TABLE II

REACTIVITY RATIO DETERMINATIONS WITH STYRENE

Sample Number	Charge/ Weight Ratio[a]	Benzene, ml.	Time, hours	Nitrogen, %
2-METHYL-5-CINNAMOYLPYRIDINE				
24-A	85/15	7	3	0.98
24-D	72/25	12	3	1.40
24-C	50/50	22	5	2.64
r_2 (2-methyl-5-cinnamoylpyridine) = −0.15 ± 0.2				
r_1 (styrene) = 0.92 ± 0.08				
3-CINNAMOYLPYRIDINE				
23-2	75/25	13	3	1.84
23-3	60/40	20	3	2.44
23-4	40/60	35	5.3	3.39
r_2 (3-cinnamoylpyridine) = 0.09 ± 0.1				
r_1 (styrene) = 0.85 ± 0.05				
3-PYRIDALACETOPHENONE				
23-III	85/15	20	3	1.52
23-II	75/25	25	3	2.08
23-IV	60/40	44	3	2.97
r_2 (3-pyridalacetophenone) = 0.00 ± 0.25				
r_1 (styrene) = 0.50 ± 0.1				

[a] Styrene/Ketone.

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3-Dehydro Derivatives of Some Indole Alkaloids

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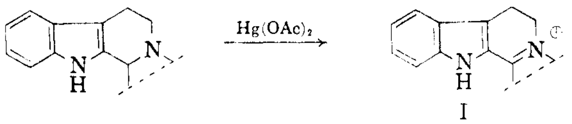
As part of an extensive study of dehydrogenation of indole alkaloids it was of interest to investigate the action of mercuric acetate on these natural products. In view of a recent publication[1] on the same subject, this phase of the study is presented at this time.

While much experimentation, especially in recent years,[2] on model compounds as well as alkaloids has shown that tertiary amines can be oxidized to immonium salts by mercuric acetate, there has been only one report on this reaction in the field of yohimbé or rauwolfia alkaloids, *i.e.* the dehydrogenation of yohimbine to an uncharacterized, colored substance.[3]

When yohimbane, *d,l*-alloyohimbane, and ajmalicine were subjected to mercuric acetate oxidation, yellow 3-dehydro products (I) were obtained.[4] Their spectra distinguish them readily from their precursors as well as from tetradehydro products. The infrared spectra exhibit characteristic 1625, 1570, and 1540 cm.$^{-1}$ peaks, while the ultraviolet spectra show maximum absorption at 248 mμ (log ϵ 4.10) and 353 mμ (log ϵ 4.41) (*cf.* Figure 1). Because of its additional chromophore in ring E ajmalicine showed slight deviations in its ultraviolet absorption curve (*cf.* Figure 1).



I

d,l-Epialloyohimbane yielded no appreciable dehydro product, even under forcing conditions. The reason for this inertness is obscure, although it must be intimately connected with the steric requirements of the transition complex of the mercuric acetate reaction. In their dehydrogenation studies Weisenborn and Diassi[1] discovered that *normal*[5] and *allo* compounds undergo the oxidation, while *pseudo* and *epiallo* systems do not, and ascribed this phenonomenon to the necessary availability of an axial C_3-H bond in order to accommodate a coplanar transition state in the reaction mechanism originally proposed by Leonard.[2] While this argument satisfies the behavior of the conformationally unequivocal *normal* and *pseudo* compounds, it appears ambiguous for the *allo* and *epiallo* substances, one of whose two all-chair, C/D trans conformations always possesses an axial C_3 hydrogen atom.[6] Whereas admittedly in such unreactive compounds as reserpine, methyl reserpate, and deserpidine[1] this conformation is the less favorable one,[6,7] the opposite is the case with the essentially inert *d,l*-epialloyohimbane.[6] In short, the mechanism of the mercuric acetate oxidation of amines will require much refinement before its steric course will become clear.

All Δ^3 products reverted to their dehydro precursors on sodium borohydride reduction as well as catalytic hydrogenation. Three previous examples of reductions of 3-dehydro compounds concur with

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(1) F. L. Weisenborn and P. A. Diassi, *J. Am. Chem. Soc.*, **78**, 2022 (1956).

(2) *Cf.* N. J. Leonard, W. J. Middleton, P. D. Thomas, and D. Chaudhury, *J. Org. Chem.*, **21**, 344 (1956) and preceding papers.

(3) A. Schomer, *Archiv. Pharm.*, **265**, 509 (1927).

