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2,4-Dimethyl-5-hydroxymethylpyrimidine (1)

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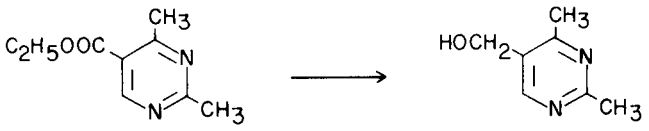
Sir:

We have synthesized 2,4-dimethyl-5-hydroxymethylpyrimidine. Preliminary studies have indicated that it is an effective pyridoxine antagonist.



This compound was most conveniently synthesized by reduction of 2,4-dimethyl-5-carbethoxypyrimidine (2) with lithium aluminum hydride at -70°. Satisfactory analytical data have been obtained from a sample which was recrystallized from high boiling ligroin and which melted at 59.5-61.0°.

2,4-Dimethyl-5-hydroxymethylpyrimidine produced lethal convulsions in Ha/ICR Swiss mice within two hours of intraperitoneal injection of doses as low as three milligrams per kilogram. The seizures were prevented by pyridoxine given simultaneously in equivalent doses to those of 2,4-dimethyl-5-hydroxymethylpyrimidine. The reversal was found to be competitive over the nine-fold range tested (3 to 27 mg./kg.). The seizure prevention was thus dependent upon a pharmacologic and not a catalytic (vitamin) role of pyridoxine.

Details of experimental procedures and further biological studies will be reported.

REFERENCES

(1) This investigation was supported by Public Health Service Grant No. CA-02857 from the National Cancer Institute.

(2) R. Urban and O. Schnider, *Helv. Chim. Acta*, **41**, 1806 (1958).

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