l-abietic acid and 2% neoabietic acid. The observed specific rotation and the calculated specific rotation were in excellent agreement, −93 and −92°, respectively.

Isolation of Isomerization Products of Levopimaric Acid. —Five-gram samples of levopimaric acid were allowed to isomerize the desired lengths of time and the isomerization stopped by pouring the solution into water and removing the precipitated resin acids by ether extraction. The product was isolated as described above in the isomerization of *l*-abietic acid.

Analysis of Products of Isomerized Levopimaric Acid.—The specific rotation, ultraviolet absorption

analysis, levopimaric acid content and chromatographic analysis were obtained on each product isolated. A summary of these analyses and the calculated specific rotations and specific extinction coefficients is recorded in Table III. The identity of palustric, *l*-abietic and neoabietic acids was confirmed by isolation by means of large scale chromatography. Acids with specific rotations of +71.2, −104.5 and +160°, respectively, were obtained.

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COMMUNICATIONS TO THE EDITOR

THE COMPOUND Fe₃S₄ (SMYTHITE) FOUND IN NATURE

Sir:

We have found minute, plate-like crystal inclusions in calcite crystals from Bloomington, Indiana, to be a new iron sulfide, with chemical and physical properties similar to those of pyrrhotite. The crystals are opaque, have a dark bronzy color, and are strongly ferromagnetic, but they give a wholly distinct powder diffraction pattern. Insufficient material is available for quantitative chemical analysis, even by microtechniques, but an ideal formula, Fe_3S_4, is postulated on the basis of our study of the crystal structure by X-ray diffraction methods. The mineral is named smythite (pronounced smīth'ite) in honor of Professor C. H. Smyth, Jr., who was one of the earliest to recognize the occurrence of pyrrhotite in sedimentary rocks.

Microanalytical techniques by X-ray fluorescence, confirmed by qualitative microchemical tests, have shown the major metallic constituent to be iron, with a small amount of nickel also present. A satisfactory microchemical test also was obtained for sulfur. Buerger precession X-ray photographs of single crystals show that they are rhombohedral with a probable space group $R\bar{3}m$ (D_{3d}^5), and hexagonal unit cell dimensions $a_0 = 3.47$ Å., $c_0 = 34.5$. This unit cell accounts quantitatively for the powder pattern. The specific gravity as measured by flotation is 4.06 ± 0.03, in good agreement with the value 4.09 as calculated from the unit cell with contents $3Fe_3S_4$.

The formula was first arrived at through a study of the crystal structure, which shows a striking relationship to that of pyrrhotite. The similarity of dimensions (pyrrhotite is hexagonal with space group $P6_3/mmc$, $a_0 = 3.44$ Å., $c_0 = 5.68$, $6 \times c_0 = 34.1$) indicates that a similar type of structure is involved, but the rhombohedral symmetry shows that the basic pyrrhotite framework is interrupted periodically to produce layers. A structure has been evolved which gives a reasonable agreement between observed and calculated diffraction intensity. The pyrrhotite-layer structure hypothesis leads directly to the formula Fe_3S_4.

The compound Fe_3S_4 has long been postulated, usually by analogy to the minerals linnaeite (Co_3S_4,

spinel structure) and violarite ($FeNi_2S_4$, spinel structure), but its existence never has been proved. For example, Sidot[1] claimed to have prepared Fe_3S_4 by the reaction of magnetite (Fe_3O_4) with H_2S at red heat, but attempts by de Jong and Willems[2] and Fontana[3] to repeat this and other previously reported syntheses were unsuccessful. So far we have not been able to achieve synthesis of smythite by fusion or by precipitation from water solutions.

A more detailed description of the occurrence, properties, and structure of smythite will be published at a later date.

(1) Th. Sidot, *Compt. rend.*, **66**, 1257 (1868).
(2) W. F. de Jong and H. W. V. Willems. *Z. anorg. allgem. Chem.*, **161**, 311–5 (1927).
(3) C. Fontana. *Atti acad. Lincei*, [6] **5**, 579–81 (1927).

