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

Cyclic Aminoacyloins and Aminoketones. IV. Dependence of Transannular Interaction Upon the Relative Location of N and C_{CO}[1]

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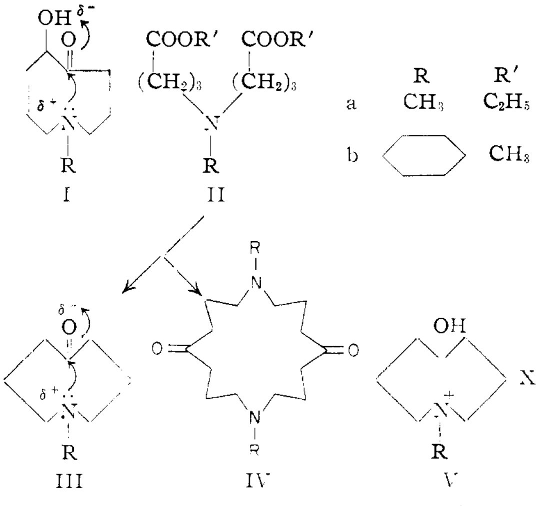
RECEIVED JULY 5, 1955

On the basis of infrared absorption spectra, the eight-membered ring aminoketone, 1-cyclohexyl-1-azacyclooöctan-5-one, shows less transannular nitrogen–carbonyl interaction than does 1-methyl-1-azacyclooöctan-5-one, consistent with the greater steric hindrance to N–C_{CO} interaction provided by the cyclohexyl group. A comparison of the infrared spectra of the isomeric ten-membered ring aminoketones, 1-methyl-1-azacyclodecan-6-one and 1-methyl-1-azacyclodecan-5-one, and their salts, indicates that the formation of a transannular bond across a ten-membered ring occurs more readily between the 1,6-positions than between the 1,5-positions, reflecting less steric interference between the alkylene chains to N–C_{CO} bonding in the former case. As additional products in the synthesis of the eight- and ten-membered ring aminoketones (IIIa, VII), when potassium *t*-butoxide was used to effect the ring closure of the corresponding methyliminodiesters, were obtained 16- and 20-membered ring diaminodiketones (IVa, VIII).

We have shown that the occurrence of transannular nitrogen–carbonyl interaction[2] in cyclic aminoacyloins (as in I) depends upon ring size,[3,4] steric strain[5] and environmental factors.[4] It was of interest to demonstrate an additional dependence—within a ring of size capable of sustaining transannular interaction—upon the relative positions occupied by tertiary amino nitrogen and carbonyl carbon. The models selected for synthesis and investigation were the isomeric cyclic aminoketones, 1-methyl-1-azacyclodecan-6-one (VII) and 1-methyl-1-azacyclodecan-5-one (XII). Incidental to this study, we have obtained information relating to the ring-size and steric-strain limitations of transannular interaction between N and C_{CO} in cyclic aminoketones, and we have uncovered an unusual method of making 16- and 20-membered ring diaminodiketones.

The eight-membered ring aminoketone, 1-methyl-1-azacyclooöctan-5-one (IIIa),[3,4] shows transannular interaction between N and C_{CO} on the basis of pK'_a determinations and the infrared spectra of the base and its perchlorate. Thus, the broad infrared carbonyl maximum (centered at 1683 cm.$^{-1}$ for a 5%, 1681 cm.$^{-1}$ for a 0.25% solution in carbon tetrachloride) is at lower than normal frequency for C=O stretching, a fact which can be accounted for by the occurrence of transannular interaction across the eight-membered ring of III in this solvent, thereby decreasing the double bond character of the carbonyl group. The interaction between N and C_{CO} attains the extreme of a full transannular bond in the salts, picrate and perchlorate, of 1-methyl-1-azacyclooöctan-5-one, which can be represented by formula V (R and OH probably *cis*), since both are transparent in the 6 μ region of the infrared (mull) but absorb in the 3 μ region.[6] The decrease in pK'_a observed for 1-methyl-1-azacyclooöctan-5-one perchlorate in making the change from 66% dimethylformamide (9.75) to water (8.75) is typical of enols and acids and indicates that the proton is attached to oxygen (V) in the conjugate acid of III in solution. This was confirmed readily by determination of the infrared spectrum of 1-methyl-1-azacyclooöctan-5-one perchlorate in D_2O, which permits examination of the C=O region. No carbonyl absorption was observed

