positive bromine were used, each isomer gave predominantly one product. *trans*-4-Methylcyclohexylmercuric bromide was cleaved with bromine in pyridine in air to yield pure *trans*-4-methylcyclohexyl bromide, b.p. 57.0° (9.5 mm.), m.p. 25.5–26.0°, $n^{29.9}\text{D}$ 1.4800, which had a strong characteristic equatorial C–Br infrared band at 704 cm.$^{-1}$. Similarly, *cis*-4-methylcyclohexylmercuric bromide yielded pure *cis*-4-methylcyclohexyl bromide, b.p. 57.0–57.8° (9.5 mm.), $n^{29.9}\text{D}$ 1.4843, which had a strong characteristic axial C–Br infrared band at 685 cm.$^{-1}$. The assignment of structure was made on the basis of the known stretching frequencies for equatorial and axial C-Br linkages,[4] and the physical properties of the isomeric bromides. Within the sensitivity of our methods for detecting each isomer (less than 2%), the reactions in pyridine are quantitatively stereospecific.

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(4) D. H. R. Barton, J. E. Page, and C. W. Shopee, *J. Chem. Soc.*, 331 (1956).

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FLUORINATED STEROIDS. I. THE SYNTHESIS OF 2α-FLUOROHYDROCORTISONE

Sir:

The introduction of fluorine into the 6α-,[1] 9α-[2] and 12α-[3] positions of the hydrocortisone structure has resulted in dramatic increases in the glucocorticoid activity of this hormone.[4] It was, therefore, of considerable interest to prepare and test 2α-fluorohydrocortisone (I). Reaction of the sodium salt of 20-ethylenedioxy-2-methoxalyl-11β,17α,21-trihydroxy-4-pregnen-3,20-dione[5] with perchloryl fluoride[6,7] in methanol, followed by base catalyzed cleavage of the methoxalyl group afforded 20-ethylenedioxy-2α-fluoro-11β,17α,21-trihydroxy-4-pregnen-3,20-dione (II), m.p. 224–226°, $[\alpha]^{25}\text{D} + 132°$ (c, 0.63 in $CHCl_3$); $\lambda_{\max}^{\text{MeOH}}$ 242 mμ (ϵ, 14,000); $\lambda_{\max}^{\text{KBr}}$ 5.87 μ (3-keto-Δ^4). *Anal.* Found: C, 64.87; H, 8.45; F, 4.43. Hydrolysis with 8% aqueous sulfuric acid in methanol gave I with m.p. 216–220°, $[\alpha]^{25}\text{D} + 190°$ (c, 0.76 in MeOH); $\lambda_{\max}^{\text{MeOH}}$ 241 mμ (ϵ, 14,800); $\lambda_{\max}^{CHCl_3}$ 5.90 μ (3-keto-Δ^4,20-keto). *Anal.* Found: C, 66.02; H, 7.82; F, 5.00. The α-configuration of the fluorine in I and II is assumed from spectral evidence, on the basis that a fluorine atom at C-2 would have effects on the infrared and ultraviolet absorption spectra similar to those exhibited by chlorine and bromine atoms at this position.[8] The apparent formation of the α-epimer is interesting since, in comparison with bromo, chloro and methyl substituents, the probability of steric interaction of a 2β-fluorine with the angular methyl group at C_{10} is at a minimum and the probability of electrostatic repulsion between a 2α-fluorine and the 3-keto group is at a maximum.[9]

In contrast to the activity of the above-mentioned fluorohydrocortisone derivatives, the activity of I is undistinguished, being approximately one-third that of hydrocortisone as measured by the liver glycogen, thymus involution and asbestos pellet granuloma inhibition tests in adrenalectomized rats.[10] This relatively low activity of I stands in contrast to the high activity of 6α-fluorohydrocortisone[1] and is interesting when one considers the high activity of both the 2α-methyl[11] and 6α-methylhydrocortisone derivatives.[12]

We have prepared other 2-fluoro steroids by this procedure and have studied the utility of perchloryl fluoride for the introduction of fluorine at other sites in the steroid molecule. These results will be published in the near future.

