8.75 (H-pyridine), 10.25 (CH=O). *Anal.* ($C_{10}H_{11}NO_3$) C, H, N.

Diethyl [2-(5-Acetoxy-4,6-dimethyl-3-pyridyl)vinyl]phosphonate·HCl (XVII).—Tetraethyl methylenediphosphonate[10] (11.5 g, 0.04 mole) was added dropwise in 15 min at room temp to a stirred mixt of NaH (1.92 g, 50% oil dispersion, 0.04 mole) in 200 ml of dry 1,2-dimethoxyethane. After stirring 1 hr, the homogeneous system was treated with XVI (6 g, 0.031 mole) batchwise in 5 min, and the soln was stirred overnight. A syrup pptd during the stirring period. Evapn of the solvent, addn of 50 ml of H_2O, and overnight extn with EtOAc yielded the crude product in the org layer. The solvent was removed, and the residue in Et_2O was treated with dry HCl until pptn of an oil was complete. After stirring 15 min, the ppt (now crystalline) was collected by filtration: yield 6.5 g (45%). Crystn from Et_2O–EtOAc gave the purified product: mp 125–127°; mass spectrum (*m/e*), 327 (M^+), 285 ($M^+ - COCH_3 + H$), 282 ($M^+ - OEt$), 248.4 (metastable, 327 → 285), 177 ($M^+ - CHPO_3Et_2$), 176 (177 − H), 149 (177 − CO), 148 (177 − HCO), 36 (base peak, HCl).

Diethyl [2-(5-Hydroxy-4,6-dimethyl-3-pyridyl)ethyl]phosphonate Acetate Ester·HCl (XVIII).—XVII (1 g) in 50 ml of EtOH was treated with 1 g of 5% Pd/C and hydrogenated at room temp with shaking for 7 hr at an initial pressure of 3.5 kg/cm². Removal of the catalyst by filtration and evapn of the filtrate gave a syrup. This was sublimed *in vacuo* (*ca.* 0.02 mm) at 100° and yielded a white, cryst sublimate: mp 100–102°; yield 180 mg; mass spectrum (*m/e*) 329 (M^+), 314 ($M^+ - CH_3$), 300 ($M^+ - C_2H_5$), 287 ($M^+ - COCH_3 + H$), 272 (*m/e* 287 − CH_3), 258 (*m/e* 287 − C_2H_5), 242 (*m/e* 287 − OC_2H_5), 192 ($M^+ - PO_3Et_2$), 150 (*m/e* 287 − PO_3Et_2). *Anal.* ($C_{15}H_{24}NO_5P·HCl$) C, H, Cl, N, P.

[2-(5-Hydroxy-4,6-dimethyl-3-pyridyl)vinyl]phosphonic Acid (XIX).—XVII (200 mg) in 10 ml of concd HCl was refluxed for 5 hr, and the resulting soln was evapd to dryness *in vacuo*. Trituration of the residue with Et_2O and filtration gave a white solid: mp > 260°; yield 130 mg. The solid was crystd from EtOH–H_2O: mp >260°; yield 50 mg (40%); nmr (DMSO-d_6), 2.4, 2.65 (2- and 4-CH_3-pyridine), 7.05 (multiplet, *trans*-HC=CH), 8.45 (H-pyridine), 10.7 (OH and H_2O). *Anal.* ($C_9H_{12}NO_4P·H_2O$) C, H, N, P.

[2-(5-Hydroxy-4,6-dimethyl-3-pyridyl)ethyl]phosphonic Acid (II).—XIX (500 mg) suspended in 25 ml of H_2O was treated dropwise with 1 *N* KOH until homogeneous. To the soln (pH 7–8) was added 500 mg of 5% Pd/C, and the mixt was hydrogenated at room temp with shaking for 12 hr at an initial pressure of 3.5 kg/cm². The catalyst was removed by filtration, and the reduced product was isolated from the filtrate as described by Hullar[4] for the corresponding pyridoxine analog: mp >260°; yield 100 mg (20%); nmr (CF_3COOD), 2.4, 3.2 (pair of complex multiplets, CH_2CH_2), 2.6, 2.75 (2- and 4-CH_3-pyridine), 8.1 (H-pyridine), 11.25 (OH). *Anal.* ($C_9H_{14}NO_4P$) C, H, N.

