resulting brown solid residue was extracted into dry ether (100 ml). This solution was concentrated to dryness and extracted into warm benzene (100 ml), which was cooled and concentrated to a small volume, whereupon small golden red crystals of product were deposited. Recrystallization from benzene afforded bronze crystals of IX (0.23 g, 15%) which charred above 130° and did not melt. The product was stable only when stored under nitrogen in the dark.

Anal. Calcd for $C_{21}H_{17}N_3$: C, 81.00; H, 5.50; N, 13.49; mol wt, 311.4. Found: C, 80.77; H, 5.71; N, 13.27; mol wt, 306 (cryoscopic in benzene).

Alternatively, pyridine-4-carboxaldehyde (0.54 g, 0.005 mole) and methyl benzenesulfonate (0.86 g, 0.005 mole) were heated together in refluxing acetonitrile (20 ml) for 72 hr under nitrogen. The solvent was removed *in vacuo* and the resulting syrup, dissolved in glacial acetic acid (50 ml), was heated with benzil (1.06 g, 0.005 mole) and ammonium acetate (10 g, 0.13 mole) under nitrogen for 12 hr. The solution, initially deep green, became orange. It was poured into ice water (200 ml) and neutralized with solid sodium carbonate. The orange solution was immediately extracted with four 15-ml portions of $CHCl_3$ and the extract was dried with sodium sulfate and evaporated *in vacuo*. The brown solid was crystallized from benzene to yield IX as bronze crystals (0.19 g, 12%). Its spectral properties were identical with those of the product from the previous preparation. Tlc on buffered Kieselguhr-G with pyridine elution showed only one spot from both preparations (R_f 0.87).

Registry No.—I, 13341-64-5; II, 13341-65-6; IV, 13341-66-7; VI, 1970-91-8; VII, 13319-97-6; VIII, 13341-68-9; IX, 13341-69-0.

Acknowledgments.—The nmr spectra of II and VI were determined by Dr. R. E. K. Winter at the Polytechnic Institute of Brooklyn. Support for this work by a Frederick Gardner Cottrell Grant from Research Corp. is gratefully acknowledged.

Elimination During the Reduction of Pyridinium Salts

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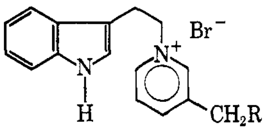
The reduction of N-[β-(3-indolyl)ethyl]pyridinium salts with metal hydrides has been studied by a number of investigators[2-5] in an attempt to prepare compounds amenable to the construction of indole alkaloids. Wenkert and co-workers[4] have reported that treatment of the pyridinium salt **1a** with lithium aluminum tri-*t*-butoxyhydride in dry tetrahydrofuran followed by exposure to aqueous acid afforded the tetracyclic **2a** whereas reduction with sodium borohydride or lithium aluminum hydride gave tricyclic **3a**. With the latter reagent, small amounts of tetracyclic **2a** were also obtained.

In an attempt to prepare the allylic alcohol **2b**, the pyridinium salt **1b** was subjected to the conditions[6] for



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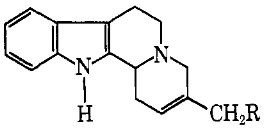
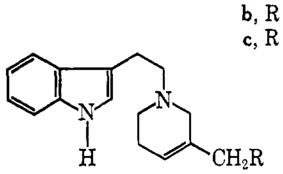


2a, R = CH_3
b, R = OH
c, R = OAc



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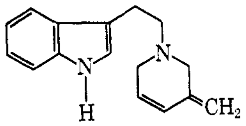
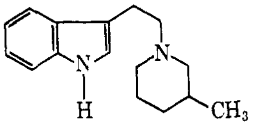
cyclization, affording two crystalline products which were readily separated by chromatography on acid-washed alumina. The more polar of the two substances was identified as the allylic alcohol **3b** (*m/e* 256), whose nmr spectrum displayed a broad two-proton singlet at δ 3.85 (CH_2O) and a broad one proton singlet at 5.65 (vinyl). The less polar component (*m/e* 238) was assigned structure **4** based upon the following data.



