Methylation with Diazomethane.—A solution of 1.00 g. of DF in 250 ml. of ether was cooled to −40° and treated with a dried (KOH pellets) ethereal solution of 0.58 g. (2.04 moles) of diazomethane. A white flocculent precipitate appeared almost at once. The reaction mixture was evaporated *in vacuo* to 100 ml. and the solid (0.37 g.) filtered off. Evaporation to 50 ml. yielded further material (0.10 g.) which gave a faint DF reaction with $FeCl_3$. The first crop showed all the reactions of the methyl ester prepared by the previous method and when recrystallized from MeOH it yielded the same characteristic mixture of crystal types; m.p. 178–180°, mixed m.p. with previous sample 178–180°.

Anal. Calcd. for $C_6H_8O_6$: C, 40.9; H, 4.55. Found: C, 40.5; H, 4.55.

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

Rearrangement of α-Aminoketones During Clemmensen Reduction. XI. The Reduction of Atom-bridged Bicyclic α-Aminoketones[1,2]

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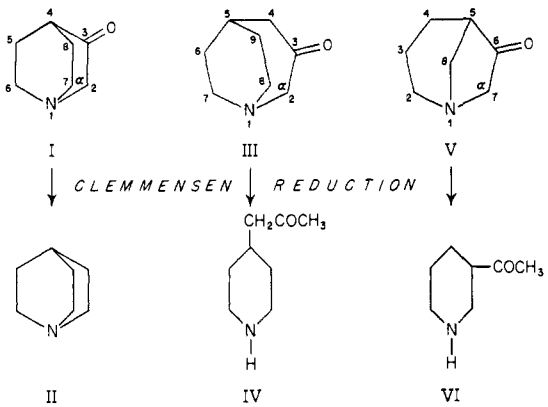
Unlike 3-ketoquinuclidine, which undergoes no C_α–N bond cleavage on Clemmensen reduction, two related atom-bridged bicyclic α-aminoketones, 3-keto-1-azabicyclo[3.2.2]nonane and 6-keto-1-azabicyclo[3.2.1]octane, were found to give ring-cleaved reduction products. Thus, the former yielded some 4-piperidylacetone and the latter, 3-acetylpiperidine under Clemmensen reduction conditions.

An exception to cleavage of the C_α–N bond which has been found to occur generally during the Clemmensen reduction of an α-aminoketone[1] lies in the behavior of 3-ketoquinuclidine (I), which is converted to quinuclidine (II).[3,4] Since compound I is also the only example of an α-aminoketone of the atom-bridged bicyclic type which has been investigated with respect to its Clemmensen reduction product, it was of interest to determine whether the exceptional behavior, *i.e.*, non-cleavage of the C_α–N bond, was exhibited by other atom-bridged bicyclic α-aminoketones. 3-Keto-1-azabicyclo[3.2.2]nonane (III) and 6-keto-1-azabicyclo-[3.2.1]octane (V) were selected as examples for study, the first as a ring homolog of I and the second as a ring isomer of I.



The synthesis of 3-keto-1-azabicyclo[3.2.2]nonane was modeled after the Clemo and Metcalfe method for 3-ketoquinuclidine,[3] but difficulty was encountered in the Dieckmann closure of the second ring. The quaternary salt from ethyl 4-pyridylacetate and ethyl bromoacetate was hydrogenated in aqueous acetic acid in the presence of platinum to give diethyl piperidyl-1,4-diacetate. The ring closure of this diester was effected in less than 1% yield, even under the most favorable conditions: potassium *t*-butoxide in xylene at high dilution under nitrogen.[5] Following hydrolysis and decarboxylation steps, an aminoketone was obtained which was assigned structure III on the basis of analysis, infrared spectrum and the structures of its precursors. 6-Keto-1-azabicyclo[3.2.1]octane (V) was synthesized by the method of Sternbach and Kaiser.[6]