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(10) G. M. Kosolapoff, *J. Amer. Chem. Soc.*, **75**, 1500 (1953).

Alkaloid Studies. 7.[1] Reactions of 18-Hydroxymethyleneyohimban-17-one and the Preparation of Yohimbano[17,18-*c* and 18,17-*d*]pyrazoles

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Some reactions of 18-hydroxymethyleneyohimban-17-one (**1**) were investigated. Hydrazine and **1** gave yohimbanopyrazole **2**, acylation of which produced acetyl and 3,4,5-trimethoxybenzoyl derivatives **8** and **9**. Phenylhydrazine and **1**, or its isobutyl ether **5**, produced isomeric phenylyohimbano[17,18-*c* and 18,17-*d*]-pyrazoles **3** and **4**. Methylhydrazine and **1** produced isomeric methylyohimbano[17,18-*c* and 18,17-*d*]-pyrazoles **11** and **10**. Structural assignments of N-substituted pyrazoles based on pmr measurements are discussed. *O*-Benzoyl and *O*-3,4,5-trimethoxybenzoyl derivatives **12** and **13** were prepared by acylation of **1**. Potent CNS depressant activity in laboratory animals was exhibited by **1**, **2**, **5**, **10**, and **11**.

Our interest in the introduction of substituents into the E ring of yohimbanones and in further modification of the E ring led us to study the chemistry of C-18 substituted yohimban-17-ones. In a previous publication[2] we have described the synthesis of C-18 substituted yohimban-17-ones and presented evidence for substitution at C-18 in carboxylation and formylation of yohimban-17-one. A study of the chemistry of 18-hydroxymethyleneyohimban-17-one[2] (**1**) was undertaken since hydroxymethylene ketones[3] are reactive intermediates which undergo numerous condensation reactions. Reactions with amines give aminomethylene derivatives,[4,5] while reactions with alcohols afford alkoxymethylene ketones; heterocyclic pyrazoles are

(1) Alkaloid Studies. VI: J. D. Albright, L. A. Mitscher, and L. Goldman, *J. Heterocycl. Chem.*, **7**, 623 (1970).

(2) J. D. Albright, L. A. Mitscher, and L. Goldman, *J. Org. Chem.*, **28**, 38 (1963).

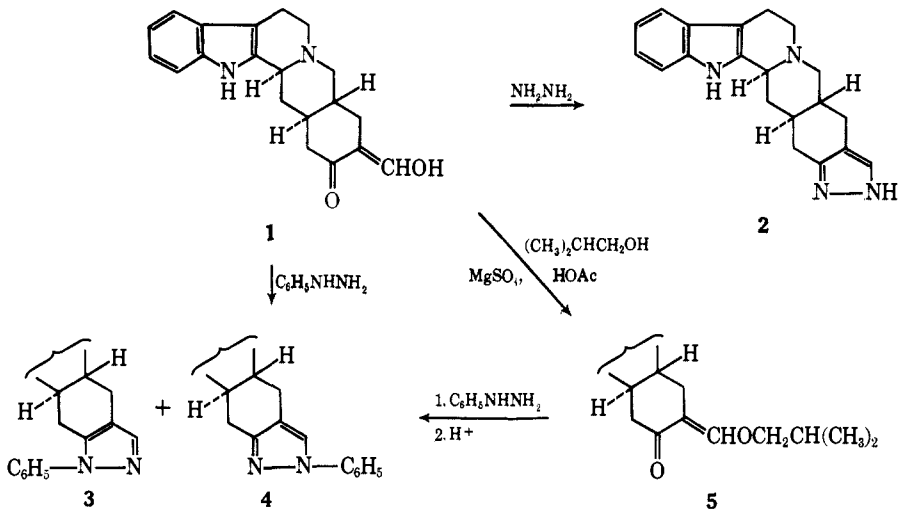
(3) For the preparation of 2-hydroxymethylene 3-ketosteroids see: (a) H. J. Ringold, E. Batres, O. Halpern, and E. Necoechea, *J. Amer. Chem. Soc.*, **81**, 427 (1959); (b) F. L. Weisenborn and H. E. Appelgate, *ibid.*, **81**, 1960 (1959).

