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Note

3-(*p*-Aminophenethyl)-5-methyl-oxazolidine-2,4-dione

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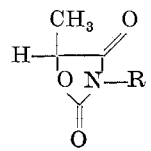
The enhancement of analgesic activity obtained with 4-pyridylethyl or *p*-aminophenethyl substituents replacing the *N*-methyl group of meperidine[1] and the noted tranquillizing activity of (Ia)[2] have suggested exploration of (Ib) as a central nervous



(I)

(Ia); R = 4-pyridylethyl-
(Ib); R = *p*-$NH_2C_6H_4CH_2CH_2$-

system (CNS) depressant. This compound is also structurally related to α-(*p*-aminophenyl)-α-ethylglutarimide recently described as an anticonvulsant.[3]

The synthesis was effected from *N*-(*p*-aminophenethyl)amine, ethyl lactate and diethyl carbonate under alkoxide catalysis.[4] In addition, *N*-(*p*-aminophenethyl)-lactamide (II) was prepared.

Methods

N-(p-*Aminophenethyl*)-*lactamide* (II). A mixture of ethyl lactate (8·5 g, 0·022 mole) and *p*-aminophenethylamine (10·0 g, 0·074 mole) was heated under reflux for 15 min with vigorous exothermic reaction. When cool, 3·8 ml (90 per cent) of the theoretical ethanol was separated and the gummy residue distilled to yield the product (6·3 g, 42 per cent), b.p. 218–220°/0·08 mm; bath 265–270°.

Anal. Calcd. for $C_{11}H_{16}N_2O_2$: N, 13·5. Found: N, 13·4.

3-(p-Aminophenethyl)-5-methyloxazolidine-2,4-dione (Ib). A mixture of *p*-aminophenethylamine (8·65 g, 0·064 mole), ethyl lactate (7·5 g, 0·064 mole) and diethyl carbonate (28 ml, excess) was treated successively with catalyst (0·1 g sodium in 2 ml of ethanol), refluxed for 1 h and the alcohol which formed was removed. After this process had been repeated four times, the theoretical quantity of ethanol was obtained. After filtration, the reaction mixture was distilled and the product (1·6 g, 11 per cent) was obtained, b.p. 176–182°/0·08 mm; bath 280°. The product solidified on standing, and upon recrystallization (ethyl acetate–hexane), melted at 135–140°.

Anal. Calcd. for $C_{12}H_{14}N_2O_3$: N, 12·0. Found: N, 12·1.

The pharmacological procedures employed have been previously described.[4]

Results

Evaluation of (Ib) (LD_{min} = 750 mg/kg) indicated absence of hypnotic or anticonvulsant activity at 350 mg/kg, no depression in motor activity at 100 mg/kg, and a 283 per cent increase in hexethal sleeping time when evaluated at 50 mg/kg. Neither hypnotic nor anticonvulsant activity was demonstrable with (II) (LD_{min} = > 1000 mg/kg) at 350 mg/kg, but a 400 per cent increase in hexethal sleeping time was noted at 300 mg/kg.

The principal activity was potentiation of CNS depression of other compounds, in the absence of CNS depression with either (Ib) or (II) when tested *per se*.

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