The Clemmensen reduction of 3-keto-1-azabicyclo[3.2.2]nonane (III) was carried out under the usual conditions, and the only isolable product was obtained as a picrate, m.p. 141.5–143°, with a composition satisfying the molecular formula $C_{14}H_{18}N_4O_8$. The nature of the oxygen atom in the base was revealed as that of a ketone carbonyl group by the infrared absorption peak at 1708 cm.$^{-1}$. The infrared data, together with the melting point of the picrate, precluded the possibility of this product being 1-azabicyclo[3.2.2]nonane (C=O reduction, no C_α–N cleavage: picrate, m.p. 288–289°),[7] 2-methylquinuclidine (cleavage + rearrangement: picrate, m.p. 282–283°)[8] or 4-*n*-propylpiperidine (cleavage + C=O reduction: picrate, m.p. 108–109°),[8] and suggested that some 4-piperidylacetone (IV) had been formed by the incomplete reduction of III. An authentic sample of 4-piperidylacetone, made by the mixed Claisen condensation of ethyl 1-benzoyl-4-piperidylacetate and ethyl acetate, followed by hydrolysis and decarboxylation, was converted to the picrate, m.p. 146–147°. A comparison of the two picrates indicated that the sample from the Clemmensen reduction product contained some impurity along with the 4-piperidylacetone picrate, but the very

(1) For article X in this series, see N. J. Leonard, G. Fuller and H. L. Dryden, Jr., THIS JOURNAL, **75**, 3727 (1953).

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

(3) G. R. Clemo and T. P. Metcalfe, *J. Chem. Soc.*, 1989 (1937).

(4) Dr. S. H. Pines, in this Laboratory, has determined the absence of any secondary amine (C_α–N cleavage) and also of 7-methyl-1-azabicyclo[2.2.1]heptane (C_α–N cleavage + rearrangement) in the reduction product.

(5) N. J. Leonard and R. C. Sentz, THIS JOURNAL, **74**, 1704 (1952).

(6) L. H. Sternbach and S. Kaiser, *ibid.*, **74**, 2215 (1952).

(7) V. Prelog and E. Cerkovnikov, *Ann.*, **532**, 83 (1937).

(8) S. Wawzonek, M. F. Nelson, Jr., and P. J. Thelen, THIS JOURNAL, **73**, 2806 (1951).

small amounts available prevented identification of the attendant products. The establishment of 4-piperidylacetone (IV) as one of the products from 3-keto-1-azabicyclo[3.2.2]nonane (III) is eloquent evidence of the occurrence of C_α–N bond cleavage in this ring system, whereas carbonyl reduction occurs to the exclusion of C_α–N bond cleavage in the 1-azabicyclo[2.2.2]octane ring system (I).

The Clemmensen reduction of 6-keto-1-azabicyclo[3.2.1]octane (V) gave two products which could be identified. The first of these formed a picrate, which by its melting point, 293–293.4°, and analysis was suggestive of 1-azabicyclo[3.2.1]-octane picrate.[9] Identification was made possible by direct comparison with an authentic sample. The process responsible for the formation of this Clemmensen product from V involves carbonyl reduction and no C_α–N cleavage, just as in the reduction of 3-ketoquinuclidine to quinuclidine. The other Clemmensen product from V, $C_7H_{13}NO$, contained oxygen in a ketone carbonyl function and was identified as 3-acetylpiperidine (VI), the result of C_α–N cleavage and no carbonyl reduction. Authentic 3-acetylpiperidine was made for comparison by condensation of ethyl N-benzoylnipecotate with ethyl acetate, followed by hydrolysis and decarboxylation.

Our results indicate that in the Clemmensen reduction of atom-bridged bicyclic α-aminoketones, the extent of the two competing reactions, (a) $CO \rightarrow CH_2$ and (b) C_α–N cleavage, varies with the ring system, and thus may be simultaneously a function of ring strain and the steric environments of the C=O and C_α–N bonds.

Acknowledgment.—The authors are greatly indebted to Dr. S. Wawzonek, University of Iowa, for generous samples of 2-methylquinuclidine picrate and 4-*n*-propylpiperidine and its picrate, and to Dr. V. Prelog, Eidgenossische Technische Hochschule, Zürich, for his kindness in providing an authentic sample of 1-azabicyclo[3.2.1]octane picrate.

