Synthesis of Vertical-type Bis(pyridodipyrimidines) as a Redox Catalyst and Their Autorecycling Oxidation of Alcohols

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Condensation of bis(3-methyluracil-6-ylamino)alkanes with 6-chloro-5-formyl-3-methyluracil or 2,4,6-trichloropyrimidine-5-carbaldehyde in acetic acid gave the respective bis(pyridodipyrimidin-10-yl)alkanes (vertical-type bis(pyridodipyrimidines)). The vertical-type bis(pyridodipyrimidines) exhibited autorecycling turnover oxidation toward cyclopentanol and *l*-menthol to give the corresponding carbonyl compounds.

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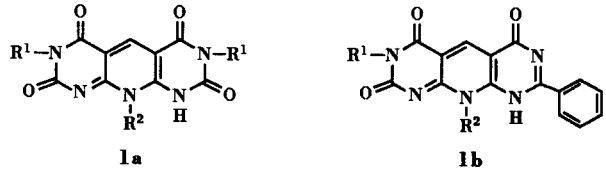
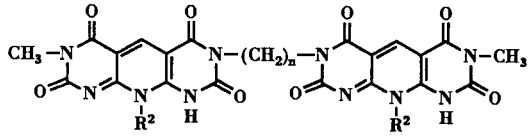
Pyridodipyrimidines **1** as a new NAD-type redox catalyst have been found to exhibit autorecycling oxidation toward alcohols under neutral conditions to yield the corresponding carbonyl compounds [1]. Furthermore the horizontal-type bis(pyridodipyrimidines) (bis-PP) **4** oxidized alcohols more efficiently than the corresponding monomeric pyridodipyrimidines **1** [2] (Scheme 1). This result could suggest that one pyridodipyrimidine moiety in the bis-PP accepts electrons to give the reduced-type pyridodipyrimidine moiety which would immediately form the intramolecular charge-transfer complex or radical pair with the other pyridodipyrimidine moiety. The formation of the intramolecular charge-transfer complex or radical pair seems to heighten the reactivity for alcohol oxidation

Scheme 1

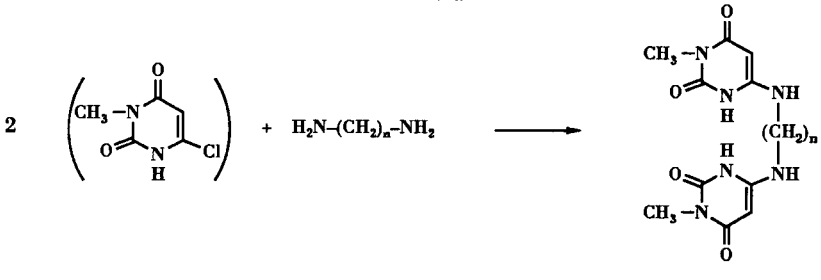


1a **1b**

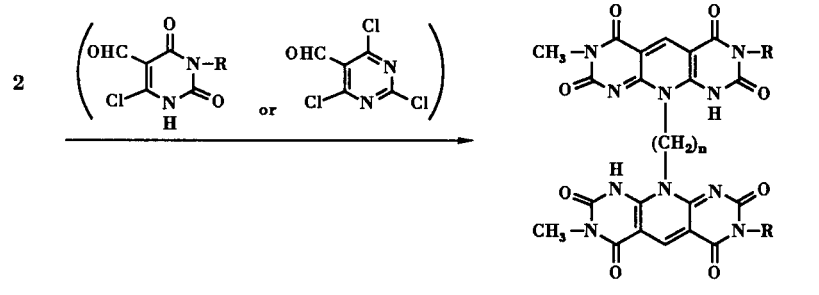


Horizontal-type Bis(pyridodipyrimidine) (4)

Scheme 2



2a (n = 6)
2b (n = 10)
2c (n = 12)



Vertical-type Bis(pyridodipyrimidine)

3a-e

Table 1

Synthesis of Bis(pyridodipyrimidine-10-yl)alkanes (Vertical-type Bis-PP's) **3a-e**

