **8**, Fig. 1 for **9** and **10**, and Fig. 2 for **11** and **12**, in which chemical shifts are correlated with the chain length. Although it is difficult to distinguish the effects of intermolecular and/or intramolecular interactions on the chemical shift changes, certain features are noteworthy. In general, it is seen that proton chemical shifts move to lower field as the methylene chain becomes longer. A linear correlation is apparent for C_6–$\underline{H}$, pyr–$^{4'}C\underline{H}_2$–O, pyr–$^{5'}C\underline{H}_2$–N, and $C(C\underline{H}_3)_2$ in **9**, and for pyr–$^{5'}C\underline{H}_2$–N, $C_6\underline{H}$, pyr–$^{4'}C\underline{H}_2$–O, ^{5}C–N–$C\underline{H}_2$–C, and $C(C\underline{H}_3)_2$ in **10**

in the order of the slope magnitude, respectively, in contrast to nonlinear correlation of –NHTs, $^{5'}C$–N–CH_2–C (triplet), and HN–CH_2–C (quartet) in **9**, and the other –CH_2– in **9** and **10**. A constant chemical shift is shown for C_2–CH_3 and –$SO_2C_6H_4$–CH_3 in both **9** and **10**. As for **11** and **12**, no proton chemical shift in **11** is linearly correlated with the chain length except for the constant signals of C_5–CH_3 and –$SO_2C_6H_4$–CH_3, although pyr–$^{2'}CH_2$–N, C_6–H, $C(CH_3)_2$, and pyr–$^{4'}CH_2$–O in **12** have a linear correlation in the order of slope magnitude.

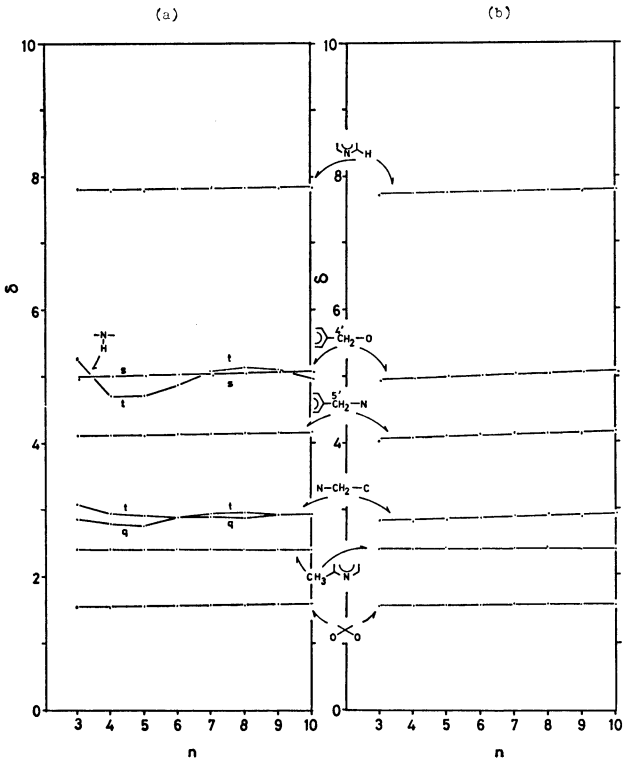


Fig. 1. Correlation of chemical shifts with the methylene chain length in ^1H NMR spectra of (a) **9** and (b) **10**, in $CDCl_3$.

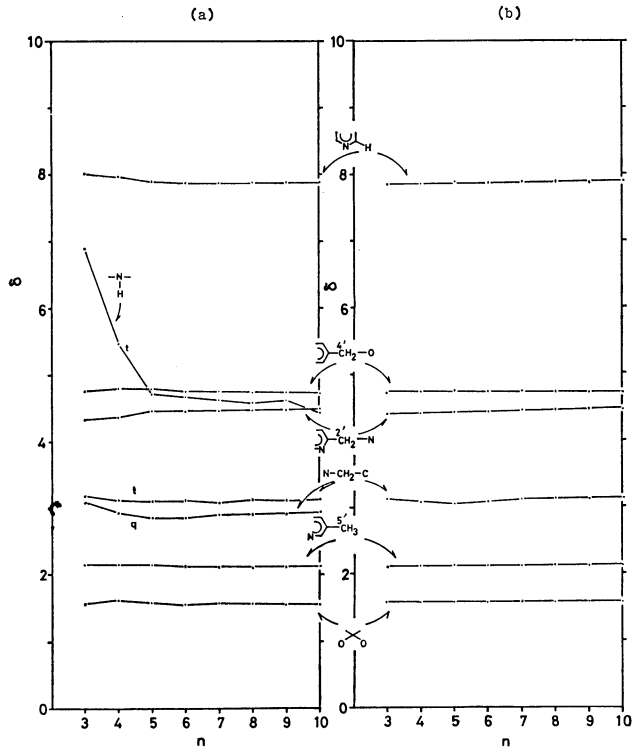


Fig. 2. Correlation of chemical shifts with the methylene chain length in ^1H NMR spectra of (a) **11** and (b) **12**, in $CDCl_3$.