Experimental[10]

Ethyl 4-Piperidylacetate.—A solution of 5.0 g. (0.03 mole) of ethyl 4-pyridylacetate[11–13] in 50 ml. of absolute ether was treated with dry hydrogen chloride gas for 1.5 hours, and the ether was then removed *in vacuo*. The residue dissolved in 110 ml. of 90% aqueous acetic acid was subjected to hydrogenation at 25° and 2–3.5 atm. in the presence of 0.20 g. of platinum oxide catalyst. Hydrogen uptake ceased after 14 hours. The catalyst and solvent were removed, the residue was made strongly alkaline by the addition of 100 ml. of 25% aqueous sodium hydroxide, and the alkaline mixture was extracted with seven 100-ml. portions of ether. The combined ethereal extracts were dried, the ether was removed, and the residue was distilled at 67° (0.3 mm.), $n^{20}D$ 1.4662, yield 2.0 g. (39%).

Anal. Calcd. for $C_9H_{17}NO_2$: C, 63.12; H, 10.01; N, 8.18. Found: C, 62.96; H, 10.05; N, 8.44.

The N-benzoyl derivative was made as follows. To a stirred solution of 5.0 g. (0.029 mole) of ethyl 4-piperidylacetate in 90 ml. of chloroform was added 2 ml. of water and 24 g. of potassium carbonate. With continued stirring, 4.7 g. (0.033 mole) of benzoyl chloride was added slowly during 20 minutes. The resulting mixture was boiled under reflux for 30 minutes, cooled and filtered. The potassium carbonate was washed with 50 ml. of chloroform, and the combined filtrate and washings were dried. After removal of the chloroform, distillation of the residue yielded 7.0 g. (90%) of pale yellow oil, b.p. 163° (0.05 mm.), $n^{20}D$ 1.5330, which was used directly in the next step.

4-Piperidylacetone Picrate.—The general procedure of Kolloff and Hunter,[14] as modified by Prelog,[15] was used. A solution of 6.8 g. (0.024 mole) of ethyl 1-benzoyl-4-piperidylacetate and 4.3 g. (0.048 mole) of ethyl acetate in 25 ml. of dry benzene was added slowly with stirring to 2.3 g. (0.033 mole) of ethanol-free sodium ethoxide. The mixture was boiled under reflux for 9 hours with stirring. After cooling and treating the mixture with 50 ml. of water, the benzene layer was decanted and the aqueous layer was extracted once with 100 ml. of benzene. The aqueous layer was acidified with 50 ml. of 12 *N* hydrochloric acid and the resulting solution was boiled under reflux for 4 hours. The solution was evaporated to near dryness *in vacuo*, the residue was made alkaline with excess aqueous potassium carbonate, and the resulting alkaline solution was extracted with ether. The ether extracts were dried, the ether was removed, and the residue was distilled *in vacuo*. **The picrate** was formed directly in ether solution and recrystallized as yellow needles from ethanol, m.p. 146–147°, yield 0.30 g. (3.3%).

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.41; H, 4.90; N, 15.13. Found: C, 45.70; H, 4.88; N, 15.24.

Diethyl Pyridinium-1,4-diacetate Bromide.—To a solution of 54.4 g. (0.35 mole) of ethyl 4-pyridylacetate in 100 ml. of anhydrous ether and 10 ml. of absolute ethanol was added 59.1 g. (0.35 mole) of ethyl bromoacetate. The reaction mixture was stirred briefly and then allowed to stand at 25° for 5 hours. The precipitate was collected by filtration and to it was added further insoluble material obtained by concentrating the filtrate. Recrystallization from absolute ethanol containing a small amount of anhydrous ether gave colorless leaflets, m.p. 167–167.5°, yield 98.0 g. (83%).

Anal. Calcd. for $C_{13}H_{18}BrNO_4$: C, 47.00; H, 5.46; N, 4.22. Found: C, 46.69; H, 5.56; N, 3.97.