(4) For the preparation of 2-aminomethylene 3-ketosteroids see: (a) J. A. Zderic, O. Halpern, H. Carpio, A. Ruiz, D. C. Limon, L. Magana, H. Jimenez, A. Bowers, and H. J. Ringold, *Chem. Ind. (London)*, 1625 (1960); (b) G. de Stevens and A. Halamandaris, *J. Org. Chem.*, **26**, 1614 (1961).

(5) Reactions of 18-hydroxymethyleneyohimban-17-one (**1**) with amines will be described in a forthcoming publication.

prepared by reaction with hydrazine or substituted hydrazines. Numerous steroidal heterocyclic pyrazoles[6] have been prepared from the appropriate steroidal hydroxymethylene ketones and some of these derivatives have shown interesting biological properties.

Reaction of 18-hydroxymethyleneyohimban-17-one[2] with hydrazine gave pyrazole **2**, while condensation with phenylhydrazine afforded two isomeric phenylpyrazoles **3** and **4** which were separated by fractional crystallization.[7] The isomer melting at 206–210° dec was assigned structure **3**, while the isomer melting at 248–255° dec was assigned structure **4** on the basis of their uv spectra. Isomer **3** showed an absorption maximum at 255 nm (ϵ 13,400) while **4** absorbed at 270 nm (ϵ 27,000). It has been shown that, in isomeric substituted pyrazoles, steric inhibition of resonance causes a shift in uv absorption to lower wavelength with a decrease in intensity of the band.[6c,d,8] On this basis the isomer which showed a decreased absorption at lower wavelength in the uv spectrum was assigned structure **3**.



The 18-isobutoxymethylene ketone **5** was prepared (*vide infra*) and its reaction with phenylhydrazine was studied in order to determine whether isomer **4** could be formed exclusively through intermediate **6** or whether 1,4 addition would occur to give **3** *via* intermediate **7**. It has been observed previously that a hydroxymethylene ketone and its enol ether may give different pyrazoles.[6c,9] However, the reaction did not produce **6** or **7**, selectively, since both isomers **3** and **4** were formed.

The pmr spectra (in $CDCl_3$) of the phenylpyrazoles were measured in order to determine whether a differentiation between structures **3** and **4** could be made on the basis of the chemical shifts of the protons on the pyrazole rings. However, the signals of the pyrazole ring protons could not be observed due to overlap with proton signals of the phenyl groups.

Acylation of yohimbano[17,18-*c*]pyrazole (**2**) with AcCl and with 3,4,5-trimethoxybenzoyl chloride gave the *N*-acyl derivatives **8** and **9**, respectively. Whereas acylation of either of the two pyrazole N atoms is possible, only one isomer was isolated in each case. The basis for assignment of the position of the acyl groups in **8** and **9** rests on pmr spectral data.[10] The pmr spectrum of **8** (in DMSO-d_6) showed a 3-proton singlet at δ 3.53 ($NCOCH_3$), a 4-proton multiplet at 6.8–7.4 (arom protons), a 1-proton singlet at 7.97 (5′-pyrazole proton), and a 1-proton singlet at 10.32 (indole NH). The pmr spectrum of **9** (in $CDCl_3$) exhibited 2 one-proton singlets at δ 7.96 and 8.12, and a 6-proton multiplet at 6.9–7.6 (arom protons). The δ 7.96 signal disappeared on exchange of the sample with CD_3OD and, therefore, the signal at δ 8.12 is attributed to the proton attached to the 5′ position of the pyrazole moiety. In pyrazole **2** the signal from the 3′(5′) proton of the pyrazole ring is found (in $CDCl_3$ + CD_3OD added to aid solubility) under the multiplet for the aromatic protons at δ 6.1–6.8 and, thus, it is seen that acylation produced a downfield shift of the 3′(5′) proton which is attributed to deshielding by the proximate trimethoxybenzoyl and Ac groups.

