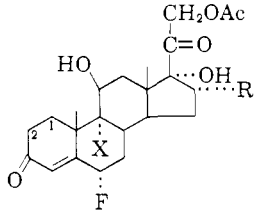
pyridine–dimethylformamide provided 6α-fluoro-16α-methyl-$\Delta^{4,9(11)}$-pregnadiene-3,20-dione-17α,21-diol 21-acetate (m.p. 188–190°, $[\alpha]D$ +74° (all rotations in $CHCl_3$), λ_{max}^{EtOH} 235, log ε 4.17; *Anal.* found for $C_{24}H_{31}O_5F$: C, 69.28, H, 7.24, F, 3.99), which was treated with N-bromoacetamide in aqueous dioxane in the presence of perchloric acid[7] and the bromohydrin cyclized directly with potassium acetate in acetone to afford 6α-fluoro-16α-methyl-9β,11β-oxido-Δ^4-pregnene-3,20-dione-17,21-diol 21-acetate (m.p. 188–191°). Opening of the epoxide with hydrogen fluoride in methylene chloride–tetrahydrofuran[8] led to 6α,9α-difluoro-16α-methylhydrocortisone acetate (II) (m.p. 255–260°, $[\alpha]D$ +113°, λ_{max}^{EtOH} 234 mμ, log ε 4.22; *Anal.* found for $C_{24}H_{32}O_6F_2$: C, 63.15; H, 6.96; F, 8.01), while oxidation of II with selenium dioxide[9] provided 6α,-



I, X = H, R = CH_3
II, X = F, R = CH_3
III, X = F, R = CH_3 with 1–2-double bond
IV, X = F, R = H
V, X = F, R = H with 1–2 double bond

9α-difluoro-16α-methylprednisolone acetate (III) (m.p. 260–264°, $[\alpha]D$ +91°, λ_{max}^{EtOH} 237 mμ, log ε 4.16; *Anal.* found for $C_{24}H_{30}O_6F_2 \cdot CH_3COCH_3$: C, 63.90, H, 7.40). This latter substance combines in one molecule four substituents (Δ^1-double bond,[10] 6α-fluorine,[1,2,3] 9α-fluorine,[7] 16α-methyl group[4,5]) known to increase individually anti-inflammatory activity.

TABLE I

Compound	Anti-inflammatory[a] activity
6α-Fluoro-16α-methylhydrocortisone acetate (I)	5[b]
6α,9α-Difluoro-16α-methylhydrocortisone acetate (II)	50[c]
6α,9α-Difluoro-16α-methylprednisolone acetate (III)	120[c]
6α,9α-Difluorohydrocortisone acetate (IV)	100[b]
6α,9α-Difluoroprednisolone acetate (V)	200[b]

[a] Assays in immature adrenalectomized rats, cotton pellet implant, hydrocortisone acetate = 1. [b] Assays by Dr. R. I. Dorfman, The Worcester Foundation for Experimental Biology; oral route. [c] Assays by the Endocrine Laboratories, Madison, Wisconsin; subcutaneous route.

Preliminary biological data covering these three substances (I, II, III) as well as 6α,9α-difluoro-hydrocortisone acetate (IV)[1,3] and 6α,9α-difluoroprednisolone acetate (V)[1,3] are summarized in the accompanying table. Pronounced sodium excretion was exhibited by I, II and III in the rat.[11]

(11) Salt assays in adrenalectomized rats without sodium chloride load, subcutaneous route. We are indebted to Dr. E. Rosemberg and Dr. R. I. Dorfman, Worcester Foundation for Experimental Biology, for these assays.

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RECEIVED MARCH 20, 1959

fully characterized and analyzed, but the data were not included for reasons of editorial policy.

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

(8) R. F. Hirschmann, R. Miller, J. Wood and R. F. Jones, *ibid.*, **78**, 4956 (1956).

(9) H. J. Ringold, G. Rosenkranz and F. Sondheimer, *J. Org. Chem.*, **21**, 239 (1956); C. Meystre, H. Frey, W. Voser and A. Wettstein, *Helv. Chim. Acta*, **39**, 734 (1956); S. A. Szpilfogel, T. A. P. Posthumus, M. S. De Winter and D. A. Van Dorp., *Rec. Trav. Chim.*, **75**, 475 (1956); K. Florey and A. R. Restivo, *J. Org. Chem.*, **22**, 406 (1957).