Diethyl Piperidyl-1,4-diacetate.—A solution of 20 g. (0.06 mole) of diethyl pyridinium-1,4-diacetate bromide in 150 ml. of acetic acid and 50 ml. of water was hydrogenated at 25° and 2–3 atm. in the presence of 0.3 g. of platinum oxide during 35 minutes. The combined reaction mixtures from *five* such runs were filtered to remove catalyst and concentrated to a sirup *in vacuo*. The residue was basified, with cooling, with 25% aqueous sodium hydroxide and extracted exhaustively with ether. The combined ether extracts were dried and the ether was removed. The residue was distilled as a colorless, nearly odorless liquid, b.p. 111–112° (0.2 mm.), $n^{20}D$ 1.4607, d^{20}_4 1.0493, yield 59.0 g. (78%). The infrared spectrum of the pure liquid indicated absorption at 1745 and 1726 cm.$^{-1}$.

Anal. Calcd. for $C_{13}H_{23}NO_4$: C, 60.67; H, 9.01; N, 5.44; MR_D, 67.30. Found: C, 60.86; H, 9.03; N, 5.66; MR_D, 67.25.

The picrate, formed in and recrystallized from ethanol, separated as yellow prisms, m.p. 107.5–108.5°.

Anal. Calcd. for $C_{19}H_{26}N_4O_{11}$: C, 46.92; H, 5.39; N, 11.52. Found: C, 46.91; H, 5.36; N, 11.61.

3-Keto-1-azabicyclo[3.2.2]nonane.—The Dieckmann ring closure of diethyl piperidyl-1,4-diacetate was carried out under high dilution conditions.[5] To a mixture of 8.8 g. (0.23 gram atom) of finely divided potassium in 1 l. of anhydrous xylene was added 63.5 ml. (0.68 mole) of *t*-butyl alcohol, freshly distilled from sodium.[16] A stream of purified nitrogen was passed over the mixture during this process and during the ring closure. The reaction mixture was

(9) V. Prelog, S. Heimbach and E. Cerkovnikov, *J. Chem. Soc.*, 677 (1939).

(10) All melting points are corrected. Microanalyses were performed by Miss Emily Davis, Mrs. Jean Fortney, Mrs. Katherine Pih, Mrs. Esther Fett and Mr. Joseph Nemeth, and the infrared absorption spectra were determined by Miss Helen Miklas.

(11) F. B. LaForge, THIS JOURNAL, **50**, 2477 (1928).

(12) R. L. Malan and P. M. Dean, *ibid.*, **69**, 1797 (1947).

(13) R. Lukeš and I. Ernest, *Collection Czechoslov. Chem. Communs.*, **14**, 679 (1949).

(14) H. G. Kolloff and J. H. Hunter, THIS JOURNAL, **63**, 490 (1941).

(15) V. Prelog, *Collection Czechoslov. Chem. Communs.*, **10**, 380 (1938).

(16) W. S. Johnson and G. H. Daub, in "Org. Reactions," **6**, 44 (1951).

stirred with heating under reflux until all of the potassium had reacted. Refluxing was continued and the *t*-butyl alcohol–xylene azeotrope was removed periodically until the distillate was pure xylene (235 ml. of distillate was collected). With continued stirring and refluxing, 23.5 g. (0.091 mole) of diethyl piperidyl-1,4-diacetate in 200 ml. of dry xylene was added slowly (4 drops per minute). The ethanol–xylene azeotrope was distilled periodically as the reaction proceeded (24.5 hours). The reaction mixture was stirred with refluxing for an additional four hours, after which it was cooled and treated, with stirring, with 100 ml. of 6 *N* hydrochloric acid. The xylene layer was extracted with four 50-ml. portions of 6 *N* hydrochloric acid, or to a negative ferric chloride test. The combined acid extracts were boiled under reflux for 12 hours. The solution was concentrated *in vacuo* and the residue was basified carefully with 125 ml. of 50% aqueous potassium carbonate. The basic mixture was extracted five times with methylene chloride, the combined extracts were dried, and most of the solvent was removed by distillation at reduced pressure through a six-inch helices-packed column. The final removal of solvent was accomplished in a 200 × 30 mm. test-tube, in which the residue was then sublimed at 80–100° (4–5 mm.), colorless prisms, m.p. 128.5–131.5°, yield 0.09 g. (0.7%).

