30. *Macrocyclic Compounds. Part VII.*[1] *Conformations of Symmetrical Cyclic Diamides and Dilactams.*

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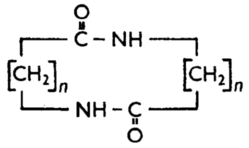
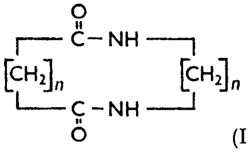
Cyclic diamides having 12—20 ring atoms have been prepared by pyrolytic depolymerization of the corresponding polyamides. Lower and higher members had to be prepared by high-dilution condensation. Alternation in depolymerization yields, melting point, solubility, and association tendency in dilute carbon tetrachloride solution in the series of cyclic diamides is explained by conformational considerations.

THE physical properties of the amide group in monolactams have been studied extensively as a function of ring size by Huisgen and his collaborators.[2,3] However, the only conclusion of structural interest that could be drawn, based on molar polarization [2] and infrared and ultraviolet spectra,[3] was that the change from the unstable *cis*-amide to the stable *trans*-amide configuration starts in the 9-membered and is completed in the 10-membered ring. No finer conformational details could be revealed, probably because the orientation of the amide group with respect to amide groups in other molecules is rather insensitive to the conformational situation in the ring itself.


(I)


(II)

It was considered that more information might be obtainable by studying the interaction between two amide groups in the same macrocyclic skeleton, as their mutual arrangement should depend very critically on subtle conformational factors. The simplest systems of this kind are the two symmetrical series of dilactams (I) and cyclic diamides (II).

As discussed in Part III,[4] the series of dilactams (I) should show an alternation in melting point: high for odd n, low for even n. The series of cyclic diamides (II) should in principle show a similar behaviour if only the angular (Baeyer) and torsional (Pitzer) strain were considered, but the alternation may be counteracted by intramolecular dipole interaction. Thus, whereas the ideal strain-free conformations of the dilactams with odd n are stabilized by the opposite orientation of the two dipoles, as illustrated in Fig. 1a for $n = 7$, and should be particularly high-melting, the corresponding cyclic diamides must have their dipoles oriented parallel (Fig. 1b) and become destabilized; their melting points should therefore lie lower. It is evident that the effect must be most marked when n is small, and the two dipoles are close, and must diminish as they become more widely separated by longer saturated chains. For the members with even n it might be expected that the dipole orientation should have the opposite effect in the two series, as for either of the two most probable conformational types illustrated for $n = 8$ in Fig. 2 the dipoles are oriented roughly parallel for the dilactams (*a* or *c*) and in opposition for the diamides (*b* or *d*). However, no conformational homogeneity is expected anyway in these cases so the dipole interaction may not manifest itself in the melting point.

Very recently, Rothe [5] has completed the whole series of dilactams (I) having $n = 1$—10. A very strong alternation in melting point, starting from the 12-membered ring ($n = 4$), is indeed observed (Fig. 3). The smallest dilactam with a *trans*-amide configuration is

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[1] Part VI, Dale and Hubert, *J.*, 1963, 5475.
[2] Huisgen and Walz, *Chem. Ber.*, 1956, **89**, 2616.
[3] Huisgen, Brade, Walz, and Glogger, *Chem. Ber.*, 1957, **90**, 1437.
[4] Dale, *J.*, 1963, 93.
[5] Rothe, *Angew. Chem.*, 1962, **74**, 725.

actually the 10-membered ring ($n = 3$), but its melting point is certainly influenced by the tension caused by strong transannular repulsion between the amide groups, which would be placed parallel and only 2·5 Å apart in a hypothetical ideal conformation.

Of the cyclic diamides (II) only those with even n have been prepared before; the method used was a high-dilution condensation of dichlorides of dicarboxylic acids with αω-diaminoalkanes.[6,7] We have now completed this series, partly (n = 3 and 9) by the same method, and partly by a simple pyrolytic depolymerization of corresponding polyamides in the presence of a catalyst (metallic sodium). This method is analogous to

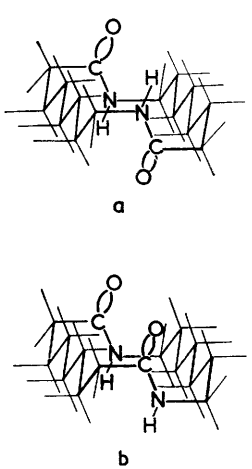

FIG. 1. Strain-free compact conformations of (a) a dilactam (I) and (b) a cyclic diamide (II), both with odd n (=7).