Isomeric *N*-methylpyrazoles **10** and **11** were obtained by the action of methylhydrazine on **1**, but could not be differentiated on the basis of their uv absorption spectra. Structural assignments could, however, be made on the basis of their pmr spectra. The isomer of mp 245–250° dec showed (in $CDCl_3$) a 3-proton singlet at δ 3.73 (NCH_3) and a 1-proton singlet at 7.35 [pyrazole-3′(5′)-H] with a $|\delta_H - \delta_{NCH_3}|$ of 3.62, while the isomer of mp 255–260° dec showed a 3-proton singlet at δ 3.83 and a 1-proton singlet at 7.13 with a $|\delta_H - \delta_{NCH_3}|$ of 3.30. We have shown[11] that these chemical shift differences are characteristic for isomeric *N*-methyl-3(5)-*H*-pyrazoles and, thus, a structural assignment of **10** to the lower melting isomer and **11** to the higher melting isomer can be made.

(6) (a) R. O. Clinton, A. J. Manson, F. W. Stonner, H. C. Newman, R. G. Christiansen, R. L. Clarke, J. H. Ackerman, D. F. Page, J. W. Dean, W. B. Dickinson, and C. Carabateas, *J. Amer. Chem. Soc.*, **83**, 1478 (1961). (b) R. O. Clinton, R. L. Clarke, F. W. Stonner, A. J. Manson, K. F. Jennings; and D. K. Phillips, *J. Org. Chem.*, **27**, 2800 (1962); (c) R. Hirschmann, N. G. Steinberg, P. Buchschacher, J. H. Fried, G. J. Kent, M. Tishler, and S. L. Steelman, *J. Amer. Chem. Soc.*, **85**, 120 (1963); (d) J. H. Fried, H. Mrozik, G. E. Arth, T. S. Bry, N. G. Steinberg, M. Tishler, R. Hirschmann, and S. L. Steelman, *ibid.*, **85**, 238 (1963).

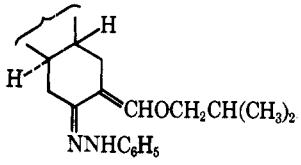
(7) We have shown previously that reaction of 18-hydroxymethyleneyohimban-17-one (**1**) with hydroxylamine gives a mixture of isomeric yohimbano[17,18-*c* and 18,17-*d*]isoxazoles.[2]

(8) W. B. Wright, Jr., H. J. Brabander, R. A. Hardy, Jr., and W. Fulmor, *J. Amer. Chem. Soc.*, **81**, 5637 (1959).

(9) T. L. Jacobs, *Heterocycl. Compounds*, **5**, 51 (1957).

(10) A pmr spectral analysis of 1-acylpyrazoles is described by J. K. Williams, *J. Org. Chem.*, **29**, 1377 (1964), but is not applicable to pyrazoles **8** and **9**.

(11) J. D. Albright and L. Goldman, *ibid.*, **31**, 273 (1966).



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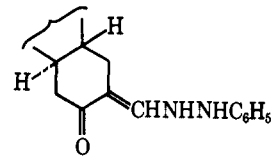

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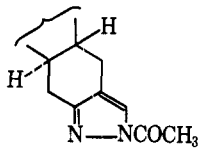

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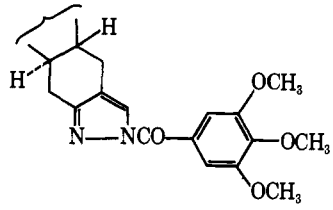

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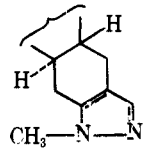