The drastic chemical shift change for amino proton (triplet) and methylene protons (quartet) contiguous to the amino proton in both **9** and **11** suggests that intermolecular and/or intramolecular interaction is involved in the molecule through N–H···N or N–H···O hydrogen-bonding. It is very significant that the change becomes rather little when the methylene chain becomes longer than around six.

Experimental

The ^1H NMR spectra were recorded on a Varian HA-100D apparatus, with TMS as the internal standard in chloroform-*d*; the chemical shift and coupling constant are presented in ppm and Hz, respectively. Merck silica gel 60 (Art. 7734, 0.063—0.20 mm) was used for the column chromatography and Wakogel B-5 FM (Wako pure and Chem. Co., Ltd.) for the thin layer chromatography (TLC), in which products were visualized in an iodine-vapor bath. DMF was dried over molecular sieve (type-4A) and the supernatant was used directly for the reaction. The uncorrected mp were measured in a bilayered cover glass (18 m/m) with a micro melting point apparatus (Yanagimoto Seisakusho, serial No. 2647). For column chromatography and TLC analysis, benzene–ethyl acetate (3:2 v/v) (solvent A) was used as an eluent. 5′-Deoxy-5′-chloro-3,4′-*O*-isopropylidenepyridoxine hydrochloride (**1**) was prepared by a known method[8] from pyridoxine hydrochloride.

*Preparation of 5′-Deoxy-3,4′-*O*-isopropylidenepyridoxine 1-Oxide (**6**).* To 10.21 g (0.053 mol) of 5′-deoxy-3,4′-*O*-isopropylidenepyridoxine (**5**), which was prepared by the known method[8] from pyridoxine hydrochloride, in 150 ml of chloroform, 10.94 g (1.2 mol equiv. as 85% purity) of *m*-chloroperbenzoic acid was added at ambient temperature. After the mixture was stirred for *ca.* 3 h, it was neutralized with 2.55 g of sodium hydroxide and then extracted with chloroform. The extract was washed with water, dried over $MgSO_4$, and then evaporated to dryness to give a colorless powder; this was recryst. from acetone–diisopropyl ether to afford 9.67 g of **6** (87% yield); mp 157—158 °C. Found: C, 63.07; H, 7.27; N, 6.69%. Calcd for $C_{11}H_{15}O_3N$: C, 63.14, H, 7.23; N, 6.69%.

*Preparation of 5′-Deoxy-2′-acetoxy-3,4′-*O*-isopropylidenepyridoxine (**7**).* The mixture of 9.67 g of **6** in 20 ml of acetic anhydride and 30 ml of chloroform was refluxed for 2 h in an oil-bath. Solvents were evaporated under reduced pressure and the residue was chromatographed on a silica gel (250 g) column eluted with solvent A to give 10.58 g of **7** (91% yield) as a viscous liquid; R_f 0.43 (solvent A). Found: C, 61.97; H, 6.70; N, 5.50%. Calcd for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.82; N, 5.57%.

*Preparation of 5′-Deoxy-2′-hydroxy-3,4′-*O*-isopropylidenepyridoxine (**8**).* To sodium methoxide in 200 ml of methanol, prepared by addition of 0.97 g of metal sodium, 10.08 g of **7** in 50 ml of methanol was added dropwise and the mixture was stirred for 1 h at ambient temperature; the reaction was completed instantly, monitored on TLC (R_f 0.3 (solvent

A)). The mixture was neutralized with the occasional addition of pieces of solid carbon dioxide, and then evaporated to dryness. The residue was triturated several times with chloroform and filtered through Celite (No. 545). The filtrate was evaporated to dryness and the residue was recrystallized from benzene (minor)–hexane (major) to give 7.51 g of **8** (89% yield), as colorless crystals; mp 125—126 °C. Found: C, 63.22; H, 7.16; N, 6.62%. Calcd for $C_{11}H_{15}O_3N$: C, 63.14; H, 7.23; N, 6.69%. IR (KBr disk): *ν* 3180, 2990, 1600, 1570, 1450, 1405, 1387, 1377, 1350, 1292, 1280, 1270, 1252, 1196, 1140, 1050, 935, 855, 770, 732, 670, and 570 cm^{-1} as relatively strong characteristic bands.