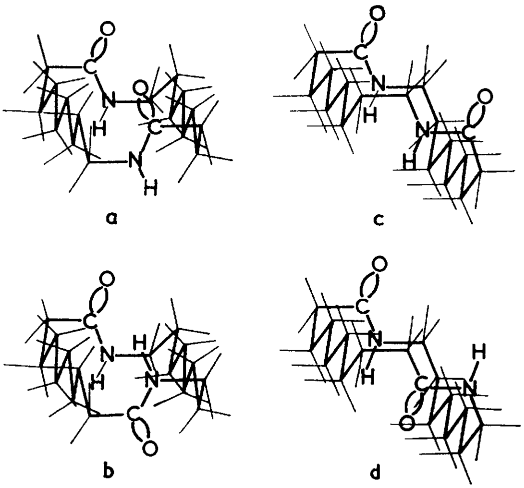

FIG. 2. Strained compact conformations (a and b) and strained open conformations (c and d) of a dilactam (I) (a and c) and a cyclic diamide (II) (b and d), both with even n (=8).

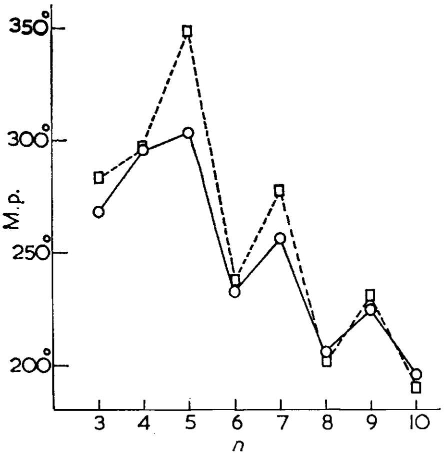

FIG. 3. Melting points of (□) *trans,trans*-dilactams (I) (Rothe [5]) and of (○) cyclic *trans,trans*-diamides (II).

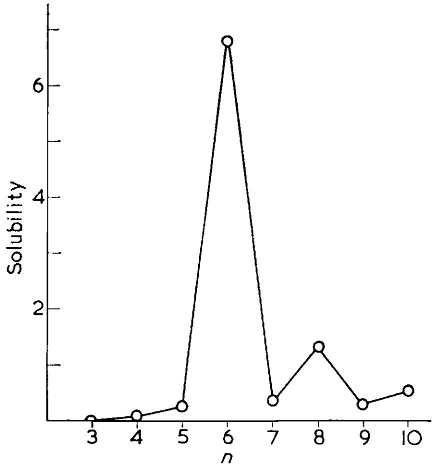

FIG. 4. Solubilities (g. per 100 g. of solution) of cyclic diamides (II) in chloroform at 20°.

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[6] Stetter and Marx, *Annalen*, 1957, **607**, 59.

[7] Rothe and Timler, *Chem. Ber.*, 1962, **95**, 783,

Carothers's cyclic ester synthesis by depolymerization of polyesters,[8] but it is more limited in scope and gives poorer yields. Thus, only the diamides with $n = 4$—8 could be obtained, and all yields were below 20%. A striking alternation was observed (Table 1); the higher yields when n is odd reflect probably the conformational stability which leads to a higher concentration of diamide in the equilibrium mixture at the pyrolysis temperature. For the higher diamides the volatility is too low and destruction took place. In the case of the smaller ring ($n = 3$) pyrolysis could not even be attempted because the corresponding polymer was not obtainable from glutaric acid and 1,3-diamino-propane.

TABLE 1.

Cyclic diamides (II).