1-Cyclohexyl-1-azacyclooöctan-5-one (IIIb) was synthesized for comparison with IIIa by a similar Dieckmann ring closure using dimethyl γ,γ′-cyclohexylimino-bis-butyrate (IIb) under high dilution conditions. The cyclohexyl group on nitrogen should offer greater steric hindrance than methyl to transannular interaction between N and C_{CO}, just as increasing the bulk of the alkyl group in I, R = CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9, reduces such interaction in the nine-membered ring aminoacyloins.[5]



Consistent with this concept, the infrared carbonyl band is shifted from 1681 cm.$^{-1}$ for IIIa to 1690 cm.$^{-1}$ for IIIb, as determined under optimum comparative conditions with dilute solutions in carbon tetrachloride.

Transannular N–C_{CO} interaction has been observed for two ten-membered ring aminoketones, namely, cryptopine[7] and protopine[8] in which the ter-

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(1) Presented at the Fourteenth National Organic Chemistry Symposium of the American Chemical Society, Lafayette, Ind., on June 14, 1955.

(2) The development of the concept of transannular interaction has been traced in earlier articles of this series. The apparent origin of the idea may be found in a footnote to the paper by W. O. Kermack and R. Robinson, *J. Chem. Soc.*, **121**, 427 (1922).

(3) N. J. Leonard, R. C. Fox, M. Ōki and S. Chiavarelli, THIS JOURNAL, **76**, 630 (1954).

(4) N. J. Leonard, R. C. Fox and M. Ōki, *ibid.*, **76**, 5708 (1954).

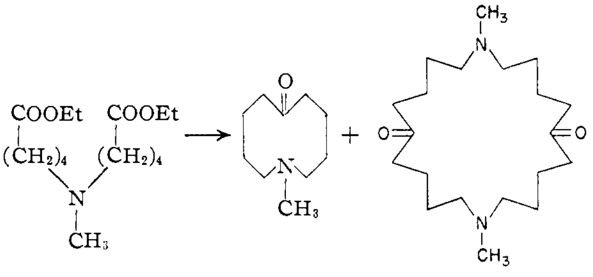
(5) N. J. Leonard and M. Ōki, *ibid.*, **76**, 3463 (1954).

(6) The detection of O–H in the perchlorate (3380 cm.$^{-1}$) is definitive in the case of the cyclic aminoketone, whereas more reliance had to be placed on the absence of C=O absorption for the salts of the cyclic aminoacyloins since O–H was already present.[4,5]

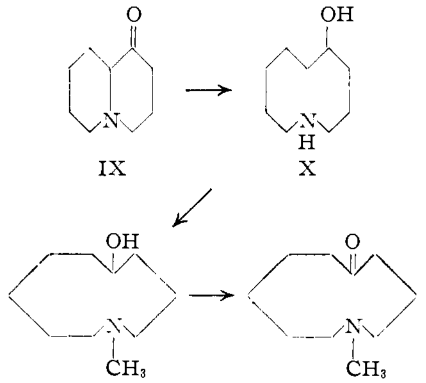
(7) F. A. L. Anet, A. S. Bailey and Sir Robert Robinson, *Chemistry & Industry*, 944 (1953).

(8) E. H. Mottus, H. Schwarz and L. Marion, *Can. J. Chem.*, **31**, 1144 (1953); F. A. L. Anet and L. Marion, *ibid.*, **32**, 452 (1954).

tiary amino nitrogen and the carbonyl carbon are in the 1,6-relation to each other and the ring bears lateral dibenzo-substitution. The simplest model bearing N and C_{CO} in the same relation in a ten-membered ring would be 1-methyl-1-azacyclodecan-6-one (VII), which we have now obtained *via* ring closure of diethyl δ,δ'-methylimino-bis-valerate (VI) with potassium *t*-butoxide under nitrogen in refluxing xylene, using high speed stirring and high dilution conditions. Apparently this is the first successful synthesis of a ten-membered ring by the Dieckmann reaction. For comparison with VII on the basis of the relative positions occupied by N and C_{CO}, the obvious choice was XII with nitrogen and carbonyl carbon in the 1,5-relation to each other. A logical precursor was available from the electrolytic reduction of 1-ketoquinolizidine (IX) at 60° in a 30% sulfuric acid catholyte at a lead cathode to give 1-azacyclodecan-5-ol (X),[9] followed by N-methylation with formaldehyde–formic acid to give 1-methyl-1-azacyclodecan-5-ol (XI).[9] Oxidation of XI to 1-methyl-1-azacyclodecan-5-one was accomplished with sodium dichromate in sulfuric acid at 0–10°, allowing a reaction time of less than one minute. The structures of the intermediates X and XI had been established previously. Proof of the structural relation of the aminoketones VII and XII to each other and confirmatory proof that they are indeed constituted as ten-membered rings was obtained by their separate conversions, by means of Wolff–Kishner reduction, to an identical product, 1-methyl-1-azacyclodecane.