Preparation of 5′-Deoxy-2′-chloro-3,4′-O-isopropylidenepyridoxine Hydrochloride (2). To a stirred suspension of 2 g of **8** in 40 ml of benzene, 0.7 ml (1 mol equiv.) of thionyl chloride in 10 ml of benzene was added dropwise at ambient temperature, resulting in an immediate clear solution and then in a precipitate. The precipitation was promoted by addition of 50 ml of dry diethyl ether. The colorless precipitate was collected by filtration, washed several times with dry diethyl ether, and then recryst. from acetone to give 2.39 g of **2** (95% yield) as colorless crystals; mp 140 °C (starts to become brown) and at 148 °C (darkening). Found: C, 50.13; H, 5.68; N, 5.36; Cl, 26.30%. Calcd for $C_{11}H_{15}O_2NCl_2$: C, 50.01; H, 5.72; N, 5.30; Cl, 26.85%. IR (KBr disk): *ν* 3060, 3010, 2970, 2320, 2025, 1552, 1480, 1465, 1445, 1420, 1385, 1370, 1310, 1278, 1260, 1204, 1125, 1078, 1060, 867, 831, 770, 651, 582, and 560 cm^{-1} as relatively strong characteristic bands.

Preparation of N,N′-*Bis(*p-*tolylsulfonyl)-α,ω-alkanediamines (3) (n=3, 4, 5, 6, 7, 8, 9, 10).* To a α,ω-alkanediamine in pyridine, three molar equivalents of *p*-toluenesulfonyl chloride were added and the mixture was stirred at 80—90 °C for 0.5—1 h. The mixture was poured into water; after cooling, a precipitate resulted. This was collected by filtration and recryst. from ethanol. All the elemental analyses for C, H, N, and S (omitted) were coincident with those calculated. Mp 134—136 °C (**3a**), 125—126 °C (**3b**), 137—138 °C (**3c**), 155—156 °C (**3d**), 144.5—145.5 °C (**3e**), 151—152 °C (**3f**), 93.5—94 °C (**3g**), and 128—129 °C (**3h**).

Preparation of N,N′-*Bis(*p-*tolylsulfonyl)-α,ω-alkanediamine Disodium Salts (4) (n=3, 4, 5, 6, 7, 8, 9, 10) and Its Reaction with 1 and 2.* To a stirred sodium ethoxide solution, prepared by addition of three gram-atom equivalents of metal sodium to ethanol (*e.g.*, 30 ml), one molar equivalent of **3** (*e.g.*, 0.5 g) was added. The mixture was refluxed for 1 h, followed by complete evaporation of ethanol under reduced pressure. DMF (*e.g.*, 50 ml) was readded to the resulting powder (**4**); to this a solution[9] of one molar equivalent of **1** or **2** in DMF (*e.g.*, 15 ml) was added dropwise with stirring at around 90 °C over the period of 2—3 h. After cooling, the brown mixture was poured into water (*e.g.*, 700 ml). Precipitation was promoted by addition of sodium chloride (*e.g.*, 10 g) (salting out effect). The precipitate was collected by filtration. Thus, by silica gel chromatography of the precipitate eluted with solvent A, the following were isolated: *N*-[2,2,8-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-5-ylmethyl]-*N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine (**9**) and *N*,*N*′-bis[2,2,8-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-5-ylmethyl]-*N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine (**10**) prepared from **1**, or *N*-[2,2,5-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-8-ylmethyl]-*N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine (**11**) and *N*,*N*′-bis[2,2,5-trimethyl-4*H*-[1,3]dioxino[4,5-*c*]pyridin-8-ylmethyl]-*N*,*N*′-bis(*p*-tolylsulfonyl)-α,ω-alkanediamine (**12**) prepared from **2**.

All elemental analyses are tabulated in Table 4 for **9**, Table 5 for **10**, and Table 6 for **11** and **12**. ^1H NMR spec-

Table 4. Elemental analyses of **9**

	State	Calcd(%)				Found(%)			
		C	H	N	S	C	H	N	S
9a	am[a]	58.61	6.15	7.32	11.18	59.20	6.24	7.51	10.90
9b	liq[b]	59.26	6.35	7.15	10.91	59.27	6.45	6.96	10.85
9c	liq	59.87	6.53	6.98	10.66	59.81	6.45	6.91	10.51
9d	am	60.46	6.71	6.82	10.41	60.35	6.74	6.62	10.45
9e	am	61.02	6.88	6.67	10.18	60.98	6.92	6.62	10.10
9f	am	61.56	7.05	6.53	9.96	61.38	6.91	6.48	10.15
9g	am	62.07	7.20	6.39	9.75	62.23	7.27	6.29	9.74
9h	liq	62.56	7.35	6.25	9.54	62.36	7.13	6.19	9.65

a) Amorphous powder. b) Liquid.