(10) H. L. Herzog, A. Nobile, S. Tolksdorf, W. Charney, F. B. Hershberg, P. L. Perman and M. M. Pechet, *Science*, **121**, 176 (1955).

MASS SPECTROMETRIC EVIDENCE FOR HEPTABORANE

Sir:

In mass spectrometric examination of tetraborane prepared by the method of Klein, Harrison and Solomon[1] mass number *versus* intensity patterns were found corresponding to B_6H_{10}, B_5H_9 and B_5H_{11}, B_4H_{10} and B_2H_6 with the B_4H_{10} pattern accounting for 94 to 97% of the total pressure. In addition, a new group of peaks was observed from mass numbers 77 through 89 with the principal peak at 83. In 5 of 6 samples examined there was no evidence of higher boranes up to mass number 150. In the sixth sample, a small amount of octaborane was found. The samples were obtained from three separate preparations of tetraborane.

Spectra were obtained using a Model 21–620 Consolidated Electrodynamics Corporation mass spectrometer with a modified d.c. amplifier circuit for greater sensitivity. The patterns from mass 77 through 89 for the 5 samples and the sixth with the octaborane subtracted were identical within the limits of instrument reproducibility. The height of the peak at mass 83 was over 80 recorder units read to ± 0.3 for each sample. The representative pattern obtained is shown in Fig. 1.

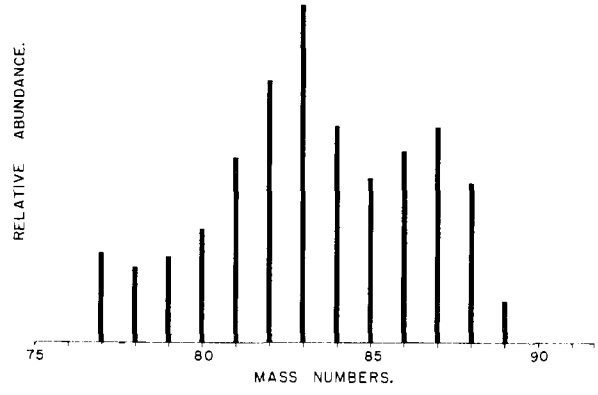

Fig. 1.

The range of mass numbers would necessitate a β_7^- compound and the sharp cutoff at mass 89 would indicate a minimum formula of B_7H_{12}. This formula does not fit either the stable B_nH_{n+4} series or the less stable B_nH_{n+6} series proposed by Wiberg.[2] The parent peak of the proposed B_7H_{13} compound from Wiberg's B_nH_{n+6} series

(1) M. J. Klein, B. C. Harrison and I. J. Solomon, THIS JOURNAL, **80**, 4149 (1958).

(2) E. Wiberg, *Ber.*, **69B**, 2816 (1936).

either may be too small in intensity to be seen or may be absent entirely. From this consideration it would seem that B_7H_{13} is a likely formula.

The possibility of a B_7 compound has been mentioned previously from mass spectral data[3] but no pattern or formula was reported because of the masking effect of higher boranes present.

After submission of this communication, our attention was called to a report of Professor Riley Schaeffer at the Boston meeting of the American Chemical Society (April 6–10, 1959) that he had evidence for a heptaborane. He reported mass peaks up to 91 with a minimum formula B_7H_{14} and, therefore, suggested that the hydride may be B_7H_{15}.

(3) R. E. Dickerson, P. J. Wheatley, P. A. Howell and W. N. Lipscomb, *J. Chem. Phys.*, **27**, 200 (1957).

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TRANSMISSION OF ELECTRONIC EFFECTS BY THE CYCLOPROPANE RING. RATES OF ALKALINE HYDROLYSIS OF SOME ETHYL *p*-SUBSTITUTED 2-PHENYLCYCLOPROPANECARBOXYLATES

Sir:

Considerable controversy exists over the ability of the cyclopropane ring to transmit conjugative effects. Spectral studies of the excited state often have indicated some "double bond character" of the three-membered ring,[1] although there is evidence that the ring does not transmit conjugative effects in certain cases.[2] Information on molecules in the ground state also is inconsistent. Dipole moment studies[3] suggest an electronic interaction of the cyclopropane ring (with an attached chlorine atom), as does the 1,6-addition of diethyl malonate anion to diethyl vinylcyclopropane-1,1-dicarboxylate.[4] In contrast is a recent evaluation of the relative transmission ability of the ethylenic unit (–CH=CH–), the saturated dimethylene group ($-CH_2CH_2-$), and the cyclopropane ring via a comparison of the ionization constants of *trans*-cinnamic acids, β-phenylpropionic acids, and *trans*-2-phenylcyclopropanecarboxylic acids.[5] Comparison of the Hammett[6] ρ value for the three series showed that the cyclopropane ring was about as good as the dimethylene group but inferior to the ethylenic group in transmitting electronic effects.

