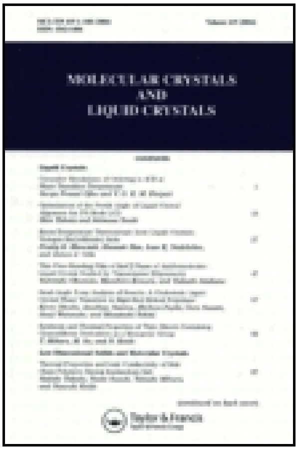

Molecular Crystals

Scanning Calorimetry of Aromatic, Difunctional, Unsaturated, and Substituted Acid Esters of Cholesterol

Edward M. Barrall [a c d] , Julian F. Johnson [b] & R. S. Porter [b]

[a] Chevron Research Company Richmond, California, 94802

[b] University of Massachusetts

[c] University of Connecticut, Dept. of Chemistry, Storrs, Conn., 06268

[d] IBM Research, San Jose, Calif

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Scanning Calorimetry of Aromatic, Difunctional, Unsaturated, and Substituted Acid Esters of Cholesterol‡

EDWARD M. BARRALL II§ and JULIAN F. JOHNSON||

Chevron Research Company
Richmond, California 94802

and

R. S. PORTER

University of Massachusetts

Abstract—Ten nonaliphatic esters of cholesterol, including three difunctional acid esters, have been studied by differential scanning calorimetry. The heats of transition for the smectic, cholesteric, and liquid-phase transitions are compared with previously published data on the aliphatic esters of cholesterol. The nonaliphatic esters follow the same entropy chain length relationship as the previously discussed aliphatic esters. The difunctional acid esters show anomalously high heats of transition from the cholesteric to the isotropic liquid. This is to be expected if both cholesterol rings participate in the cholesteric mesophase formation. A theory is proposed which accounts for much of the observed thermodynamic, optical, and rheological behavior of cholesteryl esters.

On heating or cooling, the esters of cholesterol are known to form phases (mesophases) which are intermediate in structure between a true solid and an isotropic liquid.[1] These mesophases, sometimes called liquid crystals,[2] have a structure along one or more crystal axes similar to a solid; and along one or more other axes liquid disorder exists. Brown and Shaw[1] and Chistyakov[3] have presented complete reviews of the thermal and physical data available on both cholesteric and other liquid crystal forming materials.

Scanning calorimeteric data have been reported for all the

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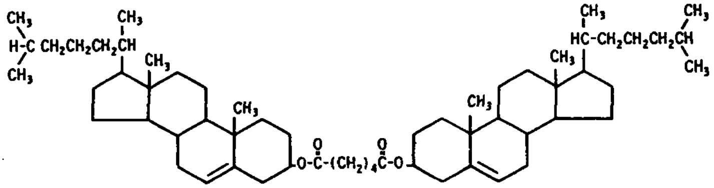
‡ Part XIX of a series on "Order and Flow of Liquid Crystals".

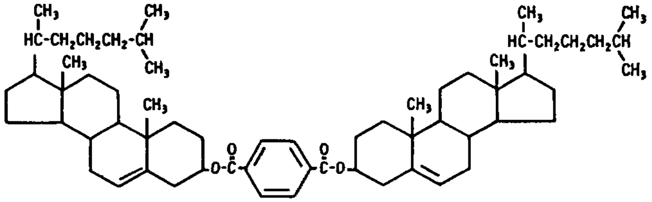
§ Present address, IBM Research, San Jose, Calif.

|| Present address, University of Connecticut, Dept. of Chemistry, Storrs, Conn. 06268.

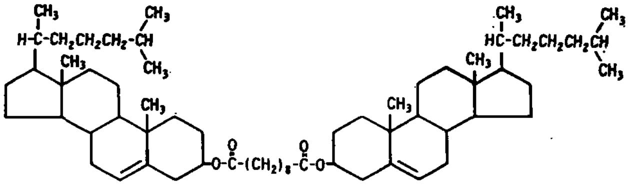
Table 1 Structural Formulae of Some Higher Cholesteryl Esters



