as an aerosol propellant. The toxicity of CCl_4 is believed to be a function of its metabolism (McLean & McLean, 1966), possibly as a result of the formation of a free radical (Butler, 1961; Slater, 1966). Similarly, the low toxicity of CCl_3F has been attributed to its inertness due to the stabilizing effect of the fluorine atom on the C-Cl bond (Slater, 1965; Clayton, 1966).

Distribution studies show that after a single dose of CCl_3F to Wistar rats a total of 97% of the dose is expired unchanged within 6h, whereas CCl_4 is excreted more slowly, only 75% being expired unchanged in 18h (Paul & Rubinstein, 1963). Possible metabolites of CCl_3F are dichlorofluoromethane (CHCl_2F) and tetrachlorodifluoroethane ($\text{C}_2\text{Cl}_4\text{F}_2$), which could be formed by reductive dehalogenation, via the production of a free radical. No dichlorofluoromethane was detected (<0.2% of substrate) in extracts of incubations of CCl_3F with microsomal preparations from rat and chicken, or from rat, mouse, guinea-pig and hamster pretreated with phenobarbital (100mg/kg body wt. daily for 3 days). The effect of CCl_3F on lipid peroxidation was investigated as an index of the formation of free radicals. Using the production of thiobarbituric acid-positive materials as a measure of lipid peroxidation, we found no evidence of free-radical formation from CCl_3F in rats and mice even after pretreatment of the animals with phenobarbital to stimulate any potential metabolism, but as reported by Slater & Sawyer (1971) CCl_4 did produce large increases of thiobarbituric acid-positive material.

However, CCl_3F is not completely inert biologically and has been shown to exhibit characteristic binding spectra with hepatic microsomal preparations, giving a type I spectrum, as does CCl_4 , with a similar K_s value (for CCl_4 , 1.1mM; for CCl_3F , 2.3mM). This binding constant (K_s) has been closely associated with the Michaelis constant for the affinity of compounds for the drug-metabolizing enzyme cytochrome *P*-450 (Schenkman *et al.*, 1967; Degkwitz *et al.*, 1969). Thus, although there is no evidence of significant metabolism of CCl_3F , it has been shown to interact with hepatic cytochrome *P*-450, which is believed to be concerned with the metabolic dechlorination of CCl_4 (McLean & McLean, 1966).

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The Metabolism of (+)- and (-)-Amphetamine and (+)- and (-)-Dimethylamphetamine in Rabbits *in vivo*

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After the intraperitoneal administration of either (+)- or (-)-amphetamine to male New Zealand white rabbits, the following compounds were detected in ethereal extracts of pooled urine: amphetamine, benzyl methyl ketone, α -methyl- β -phenylethanol, α -methyl- β -phenylethylhydroxylamine and *syn*- and *anti*-phenylacetone oximes. The urine was adjusted to pH 7.4 before exhaustive extraction.

When the aqueous phase was made alkaline (pH 12-13) further ether extraction gave α -methyl- β -phenylethylhydroxylamine and the above oximes, indicating the presence in urine of the hydroxylamine and the oximes in conjugated form.

When (+)- or (-)-dimethylamphetamine was administered as above, the following compounds were identified in addition to those derived from (+)- or (-)-amphetamine: dimethylamphetamine, dimethylamphetamine *N*-oxide, methylamphetamine and *N*-methyl- α -methyl- β -phenylethylhydroxylamine.

The urinary excretion products of amphetamine were determined as already reported (Beckett & Al-Sarraj, 1972). Dimethylamphetamine *N*-oxide was characterized by t.l.c. and by reduction to dimethylamphetamine with TiCl_2 (cf. Beckett *et al.*, 1971a). The presence of the *N*-methylhydroxylamine was demonstrated by comparison with authentic material (A. H. Beckett, J. W. Gorrod & H. N. Chissick, unpublished work) on g.l.c., t.l.c. and alkaline treatment to give the above *syn*- and *anti*-phenylacetone oximes in constant ratio.

Only the *N*-oxide and the two hydroxylamines detected result from direct metabolic oxidation; the other compounds are metabonates (Beckett *et al.*, 1971b) arising from chemical breakdown of metabolites or further enzymic attack on the chemical breakdown products.

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