VI VII VIII



IX X

XI XII

A comparison (Table I) of the infrared data for the aminoketones VII and XII and their respective salts leads to the conclusion that there is a difference in the extent of N–C_{CO} interaction in these isomeric models. The difference in wave number between the C=O maxima of the symmetrical (VII) and unsymmetrical (XII) aminoketones is not great but is deemed to be beyond the limit of error, especially in the dilute solution measurements. Moreover, the observed differences are equivalent for both dilute and concentrated solutions in carbon tetrachloride. While these observations are suggestive that transannular nitrogen–carbonyl interaction may occur to a slight extent in 1-methyl-1-azacyclodecan-6-one (VII), the 6 μ region transparency of the corresponding picrate and perchlorate salts indicates that a full transannular bond is present in such salts. By contrast, the salts of 1-methyl-1-azacyclodecane-5-one (XII) (the picrate is the more reliable) show carbonyl absorption, indicating that transannular bonding cannot be complete in these salts, at least under the comparable conditions here specified.

TABLE I

INFRARED MAXIMA, CM.$^{-1}$

	VII	XII
Base, 10% in CCl_4	1694	1700
Base, 1.23×10^{-2} *M* in CCl_4	1697	1703
Picrate, mull	3100, 3260	1702, 3230
Perchlorate, mull	3400	1698, 3400 (?)

The main driving force behind transannular nitrogen–carbonyl interaction and bonding as discussed here and in previous papers would appear to be the energy to be derived from the combination (neutralization)[7] of the nucleophilic and electrophilic groupings. In certain cases, the formation of a transannular bond may be assisted by relief of steric strain associated with the change from the monocyclic to the effectively bicyclic system. The apparent absence of intermolecular tertiary N–C_{CO} bonding and of intramolecular interaction in rings of unfavorable size[3,4] may be explained on the basis of an adverse entropy effect. Similarly, steric hindrance may diminish the extent of transannular nitrogen–carbonyl interaction.[5] From the results provided in Table I, it is apparent that the formation of a transannular bond across a ten-membered ring occurs more readily between the 1,6-positions (creating effectively two six-membered rings) than between the 1,5-positions (a five- and a seven-membered ring), reflecting less steric interference between the alkylene chains to N–C_{CO} bonding in the former case.

As co-products in the synthesis of the eight- (IIIa) and ten-membered (VII) ring aminoketones, when potassium *t*-butoxide was used to effect the ring closure of the corresponding diesters, were obtained sixteen- (IVa) and twenty-membered (VIII) ring diaminodiketones. The structures were assigned on the basis of the precursor esters and aminoketone products, analysis, molecular weight determination and physical properties. The yields of about 30% obtained for both 1,9-dimethyl-1,9-diazacyclohexadecane-5,13-dione (IVa) and 1,11-dimethyl-1,11-diazacycloeicosane-6,16-dione (VIII) suggest a fair practicality for this method. The corresponding sixteen- and twenty-membered ring diketones in the carbocyclic series have not been made by the Dieckmann reaction, but by the action of triethylamine on the chlorides of the dicar-

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[9] N. J. Leonard, S. Swann, Jr., and J. Figueras, Jr., THIS JOURNAL, **74**, 4620 (1952).

boxylic acids[10] or by thermal decomposition of the salts of these acids.[11,12]

Experimental[13,14]

γ,γ'-Cyclohexylimino-bis-butyronitrile.—A mixture of 50 g. (0.5 mole) of cyclohexylamine, 198 g. (1.0 mole) of γ-iodobutyronitrile, 138 g. (1 mole) of potassium carbonate and 500 ml. of absolute ethanol was heated under reflux with stirring for 20 hours. The mixture was cooled, the solids were removed by filtration, the ethanolic filtrate was evaporated under reduced pressure and the residue was taken up in ether. Following filtration and evaporation of the ether, the dinitrile was collected by fractional distillation, b.p. 166–168° (0.3 mm.), $n^{22.5}\text{D}$ 1.4842, yield 70 g. (60%), characteristic nitrile infrared maximum at 2250 cm.$^{-1}$ (liquid film).