4



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Catalytic hydrogenation in ethanol over 10% palladium on charcoal proceeded with the uptake of 2 equiv of hydrogen, affording a compound which was identical (undepressed mixture melting point and superimposable infrared spectrum) with the amine **5** prepared from tryptophyl bromide and 3-methyl piperidine. The presence of a diene chromophore was evident in the ultraviolet spectrum of **4**. The absorption band in the region of 220 mμ had an extinction coefficient greater by about 10,000 than the corresponding reduced product **5**. The substitution pattern of the diene was revealed by its nmr spectrum, showing a broad two-proton singlet at 5.0 (methylene vinyl) and a two-hydrogen multiplet at 5.8–6.7 (vicinal vinyl).

The diene can be thought to arise by Scheme I. It was felt that the diene could be derived from that amount of salt **1b** which was present as the aluminate of the alcohol function, whereas any uncoordinated alcohol would give rise to the allylic alcohol. Consequently, reduction with lithium aluminum hydride would be expected to give predominately the diene, and sodium borohydride, in turn, the allylic alcohol. Reduction of salt **1b** with lithium aluminum hydride in tetrahydrofuran yielded the diene in 50% yield as the only reduction product, whereas sodium borohydride in ethanol afforded the allylic alcohol **3b** in 73% yield, exclusive of the diene.[7]

Reduction of the pyridinium salt **1c** with either sodium borohydride, lithium aluminum tri-*t*-butoxyhydride, or lithium aluminum hydride gave the diene in 29, 30, and 45% yields, respectively, exclusive of the

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[1] National Institutes of Health Predoctoral Fellow, 1966–1967.

[2] For a general review, see R. E. Lyle and P. S. Anderson, *Advan. Heterocyclic Chem.*, **6**, 46 (1966).

[3] R. C. Elderfield, B. C. Fischer, and J. M. Lagowski, *J. Org. Chem.*, **22**, 1376 (1957).

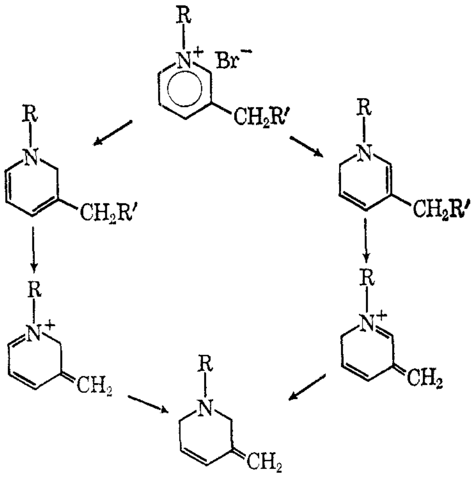
[4] E. Wenkert, R. A. Massy-Westropp, and R. G. Lewis, *J. Am. Chem. Soc.*, **84**, 3732 (1962).

[5] K. T. Potts and I. D. Nasri, *J. Org. Chem.*, **29**, 3407 (1964).

[6] The nature of the products in all the reactions studied was unaltered when the aqueous acid treatment was omitted.

[7] The crude reaction mixtures were examined by thin layer chromatography to determine their composition.

Scheme I



R = 2-(3-indolyl)ethyl
R′ = OAc or O-aluminate

allylic alcohol **3b**. In such a case, reductive elimination appears to be the preferred mode of reaction. Since the pyridinium salt contains an effective leaving group, the course of the reduction is not governed by the nature of the reducing agent.

Experimental Section[8]

Pyridinium Salt 1b.—The pyridinium salts were prepared by the method of Wenkert.[3] A mixture of 10.00 g (0.046 mole) of tryptophyl bromide and 10.00 g (0.092 mole) of 3-pyridylcarbinol was heated under nitrogen at 80° for 8 hr. The reaction mixture was cooled and the resultant solid cake was triturated with 10 ml of methanol and filtered. Recrystallization from acetone–methanol afforded 7.74 g of a bright yellow solid, mp 191–193°. An additional 0.77 g (57% yield over-all) was obtained from concentration of the mother liquors.