Table 5. Elemental analyses of **10**

	State	Calcd(%)				Found(%)			
		C	H	N	S	C	H	N	S
10a	liq[a]	61.23	6.33	7.33	8.38	60.70	6.21	7.21	8.36
10b	am[b]	61.67	6.47	7.19	8.23	61.40	6.33	7.23	8.10
10c	c)	62.10	6.61	7.07	8.09	62.76	6.67	7.34	7.88
10d	d)	62.50	6.74	6.94	7·95	62.10	6.69	6.67	7.97
10e	am	62.90	6.88	6.82	7.81	62.75	6.94	6.90	7.70
10f	am	63.28	7.00	6.71	7.68	63.41	7.10	6.82	7.52
10g	am	63.65	7.12	6.60	7.55	63.41	7.25	6.41	7.60
10h	e)	64.01	7.24	6.49	7.43	64.09	7.30	6.15	7.50

a) Liquid. b) Amorphous powder. c) Mp 161—162 °C. d) Mp 217—218.5 °C. e) Mp 169—171 °C.

Table 6. Elemental analyses of **11** and **12**

	11a[a], Found (%)				**12**[b], Found (%)				
	State	C	H	N	S	State	C	H	N	S
a	c)	58.55	6.17	7.32	11.18	liq	60.93	6.38	7.10	8.23
b	liq[d]	58.93	6.39	6.97	10.95	liq	61.32	6.49	7.07	8.02
c	liq	59.77	6.60	6.74	10.70	am[e]	61.89	6.66	6.79	8.01
d	liq	60.05	6.72	6.56	10.28	liq	62.31	6.82	6.68	7.90
e	liq	61.03	6.95	6.55	10.20	liq	63.40	7.02	6.42	7.71
f	liq	61.46	7.10	6.40	9.78	liq	63.15	7.07	6.49	7.60
g	liq	62.07	7.23	6.32	9.72	liq	63.59	7.12	6.52	7.71
h	liq	62.30	7.33	6.10	9.58	liq	63.81	7.30	6.35	7.21

a) Calcd % values correspond to those for **9** in Table 4. b) Calcd % values correspond to those for **10** in Table 5. c) Mp 135—136 °C. d) Liquid. e) Amorphous powder.

tral data are illustrated in Figs. 1 and 2. IR, as common relatively strong bands through **9a** to **9h**, 3280, 2930, 1600, 1570, 1410, 1390, 1378, 1330, 1160, 1090, 1064, 860, 813, 655, and 548 cm^{-1}; as common relatively strong bands through **10a** to **10h**, 2930, 1600, 1570, 1450, 1407, 1385, 1372, 1340, 1159, 856, 653, 568, and 545 cm^{-1}; as common relatively strong bands through **11a** to **11h**, 3270, 2990, 2930, 2850, 1600, 1570, 1450, 1400, 1375, 1330, 1290, 1153, 858, 810, and 650 cm^{-1}; as common relatively strong bands through **12a** to **12h**, 2990, 2940, 2850, 1600, 1570, 1450, 1405, 1385, 1375, 1335, 1292, 1152, 1065, 855, 810, 710, 650, and 540 cm^{-1}.

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References

1) Partly reported at the 44th National Meeting of the Chemical Society of Japan, Okayama, October 1981, Abstr. No. 2H27.

2) E. E. Snell and W. T. Jenkins, *J. Cell. Comp. Physiol.*, **54**, *Suppl.*, **1**, 161 (1959); A. E. Braunstein, "The Enzymes," 3rd ed, ed by P. D. Boyer, Academic Press, New York and London (1973), Vol. 9, p. 379.

3) E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 826 (1962); *Biochemistry*, **1**, 773 (1962); T. C. Bruice and R. M. Topping, *J. Am. Chem. Soc.*, **85**, 1493 (1963); T. C. French, D. S. Auld, and T. C. Bruice, *Biochemistry*, **4**, 77 (1965).

4) G. E. P. Smith, Jr., and F. W. Bergstrom, *J. Am. Chem. Soc.*, **56**, 2095 (1934); T. I. Crowell and D. W. Peck, *ibid.*, **75**, 1075 (1953); C. Schroeder, S. Preis, and K. P. Link, *Tetrahedron Lett.*, **1960**, 23; M, Iwata, *Bull. Chem. Soc. Jpn.*, **54**, 2835 (1981).

5) T. L. Fisher and D. E. Metzler, *J. Am. Chem. Soc.*, **91**, 5323 (1969).

6) M. Iwata and H. Kuzuhara, *Chem. Lett.*, **1981**, 1749.

7) For example, dithia(2,5)pyridinophane models for pyridoxal revealed comparable catalytic potency to that of pyridoxal in a nonenzymic system; M. Iwata and H. Kuzuhara, *Chem. Lett.*, **1981**, 5.

8) W. Korytnyk and M. Ikawa, "Methods in Enzymology," ed by D. B. McCormick and L. D. Wright, Academic Press, New York and London (1970), Vol. 18A, p. 524.

9) **2** is more soluble into DMF than **1**.