Anal. Calcd. for $C_8H_{13}NO$: N, 10.06. Found: N, 10.11.

The infrared spectrum in chloroform showed bands at 1705 and 1410 cm.$^{-1}$ indicative of a ketone carbonyl and an α-methylene group.

Clemmensen Reduction of 3-Keto-1-azabicyclo[3.2.2]nonane.—To zinc amalgam made from 1 g. of granulated zinc and 0.5 g. of mercuric chloride was added cautiously a solution of 61 mg. (0.44 millimole) of 3-keto-1-azabicyclo[3.2.2]nonane in 3 ml. of 12 *N* hydrochloric acid. After the initial reaction had subsided, the reaction mixture was heated under reflux. At 2–3 hour intervals, 0.2 ml. of hydrochloric acid was added to the reaction mixture, and after 18 hours, 1 g. additional of zinc amalgam. Refluxing was discontinued at the end of 41 hours and the solution was concentrated *in vacuo*. The sirupy residue was basified, while cooling, with 100 ml. of 50% aqueous potassium hydroxide. The resulting suspension was steam distilled, the distillate was cooled while excess 50% aqueous potassium carbonate was added slowly, and the resulting mixture was extracted with ether. The ether extracts were dried and then added to an absolute ether solution containing 0.1 g. of picric acid. The solution was evaporated to crystallization to yield 26 mg. (16%) of crude product which was recrystallized once from ether, m.p. 141.5–143°. The yellow crystals, while not completely pure, approximated 4-piperidylacetone picrate in composition and, in Nujol mull, showed normal infrared absorption for ketone carbonyl at 1708 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.41; H, 4.90; N, 15.13. Found: C, 45.64; H, 5.27; N, 14.83.

Admixture with authentic 4-piperidylacetone picrate, m.p. 146–147° (see above), gave a melting point of 142–144°. The infrared absorption curves for the two picrates, as obtained for Nujol mulls, were very similar throughout, but indicated—as did the melting point data—that the Clemmensen product, 4-piperidylacetone, isolated as the picrate, was attended by at least one other product as an impurity in small amount.

6-Keto-1-azabicyclo[3.2.1]octane.—This compound was made by the method of Sternbach and Kaiser.[6] The hydrochloride, colorless prisms from aqueous acetone, m.p. 290–292° (reported, no melting to 270°), had an infrared absorption peak at 1761 cm.$^{-1}$, and the **picrate**, yellow needles from ethanol, m.p. 202–203.5°, showed absorption at 1765 cm.$^{-1}$ (Nujol mull).

Clemmensen Reduction of 6-Keto-1-azabicyclo[3.2.1]octane.—To zinc amalgam made from 35 g. of granulated zinc and 3.9 g. of mercuric chloride was added 5 g. (31 millimoles) of 6-keto-1-azabicyclo[3.2.1]octane hydrochloride in 26 ml. of 12 *N* hydrochloric acid. After the initial reaction had subsided, the reaction mixture was heated under reflux. Every 2 hours, 20 ml. of hydrochloric acid was added to the reaction mixture. At the end of 12 hours and again after 22 hours, 27 g. additional of amalgamated zinc was added. The reaction was stopped at the end of 36 hours. A sequence of concentration, basification, and steam distillation was followed. The steam distillate was acidified with 12 *N* hydrochloric acid, evaporated to dryness *in vacuo*, and the residue, made alkaline with 50% aqueous potassium carbonate, was extracted with ether. The combined ether extracts were dried, the ether was removed through a helices-packed column and the product was fractionally distilled under reduced pressure. Two main fractions were obtained. The first fraction, 0.6 g., b.p. 45–49° (18 mm.), formed a **picrate** in benzene–ether which was recrystallized from ethanol and finally from methanol (more soluble component) as yellow needles, m.p. 293–293.4°.