We wish to make a preliminary report of a corresponding comparison of the rates of hydrolysis of the ethyl esters in 87.8% ethanol at 30°. In this series the ethyl phenylcyclopropanecarboxylates have an intermediate ρ value (Table I) indicating that the cyclopropane ring is better than a dimethylene group but poorer than an ethylenic unit in transmitting electronic effects. This is in agreement with the dipole moment work but at variance with the data obtained from ionization constants.

In Table I the ρ values for the ionization of the acids and for the alkaline hydrolysis of the esters are compared. In Table II are the rate constants for four ethyl *trans*-2-phenylcyclopropanecarboxylates prepared from acids which have the same physical constants as those previously reported.[7]

TABLE I

COMPARISON OF REACTION CONSTANTS

Series	*p*-Ester hydrolysis	*p*-Acid ionization
trans-Cinnamic	1.329[a]	0.466[a]
trans-2-Phenylcyclopropane	0.789[b]	0.182[c]
β-Phenylpropionic	0.489[a]	0.212[a]

[a] Taken from the compilation by H. H. Jaffe, *Chem. Revs.*, **53**, 191 (1953). [b] This work. [c] Ref. 5.

TABLE II

RATES OF ALKALINE HYDROLYSIS OF ETHYL *trans*-2-(*p*-SUBSTITUTED-PHENYL)-CYCLOPROPANECARBOXYLATES IN 87.8% ETHANOL AT 30°

Substituent	$k \times 10^3$ l. mole^{-1} sec.$^{-1}$[a]	Melting point, °C.
p-NO_2	6.40	50.4–51.0
p-Cl[b]	2.37	(87.5–88.0)[c]
p-H	1.38	37.5–38.4
p-CH_3O	1.00	82.0–82.8

[a] Average of two determinations: initial (KOH) = 0.04 *M*, (RCOOEt) = 0.025 *M*; temperature, 30.00 ± 0.02°. [b] $n^{24}D$ 1.5331. [c] B p. at 0.3 mm.

Other *trans* esters and several *cis* acids and esters of this series also have been prepared. The properties and rates of hydrolysis will be the subject of a subsequent article.

(7) E. N. Trachtenberg and G. Odian, THIS JOURNAL, **80**, 4015 (1958).

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RECEIVED APRIL 4, 1959

RETRACTION OF CHOLINE METHYL GROUP BIOSYNTHESIS

Sir:

Further study of the enzyme preparation reported to synthesize methyl groups of choline from formaldehyde[1] has indicated that choline is not synthesized by this preparation. It appears that the homogenate contains both the formaldehyde dehydrogenase of Strittmatter and Ball[2] and the hydroxymethyl tetrahydrofolic acid dehydrogenase of Hatefi, *et al.*[3] Much of the radioactive formaldehyde incorporated is accounted for by these two enzyme systems. In addition there is some reaction between the formaldehyde and amino-

(1) See, for example, W. W. Robertson, J. F. Music and F. A. Matsen, THIS JOURNAL, **72**, 5260 (1950); G. W. Cannon, A. A. Santilli and P. Shenian, *ibid.*, **81**, 1660 (1959), and references therein.

(2) L. I. Smith and E. R. Rogier, *ibid.*, **73**, 3840 (1951); R. H. Eastman and S. K. Freeman, *ibid.*, **77**, 6642 (1955), and preceding papers.

(3) B. I. Spinrad, *ibid.*, **68**, 617 (1946); M. T. Rogers and J. D. Roberts, *ibid.*, **68**, 843 (1946).

(4) R. W. Kierstead, R. P. Linstead and B. C. L. Weedon, *J. Chem. Soc.*, 3616 (1952).

(5) E. N. Trachtenberg and G. Odian, THIS JOURNAL, **80**, 4018 (1958).

(6) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 186.

(1) R. Venkataraman and D. M. Greenberg, THIS JOURNAL, **80**, 2025 (1958).

(2) P. Strittmatter and E. G. Ball, *J. Biol. Chem.*, **213**, 1445 (1955).

(3) Y. Hatefi, M. J. Osborn, L. D. Kay and F. M. Huennekens, *ibid.*, **227**, 637 (1957).