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.

---

[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.]

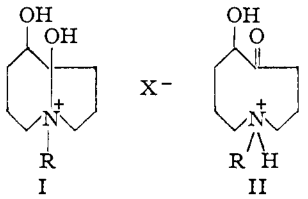
Cyclic Aminoacyloins and Aminoketones. V. Detailed Infrared Spectral Study of Transannular Interaction between N and C_{CO}[1,2]

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)

---

[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.

were in the monocyclic $-\overset{|}{\underset{|}{N}}{}^{+}-H$ form. This assumption has now been corrected by obtaining direct spectral evidence as to the state of the cations (I or II) in aqueous solution.

By determination of the infrared spectra of the perchlorates of the cyclic aminoacyloins in deuterium oxide, which permits—as water does not—an examination of the C=O stretching region, it was found that the 1-isopropyl- and 1-*t*-butyl-1-azacyclononan-5-ol-6-one salts are in the monocyclic $-\overset{|}{\underset{|}{N}}{}^{+}-H$ form (IIc, d). Both exhibited carbonyl maxima at 1706 ± 3 cm.$^{-1}$. By contrast, the spectrum of 1-ethyl-1-azacyclononan-5-ol-6-one perchlorate in D_2O was transparent in the carbonyl region, indicating that this salt is in the transannular quaternary form (Ib). It can be concluded safely that the methyl compound, which offers less steric hindrance to transannular bonding and has the same pK'_a in water, is also in this form (Ia) of the perchlorate salt in aqueous solution. The results now consistent for both water and water–dimethylformamide solutions, are indicative of the difference in hindrance provided by an N-ethyl and an N-isopropyl group in these examples and offer convincing evidence of the importance of the steric factor in the limitation of transannular N–C_{CO} bonding.

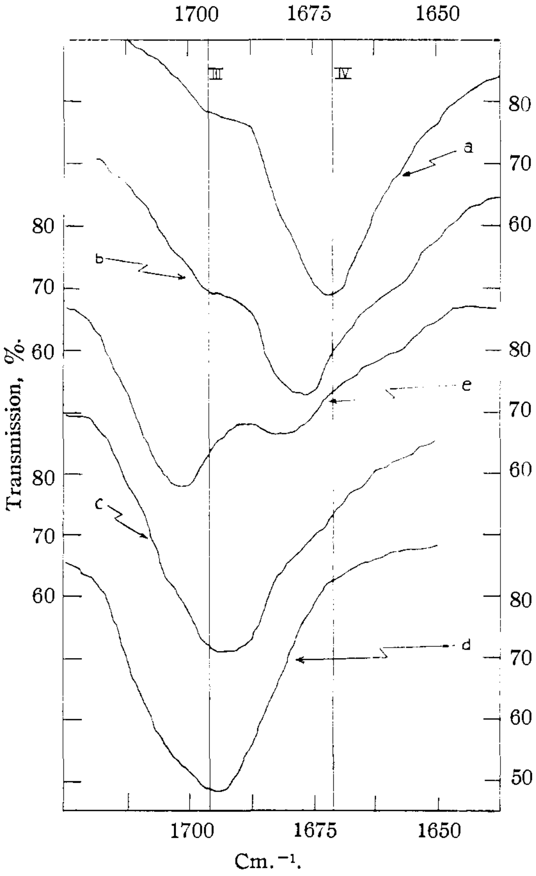
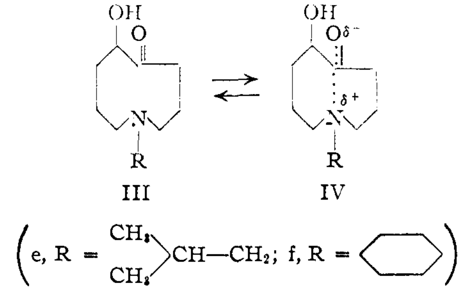


Fig. 1.—Infrared absorption spectra.

The infrared carbonyl maxima previously reported for the 1-alkyl-1-azacyclononan-5-ol-6-ones IIIa, b, c, d represented in each case the wave-number mid-point of the broad absorption band obtained for a 10% solution of the compound in carbon tetrachloride. While the shift of the band center to higher wave number with increasing bulk of the N-alkyl group was indicative of decreasing transannular interaction between N and C_{CO} for the series IIIa → d, it was desired to obtain more detailed information concerning this interaction by possible resolution of the infrared bands in the carbonyl region. We were guided by the findings of Pohland, Boaz and Woolf,[5] who detected separate infrared carbonyl bands corresponding to "interacted" and "non-interacted" forms of certain analogs of amidone, in our expectation that the spectra of dilute carbon tetrachloride solutions of the 1-alkyl-1-azacyclononan-5-ol-6-ones would reveal similarly the presence of both forms IV (interacted) and III (non-interacted).



