as previously described. Upon subsequent development of the chromatogram, three distinct spots were obtained having the following R_f values: 0.62–0.64, 0.75–0.77 and 0.86–0.88. When 5 micrograms of 3-indoleacetic acid was added to a like portion of the residue and chromatographed, the same three spots were evident with an enrichment of the colored zone having an R_f value of 0.75–0.77. A parallel chromatogram of known 3-indoleacetic acid gave an R_f value of 0.75. An acid corresponding to an R_f value of 0.75–0.77 was eluted from the papergram and applied in the form of a lanolin paste to the first internode of red kidney bean seedlings. A pronounced negative curvature was obtained. Elution of a like area of a chromatogram and treatment with the Gordon and Weber reagent[10] gave a colored product having a maximum absorption at 540 mμ. These properties described for the spot having an R_f value of 0.75–0.77 are in agreement with those of 3-indoleacetic acid.

Two other spots were obtained on the chromatogram having R_f values of 0.86 to 0.88 and 0.62–0.64. The substance having an R_f value 0.86–0.88 produced a negative curvature when applied to the first internode of bean seedlings while the substance present in the greatest amount having an R_f

value of 0.62–0.64 showed only slight biological activity. In an effort to identify these substances a number of indole derivatives were chromatographed to find known compounds which would migrate at the rate of the unknowns. The R_f values of these substances are given in Table I.

It is evident from Table I that a number of known indole compounds migrate within the range of R_f values 0.86–0.88. However, with one exception, these are neutral compounds not generally found in appreciable amounts in an acid fraction. Bennet-Clark and Kefford[9] have reported that 3-indoleacetonitrile, although not an acid, is carried to some extent from an ether solution into sodium bicarbonate solution and back into ether on re-acidification. However, using an ethyl acetate solution of synthetic 3-indoleacetonitrile and mutually saturated solutions for extracting, with washing between extractions, extremely small amounts of 3-indoleacetonitrile were obtained.

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COMMUNICATIONS TO THE EDITOR

CYCLIC AMINOACYLOINS. RING-SIZE LIMITATION OF TRANSANNULAR INTERACTION BETWEEN N AND Cco

Sir:

A transannular amide-type neutralization,

$$R—N:\overset{|\delta^+}{\underset{|}{}} \,\,\, \overset{\frown}{C}\overset{\delta^-}{=}O$$, has been proposed by Robinson[1] as

the cause of the low frequency observed for the infrared absorption of the carbonyl group in the alkaloid cryptopine (10-membered ring) and also of the ketonic groups in N-methylpseudostrychnine and N-methylpseudostrychnidine (9-membered rings).[2]
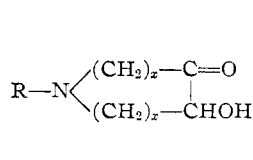
transannular interaction of RN$\lessdot$ and $\gtrdot$C=O. Moreover, we are able to assign the probable limits of ring size within which appreciable transannular interaction of these groups will occur. We have also innovated the comparison of the apparent dissociation constants of a cyclic aminoketone in solvents of different dielectric strength as a diagnostic tool for demonstrating transannular interaction.

1-Alkyl-1-azacycloalkanolones of type I (odd-membered rings) have been synthesized *via* the acyloin condensation of the corresponding aminodiesters, which were made by treatment of the pri-

		R	x	Base		Perchlorate	
	a	C_6H_5	2	1701	3458		
	b	CH_3	3	1666	3410	3440	
	c	C_2H_5	3	1671	3428	3425	
	d	CH_3	4	1700	3462	1710	3480
	e	C_2H_5	4	1705	3470		
	f	CH_3	3, no CHOH	1683		3380	

Infrared absorption maxima, cm.$^{-1}$[4]

$$R—N\underset{(CH_2)_x—CHOH}{\overset{(CH_2)_x—C=O}{\diagdown}}$$

We find that the infrared data accumulated in this Laboratory for a series of related compounds,[3] which are structurally much simpler than the alkaloid products, are consistent with the hypotheses of

mary amine with the appropriate ω-haloester. The acyloins of ring size: 11, 13, 15, 17, 19 and 23 members possess normal ketone carbonyl absorption in the infrared (1700–1713 cm.$^{-1}$), as does Ia, a 7-membered ring, while the two 9-membered ring examples (Ib, c) have infrared maxima in the 6 μ region which are at abnormally low frequency for C=O stretching in a saturated ketone. The perchlorate of the 11-membered ring (Id) shows both ketone and O–H/N–H absorption, whereas the perchlorate of the 9-membered ring (Ib, also Ic) is transparent in the 6 μ region (no C=O). The contrast between the 11- and 9-membered ring com-

