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DIFFERENTIAL SCANNING CALORIMETRIC STUDY OF THE TRANSITION HEATS OF SOME DIBENZAZEPINES, CARBAZOLES AND PHENOTHIAZINES

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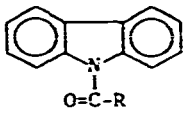
ABSTRACT

The transition temperatures and heats of two dibenzazepines, three carbazoles and three phenothiazines have been obtained. This represents a continuation of an earlier study of a series of acyldibenzazepines. Additional evidence for a back-folded acylchain in the solid state has been developed and good correlation of these bent ring molecules with well known spherical molecules on the basis of transition entropy is possible. The behaviour of the alkyl chain in acyl substituted dibenzazepines, carbazoles and phenothiazines is contrasted with other alkyl substituted ring systems.

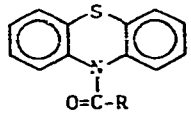
INTRODUCTION

In an earlier study the authors reported on the transition heats of twelve N-substituted derivatives of dibenzazepine[1]. It was reported in that study that these derivatives exhibited transition heats that could be correlated by assuming that the molecules behaved as oblate spheroids. In an oblate spheroid configuration, the rotational freedom of the molecules in the solid phase is more restricted than in the case of truly spherical molecules. However, the entropy change on melting is approximately intermediate between spherical and rod-like molecules. For the dibenzazepines two linear correlations were obtained when transition entropy was plotted as a function of transition temperature.

This study continues the previous work with two additional dibenzazepines, three carbazoles and three phenothiazines. The structures of these molecules are:

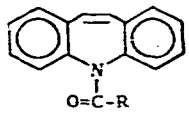


Acyl carbazole



Acyl phenothiazine

R = H, CH_3, $ClCH_2CH_2$



Acyl dibenzazepine

R = $ClCH_2$, $CH_3(CH_2)_8$

EXPERIMENTAL

Synthesis of compounds

5-Choroacetyl-5H-dibenz(b,f)azepine (compound 13a). — A mixture of 5.2 g (0.027 mole) dibenzazepine and 7.1 g (0.054 mole) chloroacetyl chloride was refluxed 18 h in 200 ml dry toluene. The mixture was cooled and then rotary evaporated to give an orange colored oil. The oil after repeated washing with petroleum ether (30–60°) and cooling solidified. Two recrystallizations from a 4:1 heptane–benzene solvent mixture and treatment with decolorizing charcoal gave 4.1 g (56.3%) of white crystals.

Anal. Calc. for $C_{16}H_{12}ClNO$: C, 71.25; H, 4.48; Cl, 13.14; N, 5.19. Found: C, 71.31; H, 4.49; Cl, 13.01; N, 5.15.

5-Decanoyl-5H-dibenz(b,f)azepine (compound 13b). — A mixture of 5.8 g (0.03 mole) dibenzazepine and 11.4 g (0.06 mole) decanoyl chloride was refluxed 18 h in 175 ml dry toluene. The mixture was cooled and then rotary evaporated to give a yellow oil. The oil was dissolved in 150 ml benzene and then passed through a 200 × 25 mm chromatographic column containing Woelm W200 neutral aluminum oxide. Unreacted dibenzazepine showing a slight red fluorescence was eluted first (benzene solvent). A second band at the top of the column was eluted from the column with diethyl ether. The ether was removed under vacuum to give the desired compound, a viscous colorless oil, in quantitative yield.

Anal. Calc. for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 82.76; H, 8.48; N, 3.98.

N-(β-Chloropropionyl)carbazole (compound 14) and N-(β-Chloropropionyl)-phenothiazine (compound 19). — The syntheses of these compounds have been previously reported[2].

The *N*-acetyl- and *N*-formyl carbazole and phenothiazine derivatives were synthesized by procedures used to prepare the analogous dibenzazepine derivatives[1].

N-Acetylcarbazole (compound 15) (30%). — *Anal.* Calc. for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.38; H, 5.30; N, 6.77.

N-Formylcarbazole (compound 16) (80%). — *Anal.* Calc. for $C_{13}H_9NO$: C, 79.78; H, 4.65; N, 7.18. Found: C, 79.97; H, 4.78; N, 7.23.

N-Formylphenothiazine (compound 17) (44%). — *Anal.* Calc. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16; S, 14.11. Found: C, 68.71; H, 4.00; N, 6.06; S, 14.12.

N-Acetylphenothiazine (compound 18) (99%). — *Anal.* Calc. for $C_{14}H_{11}NOS$: C, 69.68; H, 4.60; N, 5.80; S, 13.29. Found: C, 69.66; H, 4.63; N, 5.55; S, 13.33.