Anal. Calcd. for $C_{14}H_{23}N_3$: C, 72.05; H, 9.94; N, 18.01. Found: C, 71.68; H, 9.91; N, 18.24.

Dimethyl γ,γ'-Cyclohexylimino-bis-butyrate (IIb).—A solution of 70 g. (0.3 mole) of γ,γ'-cyclohexylimino-bis-butyronitrile in 500 ml. of methanol and 7 ml. of water was saturated with hydrogen chloride at 10°, and the mixture was heated under reflux with stirring for 2 hours. The ammonium chloride was removed by filtration following cooling, the methanol was evaporated and the residue was basified with cold aqueous sodium carbonate. Ether extraction followed by drying and evaporating operations furnished a residue which was fractionally distilled, b.p. 146–148° (0.2 mm.), $n^{22.5}\text{D}$ 1.4696, yield 65 g. (73%), characteristic ester infrared maxima at 1737 and 1175 cm.$^{-1}$ (liquid film).

Anal. Calcd. for $C_{16}H_{29}NO_4$: C, 64.18; H, 9.76; N, 4.68. Found: C, 64.37; H, 9.59; N, 4.58.

1-Cyclohexyl-1-azacycloöctan-5-one (IIIb).—The Dieckmann ring closure was run in a nitrogen atmosphere using a Morton high speed stirrer assembly[15] and high dilution conditions. To 6.0 g. (0.25 mole) of sodium hydride[16] in 1.5 l. of dry xylene was added 0.3 ml. of methanol and to the boiling mixture was then added a solution of 29.9 g. (0.1 mole) of the diester IIb in 250 ml. of xylene over a period of 24 hours. Following the addition, the reaction mixture was heated at the reflux an additional hour and then cooled. To the stirred, ice-cooled mixture was added gradually 18 g. (0.3 mole) of acetic acid followed by 100 ml. of water. The aqueous layer was separated and discarded. The xylene layer was extracted with three 70-ml. portions of 6 *N* hydrochloric acid. The combined acidic extracts were heated under reflux for 6 hours, cooled and basified with solid potassium carbonate. The product was worked up in the usual manner following ether extraction, b.p. 104° (0.2 mm.), $n^{21.5}\text{D}$ 1.5109, yield 9.4 g. (45%).

Anal. Calcd. for $C_{13}H_{23}NO$: C, 74.59; H, 11.08. Found: C, 74.93; H, 10.79.

The compound was found to be rather unstable and to discolor on standing. It melts below room temperature but is solid at 0°. The broad carbonyl band in the infrared spectrum is centered at 1687 cm.$^{-1}$ for a 5% solution in carbon tetrachloride, at 1690 cm.$^{-1}$ (unsymmetrical band) for a 0.01 *M* solution.

The picrate was made in ether and recrystallized from ethanol as yellow needles, m.p. 154–155°; infrared spectrum (Nujol mull) transparent in 6 μ region, shows O–H/N–H absorption at 3090 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{26}N_4O_8$: C, 52.05; H, 5.98; N, 12.78. Found: C, 52.06; H, 5.88; N, 12.68.

1-Methyl-1-azacycloöctan-5-one (IIIa).—The Dieckmann ring closure was run in essentially the same manner as described for IIIb except that potassium *t*-butoxide was used as the condensing agent.[3,17] When 9.75 g. (0.25 gram atom) of potassium had reacted with 50 ml. of *t*-butyl alcohol in 2 l. of xylene, excess alcohol was removed as the azeotrope until the temperature of the vapor reached 135°. To the potassium *t*-butoxide in xylene was added a solution of 25.9 g. (0.1 mole) of diethyl γ,γ'-methylimino-bis-butyrate (IIa)[18] in 300 ml. of xylene over 30 hours, during which time low boiling material was collected from a drip-tip condenser to maintain the reflux temperature at least at 135°. After an isolation procedure similar to that described above, the aminoketone was obtained as a waxy solid in 20% yield, b.p. 50° (0.3 mm.), m.p. 46–47°, which was hygroscopic and unstable. It was preserved in the form of a salt, from which it was liberated directly for infrared analysis. The broad carbonyl band in the infrared spectrum is centered at 1683 cm.$^{-1}$ for a 5% solution in carbon tetrachloride and at 1681 cm.$^{-1}$ for a *ca.* 0.02 *M* solution.

