

Preparation and Gas Chromatography of Steroid Chloromethyldimethylsilyl Ethers

By B. S. THOMAS

(Division of Chemistry and Biochemistry, Imperial Cancer Research Fund, London)

and C. EABORN and D. R. M. WALTON

(The Chemical Laboratory, University of Sussex, Brighton)

GAS-LIQUID chromatography of trimethylsilyl ethers is extensively used in the analysis of natural products, and is, for example, of great value in the identification and determination of steroids in biological fluids.¹ In view of the special sensitivity of electron-capture detectors towards organic halides, it is likely that halogenoalkylsilyl ethers will sometimes have marked advantages over trimethylsilyl ethers, and so we have prepared and examined, as simple models, some chloromethyl-dimethylsilyl ethers of steroids.

We find that steroids react with (chloromethyl-dimethylsilyl)diethylamine in the presence of chloromethyldimethylchlorosilane to give crystalline chloromethyldimethylsilyl ethers in quantitative yield. These ethers are stable under conditions of thin-layer chromatography on silica gel and of gas-liquid chromatography, and can be

TABLE. Retention time*

	Steroid	Me ₃ Si	ClCH ₂ ·Me ₂ Si
(a)	Androsterone	0·9	3·05
	Aetiocholanolone	1·06	3·54
	Dehydroepiandrosterone	1·25	4·35
(b)	Testosterone	0·66	1·55
	Epitesterone	0·57	1·31
	Dehydroepiandrosterone	—	1·03

* Relative to Cholestane = 1·00

separated from one another and from the corresponding trimethylsilyl ethers by gas-liquid chromatography. A Pye Panchromatograph with argon ionization detector was used, with an argon flow of 45 ml./min., and either (a), a 5 ft. column of 1% XE60 on Gaschrome Z (100—120 mesh) at 200°, or (b) a 3 ft. column of 3% JXR on Gas-

chrome Q (80—100 mesh) at 200°, and the retention times were as shown in the Table. The retention times are considerably shorter than those of the steroid monochloroacetates, which have been used in analysis.²

Preliminary studies show that electron-capture detectors respond satisfactorily to the chlorine-containing ethers.

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¹ M. A. Kirschner and M. B. Lipsett, *J. Clin. Endocrinol.*, 1963, **23**, 255; T. Luukkainen, W. J. A. vandenHeuvel, E. A. O. Haahti, and E. C. Horning, *Biochem. Biophys. Acta.*, 1961, **52**, 599; W. J. A. vandenHeuvel, B. G. Creech, and E. C. Horning, *Analyt. Biochem.*, 1962, **4**, 191.

² H. J. van der Molen and D. Croen, "Gas Chromatography of Steroids and Biological Fluids," ed. Lipsett, Plenum Press, New York, 1965.