Compound No.	n	R	Mp (°C)	Yield (%)	Formula	Analysis (%) Calcd. C	H	N	Found C	H	N	δ_H (Trifluoroacetic acid) C_5–H and C_5–H
3b	6	CH_3	>350	60	$C_{28}H_{28}N_{10}O_8$	53.16	4.46	22.14	52.82	4.72	22.24	9.62 (2H, s)
3b	10	CH_3	>350	42	$C_{32}H_{36}N_{10}O_8$	55.81	5.27	20.34	55.74	5.62	20.05	9.72 (2H, s)
3c	12	CH_3	345	19	$C_{34}H_{40}N_{10}O_8$	56.98	5.63	19.54	56.73	5.86	19.29	9.72 (2H, s)
3d	10	H	253	42	$C_{30}H_{32}N_{10}O_8$	54.54	4.88	21.20	54.72	4.92	21.47	9.72 (2H, s)
3e	12	H	143	63	$C_{32}H_{36}N_{10}O_8$	55.81	5.27	20.34	55.55	5.49	20.10	9.68 (2H, s)

and the sensitivity to oxygen in the turnover oxidation.

In this context, we describe here the synthesis of a series of the vertical-type bis(pyridodipyrimidines) **3** as another bis-PP's and their autorecycling turnover oxidation of alcohols.

Synthesis of Vertical-type Bis(pyridodipyrimidines) **3**.

The vertical-type bis-PP's **3** can be synthesized from bis(3-methyluracil-6-ylamino)alkanes **2**. The treatment of 6-chloro-3-methyluracil with α-ω-diaminoalkanes in boiling 1-butanol gave the corresponding bis(3-methyluracil-6-ylamino)alkanes **2** [3], which were condensed with 6-chloro-5-formyl-3-methyluracil [4] or 2,4,6-trichloropyrimidine-5-carbaldehyde [5] in acetic acid or DMF to obtain the respective bis(pyridodipyrimidine-10-yl)alkanes (vertical-type bis-PP's) **3**.

Oxidation of Alcohols with the Vertical-type Bis-PP's **3**.

The vertical-type bis-PP's **3a-e** oxidized cyclopentanol more efficiently than the corresponding monomeric PP's (Table 2). The table shows the relationship between the length of 10,10′-chain and the reactivity in the autorecycling oxidation. Decane (n = 10) has turned out to be the best among the 10,10′-chains in the oxidation of cyclopentanol. The enhanced reactivity of the bis-PP's **3** may be accounted for by acceleration of their intramolecular electron interactions. This explanation may be supported by the result that the redox potentials of **3** (-370 ~ -380 mV in DMF/$LiClO_4$ *vs.* Ag/AgCl electrode) are 250 mV or more positive than those of monomeric PP's (-620 ~ -940 mV in DMF/$LiClO_4$ *vs.* Ag/AgCl electrode). It means that the intramolecular conjugation between the PP moieties of **3** lowered the energy levels of their LUMO's.

Table 2

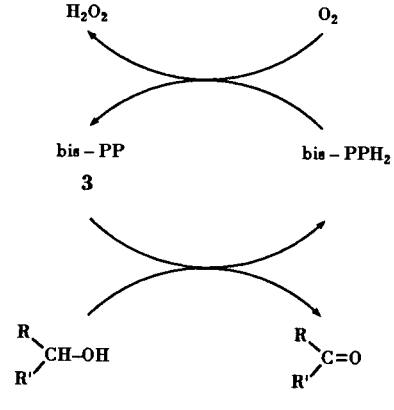
Autorecycling Oxidation of Cyclopentanol (3 ml) and *l*-Menthol (3 g) by Bis(pyridodipyrimidine-10-yl)alkanes **3** (15 mg) at 120° for 25 hours

Compound No.	R	n	Yield (%) of products Cyclopentanone	*l*-Menthone
3a	CH_3	6	18503 [a] (13.3) [b]	trace
3b	CH_3	10	36604 (24.1)	9886 [a] (11.2) [b]
3c	CH_3	12	14130 (8.73)	25715 (28.0)
3e	H	12	13920 (9.17)	9175 (10.4)

[a] Based on the catalyst. [b] Based on the starting alcolol.