The picrate separated as yellow needles from aqueous ethanol, m.p. *ca.* 300° dec.; infrared spectrum (Nujol mull) transparent in 6 μ region, maximum at 3120 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{18}N_4O_8$: C, 45.40; H, 4.90; N, 15.13. Found: C, 45.56; H, 4.86; N, 15.13.

The perchlorate crystallized from ethanol–ether as prisms, m.p. 260–261°; infrared spectrum (Nujol mull) transparent in 6 μ region, O–H maximum at 3380 cm.$^{-1}$.

Anal. Calcd. for $C_8H_{16}ClNO_5$: C, 39.75; H, 6.67; N, 5.79. Found: C, 39.85; H, 6.51; N, 5.66.

1,9-Dimethyl-1,9-diazacyclohexadecane-5,13-dione (IVa).—This compound was obtained from the higher boiling fraction, b.p. 160–180° (0.3 mm.), resulting from the Dieckmann reaction of IIa. Purification was accomplished by sublimation, colorless plates, m.p. 80–81°, yield 4.1 g. (29%); infrared maximum at 1713 cm.$^{-1}$ (5% carbon tetrachloride solution).

Anal. Calcd. for $C_{16}H_{30}N_2O_2$: C, 68.04; H, 10.71; N, 9.92; mol. wt., 282. Found: C, 68.30; H, 10.53; N, 10.19; mol. wt. (Rast, triphenylmethane), 280.

The diperchlorate separated as colorless prisms from ethanol–ether, m.p. 216–217° dec.; infrared maxima at 1688, 1706 and 3085 cm.$^{-1}$ for a Nujol mull.

Anal. Calcd. for $C_{16}H_{32}Cl_2N_2O_{10}$: C, 39.75; H, 6.67; N, 5.79. Found: C, 39.72; H, 6.33; N, 5.60.

1-Methyl-1-azacyclodecan-6-one (VII).—The ten-membered ring aminoketone was prepared from diethyl δ,δ'-methylimino-bis-valerate (VI)[4,18] by a method closely analogous to that described for 1-methyl-1-azacycloöctan-5-one. The product was distilled at 75–76° (1.4 mm.) as a colorless, rather unstable oil, $n^{19.5}\text{D}$ 1.4880, yield 10%. The compound is a solid at 0° but melts below room temperature. The carbonyl band in the infrared spectrum lies at 1694 cm.$^{-1}$ for a 10% solution in carbon tetrachloride, at 1697 cm.$^{-1}$ (unsymmetrical band) for a 1.23×10^{-2} *M* solution.

Anal. Calcd. for $C_{10}H_{19}NO$: C, 70.96; H, 11.32; N, 8.28. Found: C, 71.00; H, 11.29; N, 8.40.

The picrate crystallized as yellow prisms from ethanol, m.p. 258–259° dec.; infrared spectrum (Nujol mull) is transparent in 6 μ region, shows maxima at 3260, 3100 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{22}N_4O_8$: C, 48.24; H, 5.57; N, 14.07. Found: C, 48.50; H, 5.55; N, 14.20.

The perchlorate, prepared in ethanol, crystallized from ethanol–ether as colorless prisms, m.p. 257° dec.; infrared spectrum (Nujol mull) is transparent in 6 μ region, shows maximum at 3400 cm.$^{-1}$.

Anal. Calcd. for $C_{10}H_{20}ClNO_5$: C, 44.53; H, 7.47; N, 5.19. Found: C, 44.42; H, 7.49; N, 5.17.

1,11-Dimethyl-1,11-diazacycloeicosane-6,16-dione (VIII).—This compound was obtained as the high boiling portion of the Dieckmann product from VI and was purified by vacuum sublimation, colorless prisms, m.p. 68–69°, yield 5.1 g. (30%), infrared maximum at 1720 cm.$^{-1}$ (5% carbon tetrachloride solution).