Anal. Calcd. for $C_{13}H_{16}N_4O_7$: C, 45.88; H, 4.74; N, 16.47. Found: C, 45.92; H, 4.46; N, 16.45.

The melting-decomposition point was not depressed on admixture with an authentic sample of 1-azabicyclo[3.2.1]octane picrate, m.p. 293–293.4° (reported[9] 294–295°), and the infrared absorption spectra of the two picrate samples, as determined in Nujol mull, were identical.

The second fraction of the crude Clemmensen reduction product, 0.7 g., b.p. 53–54° (1 mm.), gave a positive test[17] for 2° amine and was shown by analysis to be an oxygen-containing substance.

Anal. Calcd. for $C_7H_{13}NO$: C, 66.10; H, 10.30; N, 11.01. Found: C, 65.78; H, 10.12; N, 11.00.

The infrared spectrum of the pure liquid showed strong carbonyl absorption at 1700 cm.$^{-1}$, and the over-all spectrum was identical with that of an authentic sample of 3-acetylpiperidine (see below).

The picrate was formed in benzene–ether and was recrystallized from ethanol as yellow prisms, m.p. 128–128.5°. The melting point was not depressed on admixture with an authentic sample of 3-acetylpiperidine picrate (see below), and the infrared absorption spectra of the two picrates were identical as determined in Nujol mull, including a carbonyl peak at 1702 cm.$^{-1}$.

Ethyl N-Benzoylnipecotate.—The method employed was similar to that used by Prelog[15] for the preparation of ethyl N-benzoylisonipecotate. To a solution of 20 g. (0.13 mole) of ethyl nipecotate[18] in 400 ml. of chloroform was added 8 ml. of water and 100 g. of anhydrous potassium carbonate. With vigorous stirring, 27 g. (0.19 mole) of benzoyl chloride was added slowly. Stirring was continued while the mixture was heated at the reflux temperature for 30 minutes. The mixture was cooled and the potassium carbonate was filtered and washed with chloroform. After removal of the chloroform from the combined filtrate and washings the residue was distilled at 166° (0.7 mm.), $n^{20.5}D$ 1.5386, yield 32.5 g. (98%).

Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33. Found: C, 69.09; H, 7.02.

3-Acetylpiperidine.—To 11.6 g. (0.17 mole) of sodium ethoxide, made from 3.9 g. of sodium, was added with stirring a mixture of 28.2 g. (0.11 mole) of ethyl N-benzoylnipecotate and 17.6 g. (0.20 mole) of ethyl acetate with 20 ml. of benzene. The reaction mixture was stirred for one-half hour, heated under reflux with stirring for 10 hours, and then allowed to stand at 25° for 8 hours. Water (150 ml.) was added to the reaction mixture with stirring. The aqueous layer was separated and extracted with three 30-ml. portions of benzene. The aqueous solution, acidified with 150 ml. of 12 *N* hydrochloric acid, was heated under reflux for four hours, and then concentrated *in vacuo* to dryness. The residue was made alkaline with 50% aqueous potassium carbonate, and the resulting solution was extracted with ether. The combined ether extracts were dried, and the ethereal solution was treated with a solution of picric acid in benzene. **The picrate** which separated was recrystallized from ethanol as yellow prisms, m.p. 128–129°, yield 3.3 g. (9%).

Anal. Calcd. for $C_{13}H_{16}N_4O_8$: C, 43.82; H, 4.53; N, 15.73. Found: C, 43.63; H, 4.37; N, 15.68.

Part of the picrate was decomposed to give 3-acetylpiperidine, b.p. 63°(4.5 mm.), $n^{20}D$ 1.4875.

Diethyl N-Ethyliminodiacetate.—To a stirred solution of 334 g. (222 ml., 2.0 moles) of ethyl bromoacetate in 500 ml. of acetone was added dropwise over a period of two hours 187.8 g. (3.0 moles) of 70% aqueous ethylamine. When the addition was complete, the reaction mixture was heated at the reflux temperature with stirring for 1 hour. The mixture was cooled and the two layers were separated.