	Yield (%) by method		M. p.			Found (%)				Required (%)		
n	A	B	Found	Lit.	Soly.*	C	H	N	Formula	C	H	N
3	0	1	268°		0·004	56·6	8·1	16·1	$C_8H_{14}N_2O_2$	56·45	8·3	16·5
4	9		295	295[6]	0·11	60·6	9·2	13·4	$C_{10}H_{18}N_2O_2$	60·6	9·15	14·1
5	19	13	303		0·25	63·6	9·7		$C_{12}H_{22}N_2O_2$	63·7	9·8	12·4
6	7		234	232[6]	6·80	65·9	10·2		$C_{14}H_{26}N_2O_2$	66·1	10·3	11·0
7	16		256		0·33	67·7	10·7		$C_{16}H_{30}N_2O_2$	68·0	10·7	9·9
8	0·1	20	205	201[7]	1·34	69·2	10·8	9·3	$C_{18}H_{34}N_2O_2$	69·6	11·0	9·0
9	0	18	224	(145)[7]	0·27	70·9	11·5		$C_{20}H_{38}N_2O_2$	71·0	11·3	8·3
10	0	23	191	195[7]	0·54	72·1	11·6		$C_{22}H_{42}N_2O_2$	72·1	11·55	7·6

Method A: depolymerization. Method B: high-dilution condensation.

* Solubility (%) in $CHCl_3$ at 20°.

TABLE 2.

Typical infrared absorption bands (cm.$^{-1}$) of cyclic diamides (II) (shoulders in italics).

	Solid (KBr)				Solution, $CHCl_3$				CCl_4
n	νNH	νC=O	δNH *	δCH_2	νNH	νC=O	δNH	δCH_2	νNH
3	3290	1642	1552	1477 (1462) *1441*	—	1656	—	—	Insol.
4	3300	1644	1555	(1464) *1453* 1437	*3450* 3335	1661	1522	— — 1437	Insol.
5	3300	1644	1555	1464 1453 *1439*	3450 3335	1650	1527	— 1458 *1441*	3435 *3270*
6	3290	1644	1552	*1462* 1435	*3450* 3325	1661	1520	1462 *1441*	*3450* 3300
7	3290	1642	1552	1464 *1437*	*3450* 3335	1658	1520	— *1441*	3450 *3280*
8	3290	1642	1552	*1468* 1435	*3450* 3335	1661	1520	*1460* 1441	*3450* 3380
9	3290	1640	1552	1466 *1435*	*3450* 3335	1658	1520	1462 *1441*	3450 *3280*
10	3290	1640	1552	*1466* 1435	*3450* 3335	1661	1518	*1464* 1441	*3450* 3370

* All members show 2 × δNH at 3060—3085 cm.$^{-1}$ in the solid state; these bands are absent from $CHCl_3$ solutions.

The melting points of the diamides (Table 1 and Fig. 3) show an alternation similar to that of the dilactams, and the expected destabilization of the members with odd n caused by parallel dipole orientation is clearly noticeable in a lowering of the melting point, especially when the amide groups are close ($n = 5$). Even for the 10-membered diamide ($n = 3$) the melting point is somewhat lower than for the corresponding dilactam, although

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[8] Hill and Carothers, *J. Amer. Chem. Soc.*, 1933, **55**, 5031; Spanagel and Carothers, *ibid.*, 1935, **57**, 929.

the transannular repulsion may overshadow subtle conformational effects and render predictions unjustified.

Solubilities are often closely related to the melting point, and one would expect here the opposite alternation, low solubility for odd n and high for even n. The solubilities in chloroform (Table 1 and Fig. 4) show such an alternation, starting from the 14-membered ring.

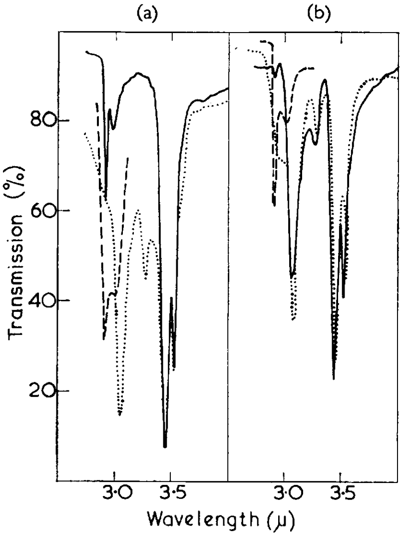

Fig. 5. Infrared spectra of cyclic diamides (II) illustrated for (a) even n with $n = 8$ and for (b) odd n with $n = 9$. Full line for CCl_4 solution in a 1 cm. silica cell; broken line for $CHCl_3$ solution in a 1 mm. cell; dotted line in KBr disks.

