The latter would be expected to give 16–17 unsaturation readily; 3α,21-diacetoxy-Δ^{16}-pregnene-11, 20-dione gives a strong Porter–Silber reaction. The sulfuric acid spectrum showed an absorption maximum at 287 (Δ^4-3-keto group) shoulder at 390 mμ.

The mobility of the free substance and its acetate suggests the presence of four, possibly five, oxygen atoms, two of which are in acetylatable hydroxyl groups. In the propylene glycol–cyclohexane system the acetate moved on paper at approximately the same rate as 11-dehydrocorticosterone acetate and considerably faster than substance S acetate. When the 3-(2,4-dinitrophenylhydrazone) of the acetate was heated one hour at 60° in 0.02 *N* perchloric acid in acetic acid the absorption maximum at 385 mμ did not change in position. This result demonstrated the absence of a 6-acetoxy group since in parallel experiments with 6α- and 6β-acetoxy-11-desoxycorticosterone 21-acetate 3-(2,4-dinitrophenylhydrazones) the absorption maxima shifted from 387 and 381 to 398 and 400 mμ. These conditions would be expected to cause loss of acetic acid from positions 1, 2 or 7 with increase in the wave length of the absorption maximum.

Hydrolysis of the acetate with citrus acetylase (courtesy of B. C. Bocklage and E. A. Doisy) gave a product which was approximately 85 times as active in the bioassay as desoxycorticosterone acetate. Paper chromatography showed the presence of two substances, one apparently completely deacetylated; crystals (m.p. 163–164°, λ_{max}^{MeOH} 240 mμ) of approximately the same activity as the crude mixture were obtained from the dry ether. The second substance, which could be converted to the first by further treatment with acetylase, crystallized from acetone–petroleum ether, m.p. 217–219°, $\lambda_{max.}^{MeOH}$ 239 mμ, and was approximately 25 times as active as desoxycorticosterone acetate.

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RECEIVED AUGUST 24, 1953

STRUCTURE OF LIGANDS IN INORGANIC COÖRDINATION COMPOUNDS BY INFRARED SPECTRA

Sir:

In addition to the active frequencies we have observed the forbidden frequencies as weak infrared absorption for such symmetrical ions as NO_3^-, SO_4^{--}, etc., when these ions are present outside the coördination sphere in complex compounds. For example, the totally symmetric frequency of the nitrate ion at 1050 cm.$^{-1}$ has been observed as a weak infrared absorption in the complex, $[Cu\{SC(NHCH_2)_2\}_4]NO_3$, and that of the sulfate ion at 980 cm.$^{-1}$ in the compound $[Cu(NH_3)_4]SO_4 \cdot H_2O$. The appearance of these forbidden symmetrical frequencies in absorption can be explained as due to the deformation of the ions in the molecular field of the crystals.

If such ions are coördinated to the central metal ion of a complex, the symmetry is disturbed much more markedly and a spectrum quite different from that expected for the free ion is observed. For example, even the strongest absorption band at 1100 cm.$^{-1}$ characteristic of the free sulfate ion disappears completely in the complex $[Co(NH_3)_5SO_4]Cl$.

However, when the ligands are coördinated by an essentially electrostatic bond, the symmetry of the ion is practically maintained. Glycinometal complexes are good examples in which carboxylate frequencies (about 1600 cm.$^{-1}$) have been observed, indicating that the carboxylate resonance in the glycino ligand is maintained nearly as in the case of potassium glycinate. If the structure in these complexes were $-C\begin{matrix}O\\ \diagdown\\ O-M\end{matrix}$, we should observe the characteristic C=O frequency (about 1700 cm.$^{-1}$), in place of the carboxylate frequency.

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RECEIVED AUGUST 31, 1953

* Member, Radiation Project operated by the University of Notre Dame and supported in part under AEC Contract AT(11-1)-38.

STRUCTURE OF RESERPIN

Sir:

Reserpin, the new sedative and hypotensive principle of *Rauwolfia serpentina* Benth. has been isolated for the first time by Mueller, Schlittler and Bein.[1] The m.p., optical rotation, characteristic bands in the ultraviolet and infrared spectra and elementary analysis were also reported; however, no empirical formula was assigned.