(17) F. R. Duke, *Ind. Eng. Chem., Anal. Ed.*, **17**, 196 (1945).

(18) S. M. McElvain and R. Adams, THIS JOURNAL, **45**, 2738 (1923).

The upper layer, consisting of an acetone solution of the iminodiester, was concentrated *in vacuo* and the residue was distilled; b.p. 109–110° (3.5 mm.), $n^{20}D$ 1.4364, d^{25}_4 1.0162, yield 175 g. (81%). The boiling point at 738 mm. was 248° (Heintz[19] reported 200–220° at atmospheric pressure for the compound prepared by a different method).

Anal. Calcd. for $C_{10}H_{19}NO_4$: C, 55.28; H, 8.82; N, 6.45. Found: C, 55.38; H, 8.86; N, 6.49.

The methiodide, prepared in the usual manner,[20] crystallized on cooling in Dry Ice. It was recrystallized from ethyl acetate, colorless needles, m.p. 62.5–64°.

Anal. Calcd. for $C_{11}H_{22}NO_4I$: C, 36.78; H, 6.17. Found: C, 36.86; H, 6.41.

N-Ethylhexamethylenimine (1-Ethylazacycloheptane).—Hexamethylenimine, as obtained[21] from ε-caprolactam, was converted by the usual alkylation procedure[22] with ethyl iodide to the N-ethyl compound in 66% yield, b.p. 90.5–91.5° (90 mm.), 153.5° (741 mm.), $n^{20}D$ 1.4571.

Anal. Calcd. for $C_8H_{17}N$: C, 75.52; H, 13.47; N, 11.01. Found: C, 75.56; H, 13.57; N, 11.21.

The picrate crystallized from ethanol as yellow needles, m.p. 173–173.5°.

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.49; H, 5.84; N, 15.72.

The methiodide crystallized from absolute ethanol as colorless leaflets, m.p. 244.5–245.5° dec.

Anal. Calcd. for $C_9H_{20}NI$: C, 40.16; H, 7.49; N, 5.20. Found: C, 40.29; H, 7.41; N, 5.17.

1-Ethyl-2-methylpiperidine.—α-Pipecoline was converted by treatment with ethyl iodide to the N-ethyl compound, b.p. 69° (50 mm.), 142° (744 mm.), $n^{20}D$ 1.4480 (reported[23,24] b.p. 148–149° (758 mm.), $n^{24.5}D$ 1.4480). **The picrate** crystallized as yellow platelets from ethanol, m.p. 189.5–190.5°.

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.47; H, 5.65; N, 15.50.

(19) W. Heintz, *Ann.*, **145**, 214 (1868).

(20) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd edition, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 180.

(21) L. Ruzicka, M. Kobelt, O. Häfliger and V. Prelog, *Helv. Chim. Acta*, **32**, 544 (1949).

(22) W. J. Hickinbottom, "Reactions of Organic Compounds," 2nd. Edition, Longmans, Green and Company, Inc., New York, N. Y., 1948, p. 299.

(23) W. Hohenemser and R. Wolffenstein, *Ber.*, **32**, 2520 (1899).

(24) A. Ladenburg, *Ann.*, **304**, 54 (1899).

The methiodide crystallized from ethyl acetate–ethanol as colorless granular crystals, m.p. 305° dec.

Anal. Calcd. for $C_9H_{20}NI$: C, 40.16; H, 7.49; N, 5.20. Found: C, 39.94; H, 7.33; N, 5.34.