Scanning calorimetry

Differential scanning calorimetry (DSC) was carried out in a Perkin–Elmer DSC-1B scanning calorimeter at a heating rate of 1.25°C/min and a sensitivity of 2 millicalories per inch. The samples were encapsulated under nitrogen in aluminum volatile sample sealers. These sealers used an additional small insert to obtain good thermal contact. The samples were positioned in the center of the cells and covered

with aluminum domes. The technique is described in detail elsewhere[3]. The calorimeter temperature axis was calibrated using 99.9999 mole % gallium, benzoic acid, indium, tin and lead. The thermal response was also calibrated in the same way. The purity analysis was made using the van't Hoff equation described previously[3–7]. The data are given in Table I. All temperatures represent the vertex of the endothermal minimum and are corrected for thermal resistence. The data are all obtained on first heating of the solvent recrystallized solids. The solids formed oils on melting which super-cooled without recrystallization. IR and UV spectra did not indicate decomposition.

DISCUSSION

Decanoyl dibenzazepine

The extension of the alkyl chain to C_{10} produces a material of low melting point and extremely low transition entropy. The melting point, 3.30 °C, is "predictable" from the melting points of the formyl, acetyl and propionyl derivatives discussed previously[1]. A general trend towards decreasing melting point and entropy of fusion with increasing acyl chain indicates that the chain is progressively shifting the total molecular configuration towards a more spherical geometry. This shift is further supported by the low transition entropy. The latter is very near the translational entropy of such well known spherical molecules as carbon tetrachloride and neopentane. In Fig. 1, the decanoyl derivative is shown to belong to the lower series of

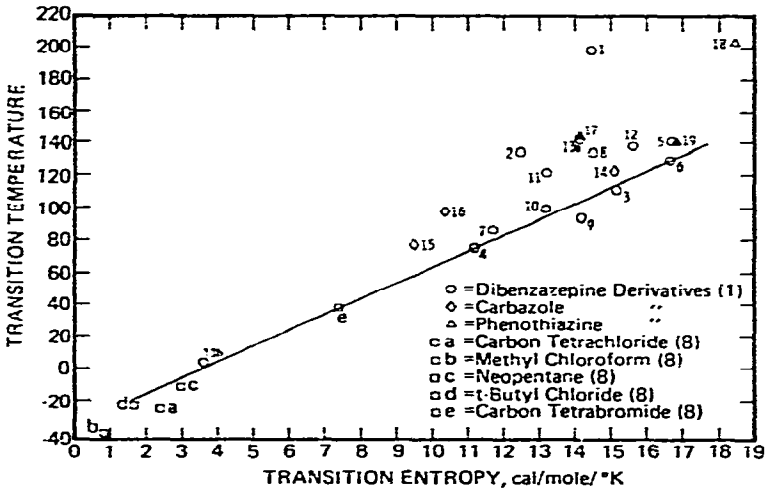


Fig. 1. Correlation of transition entropy with melting point for a group of dibenzazepines, carbazoles and phenothiazines.

dibenzazepines which contains the propionyl, chlorobutyryl, trifluoroacetyl, bromoisobutyryl, acetyl, and chloropropionyl derivatives. If the solid state had involved the decanoyl chain in a paraffinic structure, the transition entropy would be expected to increase. Assuming that the decanoyl chain added only to the molecular weight but

TABLE I

THERMODYNAMIC PROPERTIES OF SOME OBLATE MOLECULES FROM DIFFERENTIAL SCANNING CALORIMETRY

Graphical Code	*Compound*	T_m(°C)	*ΔH (cal/mole)*	*ΔS (cal/mole/°K)*	*Purity (Mole %)*	*Remarks*
1	Dibenzazepine	198.0	6840	14.5	99.6	
2	Formyl dibenzazepine	133.5	5092	12.5	99.4	
3	Acetyl dibenzazepine	112.1	5847	15.1	97.4	
4	Propionyl dibenzazepine	75.7	3904	11.2		Poorly defined peak, perhaps two
5	Isobutyryl dibenzazepine	140.4	6890	16.7	99.99	
6	Chloropropionyl dibenzazepine	129.3	6707	16.7	98.6	
7	Chlorobutyryl dibenzazepine	86.3	4186	11.7	96.3	
8	Bromoacetyl dibenzazepine	136.8	5856	14.3	97.8	
9	Bromoisobutyryl dibenzazepine	86.3	2220 Σ=5150	6.2 Σ=14.18		
		94.1	2930	7.98		Two peaks on first melt
10	Trifluoroacetyl dibenzazepine	99.2	4910	13.2	99.67	
11	Acrylyl dibenzazepine	121.9	5202	13.2	98.9	
12	Methacrylyl dibenzazepine	138.3	6435	15.6	98.95	
13a	*N*-Chloroacetyl dibenzazepine	143.2	5847	14.1	99.24	
13b	Decanoyl dibenzazepine	3.30	1001	3.66	>99.99	
14	*N*-β-Chloropropionyl carbazole	122.2	5992	15.1	99.80	
15	*N*-Acetyl carbazole	77.2	3333	9.52		Broad peak, not due to impurity
16	*N*-Formyl carbazole	98.4	3854	10.4	99.37	
17	*N*-Formyl phenothiazine	144.5	5895	14.1	99.58	
18	*N*-Acetyl phenothiazine	202.6	8778	18.5		Broad peak
19	*N*-β-Chloropropionyl phenothiazine	140.5	6964	16.8	98.29	