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(1) (a) A. Bowers and H. J. Ringold, THIS JOURNAL, **80**, 4423 (1958); (b) J. A. Hogg, *et al.*, *Chemistry and Industry*, 1002 (1958).

(2) J. Fried and E. F. Sabo, THIS JOURNAL, **79**, 1130 (1957).

(3) J. A. Hogg, Sixth Nat. Medicinal Chem. Symposium A. C. S., Madison, Wisconsin, June 23–25, 1958.

(4) 21-Fluoro-21-deoxyhydrocortisone is reported to be approximately one-half as active as cortisone acetate: J. E. Herz, J. Fried, P. Grabowich and E. F. Sabo, THIS JOURNAL, **78**, 4812 (1956).

(5) Australian Patent No. 23,672.

(6) We wish to thank the Pennsalt Chemicals Corporation for a generous sample of this material. Fluorination via the interaction of perchloryl fluoride with active methylene compounds has been reported: see C. E. Inman, E. A. Tyczkowski, R. E. Oesterling and F. L. Scott, *Experientia*, **14**, 355 (1958); C. E. Inman, R. E. Oesterling and E. A. Tyczkowski, THIS JOURNAL, **80**, 6533 (1958).

(7) Recently, Gabbard and Jensen [*J. Org. Chem.*, **23**, 1406 (1958)] reported the synthesis of 2α-fluorocholestanone by the reaction of perchloryl fluoride with cholestan-3-one pyrrolidyl enamine.

(8) (a) R. N. Jones, D. A. Ramsey, F. Herling and K. Dobriner, THIS JOURNAL, **74**, 2828 (1952); (b) B. Ellis and V. Petrow, *J. Chem. Soc.*, 1179 (1956).

(9) See E. J. Corey [THIS JOURNAL, **76**, 175 (1954)] for a discussion of the factors determining the relative stability of epimeric α-bromo ketones in the steroid field.

(10) We wish to thank L. Bortle, E. Heyder, A. Monteforte, E. Ross and I. Ringler of the Experimental Therapeutics Research Section of these Laboratories for these assays.

(11) J. A. Hogg, F. H. Lincoln, R. W. Jackson and W. P. Schneider, THIS JOURNAL, **77**, 6401 (1955).

(12) G. B. Spero, *et al.*, *ibid.*, **78**, 6213 (1956).

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ELECTROPHILIC ALIPHATIC SUBSTITUTION. II. RESOLUTION AND STEREOCHEMICAL STUDIES OF *sec*-BUTYLMERCURY COMPOUNDS[1]

Sir:

We wish to report the preparation of optically pure *sec*-butylmercuric bromides, the assignment of configuration to the enantiomorphs, and preliminary results of our stereochemical studies with these isomers.[2,3]

The assignment of configuration and maximum rotation to *sec*-butylmercuric bromide permits a broad investigation of the stereochemistry and stereospecificity of the reactions of *sec*-butylmer-

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(1) This research was supported in part by a grant from the Research Corporation.

(2) The resolution of *sec*-butylmercuric bromide recently has been reported in a communication by H. B. Charman, E. D. Hughes and C. K. Ingold, *Chem. and Ind.*, 1517 (1958). The reactions reported by us were mostly completed prior to the submission of the above communication.

(3) Several organomercury compounds containing more than one optical center have been resolved: L. T. Sandborn and C. S. Marvel, THIS JOURNAL, **48**, 1409 (1926); E. Griffith and C. S. Marvel, *ibid.*, **53**, 789 (1931); J. Romeyn and G. F. Wright, *ibid.*, **69**, 697 (1947); A. N. Nesmeyanov, O. A. Reutov and S. S. Poddubnaya, *Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk*, 649 (1953); and O. A. Reutov and Tsin-Chzhu Lu, *Doklady Akad. Nauk S.S.S.R.*, **110**, 575 (1956).