

vibration spectra of 2-pyrrolidone (I). The carbonyl frequency of the two lactams fused to cyclohexane, VI, VIII, are both 1669 cm^{-1} . The 5-membered lactam N-acetylcyclohexane-1,3-lactam (VII) has two sharp bands at 1736 and 1686 cm^{-1} . The 6-membered ring N-acetylcyclohexane-1,4-lactam also has two sharp bands, one at 1712 and the other at 1686 cm^{-1} . The two bands in each of the above two cases are of equal intensity. Presumably the band at 1686 is the normal ring lactam carbonyl (1678 – 1684 cm^{-1} for I–V) while the band at higher frequency is the acetyl carbonyl band. N-Acetylpyrrolidone⁵ has two bands, one at 1730 cm^{-1} and the other at 1686 cm^{-1} . However, N-acetylpiperidone shows only one band at 1686 cm^{-1} .

None of the lactams except N-methylpyrrolidone (V) show any ultraviolet absorption band above $200\text{ m}\mu$; there appears to be a band of high extinction just below $200\text{ m}\mu$ for the lactams which is the limit on the Cary model 11. N-Methylsuccinimide (VI) has a band at $202\text{ m}\mu$ with a molar extinction coefficient of about 5000. The 5-membered N-acetyl lactam (VII) has a peak at $217\text{ m}\mu$ with an extinction of 8700 while the 6-membered N-acetyl lactam (IX) has a peak at $218\text{ m}\mu$ molar

extinction coefficient of about 10,100. While it is true that the greater the dipole moment the lower the extinction, there is no parallel between the slopes of the plot of the maximum extinction and the dipole moment as reported for N-acetyl and N-benzoyl lactams.⁵ The fact that the 5-membered ring VII is attached to the chair form of cyclohexane, while the 6-membered ring IX is attached to the boat form of cyclohexane alters the dipole moment appreciably. N-Acetylpyrrolidone has a peak at $216\text{ m}\mu$ with extinction coefficient of 11,300, while N-acetylpiperidone has a peak at $218\text{ m}\mu$ with extinction coefficient of 8900.

Experimental

All dipole moments were measured in dioxane at 30° and calculations made using the equation and method of Halverstadt and Kumler.⁸

We wish to thank Dr. H. K. Hall, Jr., of du Pont for providing the compounds.⁹

All spectrographic measurements were made by Mr. M. K. Hrenoff of the Spectrographic Laboratory of the School of Pharmacy. Infrared spectra were run on Perkin-Elmer model 21 and ultraviolet spectra on Cary model 11.

(8) I. F. Halverstadt and W. D. Kumler, *J. Am. Chem. Soc.*, **64**, 2933 (1942).

(9) H. K. Hall, Jr., *ibid.*, **80**, 6404 (1958).

[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, SCHOOL OF PHARMACY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO MEDICAL CENTER, SAN FRANCISCO, CALIF.]

The Dipole Moment and Structure of the Carbamate Group

BY CALVIN M. LEE AND W. D. KUMLER

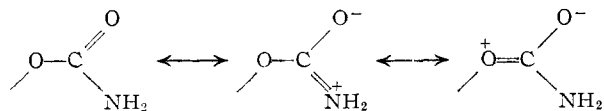
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The carbamate group, $\text{O}=\text{C}-\text{N}<$, can theoretically be in two conformations, the *cis* and the *trans* (position of the carbonyl group with respect to the R group) (Fig. 1). In cyclic carbamates of ring size five to seven only the *trans* conformation is permitted. The dipole moments of the free carbamates ethyl carbamate (I) and emylcalmate (II) are 2.59 and 2.64 D., resp. The moments of the five- and six-membered cyclic carbamates III and IV are 5.07 and 5.10 D., resp. Comparison of these experimental moments with theoretical moments indicates that the free carbamate group takes up the *cis* conformation while the cyclic carbamates of low ring size are in the *trans* conformation. Fusion of the carbamate group to the 1,3- and 1,4-position of cyclohexane (V, VI) show a slightly increased moment (0.6 D.) over the cyclic carbamates; an explanation in terms of rehybridization of ring bonds is offered. The low dipole moment of N-acetylloxazolidone (VII), 2.81 D., indicates that it is in the *cis-trans* conformation where the carbonyl groups are farthest apart. Low dipole moments (1.7 D.), examination of models, infrared and ultraviolet spectra of some oxazolidine 2,4-diones VIII and IX all indicate that there is only a very small amount of resonance in these compounds as would be predicted.