Anal. Calcd. for $C_{20}H_{38}N_2O_2$: C, 70.96; H, 11.32; N, 8.28; mol. wt., 338. Found: C, 70.62; H, 11.31; N, 8.16; mol. wt. (Rast, triphenylmethane), 311.

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[10] A. T. Blomquist and R. D. Spencer, U. S. Patent 2,584,664 (Feb. 5, 1952).

[11] L. Ruzicka, W. Brugger, C. F. Seidel and H. Schinz, *Helv. Chim. Acta*, **11**, 496 (1928).

[12] L. Ruzicka, M. Stoll and H. Schinz, *ibid.*, **11**, 670 (1928).

[13] All melting points are corrected.

[14] We wish to thank Miss Helen Miklas and Mr. James Brader for determination of the infrared absorption spectra and Mrs. R. Maria Benassi, Mrs. Lucy Chang, Mrs. Esther Fett, Mr. Joseph Nemeth and Mr. R. J. Nesset for the microanalyses.

[15] A. A. Morton, B. Darling and J. Davidson, *Ind. Eng. Chem.*, **14**, 734 (1942).

[16] F. F. Blicke, J. Azuara, N. J. Doorenbos and E. B. Hotelling, THIS JOURNAL, **75**, 5418 (1953).

[17] N. J. Leonard and R. C. Sentz, *ibid.*, **74**, 1704 (1952).

[18] E. A. Prill and S. M. McElvain, *ibid.*, **55**, 1233 (1933).

The diperchlorate crystallized from ethanol–ether as colorless plates, m.p. 216–217°; infrared maxima (Nujol mull) at 1706 and 3130 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{40}Cl_2N_2O_{10}$: C, 44.53; H, 7.47; N, 5.19. Found: C, 44.74; H, 7.39; N, 4.85.

1-Methyl-1-azacyclodecan-5-one (XII).—To a solution of 3.42 g. (20 mmoles) of 1-methyl-1-azacyclodecan-5-ol (XI)[9] in 5 g. of water and 10 g. of concentrated sulfuric acid was added with swirling 2.20 g. (7.4 mmoles) of sodium dichromate in a minimum amount of water. The temperature was kept low by immersion in an ice-salt-bath. After 30 seconds the reaction mixture was basified with potassium carbonate and extracted with ether. On fractionation an oil, b.p. 65–70° (0.7 mm.), was obtained and was converted to the picrate. **The picrate** was recrystallized from ethanol, yellow prisms, m.p. 194–195° dec.; infrared maxima (Nujol mull) at 1702 and 3230 cm.$^{-1}$.

Anal. Calcd. for $C_{16}H_{22}N_4O_8$: C, 48.24; H, 5.57; N, 14.07. Found: C, 48.31; H, 5.65; N, 14.09.

The picrate was converted to free base in the usual manner. The pure aminoketone distilled at 66–67° (0.8 mm.) and the distillate was collected as a colorless, waxy and hygroscopic solid, m.p. 40°, yield 1.52 g. (45%).

Anal. Calcd. for $C_{10}H_{19}NO$: C, 70.96; H, 11.32. Found: C, 70.60; H, 11.53.

The compound discolors readily at room temperature. The carbonyl band in the infrared spectrum lies at 1700 cm.$^{-1}$ for a 10% solution in carbon tetrachloride, at 1703 cm.$^{-1}$ (symmetrical) for a 1.23×10^{-2} *M* solution.

Attempted formation of the **perchlorate** resulted in an oil which, as a liquid film, showed absorption at 3400 and 1698 cm.$^{-1}$ in the infrared. Analysis indicated that purity had not been achieved for the oil following drying *in vacuo*.

Anal. Calcd. for $C_{10}H_{20}ClNO_5$: C, 44.53; H, 7.47. Found: C, 44.06; H, 7.01.

Conversion of 1-Methyl-1-azacyclodecan-6-one and 1-Methyl-1-azacyclodecan-5-one to 1-Methyl-1-azacyclodecane.—A solution of 1.0 g. of VII and 2.0 g. of 85% hydrazine hydrate in 10 ml. of diethylene glycol was heated under **reflux** for 5 hours. Excess hydrazine and water were removed by distillation until the temperature of the mixture reached 200°. To the mixture was added 2.0 g. of potassium hydroxide and the reflux temperature was maintained for 5 hours. The amine was steam-distilled from the reaction mixture and the steam distillate was extracted with ether. The ethereal solution was dried, the ether was removed and the residue consisting of 0.3 g. (33%) of colorless liquid was converted directly to its **picrate**, recrystallized from aqueous ethanol as yellow needles, m.p. 199–200° (reported[19] 198–199°).