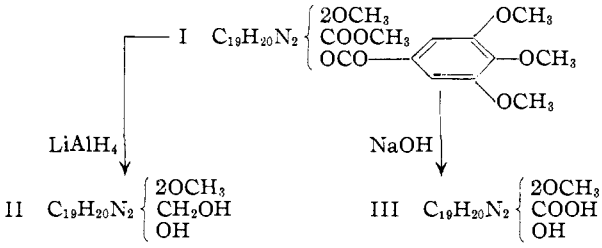
We have been able to establish the empirical formulas of Reserpin[2] and its degradation products. The alkaloid was isolated by chromatography of the Oleoresin fraction on acid-washed alumina. The repeatedly recrystallized material melted at 264–265° (dec.) and was dried for eight hours at 120° and 0.05 mm. for analysis. Calcd. for $C_{33}H_{40}O_9N_2$: C, 65.11; H, 6.62; N, 4.60; OCH_3 (6), 30.59. Found: C, 65.31, 65.11, 65.00; H, 6.88, 6.83, 6.68; N, 4.79; OCH_3, 30.22. *Mol. wt.* Calcd. 608.67; found: 586 ± 20 (electrometric titration, *pK'*a 6.6 in 66% dimethylformamide); 610 (X-ray methods), no C-methyl. The ultraviolet spectrum of Reserpin showed the following bands: $\lambda_{max.}$ 216 mμ (log ε = 4.79), $\lambda_{max.}$ 267 mμ (log ε = 4.23), $\lambda_{max.}$ 295 mμ (log ε = 4.07), shoulder at 225 mμ, $\lambda_{min.}$ 246 mμ (log ε = 3.99), $\lambda_{min.}$ 286 mμ (log ε = 4.00). The maleate salt of Reserpin melted at 226–227° (dec.). Calcd. for $C_{33}H_{40}O_9N_2 \cdot C_4H_4O_4$: C, 61.31; H, 6.12; N, 3.86. Found: C, 61.5; H, 6.3; N, 3.83. Basic hydrolysis of Reserpin, using dilute sodium hydroxide in methanol yielded two fragments. One was readily identified as 3,4,5-trimethoxybenzoic acid, identical in each respect with an authentic sample (X-ray patterns, infrared ultraviolet, m.p. and mixed m.p.). The second fragment for which we propose the name Reserpic acid was isolated as the hydrochloride of an amino acid, m.p. 274–275° (dec.). It crystallized with one mole of methanol and was

(1) J. M. Mueller, E. Schlittler and H. J. Bein, *Experientia*, **8**, 338 (1952).

(2) Our Reserpin was spectrally identical with a sample obtained through the courtesy of Dr. E. Schlittler of Ciba Pharmaceutical Products, Summit, N. J.

dried for analysis three hours at room t. and 0.05 mm.: Calcd. for $C_{22}H_{23}N_2O_5 \cdot HCl \cdot CH_3OH$: C, 58.90; H, 7.09; Cl, 7.56. Found: C, 58.84; H, 6.85; Cl, 7.53. *Mol. wt.* Calcd. 468.93; found 454 ± 20 (electrometric titration in 66% dimethylformamide, *pK'*a 6.2 and 8.2). Reduction of Reserpin using lithium aluminum hydride in tetrahydrofuran also yielded two products. One was identified as 3,4,5-trimethoxybenzyl alcohol. The *p*-nitrobenzoate was prepared and shown to be identical with the derivative obtained from an authentic sample of the alcohol (infrared, m.p. and mixed m.p.). The apparently new derivative melts at 143°. Calcd. for $C_{17}H_{17}O_7N$: C, 58.79; H, 4.93; N, 4.03. Found: C, 58.78; H, 5.02; N, 4.01. The second fragment for which we propose the name Reserpic alcohol crystallizes with one mole of water, m.p. 216–217° (dec.). Calcd. for $C_{22}H_{30}O_4N_2 \cdot H_2O$: C, 65.32; H, 7.97; N, 6.93; OCH_3 (2), 15.33; act. H, 5 moles. Found: C, 65.12, 65.40; H, 7.99, 7.99; N, 6.67; OCH_3, 15.07; act. H, 4.82 moles. *Mol. wt.* Calcd. 404; found, 409 ± 10 (electrometric titration, *pK'*a 7.7).

As a result of these data the following partial structures are suggested for Reserpin (I), Reserpic alcohol (II) and Reserpic acid (III)



A. Stoll and A. Hofmann[3] have just reported the isolation of a new alkaloid from *Rauwolfia serpentina* Benth. which they named Sarpagin and formulated as a $C_{19}H_{22}O_2N_2$ compound. There appears to be a relationship between Reserpic alcohol and Sarpagin. This relationship is substantiated by the properties of the demethylation product of Reserpic alcohol (with HBr in AcOH). Like Sarpagin this substance reduces Fehling solution and silver nitrate in ammonia solution in the cold. Furthermore, it gives a blue color with Folin–Ciocalteu reagent[4] (positive phenol test).