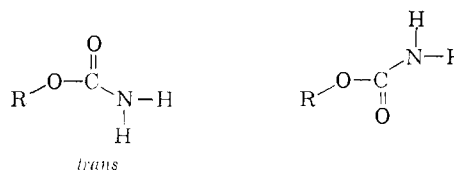
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Introduction

The carbamate group, $\text{O}=\text{C}-\text{NH}_2$, has increasingly appeared in many drug classes such as hypnotics, muscle relaxants, antiepileptics and anticancer agents. It is flat because of the resonance and there are two possible conformations,



cis and *trans*, depending on the position of the carbonyl group with respect to the R group. Either the *cis* or *trans* conformations might be expected in free carbamates while only the *trans* conformation would be expected in five-, six- and seven-



membered cyclic carbamates. The dipole moments of free and cyclic carbamates and related compounds were measured to determine which conformations are present.

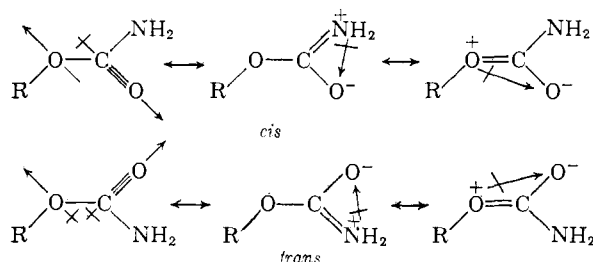
Results and Discussion

Figure 2 gives the dipole moments in dioxane at 30° for these compounds. Free carbamates have a much lower moment than cyclic carbamates (compare I–IV).

Both urethan (I), a hypnotic and anticancer agent, and emylcalmate (II), a "tranquilizing and

muscle relaxing compound," have about the same moment, 2.59 and 2.64 D., respectively. The five- and six-membered ring carbamates III and IV have about the same moment, 5.07 and 5.10 D., respectively.

Resonance in the *cis* and *trans* forms of the carbamate group involves both the ring nitrogen and the ring oxygen conjugating with the carbonyl oxygen.



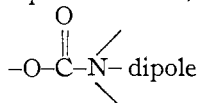
In the case of the *cis* conformation the carbonyl dipole $O^+ O^-$ and $N^+ O^-$ dipoles all point away from the $C-O-C$ ether dipole; this conformation would be expected to have a low dipole moment. In the *trans* conformation all dipoles point in the same general direction increasing the moment.

With the free carbamate group as in I and II one would expect the *cis* conformation to be favored as there is electrostatic repulsion between the carbonyl dipole and the $C-O-C$ dipole and steric interference between the NH_2 group and the R group in the *trans* conformation. As a first approximation for calculation of theoretical moments we can assume the dipole moment to be composed of two resultant dipoles, one being a dipole due to the $C-O-C$ bond with a resultant bisecting the 110° ether angle, the other being the dipole due to the carbonyl group and $N^+ O^-$ and $O^+ O^-$ dipoles (these latter make angles of 120° with the carbonyl group so their resultant is nearly in the direction of the carbonyl dipole). In the *trans*

conformation the ether resultant and the $O=C-N$ resultant make an angle of about 50° with one another (measured on Stuart-Briegleb models). In the *cis* conformation the ether resultant and the

$O=C-N$ resultant are about 180° to one another.

The dipole moment of ethyl ether is 1.3 D.¹; in the *trans* conformation the angle between the two dipoles is about 50° and the resultant moment is about 5.1 D. One can then solve the following equation for X, which is the moment for the