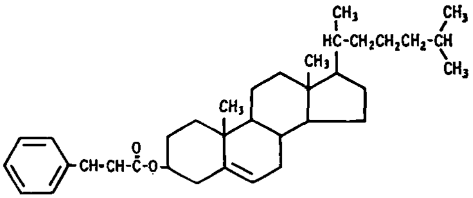
DICHOLESTERYL ADIPATE



DICHOLESTERYL PHTHALATE

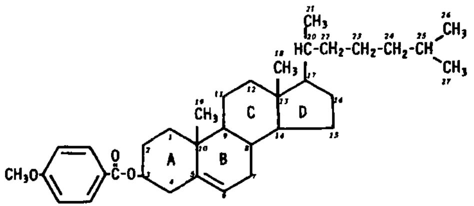


DICHOLESTERYL SEBACATE

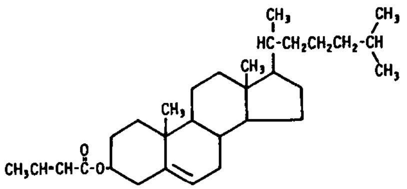


CHOLESTERYL CINNAMATE

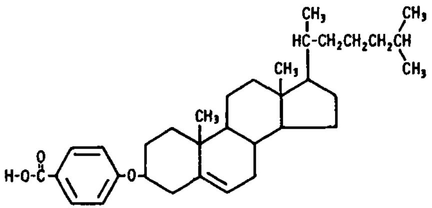
TABLE 1 (*continued*)



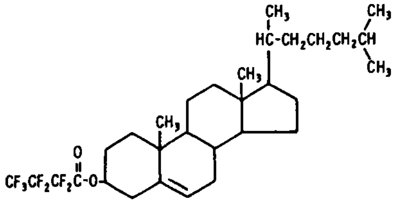
CHOLESTERYL ANISOATE



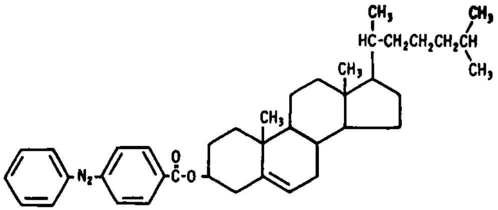
CHOLESTERYL CROTONATE



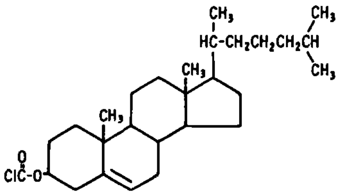
CHOLESTERYL HYDROGEN PHTHALATE



CHOLESTERYL HEPTAFLUOROBUTYRATE



CHOLESTERYL p-PHENYLAZOBENZOATE



CHOLESTERYL CHLOROFORMATE

normal saturated acid cholesteryl esters from formic to decanoic.[4,5] Data are available for the even numbered straight chain cholesteryl esters through stearic.[4,5] The heats of transition from solid to mesophase, mesophase to mesophase, and mesophase to isotropic liquid form a homogeneous body of data with the heat of a given type of transition increasing with increasing acid chain length.[5] A discontinuity in the regularly increasing trend is noted between cholesteryl caprylate and nonate (12.9 and 14.3 Å extended acid chain length).[5] No even-odd alternation in the entropy or heat of transition has been reported.[5] With the exception of cholesteryl benzoate,[6] no calorimetric investigations have been reported on the cholesteryl esters of difunctional, unsaturated, and substituted acids. However, it is well known that many of these esters exhibit mesophases which are as well defined as those reported for the normal alkyl acid esters[1,3,7] In the present study we investigated the heats and entropies of transition of a group of ten esters and compare the results with the previously reported data on this interesting group of compounds. The esters investigated are shown structurely in Table 1.

Experimental

The cholesteryl esters used in this study were obtained from Eastman Organic Chemicals, Distillation Products Industries, Rochester, New York, as " Red Label " products. The materials were recrystallized three times from hot ethanol as previously described.[4,5]

Using thin layer chromatography, gas chromatography, and infrared analysis, the ester and isomeric purity were determined to be better than 99.9%.[5] The cholesterol hydrogen phthalate was titrated with base using a glass electrode detector and found to be 99.9% the indicated material. By the same technique, adjusted for range, no free acid could be found in the diesters studied. NMR and elemental analysis of the heptafluorobutyrate ester indicated that this material was 99.9% pure on a formula basis.

The temperatures of transition were determined using a Du Pont 900 differential thermal analysis apparatus equipped with a micro-melting point cell. The temperature axis was calibrated with the melting points of zone refined-dotriacontane, semiconductor-grade indium, conductivity water, and zone-refined stearic acid. The heats of transition of the esters were measured with a Perkin-Elmer DSC-1B scanning calorimeter (DSC). The peak area was calibrated in terms of calories by measuring the heats of fusion of semiconductor-grade indium and zone-refined stearic acid. Vold's corrected heat of fusion for stearic acid was used.[8] The DSC attenuation system was calibrated by both pen displacement and fusion of several indium samples of differing weights.