(1) F. A. L. Anet, A. S. Bailey and Sir Robert Robinson, *Chemistry and Industry*, 944 (1953); also, Sir Robert Robinson in the Karl Folkers Lectures at the University of Illinois, September 29, 30, October 1, 1953. E. H. Mottus, H. Schwarz and L. Marion, *Can. J. Chem.*, 31, 1144 (1953), have come to a similar conclusion on the basis of spectral studies on protopine.

(2) R. Huisgen, H. Wieland and H. Eder, *Ann.*, 561, 193 (1949), suggested the contribution of a limiting electronic species,

$$—CH_2—\overset{|}{N}{}^+—\overset{|}{C}—O^-$$
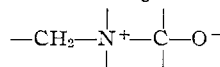
to the structure of vomicine (9-membered ring) to account for the unusual chemical behavior of the tertiary amino and ketonic groupings in this alkaloid.

(3) R. C. Fox, Ph.D. thesis, University of Illinois, 1953.

(4) We wish to thank Miss Helen Miklas for determination of the infrared absorption spectra. The bases were determined in carbon tetrachloride solution; the salts, in Nujol mull. Where the entry is blank, the infrared spectrum was not obtained.

pounds is further illustrated by their apparent dissociation constants.[5]

	pK'_a	
	66% DMF	Water
11-Membered ring (Id)	7.8	9.1
9-Membered ring (Ib)	10.6	9.2

The increment in pK'_a observed for Ib in changing solvent from 66% dimethylformamide to water is reversed in sign from that usually observed for tertiary amine-H$^+$ (compare Id, which is normal), but is typical for enols and acid types, wherein hydrogen is being removed from neutral oxygen, and is therefore evidence of the existence of the transannular quaternary form, R—N$^+$—C—OH, of the base conjugate acid in dimethylformamide.

The 8-membered ring[6] aminoketone, 1-methyl-1-azacyclooctan-5-one (If), exhibits carbonyl absorption at 1683 cm.$^{-1}$ and no absorption above 3000 cm.$^{-1}$; the perchlorate is transparent in the 6 μ region; pK'_a 9.75 in 66% DMF, 8.75 in water.

Formulations involving interaction of 3° amine and ketone functions are thus indicated for 8-, 9- and 10-membered rings in which a full transannular bond between N and Cco can create a 5- or 6-membered ring within the larger cycle.

Diethyl γ,γ'-methylimino-bis-butyrate was treated with sodium in xylene under acyloin ringclosure conditions to give (53%) 1-methyl-1-azacyclononan-5-ol-6-one (Ib), m.p. 95–97° (Calcd. for $C_9H_{17}NO_2$: C, 63.12; H, 10.01; N, 8.18. Found: C, 63.74; H, 9.98; N, 7.90); perchlorate[7] (Calcd. for $C_9H_{18}ClNO_6$: C, 39.97; H, 6.63. Found: C, 39.70; H, 6.93). Similarly, from diethyl γ,γ'-ethylimino-bis-butyrate was obtained (60%) 1-ethyl-1-azacyclononan-5-ol-6-one (Ic), b.p. 64–65° (0.15 mm.), n^{20}D 1.4999 (Calcd. for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.33; N, 7.56. Found: C, 65.12; H, 10.49; N, 7.69); perchlorate[7] (Calcd. for $C_{10}H_{20}ClNO_6$: C, 42.08; H, 7.08. Found: C 41.78; H, 7.13). From diethyl δ,δ'-methyl-imino-bis-valerate was obtained (47%) 1-methyl-1-azacyclohendecan-6-ol-7-one (Id), b.p. 85–86° (0.2 mm.), n^{20}D 1.4926 (Calcd. for $C_{11}H_{21}NO_2$: C, 66.29; H, 10.62; N, 7.03. Found: C, 66.52, H, 10.70; N, 7.21); perchlorate[7] (Calcd. for $C_{11}H_{22}ClNO_6$: C, 44.04; H, 7.39. Found: C, 44.40; H, 7.67). Diethyl δ,δ'-ethylimino-bis-valerate yielded (64%) 1-ethyl-1-azacyclohendecan-6-ol-7-one (Ie) b.p. 65° (0.02 mm.), n^{20}D 1.4907 (Calcd. for $C_{12}H_{23}NO_2$: C, 67.56; H, 10.87; N, 6.57. Found: C, 67.39; H, 10.67; N, 6.45). Dieckmann ring closure of diethyl γ,γ'-methylimino-bis-butyrate at high dilution in xylene using potassium t-butoxide,[8] followed by hydrolysis and decarboxylation, yielded (20%) 1-methyl-1-azacyclooctan-5-one, purified through the picrate, m.p. ca. 300° dec. (Calcd. for $C_{14}H_{18}$-