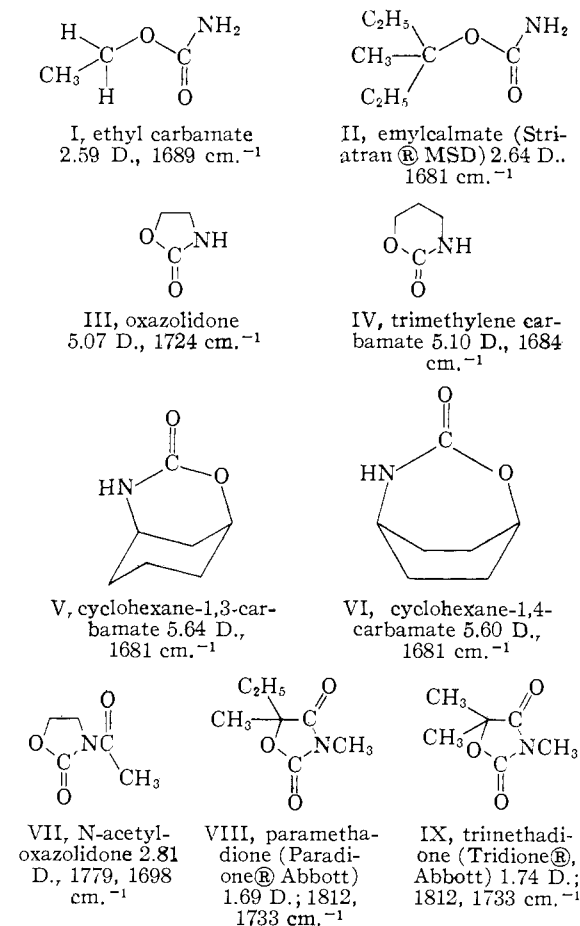


$$(5.1)^2 = (X - 1.3 \cos 130^\circ)^2 + (1.3 \sin 130^\circ)^2$$

The solution gives a value of about 4.1 D. for the

(1) L. G. Wesson, *Tables of Electric Dipole Moments*, MIT Press, 1948, p. 22.

Fig. 2.—Dipole moments in dioxane at 30° and infrared carbonyl frequencies of free and cyclic carbamates and oxazolidone-2,4-diones.



$-O-C-N$ moment. In the *cis* conformation the two moments are almost 180° to each other so the estimated moment would be (4.1-1.3) or 2.8 D. This is a fair approximation for the experimental moment of 2.6 D. considering the assumptions made.

Fischer² measured the moment of oxazolidone (III) and N-methyloxazolidone in benzene and calculated a value of 5.04 ± 0.05 D. for both. This is in good agreement with our value of 5.09 D. for III in dioxane. Kumler and Fischer³ calculated, on the basis of a theoretical moment of 3.55 D. for oxazolidone, the contributions of dipolar molecules as 21% (based on a moment of 11 D. for the dipolar molecule).

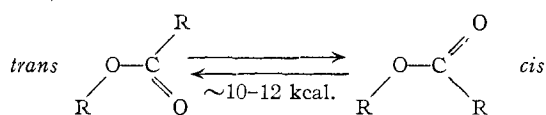
The moments of the free and cyclic carbamates confirm the prediction that the free carbamates I and II would assume the *cis* conformation while the cyclic carbamates III and IV would of necessity be in the *trans* conformation. The situation presented is analogous to that found with esters and lactones.⁴ A barrier of about 10-12 kcal./mole has been suggested in going from the more

(2) E. Fischer, *J. Chem. Soc.*, 4525 (1952).

(3) E. Fischer, *ibid.*, 2836 (1953).

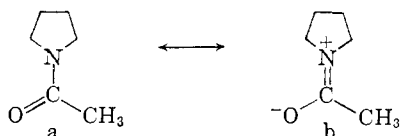
(4) R. Huisgen, *Angew. Chem.*, **69**, 341 (1957).

stable *trans* (position of R group relative to each other) to the *cis* conformation.

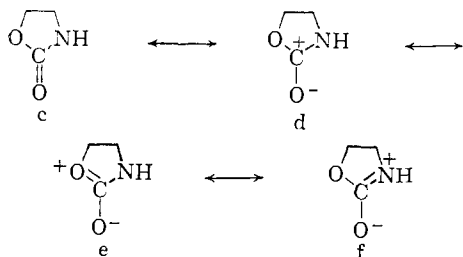


Huisgen⁴ has shown that five-, six- and seven-membered ring lactones have dipole moments of 4.1–4.5 D., while lactones with ring size 10–16 have dipole moments of 2.0–1.8 D. which is the usual ester moment. The small ring lactones are in the *cis* conformation while the larger ring lactones can assume the more favorable *trans* conformation.

