method known for the synthesis of trifluoromethyl compounds. For example, SF_4 reacts with dodecanoic acid at 130° under autogenous pressure to give 1,1,1-trifluorododecane, b.p. 92° (12 mm.), $n^{25}D$ 1.3896, in 88% yield (*anal.* calcd. for $C_{12}H_{23}F_3$: C, 64.25; H, 10.34; F, 25.41. Found: C, 64.01; H, 10.27; F, 25.81). The reaction works well with aliphatic, aromatic and polycarboxylic acids. The unusual specificity of the reaction is shown by the excellent conversion of unsaturated acids to the corresponding trifluoromethyl derivatives, *e.g.*, trifluoropropene and trifluoropropyne are now easily accessible from acrylic and propiolic acids, respectively.

Fluorination of aldehydes and ketones by SF_4 is typified by the high yield preparation of α,α-difluorotoluene from benzaldehyde and of 2,2-difluoropropane from acetone. Some quinones react like ketones, but in other cases subsequent reactions result in fluorination and aromatization of the ring. For example, chloranil in the presence of hydrogen fluoride at 270° gave 1,2,4,5-tetrachloro-3,3,6,6-tetrafluoro-1,4-cyclohexadiene, m.p. 46°, in 75% yield (*anal.* calcd. for C_6Cl_4: C, 24.86; Cl, 48.92; F, 26.22. Found: C, 25.02; Cl, 48.94; F, 26.24). However, the product from quinone was 1,2,4-trifluorobenzene in 30% yield. Such carbonyl compounds as carbon monoxide and carbon dioxide are converted to CF_4 by SF_4.[2]

Another example of the versatility of SF_4 as a fluorinating agent is the excellent conversion of benzenearsonic acid to $C_6H_5AsF_4$, b.p. 52–53° (2 mm.) (*anal.* calcd. for $C_6H_5AsF_4$: C, 31.60; H, 2.21; F, 33.33; As, 32.85. Found: C, 31.72; H, 2.48; F, 33.38; As, 32.41).

A new class of compounds, the organoiminosulfur difluorides, has been obtained from the reaction of SF_4 with compounds containing carbon-nitrogen multiple bonds. The only previously known iminosulfur difluoride was $F{-}N{=}SF_2$.[3] Examples of organoiminosulfur difluorides are the products from phenyl isocyanate and benzonitrile.[4]

$$C_6H_5N{=}C{=}O + SF_4 \longrightarrow C_6H_5N{=}SF_2 + F_2C{=}O$$
$$C_6H_5C{\equiv}N + SF_4 \longrightarrow C_6H_5CF_2N{=}SF_2$$

Phenyliminosulfur difluoride, b.p. 36° (2 mm.), was obtained in 88% yield from phenyl isocyanate at 200° (*anal.* calcd. for $C_6H_5F_2NS$: C, 44.71; H, 3.13; F, 23.58; N, 8.69; S, 19.90. Found: C, 44.12; H, 3.40; F, 24.00; N, 8.27; S, 19.76). The assigned structure is in accord with the infrared and n.m.r. spectra. Benzonitrile was converted to α,α-difluorobenzyliminosulfur difluoride, b.p. 55° (11 mm.) (*anal.* calcd. for $C_7H_4F_4NS$: F, 35.99; S, 15.18. Found: F, 35.81; S, 15.11).

Sulfur tetrafluoride has been made readily available by the discovery of a high-yield synthesis based on the reaction of SCl_2 with NaF suspended in acetonitrile at 70–80°. One distillation gives SF_4 of greater than 90% purity with thionyl fluoride as the main impurity. Sulfur tetrafluoride should be used with extreme caution because it has an inhalation toxicity comparable to that of phosgene and releases hydrogen fluoride on contact with moisture.

A large number of reactions of SF_4 and its derivatives are under investigation, and detailed reports on this research are being prepared.

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(2) W. C. Smith, U. S. Patent 2,859,245 (1958).

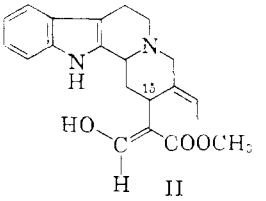
(3) O. Glemser and H. Schröder, *Z. anorg. allgem. Chem.*, **284**, 97 (1956).