Anal. Calcd for $C_{16}H_{17}BrN_2O$: C, 57.66; H, 5.11; Br, 24.02; N, 8.41. Found: C, 57.65; H, 5.22; Br, 23.80; N, 8.27.

Pyridinium Salt 1c.—A mixture of 6.20 g (0.028 mole) of tryptophyl bromide and 9.20 g (0.061 mole) of 3-acetoxymethylpyridine[9] was reacted as described above. The crude product was recrystallized from acetone–methanol to yield 8.43 g (81.3%) of bright yellow crystals, mp 160.5–161.5°.

Anal. Calcd for $C_{18}H_{19}BrN_2O_2$: C, 57.60; H, 5.07; Br, 21.33; N, 7.47. Found: C, 57.80; H, 4.98; Br, 21.55; N, 7.48.

Reduction of Salt 1b with Lithium Aluminum Tri-*t*-butoxyhydride.—To a solution of 7.00 g (0.027 mole) of lithium aluminum tri-*t*-butoxyhydride in 250 ml of dry tetrahydrofuran was added 2.00 g (0.006 mole) of pyridinium salt **1b** and the mixture was refluxed with stirring for 2 hr. The reaction mixture was cooled to room temperature, decomposed with a saturated aqueous solution of sodium sulfate, and filtered. The filtrate was treated with 20 ml of 5% aqueous hydrochloric acid and allowed to stand for 2 hr at room temperature and then 45 min at reflux. The cooled solution was neutralized with 10% aqueous sodium hydroxide, diluted with an equal volume of water, and thoroughly extracted with chloroform. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated. The residual oil was chromatographed on Merck acid-washed alumina, the 10% ether–benzene eluent affording 251 mg (17.6%) of diene **4** upon recrystallization from ether–petroleum ether (bp 30–60°): mp 109.5–110.5°; *m/e* 238, 143, 129, 108, and 93; $\nu_{max}^{CHCl_3}$ 3480, 2985, and 1455 cm^{-1}; λ_{max}^{MeOH} 291 mμ (ε 5180), 282 (5870), 274 (5370), and 220 (47,000); nmr ($CDCl_3$), δ 2.6–3.5 (8 H, m), 5.0 (2 H, br, s), 5.8–6.7 (2 H, m), 7.1 (1 H, s), 7.2–7.9 (4 H, m), 8.44 (1 H, br, s).

Anal. Calcd for $C_{16}H_{18}N_2$: C, 80.63; H, 7.61; N, 11.76. Found: C, 80.71; H, 7.72; N, 11.79.

Elution with 5% methanol–chloroform gave 429 mg (27.9%) of allylic alcohol **3b** upon recrystallization from chloroform: mp 135.5–137.5°; *m/e* 256, 144, 129, 126, 115, and 110; ν_{max}^{KBr} 3210, 1450, 1350, 1100, 1040, 845, 765, and 735 cm^{-1}; nmr (DMSO), 3.85 (2 H, br, s), 5.65 (1 H, br, s).

Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.64; H, 8.04; N, 11.01.

Reduction of Salt 1c with Lithium Aluminum Tri-*t*-butoxyhydride.—The previous procedure for the reduction of salt **1b** with lithium aluminum tri-*t*-butoxyhydride was employed, affording the diene in 30.6% yield.

Reduction of Salt 1b with Sodium Borohydride.—To a stirred suspension of 2.00 g (0.006 mole) of salt **1b** in 50 ml of absolute ethanol maintained at 0° was added 1.5 g (0.040 mole) of sodium borohydride and the mixture was allowed to react for 2 hr. The reaction mixture was diluted with 200 ml of water and thoroughly extracted with chloroform. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and evaporated to give a light yellow oil which solidified upon standing, mp 120–140°. Recrystallization from chloroform afforded 1.12 g (73% yield) of crystals, mp 135.5–137.5°.

