1, θ was determined on the basis of an assumed long spacing of 43 Å. which is an approximately average value for the acids involved. The values of θ were obtained for Cr radiation, λ 2.2909 Å. It is seen in Fig. 3 how calculated intensity (for the first six orders) varies with hydroxyl shift along the chains. The first order variation is large but not likely to be easy to observe. The relative values for 3rd and 4th order suggest an index very sensitive to hydroxyl shift. For simple identification purposes the relative intensities are particularly sensitive since odd and even acids are distinguished by short spacing; hence the problem is only to distinguish among individual even acids or among individual odd acids, as the case may be.

It was desired to compare experimental intensities with each other and with calculated intensities. It was found impossible, however, to obtain experimental intensities with sufficient reproducibility on an absolute basis to use for convenient comparison, due mainly it seemed to variations in crystallization.

To permit intercomparison of intensities it was decided to equate arbitrarily the strongest intensity, except that of the 1st order, to 1000 for any given case. (The first order was given less consideration because of uncertainties in the experimental evaluation.) The other intensities were adjusted in proportion. In Fig. 4 it is shown how the values followed an orderly sequence and showed remarkably good agreement between calculation and experiment. It is plain to see that the intensity sequence serves as a clear-cut characterization of an individual dihydroxy (or original octadecenoic) acid. This is especially evident when the alternation in m.p. and short spacings between odd and even acids is remembered. Thus a distinction to be looked for among 7,8- and 9,10- and 11,12-dihydroxystearic acids, for instance, is readily made. Accordingly it is plain that synthetic vaccenic (11-octadecenoic) acid is clearly distinguishable from synthetic or "natural" elaidic (9-octadecenoic) acid.

The agreement of calculated with experimental intensities constitutes a further confirmation of the already well-established structures of the octadecenoic acids.

Acknowledgment.—The authors are indebted to a number of members of this Laboratory for experimental assistance and advice in the preparation of this paper.

CINCINNATI 17, OHIO RECEIVED APRIL 30, 1951

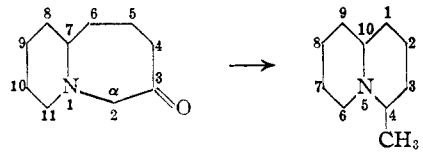
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Rearrangement of α-Aminoketones during Clemmensen Reduction. VII. The Rearrangement of 3-Keto-1-azabicyclo[5.4.0]hendecane[1]

BY NELSON J. LEONARD AND ERNEST D. NICOLAIDES

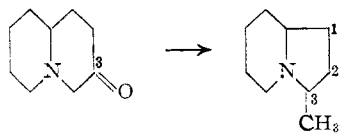
It has been shown that a bicyclic α-aminoketone having fused six- and seven-membered rings undergoes rearrangement during Clemmensen reduction. Specifically, 3-keto-1-azabicyclo[5.4.0]hendecane is converted to a mixture of the two racemates of 4-methylquinolizidine upon reduction with zinc amalgam and hydrochloric acid.

The contraction of a seven-membered monocyclic α-aminoketone during Clemmensen reduction has been established,[2] as has the similar contraction of a bicyclic α-aminoketone (6-keto-1-azabicyclo[5.3.0]decane) possessing fused five- and seven-membered rings.[3] Because of certain previously observed differences in behavior due to ring size,[4] the result of the Clemmensen reduction of a bicyclic α-aminoketone possessing fused six- and seven-membered rings was also sought. The compound 6-keto-1-azabicyclo[5.4.0]hendecane (see I for numbering system) could not serve as a model since reduction either with or without rearrangement would produce the same compound, 1-azabicyclo[5.4.0]hendecane. 3-Keto-1-azabicyclo[5.4.0]hendecane (I) was therefore selected for study, since Clemmensen reduction with rearrangement should yield 4-methylquinolizidine (II), rather than 1-azabicyclo[5.4.0]hendecane. Moreover, it has been shown recently in this Laboratory[5]



I II

that the Clemmensen reduction of the analogical 3-ketoquinolizidine (III) gives 3-methyloctahydropyrrocoline (IV) (both racemates) predominantly, rather than quinolizidine.



III IV

The two racemates represented by II have been obtained previously as their picrate derivatives, m.p. 195° and 187°,[6] but separation of the free bases was not achieved. We have now been able to separate the isomers of 4-methylquinolizidine by careful fractional distillation and to characterize both racemates by infrared absorption spectra.

(1) This work was supported by a grant from E. I. du Pont de Nemours and Company, Inc.

(2) N. J. Leonard and E. Barthel, Jr., THIS JOURNAL, **71**, 3098 (1949).