Anal. Calcd. for $C_{16}H_{24}N_4O_7$: C, 49.99; H, 6.29; N, 14.58. Found: C, 49.76; H, 6.11; N, 14.51.

The same Huang-Minlon modification of the Wolff-Kishner reaction was followed for the reduction of XII, with the exception that 2 hours were allowed for the formation of the hydrazone. The product was isolated in 30% yield as the **picrate**, m.p. 198–199°, which was identical with that described above.

Infrared Absorption Spectra.—These were obtained with a Perkin-Elmer recording spectrophotometer, model 21. For high resolution with the dilute carbon tetrachloride solutions of the aminoketones (*ca.* 0.2%), the wave number scale was expanded fourfold and maximum response and a scanning speed of 120 cm.$^{-1}$ per minute were employed. The thickness of the solution cell was about 1.0 mm. and the thickness of the solvent cell was variable so that a match could be achieved. The spectrum of 1-methyl-1-azacyclooctan-5-one perchlorate in D_2O was determined with a Beckman IR-2T infrared spectrophotometer, using a silver chloride cell. We are especially grateful to Dr. Harold E. Boaz and Mr. Donald O. Woolf, Jr., of Eli Lilly and Co., Indianapolis, Ind., for making their results available to us.

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[19] V. Prelog and R. Seiwerth, *Ber.*, **72**, 1638 (1939).

URBANA, ILLINOIS

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS AND THE LILLY RESEARCH LABORATORIES, ELI LILLY AND CO.]

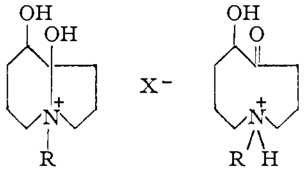
Cyclic Aminoacyloins and Aminoketones. V. Detailed Infrared Spectral Study of Transannular Interaction between N and C_{CO}[1,2]

BY NELSON J. LEONARD, MICHINORI ŌKI, JAMES BRADER AND HAROLD BOAZ

RECEIVED JULY 18, 1955

By determination of the infrared spectra of the perchlorates of nine-membered ring aminoacyloins in deuterium oxide, it has been found that the 1-isopropyl- and 1-*t*-butyl-1-azacyclononan-5-ol-6-one salts exist in the monocyclic $-\overset{|}{\underset{|}{N}}{}^{+}-H$ form in aqueous solution, whereas those of 1-methyl- and 1-ethyl-1-azacyclonan-5-ol-6-one are in the transannular quaternary form. Infrared absorption curves for dilute solutions of the cyclic N-alkylaminoacyloins in carbon tetrachloride provide a clear demonstration of the decrease in the proportion of interacted to non-interacted forms with increasing bulk of the N-alkyl group.

In our earlier investigation of the steric strain (F-strain) limitation of transannular interaction between N and C_{CO} in 1-alkyl-1-azacyclononan-5-ol-6-ones,[3] we showed by means of infrared spectra that the perchlorate salts of the methyl-, ethyl- and isopropylaminoacyloins exist in the transannular quaternary form (Ia, b, c) in the mull. In 66% dimethylformamide, the conjugate acids of the methyl- and ethylaminoacyloins are represented by formula I, and those of the isopropyl- and *t*-butylaminoacyloins, by formula II, as indicated by pK_a' determinations. Uncertainty remained as to the nature of the conjugate acids in aqueous solution. Without the benefit of direct evidence,[4] it was inferred[3] initially that all of the base-conjugate acids



I II

(a, R = CH_3; b, C_2H_5; c, *i*-C_3H_7; d, *t*-C_4H_9)

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[1] Presented at the 14th National Organic Chemistry Symposium of the American Chemical Society, Lafayette, Ind., on June 14, 1955. Supported in part by a grant from the University Research Board, University of Illinois.

[2] For preceding article in this series, see N. J. Leonard, M. Ōki and S. Chiavarelli, THIS JOURNAL, **77**, 6234 (1955).

[3] N. J. Leonard and M. Ōki, *ibid.*, **76**, 3463 (1954).

[4] No information was available to suggest whether the pK_a' of the expression Ia would be different from that of IIa in water solution.