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CATALYTIC POTENCY OF FUNCTIONALIZED (2,5)PYRIDINOPHANES AS NEW PYRIDOXAL MODEL COMPOUNDS

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Catalytic activities of new model compounds, 1a-c, 2, and 3, for the racemization of monosodium L-glutamate were shown to be more potent, ca. 1.5 fold, than that of pyridoxal, and catalyst, 1a, was stable enough to show no decomposition throughout the reaction.

Although there have been reported many model compounds for pyridoxals, embodying partial modification of the molecule or employing their functional analogues, no model compound showed superior catalytic potency to the natural coenzyme under enzymic and non-enzymic conditions, irrespectively. We would like to report alternative new model compounds, 1 through 3,[1] with extreme stability and high efficiency, in the measure of racemization reaction for monosodium L-glutamate.

Synthesis and properties of functionalized (2,5)pyridinophanes, 1 through 3, have been partly reported elsewhere.[2] Catalytic reaction was carried out as follows, after preparation of buffer,[3] amino acid,[3] and catalyst solutions.

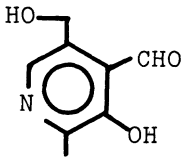
Catalyst solution: 0.5 mmol of a catalyst was dissolved into ca. 50 ml of 0.03 M borate buffer[3] and pH value was readjusted to be 10.0 by adding 2 M-NaOH. Then the mixture was adjusted to be 100 ml by addition of ethanol.

Racemization reaction: in a thermostated water bath at 25 ± 0.5 °C, 2 ml of the amino acid solution[3] and 5 ml of the catalyst solution, withdrawn from each stock solution, were mixed in a test tube equipped with a glass stopper on the top and sealed. Every 8 h, the tube was opened and 5 ml of 6 M-HCl solution was poured at once through a pipet to terminate the racemization reaction. After alleviating the temperature in the bath, the reaction solution, green colored, was transferred to a standard cell for optical rotation (α_t) measurement at 589 nm (sodium D-line). Then 2 ml of the aliquot was diluted with water to be 50 ml and the uv-vis spectrum of the solution was recorded in the range of 210-450 nm in order to estimate decomposition ratio of a catalyst during the reaction, based on optical density change of characteristic absorption maxima. The reaction was continued till racemization yield, calculated by an equation $100(\alpha_0 - \alpha_t)/\alpha_0$, becomes 56-84%. The apparent rate constant (k_{obs}) was calculated by an equation $2.30(\log \alpha_0 - \log \alpha_t)/60t$, provided that the reaction obeys the first-order kinetics.

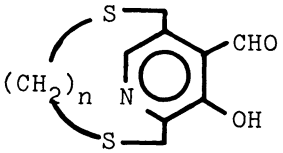
The results obtained are summarized in Table 1, involving pyridoxal itself for comparison, which clearly reveal that 1a is the first model compound, known to date, with superior properties to pyridoxal with respect to catalytic activity (1.5 fold) and to stability (no decomposition), despite of a highly strained molecule. Structurally, 2 is also highly strained, but less reactive than pyridoxal and outstandingly

Table 1. Racemization Potency of Pyridinophanes and Related Compounds for Monosodium L-Glutamate pH 10.0 at 25 ± 0.5 °C

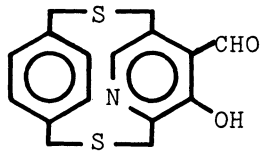
Catalyst	Reaction time, h	Final racemiztn yield, %	50% completn of racemiztn, h	$k_{obs} \times 10^4$, min^{-1}	Catalyst decomp. % (at λ_{max})
pyridoxal	188	84	55	2.09	6.6 (288)
1a	88	80	36	3.19	0 (325)
1b	96	65	37	3.13	14 (307)
1c	188	83	40	2.93	8 (305)
2	96	56	78	1.48	42 (243)
3	96	78	32	3.58	12 (305)



pyridoxal



1a (n=4)
b (n=6)
c (n=8)



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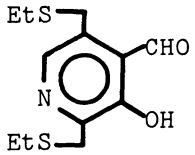

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labile. It is of interest to note that less or unstrained compounds, 1b, 1c, and 3, are yet more active than pyridoxal with compatible decomposition ratios.

In conclusion, present results suggest (a) that the replacement of the C-5' hydroxy group of pyridoxal by an aprotic substituent, preferably an electron donating group, may accelerate the nonenzymic catalytic reaction, (b) that the π-donor-acceptor relationship between the bridged chain and the pyridine ring may decrease the catalytic activity, and (c) that the ring torsion itself of the electron sink will have no effect on rate enhancement.

References and Note

1) Denotation of the compounds is as follows: 1a-c, (n+9)-hydroxy-(n+10)-formyl-2,(n+3)-dithia[m](2,5)pyridinophane [1a (n=4), 1b (n=6), 1c (n=8); m=n+4], 2, 17-hydroxy-18-formyl-2,11-dithia[3]paracyclo[3](2,5)pyridinophane, and 3, 5'-deoxy-2',5'-di(ethylthio)pyridoxal.

2)(a) M. Iwata, H. Kuzuhara, and S. Emoto, Chem. Lett., 1976, 983. (b) H. Kuzuhara, M. Iwata, and S. Emoto, J. Am. Chem. Soc., 99, 4173 (1977).

3) 0.03 M-Borate buffer (pH 10.0): 5.73 g (15 mmol) of sodium borate·10 H_2O was dissolved into 300 ml of water. A part (60 ml) of the solution was taken out to be pH 10.0 by adding ca. 35 ml of 0.1 M-NaOH solution and allowed to stand overnight. Then pH value was readjusted to be 10.0 by adding 0.1 M-NaOH solution to become 100 ml. Amino acid solution (pH 10.0): 18.7 g (0.1 mol) of monosodium L-glutamate and 0.5 g (2 mmol) of cupric sulfate·$5H_2O$ were mixed in small amount of water, followed by addition of 2 M-NaOH solution to be pH 10, and allowed to stand overnight. Then total volume of the solution was adjusted to be 100 ml by addition of water and 2 M-NaOH, readjusting pH to be 10.0.

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