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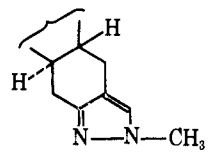
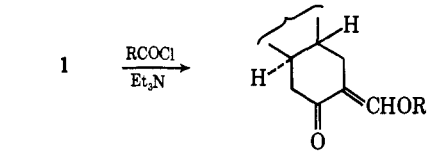
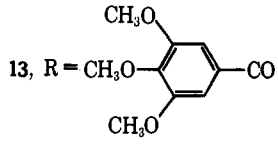


11

O-Acyl derivatives **12** and **13** were prepared by treatment of **1** with BzCl and 3,4,5-trimethoxybenzoyl chloride, respectively, in the presence of Et_3N. The trimethoxybenzoyl derivative **13** appeared to be less stable than the benzoyl derivative **12** and attempts to purify it were unsuccessful.



12, R = C_6H_5CO



13, R = CH_3O

The isobutoxymethylene derivative **5** was prepared by treatment of **1** with *i*-BuOH in the presence of glacial AcOH and anhyd $MgSO_4$. Other methods, such as *p*-TsOH and PhH with azeotropic removal of H_2O, or heating with *i*-BuOH and H_2SO_4, were less satisfactory. Some decomposition of **1** to yohimban-17-one occurred in each case. With the *p*-TsOH method, more than an equiv of acid was necessary and the acid salt formed with **1** was insol in PhH. The $MgSO_4$–AcOH method was found to be a mild and convenient procedure for preparation of compounds such as **5**.

Pharmacological Activity.—In order to find potentially useful depressants of the CNS, the compounds described in this paper were screened to determine their effect on rod-walking ability and locomotor activity of mice.[12] The most interesting CNS depressants are those listed in Table I. It was found that, at ip doses of 2–4 mg/kg, 18-hydroxymethyleneyohimban-17-one (**1**), yohimbano[17,18-*c*]pyrazole (**2**), and *N*-methylpyrazoles **10** and **11** were depressants, as measured by reduction of locomotor activity. Impairment of neurological function (ataxia) was produced by **1**, **2**, and **11** at 4–5 times this dose range. Muscle relaxant properties were exhibited by at least 55 times this dose range. With 18-isobutoxymethyleneyohimban-17-one (**5**), there was a large spread between the motor depressant dose and the doses required to produce ataxia and paralysis. When pyrazole **2** was administered ip to Cebus monkeys at 6, 8.5, and 12 mg/kg, a decrease in hostile behavior was observed at all doses.[13]

TABLE I

CNS TESTING RESULTS[a]

Compd	MDD_{50},[b] mg/kg	RWD_{50},[c] mg/kg	ISD_{50},[d] mg/kg
1	4	17	220
2	3	14	210
5	5	236	>1000
10	2	76	280
11	2	10	450

[a] Compds were administered to mice ip. No lethality was found at the ISD_{50}. [b] The dose estimated to reduce motor activity in mice to 50% of controls. [c] The dose estimated to cause 50% of the mice to be incapable of walking across a horizontal rod in a normal manner. [d] The dose estimated to cause 50% of the mice to fall off a screen inclined at 60°.

Experimental Section

Unless otherwise noted all mps were taken in sealed capillaries which were inserted in a Mel-Temp apparatus at about 10–30° below the mp. Unless otherwise noted samples were dried for analysis *in vacuo* over P_2O_5 at 100° for 18–24 hr. Uv absorption spectra were measured on a Cary recording spectrophotometer, ir spectra on a Perkin-Elmer spectrophotometer (Model 21), and pmr spectra on a Varian A-60 spectrometer or Varian Model V-4300B spectrometer operated at 56.4 MHz in $CDCl_3$ with TMS as internal standard. Where analyses are indicated only by symbols of the elements or functions, analytical results obtained for those elements or functions were within ±0.4% of the theoretical values.