Results

The cholesteryl esters examined in this study are most conveniently classified on the basis of monotropism; that is, those which exhibited a mesophase on both heating and cooling and those which exhibited mesophases only on cooling. The heats and temperatures of fusion and freezing from the DSC and DTA are given in Tables 2 and 3 for the two categories of esters. The first set of determinations for each corresponds to the heating of ethanol recrystallized material. The " second heat " results are for melt recrystallized material. Each ester was carried through the measurement sequence three times with fresh ethanol recrystallized material. The results presented in Tables 2 and 3 are the appropriate averages of the three determinations. On the basis of an average deviation test, the temperatures are reproducible to ± 0.06 °C and the heats to ± 3% on fusion and ± 5% on freezing. The column labeled T_m (endothermal minimum or exothermal maximum) has been found to correspond closely to the equilibrium melting and freezing points[9] of very pure single-transition organic compounds. These temperatures were obtained from DTA measurements made with the temperature measuring thermocouple located in the sample. The advantages of this method have been described previously.[9]

TABLE 2 DTA and DSC Thermal Data on Some Higher Cholesteryl Esters which show Mesophases on Heating

	Heating					Cooling				
Compounds	T_b	T_m	T_e	$\Delta H_{cal/g}$	$\Delta H_{kcal/Mole}$	T_b	T_m	T_e	$\Delta H_{cal/g}$	$\Delta H_{kcal/Mole}$
Cholesteryl Anisoate	177.5	181.5	185.6	16.2	8.44	153.5	150.0	146.6	13.6	7.08
	266.0	268.0	269.2	0.55	0.29	259.5	258.1	256.9	0.50	0.26
Second Heat	174.5 263.4	179.2 264.9	184.0 265.8	13.0 0.54	6.77 0.28	153.4 259.0	150.0 257.9	146.4 257.0	12.9 0.51	6.72 0.27
Dicholesteryl Adipate	189.0	193.8	196.5	10.6	9.36	190.6	189.1	185.0	6.99	6.17
	223.0	225.5	226.5	1.00	0.88	224.3	223.0	221.0	0.98	0.87
Second Heat	184.0 223.0	195.5 225.5	197.0 226.5	7.92 0.98	7.00 0.86	190.6 224.9	189.9 223.7	185.0 221.5	7.31 1.00	6.46 0.88
Cholesteryl Cinnamate	160.0	162.6	167.5	13.9	7.18	143.9	141.5	136.2	11.9	6.15
	213.2	214.5	217.0	0.31	0.16	214.9	214.0	211.0	0.35	0.18
Second Heat	160.5 214.3	162.6 215.2	167.3 217.0	13.3 0.33	6.87 0.17	144.0 215.0	141.6 213.9	136.5 211.2	11.4 0.32	5.89 0.17
Cholesteryl Crotonate	107.6	112.7	116.6	12.9	5.87	67.4	58.1	56.2	9.34	4.25
	160.6	162.0	163.0	0.65	0.30	162.0	161.2	158.5	0.66	0.30
Second Heat	107.5 160.7	112.8 162.0	116.7 163.1	13.0 0.65	5.91 0.30	67.5 162.1	58.0 161.1	56.1 158.6	9.37 0.65	4.26 0.30

TABLE 3 DTA and DSC Thermal Data on Some Cholesteryl Esters which show No Mesophases on Heating