The separation of the infrared absorption in the carbonyl region into essentially two main bands, appearing as either maxima or inflections, is seen in Fig. 1, for which the curves were obtained on dilute solutions of the 1-alkyl-1-azacyclononan-5-ol-6-ones of approximately equimolar concentration (1.23 × 10^{-2} *M*) in carbon tetrachloride. The band at higher wave number (in the range of 1696 cm.$^{-1}$) is due to C=O stretching in conformations of the monocyclic non-interacted form III, and that in the range of 1671 cm.$^{-1}$ must be due to the modified carbonyl[6] in conformations of the interacted form IV. As the steric hindrance of the substituent on nitrogen increases (CH_3, C_2H_5, *i*-C_3H_7, *t*-C_4H_9), the intensity of the band corresponding to the interacted form is progressively decreased and that of the non-interacted form is increased. At the extremes of the examples considered, the methylaminoacyloin appears to be mainly in the interacted form IVa and the *t*-butylaminoacyloin appears to be predominantly in the non-interacted form IIId. It is perhaps not surprising that the bands lack sharp definition, since the monocyclic form III can exist in a number of rotational conformations. Moreover, in consideration of form IV, if the interaction between N and C_{CO} is visualized as providing essentially a bicyclic system, the possible exist-

---

(5) A. Pohland, H. Boaz and D. D. Woolf, Jr., THIS JOURNAL (to be submitted); see also Abstracts of the 14th National Organic Chemistry Symposium of the American Chemical Society, Lafayette, Ind., June 13–16, 1955, p. 45.

(6) See N. J. Leonard, R. C. Fox, M. Ōki and S. Chiavarelli, THIS JOURNAL, **76**, 630 (1954); N. J. Leonard, R. C. Fox and M. Ōki, *ibid.*, **76**, 5708 (1954); also references included therein.

ence of *cis* and *trans* isomers[7] and attendant conformations must be appreciated. The dissymmetry of most of the curves and the additional irregularities which are apparent in some made it advisable not to attempt a calculation of molecular extinctions for the interpolated maxima.

As a further check on the steric interference of the N-alkyl group with transannular N–C_{CO} interaction, we synthesized 1-isobutyl-1-azacyclononan-5-ol-6-one by the acyloin condensation of diethyl γ,γ′-isobutylimino-bis-butyrate, with the thought that the isobutyl group should provide hindrance intermediate between that of ethyl and isopropyl. The pure N-isobutylaminoacyloin exhibited two clear maxima, at 1703 and 1682 cm.$^{-1}$, even in concentrated solution in carbon tetrachloride. The infrared absorption for a dilute (1.23×10^{-2} *M*) solution, which has been included in Fig. 1, shows that the proportion of interacted (IVe) to non-interacted (IIIe) forms is smaller than that for the N-ethyl and greater than that for the N-isopropyl compound. The infrared carbonyl absorption of 1-cyclohexyl-1-azacyclononan-5-ol-6-one (IIIf), which was synthesized by the same general method, bears closest resemblance to that of the N-isopropyl compound.

Experimental[8]

Diethyl γ,γ′-Isobutylimino-bis-butyrate.—This compound was made in a manner similar to that employed for the isopropylimino-bis-butyrate,[8] using 36.6 g. (0.5 mole) of isobutylamine, 242 g. (1.0 mole) of ethyl γ-iodobutyrate, 138 g. (1.0 mole) of potassium carbonate, 500 ml. of absolute ethanol and a reflux time of 12 hours; b.p. 106–107° (0.04 mm.), $n^{19.5}$D 1.4449, yield 82 g. (55%), characteristic infrared maxima at 1740 and 1179 cm.$^{-1}$ (liquid film).

Anal. Calcd. for $C_{16}H_{31}NO_4$: C, 63.75; H, 10.37; N, 4.65. Found: C, 63.72; H, 10.44; N, 4.65.

1-Isobutyl-1-azacyclononan-5-ol-6-one (IIIe).—The acyloin ring closure was effected in the usual way[3] using 10.1 g. (0.44 g. atom) of sodium and 30.1 g. (0.10 mole) of the diester in xylene under high dilution conditions; colorless oil, b.p. 83–85° (0.1 mm.), n^{20}D 1.4907, yield 10.3 g. (48%), representative infrared maxima at 3470, 1703, 1682 and 1100 cm.$^{-1}$ for a 10% solution in carbon tetrachloride.

Anal. Calcd. for $C_{12}H_{23}NO_2$: C, 67.56; H, 10.87. Found: C, 67.65; H, 10.86.