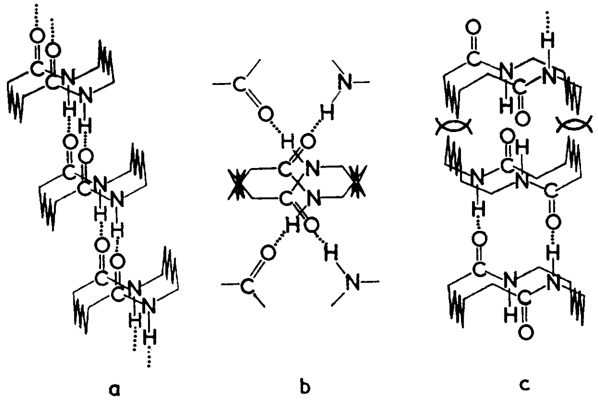

Fig. 6. Possible ways of association of cyclic diamides (II) in solution; (a) when n is odd; (b) and (c) when n is even.

The infrared spectra are similar for all the cyclic diamides in the solid state. In particular, the bands associated with the amide group, the NH-stretching, C=O stretching (" amide I "), and NH-deformation (" amide II "), remain constant (Table 2); the presence of the latter band shows that the amide groups have the *trans*-configuration.[3,9,10] The CH_2 scissoring vibration gives rise to a group of bands at 7 μ which vary along the series (Table 2). A relatively larger spread of these bands to higher frequencies in the 10-membered ring ($n = 3$) may reflect[11] medium-ring tension, while a variation in relative intensity between the α-methylene band (lower frequency) and the other methylene bands

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[9] Mizushima, Simanouti, Nagakura, Kuratani, Tsuboi, Baba, and Fujioka, *J. Amer. Chem. Soc.*, 1950, **72**, 3490.

[10] Worsham and Hobbs, *J. Amer. Chem. Soc.*, 1954, **76**, 206.

[11] Chiurdoglu, Doehard, and Tursch, *Bull. Soc. chim. France*, 1960, 1322.

along the series is more difficult to interpret; it may be caused by a different orientation of the α-methylene groups with respect to the amide group * in the two series (odd and even *n*).

In moderately dilute chloroform solution the infrared spectra of the higher members show the changes normally observed [9,12,13] with simpler amides. Thus, bands of free and associated NH coexist (Table 2 and Fig. 5), the C=O stretching is displaced to higher, and the NH-deformation to lower frequencies (Table 2). The 14-membered ring ($n = 5$) is somewhat abnormal in showing a stronger tendency to remain associated.

In very dilute carbon tetrachloride solution an interesting alternation along the series is observed (Table 2 and Fig. 5): The cyclic diamides with odd *n* have a broad NH-band at 3·1 μ and only a very weak narrow band (if at all) at 2·9 μ, hence must remain associated. The spectra of the members with even *n*, on the other hand, resemble the spectra in chloroform solution, with predominance of free NH-groups (2·9 μ), although for comparable concentrations the association is also here more pronounced in carbon tetrachloride than in chloroform, as is general [12,14] for simple amides. The abnormal behaviour is that of the series with odd *n*, as it is sterically impossible to have both NH bonds of *trans*-amide groups internally associated; at most, one would expect one associated and one free NH group per molecule at high dilution. The only logical conclusion seems to be that these molecules form long doubly associated chains, as in Fig. 6a, for which the conformation *b* of Fig. 1 is ideally suited. This is in accord with their low solubility, and also with the evidence for chain association of simple *trans*-amides obtained from infrared spectra [9] and dielectric measurements [2,9,10] in solvents (CCl_4, benzene) which do not tend to dissociate amide complexes. No chain association takes place with *N*-methylacetamide in dioxan,[9] a solvent capable of breaking the amide–amide " bonds," whose nature is now considered [12,14–16] to be more a dipole–dipole interaction than a hydrogen-bond formation.

This view is supported by our observation that chloroform is able largely to prevent the formation of doubly associated chains. Why is there then no chain association in dilute solution when *n* is even? First, the conformation *d* of Fig. 2 would be expected to give rise to doubly associated dimers (Fig. 6c), as further association would become impossible because of steric conflict between the polymethylene chains. However, each dimer should then have two free and two associated NH-groups, while mainly free groups are observed in dilute solution. The conformation *b* of Fig. 2 can form neither dimers nor polymers by double association as the bonds to be involved are no longer parallel on either side of the ring because of the twisted polymethylene chains (Fig. 6b); hence the observed normal concentration-dependent behaviour is expected. On this basis one might conclude that the conformations of the cyclic diamides with even *n* are probably of the type *b* (and not *d*) in Fig. 2, with planar *trans*-amide groups and the strain taken up as a distortion by the polymethylene chains, as proposed [16] for the case of polyamide copolymers with differing repeat unit lengths.

