REFERENCES

BECKETT, A. H., SHELLARD, E. J., PHILLIPSON, J. D. & LEE, C. M. (1966). *Planta Medica*, **14**, 266–276.

SHELLARD, E. J. & SARPONG, K. (1969). *J. Pharm. Pharmac.*, **21**, *Suppl.*, 113S–117S.

'Metabolism' of 'amphetamines' to oximes as a route to deamination

Recently, a preliminary report of the metabolism of amphetamine to benzylmethyl ketoxime (isomer not specified) appeared (Hucker, Michniewicz & Rhodes, 1970). We have found that after injection of the (+) or (−)-isomers or the racemates of amphetamine, methylamphetamine and ethylamphetamine to rabbits or guinea-pigs, *syn* and *anti*-benzylmethylketoximes are present in urine in free and conjugated forms. The metabolic conversion of the parent drugs to oxime and the stereoisomeric composition of the oxime varied with the species and with the enantiomorphs administered; in general, the *anti*-isomer predominated. In some instances, more combined oxime isomers than unchanged drug were excreted, indicating the importance of the metabolic route.

The identity and the stereoisomeric content of the oxime mixture from metabolism was established by comparison with authentic samples by mass spectrometry, polarography, nuclear magnetic resonance, t.l.c. and g.l.c. using several columns, e.g. 5% Carbowax 20 M on Chromasorb W 3 m; 140°; gas 40 ml/min *anti* 25 min, *syn* 27 min (ref *p*-chloropropiophenone 8 min): 8% Apiezon L plus 4% Carbowax 20 M on Chromosorb G, 1 m; 130°; gas 25 ml/min *anti* 34 min, *syn* 36 min (ref 16 min): 3% Carbowax 20 M on Chromosorb G 1 m; 180°; gas 30 ml/min *anti* and *syn* 6 min (ref 2·5 min).

In t.l.c. the *syn*-oxime hydrolysed to benzylmethyl ketone more rapidly than did the *anti*-isomer. In aqueous solution at pH 1, the oxime isomers were rapidly hydrolysed to benzylmethyl ketone but little hydrolysis occurred at alkaline pH values. Thus, in metabolic studies, the amount of oxime converted to ketone and its stereoisomeric content will depend upon the pH of the urine, storage time, procedures used to isolate the isomers and the method of analysis. This instability of oxime in solution may account for the fact that despite many reports of the identification of benzylmethyl ketone as a metabolite of 'amphetamines', Hucker & others (1970) were the first to record the metabolism of amphetamine to benzylmethyl ketoxime.

The 'metabolism' of 'amphetamines' to oximes which are relatively unstable in weakly acidic solutions to yield benzylmethyl ketone constitutes a route to the deamination of 'amphetamines' (cf. Hucker & others for (+)-amphetamine).

We were unable to find norephedrine recently reported (Caldwell, Dring & Williams, 1971) in urine after normal doses of methylamphetamine to guinea-pigs.

Department of Pharmacy,
Chelsea College (University of London),
London, S.W.3, U.K.
May 4, 1971

A. H. BECKETT
J. M. VAN DYK
H. M. CHISSICK
J. W. GORROD

REFERENCES

CALDWELL, J., DRING, L. G. & WILLIAMS, R. T. (1971). *Proc. biochem. Soc.*, 13.

HUCKER, H. B., MICHNIEWICZ, B. M. & RHODES, R. E. (1970). *Pharmacologist*, **12**, 255.