the urine but as a precursor (X). The rat, mouse, guinea pig and rhesus monkey did not excrete X or the ketone after being dosed with the drug. In the rabbit, as much as 22% of the dose of amphetamine (10mg./kg.) was excreted as precursor or precursors of the ketone, whereas man excreted only 2-3% and the dog 1%.

The nature of precursor X has been further elucidated. ($\pm$) Amphetamine (225mg.) was given to three rabbits over 3 days. The urine was mixed with urine from a rabbit receiving the ^{14}C -labelled drug. Precursor X was separated from the freeze-dried urine by thin-layer chromatography as a pale-yellow solid (20mg.) containing sulphur but practically no nitrogen. On acid hydrolysis it gave benzyl methyl ketone (DNP-hydrazone, m.p. and mixed m.p. 152-153°) and inorganic sulphate. Precursor X was also detected chromatographically in the urine of rabbits receiving [^{14}C]benzyl methyl ketone (1-phenyl[1- ^{14}C]propan-2-one). When $^{35}\text{SO}_4^{2-}$ was given with non-radioactive benzyl methyl ketone, the precursor X located on chromatograms contained ^{35}S . Hydrolysis of precursor X from the urine yielded benzyl methyl ketone (as DNP-hydrazone) and [^{35}S]sulphate (as $\text{Ba}^{35}\text{SO}_4$).

Gero (1954) reported that benzyl methyl ketone occurs normally in the enol form to the extent of 2.9%. We suggest that precursor X is probably a salt of the sulphate ester of 1-phenylprop-1-en-2-ol, the enol of the ketone, i.e. $\text{C}_6\text{H}_5\cdot\text{CH}:\text{C}(\text{O}\cdot\text{SO}_3^-)\cdot\text{CH}_3$. This structure was supported by nuclear-magnetic-resonance and u.v. spectra.

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Dring, L. G., Smith, R. L. & Williams, R. T. (1966). *J. Pharm., Lond.*, **18**, 402.

Gero, A. (1954). *J. org. Chem.* **19**, 1960.

expired air and a small amount (about 0.5% of the dose) in faeces. About 40% of the dose was detected in urine as two mercapturic acids, believed to be thienyl 3- and 2-mercapturic acids. No increase in the excretion of glucuronic acid or ethereal sulphate was observed and no evidence of the opening of the ring to form diethyl sulphide, as Christomanos (1930) suggested might occur in the dog, was obtained.

Chilcote (1945) suggested that 2-bromothiophen is metabolized by the rabbit in the same way as is thiophen. In the present investigation, no increase in ethereal sulphate or glucuronic acid was detected and only about 20% of a dose of 2-bromothiophen (120mg./kg.) could be accounted for as mercapturic acid-like compounds in urine. One of these acids is believed to be thienyl 2-mercapturic acid.

Böhm (1941) reported the isolation of a metabolite, believed to be benzothiophenyl 2-glucuronide, from the urine of rabbits to which benzo[b]thiophen had been administered, but we were unable to detect an increase in the excretion of either ethereal sulphates or glucuronic acid by the rabbit dosed with benzo[b]thiophen (175mg./kg.). About 80% of the dose appeared in the urine as mercapturic acid-like compounds, four of which could be separated by paper and thin-layer chromatography. One of these has been identified tentatively as benzothiophenyl 3-mercapturic acid.

A method for the synthesis of thienyl and benzothiophenyl mercapturic acids from 2-amino-3-chloropropionic acid hydrochloride and the appropriate mercaptothiophen will be described.

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Böhm, F. (1951). *Hoppe-Seyl. Z.* **269**, 17.

Chilcote, M. E. (1945). *University Microfilm, Ann Arbor, Mich.*, **6**, no. 1, 15.

Christomanos, A. A. (1930). *Biochem. Z.* **229**, 248.

Heffter, A. (1886). *Pflüg. Arch. ges. Physiol.* **39**, 420.

The Metabolism of Thiophen and Benzo[b]-thiophen

By H. G. BRAY and F. M. B. CARPANINI (*Department of Physiological Chemistry, University of Birmingham*)

In studies of the metabolic fate of thiophen Heffter (1886), Christomanos (1930) and Chilcote (1945) did not report the identification of any metabolite, although their results suggested that no ethereal sulphate was formed and that the chief metabolite might be a mercapturic acid.

We found that the rabbit excreted about 35% of a dose of thiophen (150mg./kg.) unchanged in

The Metabolism of Cyclohexylamine in Rabbits

By T. H. ELLIOTT, N. Y. LEE-YOONG and ROSALINE C. C. TAO (*School of Pharmacy, University of Singapore*)

Bernhard (1937) reported that cyclohexylamine fed to dogs disappears completely. However, in view of the widespread use of sodium cyclamate as a sweetener, and the report by Ohashi (1964) that in the presence of acid and hydrogen peroxide it is hydrolysed to cyclohexylamine, it is of some importance to know the precise metabolic fate of cyclohexylamine.