Reduction of Salt 1c with Sodium Borohydride.—The previous procedure for the reduction of salt **1b** with sodium borohydride was employed affording the diene in 29.3% yield.

Reduction of Salt 1b with Lithium Aluminum Hydride.—To a suspension of 0.500 g (0.013 mole) of lithium aluminum hydride in 50 ml of dry tetrahydrofuran was added 470 mg (1.41 mmoles) of salt **1b** and the reaction mixture was stirred for 1 hr at room temperature. The excess reducing agent was decomposed with 1 ml of saturated aqueous sodium sulfate. The reaction mixture was filtered, dried over anhydrous magnesium sulfate, refiltered, and concentrated to give a yellow oil. Chromatography on alumina (*vide supra*) afforded 167 mg (49.8% yield) of crystalline diene, mp 110–111°, from ether–petroleum ether.

Reduction of Salt 1c with Lithium Aluminum Hydride.—The previous procedure for the reduction of salt **1b** with lithium aluminum hydride was employed, yielding the diene in 45.2% yield.

Amine 5.—A mixture of 2.00 g (0.009 mole) of tryptophyl bromide and 2.00 g (0.020 mole) of 3-methyl piperidine was allowed to stand at room temperature overnight. The reaction mixture was diluted with 50 ml of methylene chloride, washed with aqueous sodium carbonate, dried over anhydrous magnesium sulfate, filtered, and concentrated. Chromatography of the residual oil on acid-washed alumina followed by recrystallization from ether–petroleum ether afforded 584 mg (27% yield) of the tertiary amine: mp 136.5–137.5°, $\nu_{max}^{CHCl_3}$ 3480, 3010, 2935, and 1455 cm^{-1}; λ_{max}^{MeOH} 291 mμ (ε 5220), 282 (5970), 273 (5410), 222 (37600); nmr ($CDCl_3$), δ 0.88 (3 H, d), 1.5–1.8 (5 H, m), 2.7–3.1 (8 H, m), 6.85 (1 H, br, s), 7.05–7.30 (4 H, m), 7.5–7.7 (1 H, br, s).

Anal. Calcd for $C_{16}H_{22}N_2$: C, 79.29; H, 9.15; N, 11.56. Found: C, 79.17; H, 9.11; N, 11.68.

Hydrogenation of Diene IV to Amine V.—A solution of 134 mg (0.56 mmole) of diene in 5 ml of absolute ethanol was hydrogenated at atmospheric pressure in the presence of 50 mg of 10% palladium on charcoal. Uptake of hydrogen ceased at 25.8 ml (2.05 equiv, cor). The catalyst was removed by filtration and the filtrate evaporated *in vacuo*. The oil was crystallized from ether–petroleum ether, affording 110 mg (81.5%) of white crystals, mp 135.5–137.5°. A mixture melting point was undepressed and had a superimposable infrared spectrum with a sample prepared in the preceeding experiment.

Registry No.—**1b**, 13426-97-6; **1c**, 13444-34-3; **3b**, 13426-98-7; **4**, 14326-99-8; **5**, 13427-00-4.

Acknowledgments.—We are indebted to Dr. Walter McMurray of the Yale Medical School for the determination of the mass spectra. F. E. Z. wishes to thank Eli Lilly and Co. for a research grant which aided in the support of this work.

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[8] All melting points are corrected. The infrared spectra were determined on a Perkin-Elmer 421 spectrophotometer. Ultraviolet spectra were recorded on a Cary 11S recording spectrophotometer. Nuclear magnetic resonance spectra were determined on a Varian A-60 spectrometer with tetramethylsilane as internal standard. Mass spectra were recorded on an A. E. I. MS-9 spectrometer. Elemental analyses were determined by Alfred Bernhardt Laboratories.

[9] M. Simonetta and G. Favini, *Gazz. Chim. Ital.*, **84**, 566 (1954).