(3) N. J. Leonard and W. C. Wildman, *ibid.*, **71**, 3100 (1949).

(4) G. R. Clemo, R. Raper and H. J. Vipond, *J. Chem. Soc.*, 2095 (1949).

(5) N. J. Leonard and S. H. Pines, THIS JOURNAL, **72**, 4931 (1950).

(6) R. Lukeš and F. Šorm, *Collection Czechoslov. Chem. Communs.*, **12**, 356 (1947).

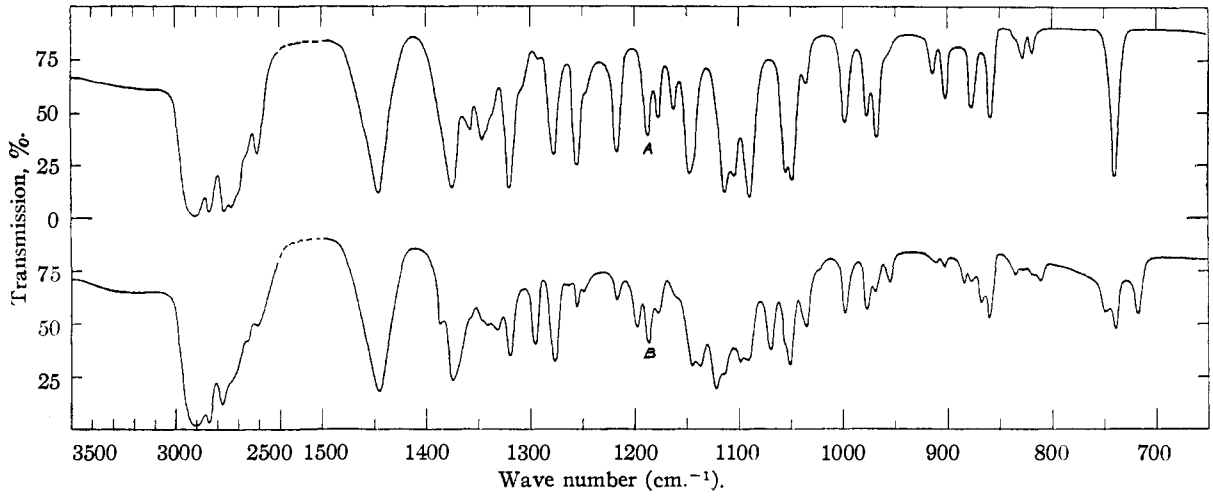
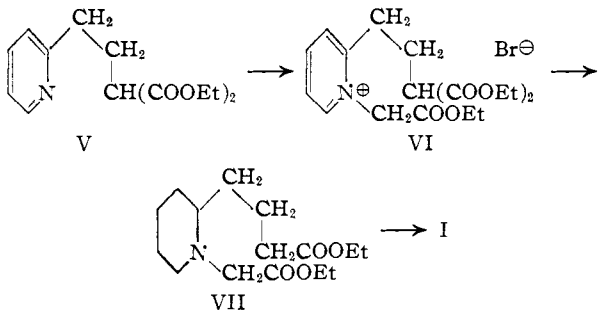


Fig. 1.—Infrared absorption of 4-methylquinolizidines.

The method used for the preparation of 4-methylquinolizidine (II) was that of Boekelheide and Rothchild[7] utilizing the catalytic hydrogenation of 1-(2′-pyridyl)-4-pentanone. These workers reported the isolation of only one racemate of II (which formed a picrate, m.p. 191–195°), whereas we were able to isolate the second racemate as well by distillation of the hydrogenation product first through a Podbielniak column and then through a Craig column.

The two racemates of 4-methylquinolizidine (II), thus obtained unequivocally by catalytic hydrogenation of 1-(2′-pyridyl)-4-pentanone, were readily identified as the main constituents of the product obtained from the Clemmensen reduction of 3-keto-1-azabicyclo[5.4.0]hendecane (I). The method used for the synthesis of the α-aminoketone I is indicated in the accompanying reaction sequence (V → VI → VII → I). Diethyl β-(2-



pyridyl)-ethylmalonate (V)[7,8] was converted to the quaternary salt VI by treatment with ethyl bromoacetate. A combination of steps, including catalytic hydrogenation, hydrolysis, decarboxylation and esterification, served for the conversion of 1-carbethoxymethyl-2-(γ,γ-dicarbethoxypropyl)-pyridinium bromide (VI) to diethyl piperidyl-1-acetate-2-γ-butyrate (VII). The Dieckmann ring closure of VII, resulting in the new seven-membered ring of I, was effected by sodium ethoxide. No attempt was made to isolate the intermediate ketoester: ring closure was followed immediately by hydrolysis and decarboxylation. The Clemmensen reduction of I was carried out in the usual manner.[3] The finding that ketone ring contraction occurred during the Clemmensen reduction of 3-keto-1-azabicyclo[5.4.0]hendecane (I) and that no 1-azabicyclo[5.4.0]hendecane[9] was produced is consistent with the results obtained earlier in this Laboratory on the Clemmensen reduction of the ring homolog, 3-ketoquinolizidine (III → IV). In addition, the conversion of I to II represents the third example (among as many differently constituted molecules)[2,3] of the contraction of a seven-membered-ring α-aminoketone in which the carbonyl and amino groups are homocyclic.