In view of previous discussions on the effect of ring size on dipole moments⁵ it may seem odd at first that five-membered carbamate III would have about the same moment, 5.07 D., as the six-membered carbamate IV, 5.10. It was pointed out by Bartlett and Stiles⁶ that the smaller the ring size, the more *p*-character is possessed by the ring bonds and the more *s*-character there is in the exocyclic bonds. We have shown a relationship between the dipole moments of N-acetyl cyclic amines and the carbonyl frequency of the same ring size cyclic ketones.⁵ The slightly higher dipole moment of the five-membered ring compounds compared with the six-membered ring compound was attributed to greater stabilization of the ionic structure b due to the greater *s*-character in the exocyclic C–N bond. Figure 2 gives the carbonyl



frequency of the various compounds. It shows that the free carbamates I and II and six- and seven-membered ring carbamates IV, V and VI have about the same frequency, 1689–1681 cm.^{-1} . The five-membered cyclic carbamate oxazolidone III, however, has a higher carbonyl frequency, 1724 cm.^{-1} , indicating the effect of increased *s*-character in the exocyclic bond. On this basis one would at first expect the five-membered ring to have a low dipole moment. Resonance hybrid d is less probable due to the greater *s*-character in the *exocyclic bonds* of the five-membered ring (indicated by the higher carbonyl frequency).



The contribution of resonance hybrids e and f is decreased because of the lower *s* character in the ring. Both effects would be expected to decrease

(5) C. M. Lee and W. D. Kumler, *J. Am. Chem. Soc.*, **83**, 4586 (1961).

(6) P. D. Bartlett and M. Stiles, *ibid.*, **77**, 2809 (1955).

the dipole moment of the five-membered compound compared to the six-membered compound.

Two additional effects, however, might cause the moments of the five- and six-membered ring compounds to be alike. One effect might partly overcome the resonance decrease in the five-membered ring and increase its dipole moment. The other might cause a decrease in the moment of the six-membered ring; the five- and six-membered carbamates fused to the cyclohexane ring V and VI have dipole moments 0.5 D. higher.

Examination of Dreiding models indicates that the formation of the five-membered carbamate ring is difficult; the distance between the nitrogen and oxygen and the carbonyl group is greater in the five-membered ring compound than in six-membered compound because of the more acute ring angles in the five-membered compound. The greater distance between ionic charges in the five-membered ring compound ($\text{O}^+ \text{O}^-$ and $\text{N}^+ \text{O}^-$) would increase its moment over that of the six-membered ring compound. This may partly offset the decreased amount of the ionic forms due to bond rehybridization.

The models also indicate that the five-membered

ring may be nearly flat with the $\begin{array}{c} \text{O} \\ || \\ \text{O}-\text{C}-\text{N} \end{array}$ group coplanar. In the six-membered ring there is some

opposition to the coplanarity of the $\begin{array}{c} \text{O} \\ || \\ \text{O}-\text{C}-\text{N} \end{array}$ group due to the buckling of the three methylene groups. The distortion of the carbamate group from coplanarity inhibits resonance to some degree and would lower the moment of the six-membered compound compared to the five-membered compound. Both effects bring the two dipole moments closer to each other.

The six-membered cyclohexane-1,3-carbamate (V) and the seven-membered cyclohexane-1,4-carbamate (VI) have about the same dipole moment, 5.64 and 5.60 D., respectively. This is fortuitous, for the 1,3-carbamate is attached to the *chair* form of cyclohexane, while the 1,4-carbamate is attached to the *boat* form of cyclohexane.

Unlike the fusion of an imide or urea to cyclohexane the fusion of the carbamate group causes distortion of the cyclohexane ring. Examination of Dreiding models shows that attachment of the carbamate group to the 1,3-diaxial position of cyclohexane as in IV requires widening of the

$\begin{array}{c} \text{O} \\ || \\ \text{O}-\text{C}-\text{N} \end{array}$ angles. The three atoms are still co-

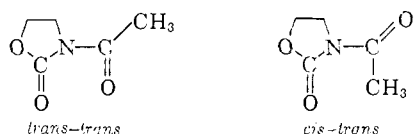
planar but widening of the angles causes rehybridization effects as mentioned previously. This is just the reverse of the case of five-membered cyclic carbamates III where the angles are decreased. Here there is more *s*-character in the ring bonds and less *s*-character in the exocyclic bonds. There is facilitation of structures e and f and resonance stabilization of structure d, and so the over-all

dipole moment of six-membered cyclohexane 1,3-carbamate (V), 5.6 D., is greater than the six-membered ring IV, 5.1 D.