did not contribute to the solid state order in any way (*i.e.*, completely random in the solid), the transition entropy should be reduced by less than one half of the formyl value, *i.e.*, approximately 6 kcal/mole. This, obviously, is not the case. The decanoyl chain must exist in the solid phase folded over the dibenzazepine rings and contributes a generally more spherical configuration to the molecule. It is possible that the rotationally frozen state was not formed. Molecules with a spherical configuration usually exibit two transitions: a rotational (solid → solid) and translational (solid → liquid). The rotational transition is usually the larger of the two[8]. The decanoyl derivative appears to show only a translational entropy. A second solid phase probably exists below −20°C (the start of this study). Indeed, all of the materials in this study may have a second low temperature form. This is indicated by a calculation using the entropy rules given by Bondi[9]. The predicted solid to liquid transition entropy for these multi-ring materials is approximately 19 cal/mole/°K (excluding symmetry factors).

Carbazoles

The three carbazole derivatives measured exibit melting points about 20° higher than predicted by analogy to dibenzazepines of the lower melting series (compounds 3, 4, 6, 7, 9, 10). This could be due to reduced midring pucker and greater molecular polarity. Both effects would tend to increase the intermolecular attraction in the solid phase. Intermolecular attraction in the solid phase is supported by the high melting point of the β-chloropropionyl derivative. The length of the side chain, *per se*, is unimportant, since no regular increase in entropy of fusion is noted with increasing side chain length for these materials. The side chain is probably folded over the rings in the solid phase and is important to the solid order only in altering the total electronic configuration.

Phenothiazines

These derivatives exhibit an entropy–fusion temperature relationship comparable to the higher series of dibenzazepines (compounds 2, 5, 8, 12 and 13 a,b). The *N*-acetyl phenothiazine has an unusually high fusion temperature; higher than dibenzazepine. This elevated temperature must be due to hydrogen bonding in the solid phase. The sulfur atom in the bridge appears to affect molecular polarity and geometry in much the same way as the double bond bridge in dibenzazepine. It has been observed that phenothiazine is isosteric with dibenzazepine in the same way that benzene is isosteric with thiophene[10].

CONCLUSIONS

The derivatives of dibenzazepine, carbazole and phenothiazine described in this paper display entropies and temperatures of fusion characteristic of oblate spherical molecules. The substitution at the nitrogen apparently folds back over the molecule to give a more spherical molecular symmetry. The decanoyl dibenzazepine derivative

has a very low entropy of fusion very close to well known spherical molecules. The solid phase of this material restricts only translational freedom; not rotational freedom. No tendency for side chains to organize along the basis of the paraffins was noted. The presence of a puckered ring system is essential for this kind of molecular symmetry. Other ring systems which have been investigated do not show any tendency to form spherical molecules in the solid phase[9,11,12].

Ring structures similar to the carbazoles and phenothiazines are found in many drugs and allied natural products. The existence of spherical or oblate spherical symmetry in the solid phase could explain the unusual melting points, solubilities and polymorphy reported by many workers.

REFERENCES

1 E. GIPSTEIN, E. M. BARRALL II AND K. E. BREDFELDT, in R. S. PORTER AND J. F. JOHNSON (Eds.) *Analytical Calorimetry*, Vol. II, Plenum Press, New York, 1970, p. 127.
2 E. GIPSTEIN, W. A. HEWETT AND O.U. NEED, *J. Polym. Sci., A1*, 8 (1970) 3285.
3 E. M. BARRALL II AND R. D. DILLER, *Thermochim. Acta*, 1 (1970) 509.
4 *Thermal Analysis Newsletter, Nos. 1–6*, Perkin–Elmer Corp., Norwalk, Conn.
5 G. L. DRISCOLL, I. N. DULLING AND F. MAGNOTTA, in R. S. PORTER AND J. F. JOHNSON (Eds.), *Analytical Calorimetry*, Vol. I, Plenum Press, New York, 1970, p. 271.
6 N. J. DEANGELIS AND G. J. PAPARIELLO, *J. Pharm. Sci.*, 57 (1968) 1868.
7 C. PLATO AND A. R. GLASGOW, JR., *Anal. Chem.*, 41 (1969) 330.
8 L. SILVER AND R. RUDMAN, *J. Phys. Chem.*, 74 (1970) 3134.
9 A. BONDI, *Chem. Rev.*, 67 (1967) 565.
10 P. N. CRAIG, B. M. LESTER, A. J. SAGGIOMO, C. KAISER AND C. L. ZIRKLE, *J. Org. Chem.*, 26 (1961) 135.
11 R. S. PORTER, E. M. BARRALL II AND J. F. JOHNSON, *Accounts Chem. Res.*, 2 (1969) 53.
12 E. M. BARRALL II, *Thermochim. Acta*, 3 (1971) 55.