Finally, we can discuss the very strong *trans*-preference of the amide group.[2,10] Repulsion between the substituents has been considered [2] as a factor destabilizing the *cis*-configuration; but, although the CN bond has some double-bond character, it is essentially a single bond,[10,17] so it seems more natural to connect the stability of the *trans*-configuration with its staggered conformation, the *cis*-configuration being totally eclipsed. The *s*-*trans*-preference of butadiene [18] represents an analogous case. In both cases a double bond is considered sterically as two bent bonds [4] and the nitrogen is tetrahedral. The

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* Cf. hexamethylenediamine adipate (Heidemann and Zahn, *Makromol. Chem.*, 1963, **62**, 123).

[12] Cannon, *Mikrochim. Acta*, 1955, 555.

[13] Beer, Kessler, and Sutherland, *J. Chem. Phys.*, 1958, **29**, 1097.

[14] Mizushima, Tsuboi, Shimanouchi, and Tsuda, *Spectrochim. Acta*, 1955, **7**, 100.

[15] Cannon, *J. Chem. Phys.*, 1956, **24**, 491; *Discuss. Faraday Soc.*, 1958, **25**, 59.

[16] Cannon, *Spectrochim. Acta*, 1960, **16**, 302.

[17] Miyazawa, Shimanouchi, and Mizushima, *J. Chem. Phys.*, 1958, **29**, 611.

[18] Aston, Szasz, Woolley, and Brickwedde, *J. Chem. Phys.*, 1946, **14**, 67.

difficulty is that the NH proton must then be considered as being bonded through both " lone pairs " in order to have a planar structure.

EXPERIMENTAL

Preparation of Cyclic Diamides (II; n = 3—5,8—10) *by High-dilution Condensation.*—These *compounds* (Table 1) were prepared by Stetter and Marx's method[6] from the dichlorides of dicarboxylic acids and αω-diaminoalkanes; spectral data in Table 2. Two of these compounds (n = 8 and 10) have been prepared by Rothe and Timler,[7] by the same method; another product claimed to be (II; n = 9) was obtained by them by rearrangement of a cyclic dioxime, but melts much too low (145°).

Preparation of Cyclic Diamides (II; n = 4—8) *by Depolymerization of Polyamides.*—The polyamides were prepared[19] by heating equimolar quantities of the dicarboxylic acid and the diamine at 200° under nitrogen, then dehydrating the product in a vacuum at temperatures up to 290°. The resulting polyamide was heated with about 1% of sodium (NaOH and tetrabutyltitanate were found ineffective as catalysts) in a distillation flask in oil-pump vacuum at 270—300°. After a few hours the cyclic diamide started to distil and solidified in the condenser. The crude product was taken up in chloroform, washed with sodium hydrogen carbonate solution, dried, and evaporated, then recrystallized from chloroform, when necessary with addition of hexane, and sublimed in an oil-pump vacuum. Data for these *compounds* are also given in Tables 1 and 2; those with even n are known compounds.[6,7]

When poly-6-hexanolactam (Nylon 6) was pyrolysed in the same manner, only the monolactam, m. p. 72°, was obtained, and none of the dilactam (I; n = 5).

Infrared Spectra of Cyclic Diamides.—These were measured on a Perkin-Elmer double-beam instrument, model 21, fitted with a sodium chloride prism. Because of the low solubility, solutions in CCl_4 had to be measured in 1 cm. silica cells at a temperature close to the b. p.; the spectra extended therefore only to 4 μ. Solutions in $CHCl_3$ could be measured at room temperature in 0·1 and 1·0 mm. sodium chloride cells and extended to 8 μ. Solid-state spectra were obtained for potassium bromide discs. The results are given in Table 2 and in part in Fig. 5.

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[19] D'Alelio, " Experimental Plastics and Synthetic Resins," John Wiley & Sons, New York, 1946, p. 140.