Yohimbano[17,18-*c*]pyrazole (2)·2HCl.—A mixt of 2.0 g (0.0060 mole) of 18-hydroxymethyleneyohimban-17-one (**1**),[1] 0.64 g (0.0061 mole) of hydrazine·2HCl, and 100 ml of MeOH was warmed on a steam bath for 5 min. After 18 hr at room temp addl MeOH was added to dissolve the ppt and the resulting soln was treated with Darco several times and filtered, and the filtrate was concd to 75 ml. Slow cooling with continual scratching of the flask afforded 1.48 g (60%) of product as tan plates, mp 300–305°. Difficulties in crystg the material were encountered due to the tendency of the mixt to form a gel. Several recrystns from MeOH with the aid of Darco gave **2**·2HCl as hygroscopic plates: mp 301–305° dec; $[\alpha]^{25}D$ −127° (*c* 0.53, H_2O). *Anal.* ($C_{20}H_{22}N_4 \cdot 2HCl \cdot 0.25H_2O$) C, H, N; Cl: calcd, 17.9; found, 17.4.

Yohimbano[17,18-*c*]pyrazole (2).—A mixt of 5.00 g (0.015 mole) of **1**, 0.80 ml of hydrazine·H_2O, and 100 ml of abs EtOH was refluxed for 0.5 hr and then allowed to stand overnight at room temp. The solvent was removed *in vacuo* to give 5.93 g of a brown glass. Crystn from aq MeOH with the aid of activated charcoal gave 4.41 g (88%) of tan crystals, mp 234–238° dec (sinters at 183–190°). A 300-mg sample was recrystd 3 times from aq MeOH to give 0.190 g of **2** as cream-colored crystals: mp 241–244° dec (sinters at 185°); $[\alpha]^{25}D$ −198° (*c* 1.36, pyridine). *Anal.* ($C_{20}H_{22}N_4 \cdot 0.25H_2O$) C, H, N, H_2O (Karl Fischer).

18-Isobutoxymethyleneyohimban-17-one (5).—A mixt of 0.331 g (0.0010 mole) of **1**, 5.0 ml of redistd *i*-BuOH, 5.0 ml of glacial AcOH, and 1.0 g of $MgSO_4$ was stirred at room temp for 20 hr. The mixt was chilled and poured into 50 ml of cold 4 *N* NaOH and then extd with $CHCl_3$. The $CHCl_3$ ext was dried (Na_2SO_4) and concd *in vacuo* to a glass. The glass (0.204 g) was dissolved in Me_2CO, and the soln was filtered through diatomaceous earth.

(12) For screening procedures see: W. B. Wright, Jr., H. J. Brabander, R. A. Hardy, Jr., and A. C. Osterberg, *J Med. Chem.*, **9**, 852 (1966).

(13) Behavioral studies in monkeys were carried out by Drs. C. N. Latimer and B. M. Bernstein, Experimental Therapeutics Research Section, Pearl River, N. Y.

The filtrate was dild with H_2O, chilled, and filtered to give 0.142 g (35%) of tan needles, mp 119–123°. Recrystn from Me_2CO–H_2O afforded 0.055 g of **5** as off-white needles, mp 119–124°. After drying over P_2O_5 *in vacuo* the sample melted at 176–182° dec; $[\alpha]^{25}D$ −157° (*c* 1.05, $CHCl_3$). *Anal.* ($C_{24}H_{30}N_2O \cdot 1.5H_2O$) C, H, N.

1′-Phenylyohimbano[18,17-*d*]pyrazole (3) and 1′-Phenylyohimbano[17,18-*c*]pyrazole (4). A.—A mixt of 5.00 g (0.015 mole) of **1**, 1.05 ml of phenylhydrazine, and 100 ml of abs EtOH was refluxed for 0.5 hr and then allowed to stand overnight at room temp. The solvent was removed *in vacuo* to give 6.55 g of a brown glass. Crystn from 40 ml of EtOAc containing several drops of H_2O gave 3.91 g of crystals, mp 195–212° dec. This was dissolved in 250 ml of MeOH, treated with activated charcoal, and filtered, and the filtrate was dild with 75 ml of H_2O. Cooling gave 1.44 g of tan crystals, mp 195–202° dec. Recrystn from 50 ml of EtOAc gave 1.15 g of **3** as tan needles, mp 203–207° dec (sinters at 200°). Recrystn of a 0.150-g sample from EtOAc–H_2O gave 0.070 g of **3** as tan needles: mp 206–210° dec (sinters at 200°); $[\alpha]^{25}D$ −180° (*c* 1.25, pyridine); $\lambda_{max}^{CH_3OH}$ 223 (44,600); 255 (13,400); 282 (8130); 289 nm (ε 6,310). *Anal.* ($C_{26}H_{26}N_4$) C, H, N.