1-Ethyl-2,5-dimethylpyrrole.—The procedure used was adapted from that for 2,5-dimethylpyrrole.[25] An application of the method used by Elderfield and Hageman[26] for 1-*n*-butyl-2,5-dimethylpyrrole gave a slightly better yield but the product was impure. A mixture of 57 g. (59.5 ml., 0.5 mole) of acetonylacetone and 22.5 g. (0.5 mole) of gaseous ethylamine dissolved in 50 ml. of water was shaken, with periodic cooling under the tap, until it no longer developed heat. The mixture was allowed to stand for 1 hour. The upper, oily layer was separated, the aqueous layer was extracted once with chloroform, and the extract was combined with the organic layer. After drying the solution and removing the chloroform, the product was distilled, b.p. 103.5–104.5° (45 mm.), 174° (739 mm.) (reported[27] 102° (79 mm.)), $n^{20}D$ 1.4884, yield 46.3 g. (75%).

Anal. Calcd. for $C_8H_{13}N$: C, 77.99; H, 10.63; N, 11.37. Found: C, 77.88; H, 10.71; N, 11.42.

1-Ethyl-2,5-dimethylpyrrolidine.—The pyrrole was hydrogenated according to the procedure of Elderfield and Hageman[26] to 1-ethyl-2,5-dimethylpyrrolidine, b.p. 131.5–132.5° (744 mm.), $n^{20}D$ 1.4332; d^{25}_4 0.8063, yield 19.4 g. (42%).

Anal. Calcd. for $C_8H_{17}N$: C, 75.52; H, 13.47; N, 11.01. Found: C, 75.37; H, 13.58; N, 11.27.

The picrate crystallized from ethanol as yellow leaflets, m.p. 195–197°.

Anal. Calcd. for $C_{14}H_{20}N_4O_7$: C, 47.19; H, 5.66; N, 15.72. Found: C, 47.36; H, 5.87; N, 15.64.

Since both *cis* and *trans* forms of 1-ethyl-2,5-dimethylpyrrolidine could be formed by this method of synthesis, it was not surprising that another **picrate** derivative was isolated, yellow leaflets from ethanol, m.p. 185.5–186°.

Anal. Found: C, 47.08; H, 5.77; N, 15.76.

A methiodide was obtained which crystallized from absolute ethanol as colorless platelets, m.p. 318–318.5° dec.

Anal. Calcd. for $C_9H_{20}NI$: C, 40.16; H, 7.49; H, 5.20. Found: C, 40.00; H, 7.46; N, 5.28.

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Ethylenimine Ketones. X. The Stereoisomerism of 1-Cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine[1]

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To extend our studies of the hyperconjugating ability of three-rings with various other groups we have now synthesized and separated by chromatographic methods the *cis* and *trans* racemic forms of 1-cyclohexyl-2-methyl-3-(*p*-phenylbenzoyl)-ethylenimine from the reaction of α,β-dibromo-*p*-phenylbutyrophenone and cyclohexylamine. An examination of the diagnostic reactions of the *cis* and *trans* forms with phenylhydrazine, and an examination of the ultraviolet and infrared absorption spectra has led to the assignment of the *trans* configuration to the higher melting form and the *cis* configuration to the lower melting form in this series. The spectra studies indicate that the 2-methyl group in the *trans* form is able to interact electrically with the three-ring either inductively or possibly by a secondary hyperconjugation mode.

Six different pairs of *cis–trans* racemates of aryl aroyl ethylenimines have been obtained in previous investigations in this Laboratory from the reaction of a primary amine with an α,β-dibromoketone in dry benzene solution.[2] A detailed study of the diagnostic reactions of phenylhydrazine with the *cis–trans* isomeric pairs[2c,2d] and an examination of the ultraviolet and infrared spectra in these previous investigations was reported. It was concluded that the lower melting geometrical isomer which has its characteristic carbonyl absorption band at the lower frequency in both the ultraviolet and infrared ranges of the spectrum, and which reacts most readily with phenylhydrazine to pro-

(1) Presented at the 124th Meeting of the American Chemical Society, Chicago, Illinois, Sept., 1953.

(2) (a) N. H. Cromwell, *et al.*, THIS JOURNAL, **65**, 312 (1943); (b) *ibid.*, **71**, 708 (1949); (c) *ibid.*, **73**, 1044, 5929 (1951); (d) *J. Org. Chem.*, **17**, 414 (1952).