(4) Both yohimbine and yohimbone have been converted to their 3-dehydro derivatives. However, the former will not be treated here in deference to the prior communication by Weisenborn and Diassi,[1] and discussion of the latter will be postponed until a later date.

(5) The term *normal* is applied to those substances having the stereochemistry of yohimbine at carbons 3, 15, and 20.

(6) E. Wenkert and L. H. Liu, *Experientia*, **11**, 302 (1955).

(7) C. F. Huebner, H. B. MacPhillamy, E. Schlittler, and A. F. St. André, *Experientia*, **11**, 303 (1955).

this observation.[8-10] While little can be said about the mode of the chemical reduction, the hydrogenation requires comment. The formation of *d,l*-alloyohimbane from its dehydro derivative[8] was predictable on steric grounds, *i.e.* adsorption on the catalyst's surface, and hence hydrogen transfer to C_3, would have been expected to proceed preferentially on the side of the C_{15} and C_{20} hydrogen atoms. The exclusive formation of yohimbane,[9] instead of a mixture of it and pseudoyohimbane, appears at first glance to be an anomaly in view of the absence of any steric factors. This unambiguous case of *catalytic hydrogenation under thermodynamic control* strongly suggests that the reduction of the immonium linkage takes place unsymmetrically, *via* the transfer of a hydride ion, or its equivalent, to C_3, instead of the usual H_2 transposition onto both atoms attached to a double bond.[11] Since ajmalicine can possess the stereochemistry of *only* a *normal* or *allo* compound, because of its relationship to serpentine[12-14] its hydrogenative re-formation from its 3-dehydro product was expected.

EXPERIMENTAL

Dehydrogenation of yohimbane, d,l-alloyohimbane, ajmalicine,[15] *and d,l-epialloyohimbane.* A mixture of amine and mercuric acetate (1:4 moles) in 5% aqueous acetic acid was heated at 60–90° for two hours. The precipitated mercurous acetate (average 75% yield) was filtered, and the filtrate was heated to boiling and saturated with H_2S gas. A small amount of concentrated hydrochloric acid was added to the cooled solution and the latter was heated until the black mercuric sulfide had coagulated and separated. The mixture was filtered and the filtrate was treated with a saturated solution of potassium perchlorate. The resulting precipitate was filtered and recrystallized in methanol. The yields of 3-dehydro perchlorates ranged from 61–74%. The ultraviolet spectra are shown in Figure 1. The infrared spectra (in Nujol) showed the following characteristic peaks; 3230 (w), 1625(m), 1570(m), and 1540(m) cm.$^{-1}$

3-Dehydroyohimbane consisted of yellow needles, m.p. 273–274°, $[\alpha]^{28}_{D}$ +98.3° (methanol).

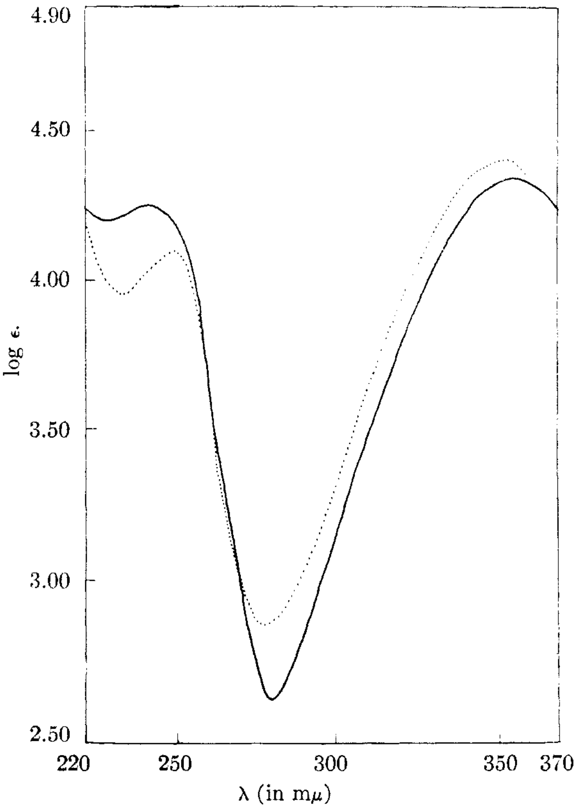

FIG. 1.—ULTRAVIOLET SPECTRA IN 95% ALCOHOL SOLUTION: ——— 3-Dehydroajmalicine; .... *d,l*-3-Dehydroalloyohimbane.