Cyclohexane-1,4-carbamate (VI) must have the carbamate fused to the boat form of cyclohexane. Models indicate that there is distortion of the boat

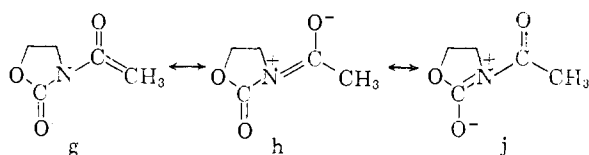
form leading to widening of the $-\text{O}-\text{C}=\text{N}$ angles so the dipole moment is greater than that of non-fused cyclic carbamates.

N-Acetyloxazolidone (VII) could be present in two conformations, the *cis-trans* or *trans-trans*



The *trans-trans* conformation would have a higher dipole moment than oxazolidone as the two carbonyl groups are lined up in the same direction; it would be expected to be unfavorable due to electrostatic repulsion. The *cis-trans* conformation, where the carbonyl groups are farthest apart, would be the favored conformation; its dipole moment would be lower than oxazolidone as the carbonyl group is pointed away from the oxazolidone resultant.

The low experimental moment of 2.81 D. for N-acetyloxazolidone indicates that the compound is in the favored *cis-trans* conformation. The carbonyl bond moment (2.4 D.) makes an angle of about 155° ($120 + 70/2$) with the oxazolidone resultant, so $\mu^2 = (5.1 - 2.4 \cos 25^\circ)^2 + (2.4 \sin 25^\circ)^2$. This calculated value of 3.1 D. is 0.3 D. higher than the observed moment. There are two new factors that we have not taken into account that would lower the observed moment; both deal with the extra resonance possible because of an additional carbonyl group. First, the new



resonance ($g \longleftrightarrow h$) creates an additional dipole directed away from the oxazolidone resultant. Secondly, this resonance competes with the usual oxazolidone resonance ($h \longleftrightarrow j$) which creates a dipole in the opposite direction.

Hall and Zbinden⁶ measured the infrared carbonyl frequency of the compound in KBr and found two bands at 1779 and 1698 cm^{-1} . They assigned the 1795 cm^{-1} band to the ring carbonyl and the 1711 cm^{-1} band to the free carbonyl in the side chain. It seems more logical to us to reverse the assignment. One would expect the ring carbonyl to have the lowest frequency (more single bond character) as it can resonate with both the ring oxygen and the ring nitrogen. The side chain carbonyl, however, can resonate only

(6) H. K. Hall, Jr., and R. Zbinden, *J. Am. Chem. Soc.*, **80**, 6428 (1958).

with the ring nitrogen and would be expected to have the higher frequency (more double bond character). That its frequency is so high indicates that the acetyl carbonyl does not resonate with the ring nitrogen to an appreciable extent. The fact that the experimental dipole moment is only a small amount (0.3 D.) less than that calculated also indicates that resonance ($g \longleftrightarrow h$) is small.

The replacement of a methylene group by a carbonyl group in oxazolidone leads to a group of useful antiepileptic and analgetic agents, the oxazolidone-2,4-diones VIII and IX. The substitution of a group having a characteristic angle of 120° (carbonyl) for a group having an angle of 109° (methylene) in a pentagon in which the angles are 108° leads to distortion of the structure.

This distortion is indicated both in the infrared spectra and the dipole moments. Paramethadione (VIII) and trimethadione (IX) both show two sharp peaks at 1812 and 1733 cm^{-1} , the first peak being of lesser intensity. Initially one might assign the peak at 1733 cm^{-1} to the oxazolidone VI carbonyl (1724 cm^{-1}) and the peak at 1812 cm^{-1} to the new carbonyl group. This explanation seems untenable, for even ketones rarely absorb above 1775 cm^{-1} ,⁷ and tertiary amides usually are much lower, being around 1650 cm^{-1} .⁷