(4) W. C. Smith, U. S. Patent 2,862,029 (1958).

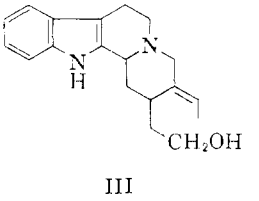
THE STRUCTURE OF GEISSOSCHIZINE

Sir:

Recently[1] we reported that treatment of geissospermine ($C_{40}H_{48}N_4O_3$, I) with concd. hydrochloric acid gave three products, *viz.*, geissoschizine ($C_{21}H_{24}N_2O_3$), apogeissoschizine ($C_{21}H_{22}N_2O_2$), and geissoschizoline ($C_{19}H_{26}N_2O$).[2] We now wish to report that geissoschizine possesses structure II.



II



III

Both the acidic character of II and the profound, reversible ultraviolet spectral changes observed on adding acid and alkali[3] suggest the presence of a readily enolizable carbonyl. To confirm this II was treated with one mole of aniline to give the expected anilinoacrylic ester ($C_{27}H_{29}N_3O_2$, m.p. 170–172°) with a carbonyl absorption at 6.11 μ as compared to 5.96 μ for II. The ethylidene side chain was shown by ozonolysis, which gave acetaldehyde, and by the observation that Kuhn–Roth oxidation of II gave one mole of acetic acid whereas oxidation after catalytic reduction gave one mole of mixed acetic–propionic acids.[4]

On boiling II with 1 *N* hydrochloric acid, an amorphous aldehyde was formed by loss of methanol and carbon dioxide, and this aldehyde with sodium borohydride gave a crystalline carbinol (III, $C_{19}H_{24}N_2O$, m.p. 210–215° dec.). Wolff–Kishner reduction of the aldehyde gave an oxygen-free compound (IV, $C_{19}H_{24}N_2$). Although III still shows the presence of only one C–CH_3, two are present in IV. Heating IV with palladized charcoal at 220° gave one mole of hydrogen and alstyrine,[5] from which *o*-aminopropiophenone and 4,5-diethylpicolinic acid were obtained on further degradation.

Additional evidence for the structure II resulted from selenium dehydrogenation studies on geis-

(1) H. Rapoport, T. P. Onak, N. A. Hughes and M. G. Reinecke, THIS JOURNAL, **80**, 1601 (1958).

(2) Satisfactory analyses have been obtained for all compounds for which molecular formulae are given. The identity of known compounds has been established by comparison with authentic samples.

(3) The ultraviolet spectrum of II in 0.1 *N* alkali could be very closely reproduced by combining the spectra of alloyohimbine and of ethyl acetoacetate in 0.1 *N* alkali.

(4) H. Bickel, H. Schmid and P. Karrer, *Helv. Chim. Acta*, **38**, 649 (1955).

(5) T. B. Lee and G. A. Swan, *J. Chem. Soc.*, 771 (1956).

sospermine derivatives.[6] When dihydrodemethoxygeissospermine ($C_{39}H_{48}N_4O_2$, m.p. 182–184°, from reduction of I with sodium in ammonia) was heated with selenium, alstyrine was formed. On the other hand, decarbomethoxygeissospermine ($C_{38}H_{46}N_4O$, m.p. 254–255°) obtained by treatment of I with methanolic potassium hydroxide, gave, as expected, a desmethylalstyrine which was further degraded to *o*-aminopropiophenone and 4-methyl-5-ethylpicolinic acid (m.p. 156–158°). The latter was identical with a synthetic sample prepared from 2-methyl-5-ethylpyridine-4-carboxaldehyde[7] by Wolff–Kishner reduction, condensation with benzaldehyde, and oxidation to the picolinic acid.

The above evidence definitely establishes the structure of the C_3-substituent as a β-aldehydo-ester. Its position is fixed at C_{15} by the nature of the various alstyrines produced, and these also establish the remaining skeletal structure of geissoschizine. Confirmation of the indolic N–H and enolic O–H was provided by infrared bands at 2.90 and 3.30 μ, respectively, which were shifted to 3.88 and 4.00 after exchange in deuterium methoxide. Thus structure II is established for geissoschizine.

