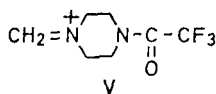
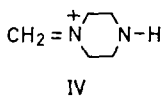
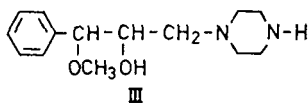
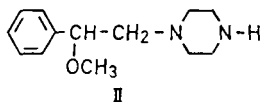
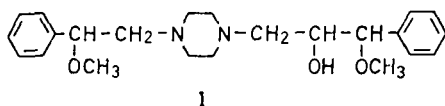


## LETTERS TO THE EDITOR

## A note on the metabolism of Respilene in man

A. H. BECKETT\*, R. ACHARI, *Department of Pharmacy, Chelsea College, University of London, Manresa Road, London, SW3 6LX, U.K.*

After oral doses of Respilene (I), a new antitussive agent, in man, the ethereal extract of basic (pH 12–13) urine revealed five products on t.l.c. (silica gel; benzene–diethylamine–methanol 80:10:10) in addition to the parent drug ( $R_f$  0.66). Spots corresponding to the main products II ( $R_f$  0.32) and III ( $R_f$  0.24) were scraped off the plate, extracted with ether, and the concentrated extract was examined by g.l.c. and g.l.c.-mass spectrometry along with the synthetic reference compounds.



All compounds were chromatographed on a Perkin-Elmer Model F.11 gas chromatograph. Columns were 1 m in length and of 3 mm i.d. glass tubing. Hydrogen

and air pressures were 140 and 175 kNm<sup>-2</sup>, respectively. Injection port temperature was 30° above column.

G.l.c. on column A (0.2% Carbowax 20 M on 60–80 mesh glass beads; nitrogen, 0.95 cm<sup>3</sup> s<sup>-1</sup>) gave peaks corresponding to compound II (Rt 6.9 min, 135°) and compound III (Rt 6.6 min, 175°), respectively. G.l.c. as trifluoroacetyl (TFA) derivatives on column B (3% OV 17 on 80–100 mesh Chromosorb G; nitrogen, 0.61 cm<sup>3</sup> s<sup>-1</sup>) gave peaks corresponding to the TFA derivatives of compound II (Rt 9.7 min, 185°) and compound III (Rt 12.1 min, 185°), respectively.

G.l.c. mass spectrometry of compound II and its TFA derivative gave the base peak at  $m/e$  99 (IV) and  $m/e$  195 (V), respectively, while the TFA derivative gave the molecular ion at  $m/e$  316. Compound III showed the molecular ion at  $m/e$  250 and the base peak at  $m/e$  99 (IV); the base peak for the TFA derivative occurred at  $m/e$  195 (V).

T.l.c. of the ethereal extract of neutral urine did not show any phenolic product when the plates were sprayed with ferric chloride solution and diazotized sulphanic acid. *N*-Oxide was not present in the urine, since the urine after extraction of Respilene and treatment with TiCl<sub>3</sub>/HCl did not give any parent amine (Rt 10.6 min, 220°), when examined by g.l.c. analysis on column C (3% XE 60 on 80–100 mesh Chromosorb G; nitrogen, 1.25 cm<sup>3</sup> s<sup>-1</sup>). The presence of the conjugates of Respilene and compounds II and III could not be demonstrated since the urine (post extraction of Respilene and compounds II and III) after enzymatic ( $\beta$ -glucuronidase-sulphatase) and acid hydrolysis did not give any of the above compounds.

We thank CERM (Riom), France, for supplying the compounds I, II, III and Dr J. F. Harper of Advisory Services (Clinical & General) Ltd. for organizing the study. R.A. also thanks Chelsea College for a studentship.

November 22, 1976

\*Correspondence.