It had been noted⁸ that anhydrides and peroxides have a doubling of carbonyl frequency, e.g., succinic anhydride has two bands at 1865 and 1782 cm^{-1} . Hall and Zbinden⁶ show that in some compounds with two equivalent carbonyl groups there is a splitting of the carbonyl band due to vibrational interaction. One can look upon oxazolidone-2,4-dione as an imide with an additional ether linkage. They showed that the splitting was symmetrical, i.e., the average of the two absorption frequencies would be at the position of a single non-interacting carbonyl group in the same ring configuration. An average of the two observed frequencies leads to a value of 1772 cm^{-1} , which is 58 cm^{-1} higher than oxazolidone III and 91 cm^{-1} higher than an unstrained carbamate (cf. I, II). This greater carbonyl frequency means that there must be less resonance interaction in the molecule so one would expect the contribution of the dipolar structures to the dipole moment to be less. In order to resonate throughout the oxazolidone-2,4-dione system there must be widening of ring angles from about 108° to about 120° ; this requirement due to ring strain would be expected to make conjugation in the system difficult.

Models indicate that the new carbonyl group in the ring is almost 180° from the resultant of the oxazolidone moment. An estimation of the moment is 2.7 D. ($5.1 - 2.4$). That the observed moment, 1.7 D., is about 1.0 D. less may be due to the two factors mentioned before regarding additional resonance between the ring nitrogen and the new carbonyl. It more likely is due to the smaller amount of the ionic structures "present" as indicated by the infrared data.

This relative lack of resonance is also indicated in the ultraviolet spectra. Compounds I-VI

(7) L. J. Bellamy, "Infrared Spectra of Complex Molecules," Methuen, London, 1958, pp. 132, 213.

(8) Reference 7, p. 127.

show no peaks above 200 $m\mu$ while N-acetyl-oxazolidone, where additional resonance is present has a peak at 204 $m\mu$ with a molar extinction coefficient of 10,300. Paramethadione (VIII) and trimethadione (IX), where one might have expected additional resonance, show no prominent peaks above 200 $m\mu$. Both have a small peak at 227 $m\mu$ with an extinction of about 150.

TABLE I

DIPOLE MOMENTS OF CARBAMATES AND OXAZOLIDINE-2,4-DIONES IN DIOXANE AT 30°

		ω_2	ϵ_{12}	ν_{12}		
I	Ethyl carbamate	0.00	2.20875	0.97450		
		.0031534	2.23644	.97428		
		.0051375	2.25643	.97406		
		$\mu = 2.59 \pm 0.02$ D.	.0064038	2.22664	.97395	
			.0071645	2.27330	.97384	
			.0094595	2.29213	.97363	
		Mol. wt. = 89.09	.0095242	2.29410	.97363	
		$\epsilon_1 = 2.20833$	$\nu_1 = 0.97452$	$P_{20} = 155.57$		
		$\alpha = 9.04181$	$\beta = -0.09147$	$P_E = 21.17$ calcd.		
		II	Emylcalmate	0.00	2.20199	0.97433
.0006329	2.20661			.97433		
$\mu = 2.64 \pm 0.06$ D.	.00101489			2.20893	.97433	
	.00226893			2.21423	.97433	
	.00329882			2.22202	.97433	
Mol. wt. = 145.20	.00398990			2.22622	.97433	
$\epsilon_1 = 2.20261$	$\nu_1 = 0.97433$			$P_{20} = 178.17$		
$\alpha = 5.72947$	$\beta = 0.00$			$P_E = 38.00$ calcd.		
III	Oxazolidone			0.00	2.20640
				.0006848	2.23054	0.97849
		.0014538	2.25765	.97828		
		$\mu = 5.07 \pm 0.01$ D.	.0019278	2.27438	.97816	
			.0023806	2.29121	.97806	
			.0028046	2.30559	.97802	
		Mol. wt. = 87.08	.0032456	2.32163	.97793	
		$\epsilon_1 = 2.20624$	$\nu_1 = 0.97861$	$P_{20} = 532.17$		
		$\alpha = 35.50570$	$\beta = -0.21670$	$P_E = 16.44$ calcd.		
		IV	Trimethylene urethan	0.00	2.20509
.0007671	2.23011			0.97854		
.0015062	2.25338			.97833		
$\mu = 5.10 \pm 0.02$ D.	.0019241			2.26654	.97825	
	.0024622			2.28380	.97812	
	.0029062			2.29609	.97804	
Mol. wt. = 101.11	.0034578			2.31361	.97786	
$\epsilon_1 = 2.20584$	$\nu_1 = 0.97872$			$P_{20} = 546.74$		
$\alpha = 31.3075$	$\beta = -0.24380$			$P_E = 23.33$ calcd.		
V	Cyclohexane-1,3-carbamate			0.00	2.20413
		.0014547	2.24068	0.97405		
		$\mu = 5.64 \pm 0.02$ D.	.0018144	2.25044	.97395	
			.0023495	2.26414	.97357	
			.0027745	2.27458	.97333	
		Mol. wt. = 154.17	.0034458	2.29230	.97318	
		$\epsilon_1 = 2.20392$	$\nu_1 = 0.97474$	$P_{20} = 674.46$		
		$\alpha = 25.57344$	$\beta = -0.47433$	$P_E = 35.84$ calcd.		
		VI	Cyclohexane-1,4-carbamate	0.00	2.20987	0.97395
				.0006989	2.22716	.97374
.0009259	2.23187			.97356		