The $C_{19}H_{22}N_2$ nucleus of Reserpin is possibly a substituted indole alkaloid of Yohimbine-like type and our spectral data are in very good agreement with such a formulation. The infrared spectrum of Reserpin in chloroform solution has a free NH band at 2.87 μ within 0.01 μ of similar bands in indole, 5,6-dimethoxyindole, 2,3-dimethyl-5,6-dimethoxyindole and tetrahydroalstonilin.[5] Two carbonyl bands have wave lengths of 5.79 μ and 5.82 μ in the spectrum (0.01 to 0.02 μ greater separation when analytically resolved). Methyl cyclohexanecarboxylate and methyl 3,4,5-trimethoxybenzoate have bands at 5.78 μ and 5.82 μ, respectively. Comparison of the above-mentioned models with Reserpin in the 6–7 μ region suggests the possibility that one of the two methoxyls in Reserpin is at the 6 position of the indole moiety. A summation of the ultraviolet absorption of 2,3-dimethyl-5,6-dimethoxyindole and methyl 3,4,5-trimethoxybenzoate in a mole per mole ratio resulted in a spectrum which contained all the significant features of the Reserpin spectrum. The computed spectrum possessed three maxima, a shoulder and two minima, at 214 mμ (log ε = 4.73), 267 mμ (log ε = 4.14), 298 mμ (log ε = 4.04), 225 mμ, 246 mμ (log ε = 3.98) and 286 mμ (log ε = 3.96), respectively. The 214 mμ band is due to the methyl 3,4,5-trimethoxybenzoate chromophore. This chromophore is also responsible for a large part of the absorption at 267 mμ. The substituted indole chromophore is the main contributor to the 298 mμ band and also the shoulder at *ca.* 225 mμ. The slight discrepancy between the sum of the absorption of the two compounds and Reserpin can be accounted for by the unknown position of the second methoxyl group in the indole ring of Reserpin.

Acknowledgment.—We would like to thank Dr. R. B. Woodward for helpful suggestions during the course of this investigation. We gratefully acknowledge the aid rendered by the following: Dr. H. A. Rose, X-ray data; Mr. E. H. Stuart, Isolation of the Oleoresin fraction; Messrs. W. L. Brown, G. M. Maciak and H. L. Hunter, elementary analyses and group determinations; Miss M. Hoffman, infrared spectra and Mr. D. O. Woolf, electrometric titration.

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RECEIVED SEPTEMBER 8, 1953

(3) A. Stoll and A. Hofmann, *Helv. Chim. Acta*, **36**, 1143 (1953).

(4) O. Folin and V. Ciocalteu, *J. Biol. Chem.*, **73**, 629 (1927).

(5) We would like to thank Dr. R. C. Elderfield, of the University of Michigan, for the sample of Tetrahydroalstonilin.

THE C-25 ISOMERISM OF SARSASAPOGENIN AND SMILAGENIN

Sir:

It has been assumed that sarsasapogenin[1] and smilagenin, yamogenin and diosgenin, and other so-called "normal" and "iso" (22a and 22b) sapogenins differ in their steric arrangement at C-22.[2] This assumption was supported by such observations as sarsasapogenin and smilagenin giving the same "pseudo" compound[3] and the same dihydrogenin.[4]

We have established a difference between pseudosarsasapogenin (I), $[\alpha]^{20}D$ +12°, m.p. 167–169°[5] (*Anal.* Found: C, 77.86; H, 10.32), and psuedosmilagenin (II), $[\alpha]^{20}D$ +24°, m.p. 158–161° (*Anal.* Found: C, 78.06; H, 10.58), and between dihydrosarsasapogenin (III), $[\alpha]^{20}D$ −4°, m.p. 165–167° (*Anal.* Found: C, 77.62; H, 11.16), and dihydrosmilagenin (IV), $[\alpha]^{20}D$ +3°, m.p. 164–

(1) We are indebted to Dr. Monroe E. Wall, Eastern Regional Research Laboratory, United States Department of Agriculture, for a generous supply of this material.

(2) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," 3rd Ed., Reinhold Publishing Corp., New York, N. Y., 1949, p. 578 ff.

(3) R. E. Marker, E. Rohrmann and E. M. Jones, THIS JOURNAL, **62**, 648 (1940).

(4) R. E. Marker and E. Rohrmann, *ibid.*, **61**, 846 (1939).

(5) Rotations, unless otherwise noted, were taken in chloroform solution. All melting points reported were taken on the Kofler block and are uncorrected.