Experimental[10]

4-Methylquinolizidine (II).—Ethyl β-(2-pyridyl)-ethylacetoacetate,[7,8] obtained by the addition of ethyl acetoacetate to 2-vinylpyridine, was converted to 1-(2′-pyridyl)-4-pentanone,[7,8] b.p. 77–87° (0.25 mm.), $n^{20}D$ 1.5093. Hydrogenation of 1-(2′-pyridyl)-4-pentanone was carried out according to the directions of Boekelheide and Rothchild[7] at 200° and 200 atm. over Raney nickel in ethanol. The 4-methylquinolizidine product (15 g.) was distilled through a Miniature Hyper-Cal Podbielniak Column of 60 theoretical plates. A reflux ratio of 20:2 and a distillation rate of 0.1 ml. per minute was used. A total of six fractions was collected within an over-all boiling point range of 1.3° (27.5 mm.) and a refractive index range of 0.0052. At the end of the distillation, the column and pot were washed out with ether and the ether was removed, leaving approximately 2 ml. of residue. A sample of distillate fraction five, b.p. 90.3–90.5° (27.5 mm.), $n^{20}D$ 1.4794, was submitted for analysis.

Anal. Calcd. for $C_{10}H_{19}N$: C, 78.36; H, 12.50; N, 9.14. Found: C, 78.25; H, 12.23; N, 9.33.

The picrate, made in ether and recrystallized from ethanol, formed yellow prisms, m.p. 191–193°.

Anal. Calcd. for $C_{16}H_{22}N_4O_7$: C, 50.25; H, 5.80; N, 14.61. Found: C, 50.24; H, 6.07; N, 14.57.

The infrared spectra[11] of the first through the fifth (curve A in Fig. 1) distillate fractions were very similar, while that of the pot residue was slightly different. This residue was distilled through a Craig column at a distillation rate of 0.3

(7) V. Boekelheide and S. Rothchild, THIS JOURNAL, **71**, 879 (1949).
(8) W. E. Doering and R. A. N. Weil, *ibid.*, **69**, 2461 (1947).
(9) N. J. Leonard and W. E. Goode, *ibid.*, **72**, 5404 (1950).
(10) All melting points are corrected. Microanalyses were performed by Miss Emily Davis, Mrs. Jean Fortney and Miss Katherine Pih.
(11) The authors are indebted to Miss Elizabeth M. Petersen for determination of the infrared absorption spectra.

ml. per hour, and three fractions were collected at a pressure of 16 mm. and a bath temperature range of 94–104°. The first fraction, $n^{20}D$ 1.4806, was found to have an infrared absorption spectrum identical with that of fraction five from the Podbielniak column (racemate "A," Fig. 1), and formed a picrate, m.p. 191–193°. The third fraction, $n^{20}D$ 1.4814, which had an infrared spectrum (curve B in Fig. 1) markedly different from "A," is regarded as the second racemate ("B") of 4-methylquinolizidine. **The picrate** of "B," prepared in ether and recrystallized from ethanol, formed yellow platelets, m.p. 182–184°.[12]

Anal. Calcd. for $C_{16}H_{22}N_4O_7$: C, 50.25; H, 5.80; N, 14.61. Found: C, 50.48; H, 5.98; N, 14.54.

The infrared absorption spectra for the two picrates, m.p. 191–193° and 182–184°, were found to be different.

1-Carbethoxymethyl-2-(γ,γ-dicarbethoxypropyl)-pyridinium Bromide (VI).—The quaternary salt VI was formed in 57% yield by heating under reflux in dry benzene solution equimolar quantities of diethyl β-(2-pyridyl)-ethylmalonate (V)[7,8] and ethyl bromoacetate. After crystallization from anhydrous ether containing a little absolute ethanol, the colorless platelets melted at 113–115°.

Anal. Calcd. for $C_{18}H_{26}BrNO_6$: C, 50.00; H, 6.06; N, 3.24. Found: C, 50.07; H, 6.33; N, 3.45.