Anal. Calc'd for $C_{19}H_{23}ClN_2O_4$: C, 60.23; H, 6.12; N, 7.39. Found: C, 60.30; H, 6.37; N, 7.36.

d,l-3-Dehydroalloyohimbane, yellow rods, m.p. 227–228°.

Anal. Calc'd for $C_{19}H_{23}ClN_2O_4$: C, 60.23; H, 6.12; N, 7.39. Found: C, 60.42; H, 6.25; N, 7.08.

3-Dehydroajmalicine, yellow needles, m.p. 264–265°, $[\alpha]^{28}_{D}$ +75.6° (methanol).

Anal. Calc'd for $C_{21}H_{23}ClN_2O_7$: C, 55.93; H, 5.14; N, 6.22. Found: C, 55.90; H, 5.48; N, 6.33.

Mercuric acetate oxidation of *d,l*-epialloyohimbane yielded no mercurous acetate, even after 22 hours. The isolated perchlorate showed an ultraviolet spectrum corresponding to approximately a 10% conversion to dehydro product. Liberation of the free amine by ammonia yielded merely starting material, as indicated by m.p., mixture m.p., and ultraviolet spectrum.

Reduction of the 3-dehydro products. (*a*) *Sodium borohydride reduction.* A mixture of the 3-dehydro perchlorate and a 25-molar excess of sodium borohydride in methanol was refluxed for three hours. The solvent was removed under a vacuum, and the residue was treated with water and extracted with chloroform. The organic solution was washed with a saturated sodium chloride solution and dried over sodium sulfate. On evaporation of the solvent a glass remained, which on recrystallization from methanol yielded yohimbane, *d,l*-alloyohimbane, and ajmalicine from their corresponding dehydro products, as identified by m.p., mixture m.p., and infrared spectra. The yields ranged from 40–90%.

(*b*) *Catalytic hydrogenation.* A mixture of the 3-dehydro perchlorate and 10% (by weight) of platinum oxide catalyst in methanol was hydrogenated at 57 lbs. pressure until hydrogen uptake had ceased. After filtration of the catalyst the solution was concentrated to a small volume, diluted with water and the free base was precipitated by adding ammonia. The precipitate was filtered, washed with water,

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(8) G. Stork and R. K. Hill, *J. Am. Chem. Soc.*, **76**, 949 (1954).

(9) E. E. van Tamelen, and M. Shamma, *J. Am. Chem. Soc.*, **76**, 949 (1954).

(10) R. B. Woodward F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kiersteadt, *J. Am. Chem. Soc.*, **78**, 2023 (1956).

(11) The production of both *normal* and *pseudo* systems on hydrogenation, followed by a rapid catalyst-induced epimerization of the *pseudo* product is a less likely alternative yet to be excluded.

(12) F. L. Weisenborn, M. Moore, and P. A. Diassi, *Chemistry & Industry*, 375 (1954).

(13) M. W. Klohs, M. D. Draper, F. Keller, W. Malesh, and F. J. Patracek, *J. Am. Chem. Soc.*, **76**, 1332 (1954).

(14) The catalytic hydrogenation of tetradehydro *normal* and *allo* systems has been shown to give exclusively *normal* and *allo* products [M.-M. Janot, Goutarel, A. Le Hir, M. Amin, and V. Prelog, *Bull. soc. chim., France*, 1085 (1952); A. Le Hir, M.-M. Janot, and R. Gotarel, *Bull. soc. chim. France*, 1027 (1953)].

(15) One of the authors (D. K. R. C.) would like to thank Drs. Hochstein and Keller for their kind gifts of serpentine.

and crystallized from methanol, yielding yohimbane, *d,l*-alloyohimbane, and ajmalicine, each from its corresponding 3-dehydro product, as identified by m.p., mixture m.p., and infrared spectra. The yields were 91, 52, and 71%, respectively.

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The Base-Catalyzed Alkylation of Fluorene with Secondary Alcohols

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Recently, the successful alkylation of fluorene with primary alcohols and their alkoxides was reported, and the general subject was reviewed.[2] It was the purpose of this investigation to determine whether the reaction could be extended to secondary alcohols as could be predicted from the postulated mechanism for the reaction.[2,3]

It has now been found that cyclopentanol and cyclohexanol together with their respective sodium salts at 220–230° do alkylate fluorene in from 24–60% yield (see Table). Furthermore, isopropyl alcohol together with its sodium salt alkylates fluorene, but in only about 1% yield. These yields are generally lower than those for primary alcohols previously reported under comparable conditions.[2,3]

Recently a number of investigators[4-8] have reported for a related reaction, the N-alkylation of aniline, that the temperature for alkylation may be lowered by the use of U. O. P. nickel or Raney nickel. In the present reaction, these results were corroborated: 9-cyclohexylfluorene was obtained in 69% yield using U. O. P. nickel and in 74% yield with Davison sponge nickel catalyst. When the use of the latter catalyst was combined with the technique of returning the refluxing solvent through a Soxhlet thimble containing calcium hydride, the yield of 9-isopropylfluorene was raised from below 1% to 52%.