The oxidation yields toward *l*-menthol (Table 2) changed drastically according to the length of the 10,10′-chains although the relationship between them is not clear. Furthermore, the presence of the acidic hydrogens at 7 and 7′ positions was not so efficient in the autorecycling oxidation of alcohols. So far the vertical-type bis-PP's **3** are a little less efficient than the horizontal bis-PP's **4** in the oxidation of cyclopentanol [2], in spite of the more positive redox potentials of **3** in comparison with those of **4** (-400 ~ -630 mV in DMF/$LiClO_4$ *vs.* Ag/AgCl electrode). These results may suggest that **3** oxidize alcohol rapidly with concomitant reduction of **3** to the vertical-type dihydro bis-PP's, which have less reactivity toward oxygen in comparison with that of the horizontal-type dihydro bis-PP's. Hence the dihydro bis-PP's may be oxidized more slowly to the original bis-PP's **3** by adventitious air in the autorecycling oxidation.

Scheme 3



EXPERIMENTAL

All melting points were determined on a Yanagimoto hot-stage apparatus and are uncorrected. The ^1H nmr were obtained on a JEOL JNM 3H-60 spectrometer (tetramethylsilane as internal

standard). Redox potentials were taken on a MCl model AS-02 cyclic boltammetry analyzer.

Bis(3-methyluracil-6-ylamino)alkanes (**2a-c**). General Procedure [3].

A mixture of 6-chloro-3-methyluracil (0.20 g, 1.25 mmoles) and α,ω-diaminoalkanes (1.25 mmoles) in *l*-butanol (40 ml) was refluxed for 6 hours. After the reaction, the precipitated crystals were collected by filtration and recrystallized from acetic acid to give colorless microcrystalline powder in 20-35% yields.

Bis{3,7-dimethylpyrido[2,3-*d*;6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,-7*H*,9*H*)tetrone-10-yl}alkanes (**3a-c**). General Procedure.

Compounds **2** (0.67 mmoles) and 6-chloro-5-formyl-3-methyluracil (0.236 g, 1.47 mmoles) were added to acetic acid (10 ml), and the mixture was refluxed for 3 hours. After cooling, the precipitated crystals were collected by filtration and recrystallized from DMF to give yellow microcrystalline powder (Table 1).

Bis{3-methylpyrido[2,3-*d*;6,5-*d'*]dipyrimidine-2,4,6,8(3*H*,10*H*,-7*H*,9*H*)tetrone-10-yl}alkanes (**3d,e**). General Procedure.

Compounds **2** (1.11 mmoles) and 2,4,6-trichloropyrimidine-5-carbaldehyde (0.70 g, 3.31 mmoles) were added to DMF (20 ml) and the mixture was stirred for 3 hours at room temperature. After the reaction, the precipitated crystals were collected by filtration and recrystallized from DMF to give yellow microcrystalline powder (Table 1).

General Procedure for Autorecycling Oxidation of Alcohol.

A mixture of the catalyst **3** (15 mg) in an appropriate alcohol (3 ml or 3 g) was stirred in a flask joined with an air condenser at 120° for 25 hours. The reaction mixture was analyzed by gas chromatography. Furthermore, the reaction mixture was diluted with ether and filtrated. The filtrate was treated with a 2 *N* hydrochloric acid solution of 2,4-dinitrophenylhydrazine to give the 2,4-dinitrophenylhydrazone of the corresponding carbonyl compounds, which was filtered off, dried and weighed.

REFERENCES AND NOTES

[1] F. Yoneda, H. Yamato, and M. Ono, *J. Am. Chem. Soc.*, **103**, 5947 (1981).

[2] F. Yoneda, K. Tanaka, H. Yamato, K. Moriyama, and T. Nagamatsu, *J. Am. Chem. Soc.*, **111**, 9199 (1989).

[3] T. Nagamatsu, Y. Hashiguchi, and F. Yoneda, *J. Chem. Soc., Perkin Trans. 1*, 561 (1984).

[4] F. Yoneda, Y. Sakuma, S. Mizumoto, and R. Ito. *J. Chem. Soc., Perkin Trans. 1*, 1547 (1976).

[5] F. Yoneda, *Methods Enzymol.*, **66**, 267 (1980).