The MeOH filtrate from the 1.44-g crop of crystals was dild with H_2O to give 1.20 g of crystals, mp 220–223° dec (sinters above 180°) (mixt of isomers, mainly isomer **4**). Further diln with H_2O afforded 0.44 g of **4**, mp 220–240° dec (sinters above 195°). Recrystn from EtOAc afforded 0.152 g of **4** as yellow irregular plates: mp 248–255° dec (sinters above 215°); $[\alpha]^{25}D$ −180° (*c* 1.1, pyridine); $\lambda_{max}^{CH_3OH}$ 220 (40,700), 270 (27,000), 289 nm (sh) (ε 13,800). *Anal.* ($C_{26}H_{26}N_4$) C, H, N.

B.—A mixt of 0.406 g (0.0010 mole) of 18-isobutoxymethyleneyohimban-17-one (**5**), 0.11 ml of phenylhydrazine, and 10 ml of EtOH was allowed to stand at room temp for 20 hr. The mixt was heated on a steam bath for 10 min and concd *in vacuo* to a dark glass. Water (1 ml) and AcOH (3 ml) were added to the residue and the mixt was heated on a steam bath for 10 min and concd *in vacuo*. The residue as partitioned between 25 ml of $CHCl_3$ and 25 ml of a satd soln of $NaHCO_3$. The org layer was sepd and the H_2O layer was extd with two 15-ml portions of $CHCl_3$. The combined $CHCl_3$ exts were washed with 25 ml of a satd soln of $NaHCO_3$, dried ($MgSO_4$), and concd *in vacuo* to give 0.450 g of a glass. This was crystd from EtOAc to give 0.106 g of **3** as tan needles, mp 200–205° dec. From the mother liquors 0.113 g of **4** was obtained as yellow irregular plates.

1′-Acetylyohimbano[17,18-*c*]pyrazole (8).—A mixt of 3.0 g of yohimbano[17,18-*c*]pyrazole (**2**), 15 ml of Et_3N, and 10 ml of Ac_2O was stirred at room temp for 22 hr. The mixt was dild with 50 ml of EtOH and concd *in vacuo*. The residue was dissolved in CH_2Cl_2 and washed with 100 ml of satd $NaHCO_3$ soln. The CH_2Cl_2 soln was sepd, dried ($MgSO_4$), and concd *in vacuo*. The residue was dissolved in C_6H_6, and the solvent was removed *in vacuo* to give a yellow glass. Trituration with EtOH gave 1.90 g of tan crystals, mp 234–236° dec. Recrystn from EtOH gave 1.20 g (36%) of **8** as light tan crystals: mp 247–250° dec; $[\alpha]^{25}D$ −203° (*c* 1.1, pyridine). *Anal.* ($C_{22}H_{24}N_4O$) C, H, N.

1′-(3,4,5-Trimethoxybenzoyl)yohimbano[17,18-*c*]pyrazole (9).—To a chilled mixt of 1.62 g of **2** and 1.3 ml of Et_3N in 72 ml of dry $CHCl_3$ was added 1.71 g of 3,4,5-trimethoxybenzoyl chloride. The soln was stirred at room temp for 18 hr and then was washed with a satd $NaHCO_3$ soln. The org phase was dried ($MgSO_4$), filtered, and concd to dryness *in vacuo* and dried further under high vacuum for several hr. The residual yellow glass was heated with 20 ml of abs EtOH, and CH_2Cl_2 was added dropwise until soln occurred. The soln was concd, cooled, and filtered to give 1.44 g (56%) of yellow crystals, mp 236–238° dec. Another recrystn from the same solvent system yielded 1.40 g (55%) of **9** as yellow crystals: mp 237–240° dec; $[\alpha]^{25}D$ −125 ± 4.6° (*c* 1.1, pyridine). *Anal.* ($C_{30}H_{32}N_4O_4 \cdot 0.5H_2O$) C, H, N.