The alkylation of fluorene was also attempted with one primary alcohol — neopentyl alcohol. It was hoped that the bulky *tert*-butyl group on the postulated intermediate fulvene would prevent further reduction.[2,3,9] However, a colorless compound corresponding in all respects to those expected for a fluorene and not a fulvene was obtained. Absorption bands at 1368 cm.$^{-1}$ and 1390 cm.$^{-1}$ are characteristic of a neopentyl group[10] and preclude the possibility of rearrangement during alkylation.

TABLE I

9-Alkylfluorenes

Alkyl Group	Method	M.P. of Product, °C.	Yield, %	M.P. of Analytical Sample, °C.	Analyses C Calc'd	C Found	H Calc'd	H Found
Cyclohexyl	I	110.0–115.6	60.5	115.3–115.7[a]	91.88	91.98	8.12	7.83
Cyclohexyl	II	112.0–116.0	69.0					
Cyclohexyl	III	113.0–116.6	74.2					
Cyclopentyl[b]	I	60.0–62.4	24.4	62.0–62.4	92.26	92.24	7.74	7.84
Cycloheptyl	III	63.0–68.8	40.0	65.6–66.8	91.55	91.32	8.45	8.49
Isopropyl	I	53.9–54.5	<1	53.9–54.5[c]				
Isopropyl	IV	50.0–54.5	52.3	53.8–54.8[c]	92.26	91.94	7.74	8.08
Neopentyl	I	79.0–79.8	35.2	79.4–79.8	91.47	91.51	8.53	8.45

[a] W. G. Brown and B. A. Bluestein, *J. Am. Chem. Soc.*, **65**, 1082 (1943), report, m.p. 116°. [b] Decomposed upon standing exposed to air for one month. [c] Footnote (*a*) reports 54–55°.

EXPERIMENTAL

Cycloheptanol. Cycloheptanone (49.0 g., 0.44 mole) was added dropwise to a stirred suspension of 5.0 g. (0.13 mole) of lithium aluminum hydride in 200 ml. of dry ether. After the addition was complete, the mixture was refluxed for three hours. Ten percent sulfuric acid then was added with stirring until a clear solution was obtained. The aqueous layer was separated, washed twice with ether, and the combined organic layers were washed with sodium carbonate solution and then with water until neutral. After drying over sodium sulfate, the ether and then the cycloheptanol distilled to give 38.8 g. (0.34 mole, 80%), b.p. 184–187°, n_D^{25} 1.4742.[11]

Alkylation reactions. Method I. Sodium (2 g., 0.087 g.-atom) was added in small pieces to 40 ml. of the required alcohol contained in a Carius tube to which a condenser had been temporarily attached. An oil-bath hastened reaction of the sodium. Upon cooling the solution to room tempera-

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[1] To whom inquiries should be sent.

[2] K. L. Schoen and E. I. Becker, *J. Am. Chem. Soc.*, **77**, 6030 (1955).

[3] See also Y. Sprinzak, *J. Am. Chem. Soc.*, **78**, 466 (1956).

[4] E. F. Pratt and E. J. Frazza, *J. Am. Chem. Soc.*, **76**, 6174 (1954).

[5] R. C. Rice and E. J. Kohn, *J. Am. Chem. Soc.*, **77**, 4052 (1955).

[6] C. Ainsworth, *J. Am. Chem. Soc.*, **78**, 1635 (1956).

[7] B. B. Corson and H. Dressler, *J. Org. Chem.*, **21**, 474 (1956).

[8] J. Horyna and O. Černý, *Chem. Listy*, **50**, 381 (1956).

[9] S. M. Linder, E. I. Becker, and P. E. Spoerri, *J. Am. Chem. Soc.*, **75**, 5972 (1953).

[10] L. Bellamy, *The Infra-red Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, 1954, p. 13.

[11] P. A. S. Smith and D. R. Baer [*J. Am. Chem. Soc.*, **74**, 6135 (1952)] reported 50% yield with the same reagent but without heating, b.p. 87–88.5° (15 mm.), n_D^{20} 1.4757.