Compound	Heating					Cooling				
	T_b	T_m	T_eT_e	$\Delta H_{cal/g}$	$\Delta H_{kcal/Mole}$	T_b	T_m	T_e	$\Delta H_{cal/g}$	$\Delta H_{kcal/Mole}$
Dicholesteryl Sebacate	172.8	180.4	182.0	10.8	10.1	153.9	149.1	145.6	11.1	10.4
	-	-	-	-	-	176.2	175.8	173.7	0.94	0.88
Second Heat	172.4 -	179.1 -	180.5 -	11.3 -	10.6 -	154.9 176.2	148.4 175.6	145.7 173.1	11.3 0.99	10.6 0.93
Dicholesteryl Phthalate	183.7	186.8	188.6	11.8	10.7	150.5	144.4	133.3	6.64	6.00
	-	-	-	-	-	-	-	-	-	-
Second Heat	164.2 162.9	167.4 186.4	169.8 187.8	-7.14 10.5	-6.45 9.49	150.4 -	142.2 -	129.3 -	6.48 -	5.85 -
Cholesteryl Heptafluorobutyrate	112.6	114.7	116.1	10.8	6.29	102.4	100.3	96.1	10.3	6.00
	-	-	-	-	-	-	-	-	-	-
Second Heat	112.1 -	114.2 -	115.2 -	10.9 -	6.35 -	102.6 -	100.1 -	96.2 -	10.3 -	6.00 -
Cholesteryl p-Phenylazobenzoate	190.5	192.7	194.2	12.2	7.32	154.9	153.8	150.4	8.35	5.00
	-	-	-	-	-	185.9	185.3	183.2	0.60	0.36
Second Heat	187.9 -	192.4 -	193.6 -	11.8 -	7.08 -	159.9 185.2	155.7 184.5	153.8 183.1	8.07 0.58	4.84 0.35
Cholesteryl Hydrogen Phthalate	162.9	169.8	172.8	17.7	9.47	-	-	-	-	-
	- -	- -	- -	- -	- -	154.4 92.0	153.4 89.1	151.9 80.2	0.15 0.91	0.080 0.49
Second Heat	79.3 - -	95.4 - -	105.4 - -	1.13 - -	0.60 - -	- 157.8 84.4	- 153.3 81.8	- 150.5 75.3	- 0.18 0.92	- 0.096 0.49
Cholesteryl Chloroformate	114.7	125.2	125.3	16.0	7.19	92.1	94.9	98.7	12.3	5.52
Second Heat	109.0	120.6	123.4	14.1	6.34	86.8	92.3	96.5	12.2	5.48

Cholesteryl anisoate exhibits a mesophase from 181.5 °C to 268.0 °C on heating. This compares well with the Eastman listing of 179–268 °C. The heat of fusion of the ethanol resrystallized solid is 3.2 cal/g greater than the melt recrystallized material. This, coupled with the reproducible data from the melt recrystallized ester, indicates that the ethanol recrystallized solid is structurally different from the melt recrystallized solid. This difference may be due to orientation of the anisoate dipoles when recrystallization is effected from ethanol. The isotropic liquid → cholesteric mesophase transition supercools somewhat, 10–13 °C, which is unusual for mesophase formation. Previous studies have indicated that the formation of the cholesteric mesophase from the melt does not supercool by more than 0–5 °C for the majority *n*-acid cholesteryl esters.[4]

The heats of the cholesteric → isotropic liquid and isotropic liquid → cholesteric mesophase transformations appear to be nearly identical within 0.05 cal/g. Although 0.05 cal/g is not significant in an absolute sense within the framework of experimental accuracy, the bias, always in favor of the cholesteric → isotropic liquid transition, *is* significant. Miscroscopic examination indicates that the cholesteric texture formed by heating the solid is different from the texture formed by cooling the isotropic liquid.[10] The present data indicate that the heat content of the solid formed cholesteric mesophase is a few hundredths of a calorie per gram greater than the liquid-formed mesophase.

The indicated path of transition is:

$$\begin{tikzcd}
C_2 \arrow[r, "131.5^\circ"] & M \arrow[r, shift left, "268.0^\circ"] \arrow[d, shift left, "150.0^\circ"] & L \arrow[l, shift left, "258.1^\circ"] \\
 & C_1 \arrow[u, shift left, "179.2^\circ"] &
\end{tikzcd}$$

where C_2 is the solid phase formed from the melt, C_1 is the solid phase formed from ethanol solution, M is the cholesteryl mesophase, and L is the isotropic liquid.

Dicholesteryl adipate on heating exhibits a mesophase from 193.8 °C to 225.5 °C. Eastman gives the range as 194 °C to 230 °C. From the data in Table 2, it is apparent that the mesophase formed from the melt is identical to that formed from the solid. The solid phase formed from the melt and from ethanol recrystallization is not identical on the basis of fusion heats (7.92 cal/g and 10.6 cal/g). Unlike many cholesteryl esters, the solid phase does not supercool excessively on freezing (4.7 °C to 5.6 °C). The path of the phase change is as follows:

$$\begin{tikzcd}
C_2 \arrow[r, "193.8^\circ"] & M \arrow[r, shift left, "225.5^\circ"] \arrow[d, shift left, "189.1^\circ"] & L \arrow[l, shift left, "223.0^\circ"] \\
 & C \arrow[u, shift left, "195.5^\circ"] &
\end{tikzcd}$$

The symbols have the same meaning as before.