1′-Methylyohimbano[18,17-*d*]pyrazole (10) and 1′-Methylyohimbano[17,18-*c*]pyrazole (11).—A mixt of 16.6 g (0.050 mole) of **1**, 240 g (0.052 mole) of methylhydrazine, and 300 ml of abs EtOH was allowed to stand at room temp overnight and was then refluxed for 2 hr. The solvent was removed *in vacuo* to give 17.1 g of a residual brown glass. Trituration with 400 ml of hot Et_2O and filtration gave 8.0 g (47%) of tan crystals, mp 235–239° dec. The filtrate, on concn *in vacuo*, gave 6.0 g (35%) of a glass which was dissolved in 80 ml of abs EtOH, treated with Darco, and filtered, and the filtrate was dild with H_2O. Scratching the flask induced crystn and filtration gave 1.18 g of pale yellow crystals, mp 159–164°. Recrystn from abs EtOH afforded 0.580 g (3%) of **10** as white crystals: mp 245–250° dec; $[\alpha]^{25}D$ −216° (*c* 1.2, pyridine). *Anal.* ($C_{21}H_{24}N_4$) C, H, N.

The first crop of crystals (8.0 g, mp 235–239° dec) was recrystd from EtOAc and from MeOH with the aid of Darco to give 5.20 g (30%) of **11** as tan crystals, mp 255–260° dec. A 1.2-g sample was recrystd from MeOH to give 0.725 g of **11** as pale yellow crystals: mp 255–260° dec; $[\alpha]^{25}D$ −185° (*c* 1.0, pyridine). *Anal.* ($C_{21}H_{24}N_4 \cdot 0.25H_2O$) C, H, N, C-$CH_3$.

18-Hydroxymethyleneyohimban-17-one *O*-Benzoate (12).—To a chilled mixt of 3.31 g (0.010 mole) of **1** and 2.66 ml of dry Et_3N in 150 ml of dry $CHCl_3$ was added 1.80 ml (0.015 mole) of BzCl and the resulting soln was stirred at room temp for 18 hr. It was washed with H_2O and with satd $NaHCO_3$ soln and the organic phase was dried ($MgSO_4$), filtered, and evapd to dryness *in vacuo* to give 6.39 g of a dark red-brown gum. The gum was dissolved in 500 ml of boiling abs EtOH. Chilling and filtering gave 2.00 g (46%) of **12** as light orange-brown crystals, mp 211–214° dec. Recrystn from abs EtOH gave orange crystals: mp 218–219° dec; $[\alpha]^{25}D$ −242° (*c* 0.58, pyridine). *Anal.* ($C_{27}H_{26}N_2O_3 \cdot 0.5H_2O$) C, H, N, H_2O (Karl Fischer).

18-Hydroxymethyleneyohimban-17-one *O*-3,4,5-Trimethoxybenzoate (13).—To a chilled mixt of 2.00 g (0.00603 mole) of **1**, 1.70 ml (0.0131 mole) of dry Et_3N, and 120 ml of dry $CHCl_3$ was added 2.79 g (0.0121 mole) of freshly prepared 3,4,5-trimethoxybenzoyl chloride. The reaction was worked up as for **12** to yield 4.24 g of a red-brown glass which was triturated with MeOH and filtered to give 2.73 g (88%) of a light brown cryst solid, mp 156–163° dec. Boiling MeOH was added to the solid followed by CH_2Cl_2 until soln occurred. After chilling and filtering, 1.43 g (46%) of **13** was obtained as red-brown crystals: mp 160–164° dec; $[\alpha]^{25}D$ −152° (*c* 0.98, $CHCl_3$). *Anal.* Calcd for $C_{30}H_{32}N_2O_6 \cdot 2H_2O$: C, 65.2; H, 6.57; N, 5.07. Found: C, 64.7; H, 6.42; N, 3.85.

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