		$\mu = 5.60 \pm 0.04$ D.	.0012897	2.24240	.97337	
			.0019000	2.25823	.97328	
			.0023709	2.26867	.97318	
		Mol. wt. = 154.17	.0024692	2.27124	.97309	
		$\epsilon_1 = 2.20966$	$\nu_1 = 0.97391$	$P_{20} = 664.96$		
		$\alpha = 25.04506$	$\beta = -0.33390$	$P_E = 35.84$ calcd.		
VII	N-Acetyl oxazolidone	0.00	2.20021	0.97840		
		.0007292	2.20596	.97817		
		$\mu = 2.81 \pm 0.02$ D.	.0012771	2.20927	.97825	
			.0019446	2.21389	.97802	
			.0022993	2.21633	.97794	
		Mol. wt. = 135.12	.0029159	2.22095	.97783	
		$\epsilon_1 = 2.20042$	$\nu_1 = 0.97840$	$P_{20} = 187.40$		
		$\alpha = 6.99420$	$\beta = -0.19701$	$P_E = 28.87$ calcd.		
		VIII	Paramethadione	0.00	2.20268
				.0008166	2.20457	0.97857
$\mu = 1.69 \pm 0.03$ D.	.0013022			2.20570	.97854	
	.0019003			2.20744	.97847	
	.0029247			2.20962	.97837	
Mol. wt. = 157.57	.0034167			2.21049	.97830	
$\epsilon_1 = 2.202623$	$\nu_1 = 0.97866$			$P_{20} = 101.23$		
$\alpha = 2.37125$	$\beta = -0.10462$			$P_E = 43.92$ calcd.		
IX	Trimethadione			0.00	2.20169
				.0010153	2.20431	0.97841
		$\mu = 1.74 \pm 0.02$ D.	.0014206	2.20527	.97832	
			.0018574	2.20614	.97826	
			.0023932	2.20771	.97824	
		Mol. wt. = 143.11	.0028651	2.20875	.97818	
		$\epsilon_1 = 2.20173$	$\nu_1 = 0.97851$	$P_{20} = 93.82$		
		$\alpha = 2.46041$	$\beta = -0.11541$	$P_E = 32.14$ calcd.		

An examination of the physical properties³ of paramethadione and trimethadione is interesting.

Compound	Mol. wt.	M.p., °C.	B.p., °C. (mm.)
Trimethadione IX	143.1	+6	78-80 (5)
Paramethadione VIII	157.2	(~0)	101-102 (11)

Even though paramethadione has a higher molecular weight, it is an oily liquid compared with trimethadione which is a white crystalline powder. This is an example of the effect that symmetry has on physical properties of a compound. The extra methyl group in paramethadione disrupts the close packing in the crystal lattice thus causing it to have a lower melting point.

Experimental

All dipole moments were measured in dioxane at 30° and calculations were made using the equation and method of Halverstadt and Kumler.³ We wish to thank Dr. H. K. Hall, Jr., of du Pont for providing compounds III, IV, V, VI and VII.^{6,10} We wish to thank Dr. A. O. Geiszler of Abbott Laboratories for the samples of Paradione® and Tridione® and Dr. E. H. MacLaughlin of Merck Sharp and Dohme for the sample of Emylcalmate. All spectrographic measurements were by Mr. M. K. Hrenoff of the Spectrographic Laboratory. Infrared spectra were run on Perkin-Elmer model 21 and ultraviolet spectra on Cary model 11.

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