Diethyl Piperidyl-1-acetate-2-γ-butyrate (VII).—Hydrogenation of 60 g. (0.14 mole) of VI in 500 ml. of aqueous acetic acid at 3–5 atm. using platinum oxide was followed by filtration and evaporation. The crude product (44 g.) was taken up in 200 ml. of 6 *N* hydrochloric acid, and the resulting solution was heated under reflux for 12 hours. After evaporation to dryness, the residue was dissolved in 300 ml. of absolute ethanol saturated with dry hydrogen chloride. After refluxing for eight hours, the solvent was removed *in vacuo*. The crude ester residue was overlayered with ether and was made basic with saturated aqueous potassium carbonate. The ether layer was separated and the aqueous layer was extracted three times with ether. The combined ethereal solutions were dried and the ether was removed. The residue distilled as a light yellow oil, b.p. 120–123° (0.15 mm.); $n^{20}D$ 1.4650; d^{20}_4 1.028; yield 20 g. (50%).

Anal. Calcd. for $C_{15}H_{27}NO_4$: C, 63.13; H, 9.54; N, 4.91; MR_D, 76.52. Found: C, 63.24; H, 9.59; N, 5.18; MR_D, 76.75.

Dieckmann Ring Closure of Diethyl Piperidyl-1-acetate-2-γ-butyrate. 3-Keto-1-azabicyclo[5.4.0]hendecane (I).—To a sodium ethoxide prepared from 1.37 g. of sodium was added slowly a solution of 17 g. (0.06 mole) of the aminodiester VII in 200 ml. of xylene. The mixture was heated under gentle reflux. Periodically the temperature was raised and the mixture of ethanol and xylene was distilled until the boiling point rose to that of pure xylene. At the end of 20 hours, no further ethanol was obtained. The xylene solution was cooled and extracted four times with water; the aqueous extracts were discarded. The xylene layer was extracted with 40-ml. portions of dilute hydrochloric acid until a negative enol test with ferric chloride was obtained. The acidic extracts were combined, 50 ml. of concentrated hydrochloric acid was added, and the solution was refluxed for 2.5 hours (negative enol test). After concentration *in vacuo*, the residue was cooled to 0° and was made basic with saturated aqueous sodium hydroxide solution. The aqueous layer was extracted with ether, the ether extracts were combined, dried and the ether was removed. The product was obtained as a colorless liquid, b.p. 130–132° (18 mm.), which darkened rapidly on exposure to air; yield 3.6 g. (36%).

Anal. Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.38. Found: C, 72.27; H, 10.23; N, 8.17.

The picrate of 3-keto-1-azabicyclo[5.4.0]hendecane was made in ether and crystallized from ethanol as yellow platelets, m.p. 157–158°.

Anal. Calcd. for $C_{16}H_{20}N_4O_8$: C, 48.48; H, 5.09; N, 14.13. Found: C, 48.73; H, 5.25; N, 13.95.

The picrolonate, prepared in ether and recrystallized from ethanol, separated as yellow needles, m.p. 203–204°.

Anal. Calcd. for $C_{20}H_{25}N_5O_6$: C, 55.67; H, 5.84; N, 16.24. Found: C, 55.93; H, 6.10; N, 16.09.

Clemmensen Reduction of 3-Keto-1-azabicyclo[5.4.0]-hendecane.—The reduction was carried out in the usual manner.[3] The hydrochloric acid solution was concentrated *in vacuo*, and the residue was made strongly basic was 50% potassium hydroxide solution and was steam distilled. The distillate was saturated with potassium carbonate and extracted with ether. The ethereal solution was dried, the ester was removed and the residue was distilled as a colorless oil, b.p. 87–89° (21 mm.); $n^{20}D$ 1.4796; yield 74%. Two grams of the product was distilled through a Craig column at the rate of 0.3 ml. per hour. A total of six fractions was collected. The infrared spectrum (curve A, Fig. 1) of the first fraction, bath temperature 86° (16 mm.), $n^{20}D$ 1.4790, was identical with that of racemate "A" of 4-methylquinolizidine, while the infrared spectrum of the sixth fraction, bath temperature 98–100° (16 mm.), $n^{20}D$ 1.4803, more closely resembled that of racemate "B," but indicated some contamination with "A."

The picrate of the first fraction melted at 191–193°, that of the sixth fraction, at 181–183°, corresponding to the picrates of racemates "A" and "B," respectively, of 4-methylquinolizidine. The picrate of 1-azabicyclo[5.4.0]-hendecane[9] showed an infrared absorption spectrum which was markedly different from the spectra of the Clemmensen reduction product picrates.

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(12) The melting points of the picrates of the two racemates obtained by Lukeš and Šorm[6] were reported as 195 and 187°.