LETTERS TO THE EDITOR

Synthesis and Anticonvulsant Activity of some *N*-phenethylacetamides

SIR,—We would like to report the synthesis of α-chloro-*N*-phenethyl-, α-chloro-*N*-*m*-chlorophenethyl-, α-chloro-*N*-*p*-chlorophenethyl-, α-chloro-*N*-*o*-methoxyphenethyl- and α-chloro-*N*-*p*-methoxyphenethyl-acetamide. These were prepared by us as intermediates for the synthesis of *N*-aminoalkylphenethylamines. However, the unexpected discovery of significant anticonvulsant activity in two of these chloroacetamides has prompted us to make this preliminary communication.

Chloroacetyl chloride (0·11 M) was added slowly to a cooled and well-stirred suspension of the desired phenethylamine (0·10 M) in 10 per cent aqueous sodium hydroxide solution (200 ml.). Stirring was continued for 2 hr. and the solid which separated was triturated with hydrochloric acid (1 :1), washed with water and recrystallised from aqueous ethanol.

(I) α-Chloro-*N*-phenethylacetamide m.p. 70–71° (Child and Pyman, 1931). (II) α-Chloro-*N*-*m*-chlorophenethylacetamide m.p. 66°, found C, 51·62; H, 4·70; N 6·12 per cent. (III) α-Chloro-*N*-*p*-chlorophenethylacetamide m.p. 91°, found C, 51·74; H, 4·71; N, 5·80 per cent; (II) and (III) $C_{10}H_{11}Cl_2NO$ require C, 51·72; H, 4·74; N, 6·03 per cent. (IV) α-Chloro-*N*-*o*-methoxyphenethylacetamide m.p. 84°, found C, 57·87; H, 6·22; N, 6·25 per cent; (V) α-chloro-*N*-*p*-methoxyphenethylacetamide m.p. 102°; found C, 57·94; H, 6·45; N, 6·4 per cent; (IV) and (V) $C_{11}H_{14}Cl\,NO_2$ require C, 58·02; H, 6·14; N, 6·15 per cent.

These compounds, administered orally in suspension in 10 per cent gum acacia, were screened for their anticonvulsant activity in albino rats given maximal electroshock seizures from corneal electrodes dipped in normal saline (Goodman, Brown and Swinyard, 1952). α-Chloro-*N*-phenethylacetamide (I) was the most active and its anticonvulsant activity was, therefore, compared to phenobarbitone, phenytoin sodium and troxidone. The ED 50 of these compounds administered orally was found to be 5 mg./kg. for α-chloro-*N*-phenethylacetamide, phenobarbitone and phenytoin sodium and 100 mg./kg. for troxidone. The percentage of protection against electroshock seizures in rats by oral doses of 5, 10 and 15 mg./kg. of the acetamide was 64, 80 and 96. The corresponding figures for phenobarbitone were 48, 76, 96; for phenytoin sodium 52, 64, 76; for troxidone 52, 64 and 72. The Peak Effect was found to be 4, 3, 4 and 2 hr. respectively.

Thus compound I appears to be as potent as phenobarbitone against electroshock seizures in rats, while α-chloro-*N*-*m*-chlorophenethylacetamide (II) was found to be about two-thirds as potent as (I). The other three compounds reported showed no significant anticonvulsant activity. None of these compounds afforded protection against leptazol induced seizures.

The pharmacological screening described here has been carried out at the Pharmacology Department of the Osmania Medical College, Hyderabad, and we record out thanks to Prof. M. Y. Ansari and Dr. P. Pentiah for this.

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