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12α-HALO DERIVATIVES OF 11β-HYDROXYPROGESTERONE

Sir:

The enhancement of adrenocorticoid activity by substitution of a halogen atom in the 9α-position of 11β-hydroxy or 11-ketopregnane derivatives was first reported from this laboratory[1] and has since been demonstrated to be of broader significance.[2] In examining available data for possible generalizations concerning the dependence of biological activity upon chemical structure one cannot fail to note the consistent parallelism between adrenocorticoid action and the electronegativity (−I effect) of the 9α-substituent.[3] Such a relationship suggested the view that enhancement in activity might be the

(1) J. Fried and E. F. Sabo, THIS JOURNAL, **75**, 2273 (1953).
(2) (a) J. Fried and E. F. Sabo, *ibid.*, **76**, 1455 (1954); (b) J. Fried, J. E. Herz, E. F. Sabo, A. Borman, F. M. Singer and P. Numerof, *ibid.*, **77**, 1068 (1955); (c) R. F. Hirschman, R. Miller, R. E. Beyler, L. H. Sarett and M. Tishler, *ibid.*, **77**, 3166 (1955); (d) J. Fried, K. Florey, E. F. Sabo, J. E. Herz, A. R. Restivo, A. Borman and F. M. Singer, *ibid.*, **77**, 4181 (1955); (e) J. Fried, *Ann. N. Y. Acad. Sci.*, **76**, 573 (1955).
(3) This relationship does not apply to halogens only but also to other substituents. *e.g.*, OH, OCH₃, OC₂H₅. A convenient numerical expression of the electro-negativity of a substituent is the pK_a of the correspondingly α-substituted acetic acid. *Cf.* C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 737.

result of an increase in the acidity constant of the important 11β-hydroxyl group (or the degree of polarization of the 11-keto group) brought about by the inductive ($-$I) effect of the neighboring 9α-substituent. Such a thesis would receive support if 12α-substituted corticoids could be shown to possess activities similar to those of their 9α-congeners. It is the purpose of the present communication to demonstrate that this is indeed true in the case of the 12α-halo-11β-hydroxyprogesterones.

11-Dehydroprogesterone[4] on treatment with N-bromoacetamide and perchloric acid in dioxane furnished 12α-bromo-11β-hydroxyprogesterone (I),[5] m. p. 220–222° (dec.); $[\alpha]^{23}$D $+128°$ (c 0.39 in CHCl₃); λ_{max}^{alc} 239 mμ (ϵ = 16,000); λ_{max}^{Nujol} 2.97, 5.96, 6.18 μ; Anal. Calcd. for $C_{21}H_{29}O_3Br$: C, 61.62; H, 7.14. Found: C, 61.99; H, 7.06. The latter on treatment with potassium acetate in alcohol yielded 11β,12β-oxidoprogesterone (II), m. p. 169–170°; $[\alpha]^{23}$D $+203°$ (c 0.81 in CHCl₃); λ_{max}^{alc} 238 mμ (16,300); λ_{max}^{Nujol} 5.90, 6.01, 6.21 μ; Anal. Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.70, H, 8.74, which with aqueous hydrochloric acid in dioxane was transformed into 12α-chloro-11β-hydroxyprogesterone (III),[6] m. p. 233–234°; $[\alpha]^{23}$D $+162°$ (c 0.60 in CHCl₃); λ_{max}^{alc} 239 mμ (17,000); λ_{max}^{Nujol} 2.98, 5.97, 6.17 μ; Anal. Calcd. for $C_{21}H_{29}O_3Cl$: C, 69.12; H, 8.01. Found: C, 69.26; H, 7.97.

Alternatively, III was prepared as follows: treatment of 12α-bromopregnane-11β-ol-3,20-dione,[5] m. p. 251–252° (dec.); $[\alpha]^{23}$D $+76°$ (c 0.37 in dioxane) with potassium carbonate in methanol yielded 11β,-12β-oxidopregnane-3,20-dione, m. p. 139–140°; $[\alpha]^{23}$D $+89°$ (c 0.38 in CHCl₃); λ_{max}^{Nujol} 5.86, 5.88 μ; Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.15; H, 8.90, which with HCl in dioxane was converted into 12α-chloropregnane-11β-ol-3,20-dione, m. p. 241–244°; $[\alpha]^{23}$D $+80°$ (c 0.31 in CHCl₃); λ_{max}^{Nujol} 2.96, 5.83, 5.95 μ. Calcd. for $C_{21}H_{31}O_3Cl$: C, 68.74; H, 8.52; Cl, 9.66. Found: C, 69.16, H, 8.50; Cl, 9.36. The latter with bromine in acetic acid afforded 12α-chloro-4β-bromopregnane-11β-ol-3,20-dione, m. p. 184–186° (dec.); $[\alpha]^{24}$D $+100°$ (c 0.50 in CHCl₃); λ_{max}^{Nujol} 2.95, 5.78, 5.92 μ, which was dehydrobrominated to III by means of lithium chloride in dimethylformamide.[7]