1-Cyclohexyl-1-azacyclononan-5-ol-6-one (IIIf).—This compound was made by the same method; viscous, rather unstable oil, b.p. 124–126° (0.25 mm.), n^{21}D 1.5177, yield 50%, infrared maxima at 3455 and 1691 cm.$^{-1}$ for a 5% solution in carbon tetrachloride, at 1687 cm.$^{-1}$ (unsymmetrical) for a 0.01 ± 0.005 *M* solution.

Anal. Calcd. for $C_{14}H_{25}NO_2$: C, 70.25; H, 10.53. Found: C, 70.58; H, 10.29.

The picrate was made in ether and recrystallized from ethanol–ether as yellow prisms, m.p. 146–148°, infrared maxima (Nujol mull) at 3480, 3075 and 1701 cm.$^{-1}$ among others.

Anal. Calcd. for $C_{20}H_{28}N_4O_9$: C, 51.27; H, 6.02; N, 11.96. Found: C, 51.36; H, 6.17; N, 12.15.

1-Methyl-, 1-ethyl-, 1-isopropyl- and 1-*t*-butyl-1-azacyclononan-5-ol-6-one[3] were freshly prepared and distilled prior to infrared spectral examination.

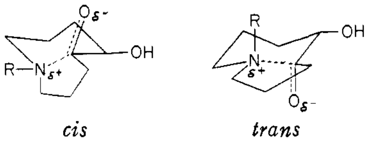
Infrared Absorption Spectra.—The spectra of the cyclic aminoacyloins were obtained with a Perkin–Elmer recording spectrophotometer, model 21. For high resolution with the dilute carbon tetrachloride solutions of the aminoacyloins, the wave number scale was expanded fourfold, and maximum response and a scanning speed of 120 cm.$^{-1}$ per minute were employed. The thickness of the sodium chloride cell was about 1.0 mm. and the thickness of the solvent cell was variable so that a match could be achieved. The concentration was $1.23 \pm 0.05 \times 10^{-2}$ *M* of aminoacyloin in Rascher and Betzold reagent carbon tetrachloride (except for the cyclohexyl compound) and the spectra were calibrated against water vapor.

The infrared spectra of the perchlorates in D_2O were determined with a Beckman IR-2T infrared spectrophotometer, using a silver chloride cell. We wish to thank Mr. Donald O. Woolf, Jr., of Eli Lilly and Company for these determinations in deuterium oxide.

URBANA, ILLINOIS
INDIANAPOLIS 6, INDIANA

---

[7] *E.g.*



cis *trans*

[8] Microanalyses by Mrs. R. Maria Benassi and Mr. Joseph Nemeth.

Cyclic Aminoacyloins and Aminoketones. VI. Effect of Transannular Interaction between N and C_{CO} on Ultraviolet Absorption[1]

BY NELSON J. LEONARD AND MICHINORI ŌKI

RECEIVED JULY 18, 1955

Since it has been found possible to use infrared absorption spectra effectively[2] in the detection of transannular interaction between N and C_{CO} in cyclic aminocyloins and aminoketones,[3–6] it was of corollary interest to ascertain the relation of ultraviolet absorption spectra to this type of interaction. Ether was selected as the solvent for the ultraviolet spectral study because of the availability of information on the absorption of tertiary amines in ether[7] and because carbon tetrachloride, which was the solvent of choice for the infrared determinations, is reported to cut off at 265 mμ. 2-Hydroxycyclononanone[8] was selected as a model since it contains the acyloin function in a nine-membered carbocyclic ring, analogous to the 1-alkyl-1-azacyclononan-5-ol-6-ones here considered. The model I exhibited two distinct ultraviolet maxima (Table I), at 217 and 264 mμ. The position of the long wave length (carbonyl) maximum is probably determined by the geometry of the α-ketol system.[9] 1-Methyl-1-azacyclononan-5-ol-6-one (II) showed very weak absorption, with no detectable maximum, in the region of 264 mμ, and had a new maximum at 228 mμ. Since this compound probably occurs predominantly in the transannular interacted form[2] in

---

[1] Presented at the Fourteenth National Organic Chemistry Symposium of the Am. Chem. Soc., Lafayette, Ind., on June 14, 1955. Supported in part by a grant from the University Research Board, University of Illinois.

[2] N. J. Leonard, M. Ōki, J. Brader and H. Boaz, THIS JOURNAL, **77**, 6237 (1955).

[3] N. J. Leonard, M. Ōki and S. Chiavarelli, *ibid.*, **77**, 6234 (1955).

[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] N. J. Leonard, R. C. Fox, M. Ōki and S. Chiavarelli, *ibid.*, **76**, 630 (1954).

[7] N. J. Leonard and D. M. Locke, *ibid.*, **77**, 437 (1955).

[8] A. T. Blomquist, L. H. Liu and J. C. Bohrer, *ibid.*, **74**, 3643 (1952).

[9] R. C. Cookson and S. H. Dandegaonker, *J. Chem. Soc.*, 352 (1955).