(5) We are indebted to Mr. Donald O. Woolf, Jr., and Dr. Harold E. Boaz of Eli Lilly and Company, Indianapolis, Ind., for the electrometric titrations and for aid in their interpretation.

(6) H. C. Brown and E. A. Fletcher, THIS JOURNAL, 73, 2808 (1951), have demonstrated the coördination of $>$N: with B$<$O— across an 8-membered ring in triethanolamine borate.

(7) Hygroscopic glass.

(8) N. J. Leonard and R. C. Sentz, ibid., 74, 1704 (1952).

N_4O_8: C, 45.40; H, 4.90; N, 15.13. Found: C, 45.56; H, 4.86; N, 15.13); perchlorate, m.p. 260–261° dec. (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).

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SELECTIVE REDUCTIONS OF AROMATIC SYSTEMS TO MONOÖLEFINS

Sir:

In an earlier publication from this Laboratory[1] we announced the surprisingly large uptake of lithium metal by aromatic ring systems in a solvent of ethylamine. Thus, in some instances, six equivalents of metal were absorbed per benzene nucleus. This clearly indicated that far more extensive reduction of the aromatic rings was occurring than had been observed previously in the sodium–ammonia system.

We now wish to announce the application of this discovery to practical organic syntheses. Thus, employing the lithium–ethylamine reducing medium, we have succeeded in reducing naphthalene, in a one-step operation, directly to $\Delta^{9,10}$-octalin in 52% yield. The nitrosyl chloride of our product melted at the same point as an authentic specimen,[2] and a mixed m.p. was not depressed. A 2,4-dinitrobenzenesulfenyl chloride derivative melted at 142–142.5°. *Anal.* Calcd. for $C_{16}H_{19}O_4N_2SCl$: C, 51.82; H, 5.14; N, 7.56. Found: C, 51.57; H, 5.46; N, 7.65.

Likewise we have shown that tetralin is reduced in 68% yield to $\Delta^{9,10}$-octalin by lithium in ethylamine, thus indicating that naphthalene may pass through this intermediate in its reduction to $\Delta^{9,10}$-octalin. Certainly the above reactions appear to be the method of choice at the moment for the preparation of this olefin. It is noteworthy that sodium in liquid ammonia is reported[3] to reduce naphthalene to tetralin. We have found that lithium in ammonia acts similarly. The greater basicity of ethylamine compared to liquid ammonia may be one of the factors causing more extensive reduction in these cases, although we have not as yet proved this point.

In another case we reduced biphenyl to 1-cyclohexylcyclohexene in 66% yield, the nitrosyl chloride derivative giving an undepressed mixed m.p. with an authentic sample.[4] Sodium in liquid ammonia is reported[5] to reduce biphenyl to 1-phenyl-1-cyclohexene, again indicating a marked difference in the two systems.

Similarly benzene is reduced by lithium–ethylamine to cyclohexene, showing again a tendency for the reagent to leave one unreduced double bond.

(1) R. A. Benkeser, R. E. Robinson and H. Landesman, THIS JOURNAL, 74, 5699 (1952).

(2) P. D. Bartlett, F. E. Condon and A. Schneider, ibid., 66, 1538 (1944).

(3) P. Lebeau and M. Picon, Compt. rend., 158, 1514 (1914). See also C. B. Wooster and F. B. Smith, THIS JOURNAL, 53, 179 (1931).

(4) R. Criegee, E. Vogel and H. Hoger, Ber., 85, 144 (1952).

(5) W. Huckel and H. Bretschneider, Ann., 540, 157 (1939).