12α-Fluoro-11β-hydroxyprogesterone IV, m. p. 182–183°; $[\alpha]^{23}$D $+193°$ (c 0.47 in CHCl₃); λ_{max}^{alc} 239 mμ (18,000); λ_{max}^{Nujol} 3.00, 5.89, 6.05, 6.20 μ. Anal. Calcd. for $C_{21}H_{29}O_3F$: C, 72.29; H, 8.39; F, 5.45. Found: C, 72.41; H, 8.32; F, 5.49, was prepared from II with hydrogen fluoride in chloroform containing 5% alcohol at 0°. Oxidation of IV with chromic acid in acetic acid furnished 12α-fluoro-11-ketoprogesterone, m. p. 147–148°; $[\alpha]^{23}$D $+271°$

(4) P. Hegner and T. Reichstein, Helv. Chim. Acta, 26, 715 (1943).

(5) The addition of the elements of HOBr to the 11,12 double bond in the pregnane series has been shown to proceed in the direction indicated; cf. P. Hegner and T. Reichstein, ibid., 26, 721 (1943).

(6) The opening of 11β,12β-oxides with hydrogen halides has been shown to lead to the all-axial 12α-halo-11β-ols; cf. J. Schmidlin and A. Wettstein, ibid., 36, 1241 (1953); J. W. Cornforth, J. M. Osbond and G. H. Phillipps, J. Chem. Soc., 907 (1954).

(7) R. P. Holysz, This Journal, 75, 4432 (1953).

(c 0.35 in CHCl₃); λ_{max}^{alc} 236 mμ (16,500); λ_{max}^{Nujol} 5.81, 5.86, 6.00, 6.20 μ.

We are indebted to F. M. Singer, W. B. Kessler and A. Borman of our laboratories for the bioassay data shown below. The activities of the 12α-halo derivatives in the rat liver glycogen assay[8] are listed in Table I and compared (cortisone acetate = 1) with those previously obtained for the corre-

TABLE I

GLUCOCORTICOID ACTIVITIES OF 12α- AND 9α-HALO-11β-HYDROXYPROGESTERONES

	12α	9α
Bromo-11β-hydroxyprogesterone (I)	0.25–0.35	0.1–0.2
Chloro-11β-hydroxyprogesterone (III)	0.5–0.6	0.35
Fluoro-11β-hydroxyprogesterone (IV)	0.6–0.9	0.85

sponding 9α-halo derivatives.[2b] The sodium-retaining activity of 9α- and 12α-fluoro-11β-hydroxyprogesterone was found[8] to be approximately equal to that of desoxycorticosterone. Recently Huggins and Jensen[9] have shown that 9α-fluorinated Δ^4-pregnene derivatives are powerful inhibitors of estrogen and androgen-induced uterine growth in the rat. IV was found to inhibit estradiol in the mouse at dose levels approximately equal to those of 9α-fluoro-11β-hydroxyprogesterone.[10]

(8) F. M. Singer and A. Borman, to be published.

(9) Charles Huggins and E. V. Jensen, J. Exp. Med., 102, 347 (1955).

(10) W. B. Kessler and A. Borman, to be published.

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ON THE RATE EQUATION FOR THE PERSULFATE OXIDATION OF ISOPROPYL ALCOHOL

Sir:

We wish to point out that the procedure followed in the development of the rate equation in our recent article[1] on the kinetics of the persulfate oxidation of isopropyl alcohol is not valid.[2] In Eq. 12 it is not permissible to substitute the quantity $[SO_4]$ $-$ $[X]$ for $[SO_4]$, since $[SO_4]$ itself already represents the concentration of free sulfur tetroxide remaining after formation of a certain quantity of complex, $[X]$.

Unless certain questionable assumptions are made about the magnitude of some of the rate constants and the concentration of the proposed intermediates, it does not appear that a rate equation of the required form, predicting a limiting rate at higher initial alcohol concentrations, can be derived from the proposed mechanism. Furthermore, newer kinetic data recently obtained in this laboratory[3] indicate that a limiting rate also is attained at higher initial concentrations of persulfate when the initial alcohol concentration is kept constant. Any correct theory of the mechanism of these oxidations must therefore take this fact into account, along with other recently observed anom-

(1) L. S. Levitt and E. R. Malinowski, This Journal, 77, 4517 (1955).

(2) As a result of discussions initiated by Dr. K. B. Wiberg, this error has come to our attention.

(3) L. S. Levitt and E. R. Malinowski, unpublished experiments.