(6) Preliminary studies showed that similar alstyrines were obtained from I and II. However, greater availability and higher yields of alstyrines made the geissospermine derivatives more suitable. Since geissoschizoline (in common with most indoline alkaloids) fails to yield alstyrines under these conditions, the products obtained must arise from the indolic portion of the geissospermine derivatives.

(7) F. D. Popp and W. E. McEwen, THIS JOURNAL, **80**, 1181 (1958).

(8) National Science Foundation Postdoctoral Fellow, 1958–1959.

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6α-FLUORO-16α-METHYL ANALOGS OF CORTICAL HORMONES

Sir:

Since the initial demonstration in these laboratories[1] of the enhanced adrenal cortical activity of the 2α-methyl analogs of corticoids, we[2] and others[3] have been investigating the effect of methyl substitution elsewhere in the hydrocortisone molecule. We have also shown[4] that the 6α-fluoro group potentiates the biological activity of hydrocortisone.

The present report concerns the synthesis of a series of highly active hydrocortisone analogs containing both the 6α-fluoro and 16α-methyl groups.[5]

16α-Methylprogesterone[6] was converted by microbial fermentation[7] to 11α-hydroxy-16α-methylprogesterone, m.p. 161–163°, $[\alpha]_D$ +149° (chf.) which was oxidized with sodium dichromate to 16α-methyl-11-ketoprogesterone, m.p. 183–185°, $[\alpha]$ +225° (chf.), λ_{max} 238 mμ (15,850). This was subjected to a process involving diglyoxalation, bromination and Faworskii rearrangement with sodium methoxide[8] to give a mixture of methyl 3,11-diketo-16α-methyl-4,17(20)-[*cis*]-pregnadien-21-oate, m.p. 175–176°, $[\alpha]_D$ +165° (chf.), λ_{max} 232.5 mμ (23,750) and methyl 3,11-diketo-16α-methyl-4,17(20)-[*trans*]-pregnadien-21-oate, m.p. 192–195°, $[\alpha]_D$ + 131° (chf.), λ_{max} 232.5 mμ (24,100). The 3-ethylene-ketal of the *trans* ester then was epoxidized with peracetic acid to give methyl 3-ethylenedioxy-5α,6α-oxido-11-keto-16α-methyl-17(20)-[*trans*]-pregnen-21-oate, m.p. 187–191°, $[\alpha]_D$ −63° (chf.), λ_{max} 225 mμ (13,850). On reaction with hydrogen fluoride the oxide was opened and the ketal lost, giving methyl 5α-hydroxy-6β-fluoro-3,11-diketo-16α-methyl-17(20)-[*trans*]-pregnen-21-oate, m.p. 230–234°, $[\alpha]_D$ −6° (chf.), λ_{max} 224 mμ (13,850). Reketalization (at C-3) with ethylene glycol, lithium aluminum hydride reduction and acetylation of the resulting 21-alcohol produced 3-ethylenedioxy-6β-fluoro-16α-methyl-17(20)-[*trans*]-pregnene-5α,11β,21-triol, 21-acetate, m.p. 176–180°, $[\alpha]_D$ −1° (chf.). Oxidation of this material with N-methylmorpholine oxide-peroxide[9] and a catalytic amount of osmium tetroxide gave 3-ethylenedioxy-6β-fluoro-5α,11β,17α,21-tetrahydroxy-16α-methylpregnan-20-one 21-acetate, which was not purified, but was treated with anhydrous hydrogen chloride in chloroform–ethanol to give 6α-fluoro-16α-methylhydrocortisone, 21-acetate (I) m.p. 242–245° (dec.), λ_{max} 237 mμ (14,950). 6α-Fluoro-16α-methylhydrocortisone, m.p. 210–216°, was obtained from this by hydrolysis with potassium bicarbonate in methanol.

Selenium dioxide dehydrogenation of I formed 6α-fluoro-16α-methylprednisolone 21-acetate (II), m.p. 173–176°, resolidifying and melting again at 232–234° (dec.). Application of the well-known series of reactions[10]: dehydration at 11, bromo-

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