Cholesteryl cinnamate when heated exhibits a mesophase from 162.6 °C to 214.5 °C, which is somewhat broader than the Eastman listing of 160 °C to 200 °C. Less than 20% of the material received from Eastman was recovered after three recrystallizations in ethanol. This was the least pure material obtained in this group of esters. The low purity could account for the narrow range reported in the Eastman list. The solid phase does not appear to be different if formed from melt rather than solution on the basis of the data in Table 2. The solid phase supercools by 20 °C on freezing, which accounts for the difference between the specific heats of freezing and of melting.

$$\begin{tikzcd}
C \arrow[r, shift left, "162.6^\circ"] & M \arrow[l, shift left, "141.5^\circ"] \arrow[r, shift left, "214.5^\circ"] & L \arrow[l, shift left, "214.0^\circ"]
\end{tikzcd}$$

Cholesteryl crotonate exhibits a stable mesophase from 112.7 °C to 162.0 °C, which is somewhat broader than that given in the Eastman list, 103 °C to 125 °C. No explanation except the improved purity of the material effected by recrystallization can be offered. The ethanol and melt recrystallized materials are identical with respect to temperature and heat of fusion. The cholesteric mesophase is not affected by the direction of the temperature program. The solid phase recrystallizes very slowly and supercools by 50 °C. The value of 9.34 cal/g for the heat of solid-phase formation from the cholesteric mesophase is the result of integrating a very broad and flat exotherm. Prompt reheating of the sample after cooling gives a heat of solid → mesophase transformation of 9.4 cal/g. Overnight standing of the sample at 30 °C produces a crystallinity comparable on the basis of specific heat of fusion to that of the ethanol recrystallized solid. The following crystallization path is proposed:

$$C_1 \underset{112.7^\circ}{\overset{58.1^\circ}{\leftrightarrows}} M \underset{162.0^\circ}{\overset{161.2^\circ}{\leftrightarrows}} L$$

The symbols have the same meaning as before.

Dicholesteryl sebacate exhibits no mesophases on heating. The diester melts directly at 180.4 °C to form the isotropic liquid. The solid phase is insensitive to the previous route of crystallization. On cooling the isotropic liquid, a cholesteric mesophase forms at 175.8 °C with a heat of formation of 0.94–0.99 cal/g. This is comparable to dicholesteryl adipate. At 149.1 °C the solid phase reforms sharply and liberates 11.1 cal/g. The crystallization path is proposed as follows:

$$\begin{tikzcd} C \arrow[r, "180.4^\circ"] & L \arrow[d, "175.8^\circ"] \\ & M \arrow[ul, "149.1^\circ"] \end{tikzcd}$$

The Eastman list gives the mesophase range from 180 °C to 185 °C. This should be very dependent on how the sample is cooled.

Dicholesteryl phthalate exhibits no mesophases on heating or cooling at the rates used in this study. The ethanol recrystallized material melts to form the isotropic liquid at 186.8 °C and freezes to a disordered form of the solid at 144.4 °C. On reheating the solid phase formed from the melt, an exotherm appears at 167.4 °C which liberates 7.14 cal/g. This solid then melts at 186.4 °C requiring 10.5 cal/g. The endotherms on the DSC are broad. The Eastman list gives a mesophase range of 186–189 °C. Since separate transitions 3 °C apart can be resolved by DTA, the mesophase must interpenetrate the solid phase. This interpenetration of phases has been noted previously for cholesteryl heptylate.[4]

Cholesteryl heptafluorobutyrate does not exhibit a distinct mesophase on either heating or cooling. A simple endotherm appears at 114.7 °C with 10.8 cal/g required with ethanol recrystallized material. The melt recrystallized material is essentially the same. Cooling the isotropic liquid produces a single exotherm at 100.3 °C liberating 10.3 cal/g. The Eastman catalog gives a mesophase range from 116 °C to 118 °C. The loss of mesophase may have been caused by impurities which were not removable by ethanol recrystallization. However, this seems unlikely, since ethanol recrystallization appears to have been successful with the other esters of far lower initial purity than the Eastman products.[4,11]

Cholesteryl p-phenylazobenzoate exhibits a single endotherm on heating at 192.7 °C requiring 12.2 cal/g. On cooling, a mesophase forms at 185.3 °C which liberates 0.60 cal/g. The solid phase forms at 153.8 °C liberating 8.35 cal/g. Immediate reheating produces an endotherm at 190 °C which required 9.00 cal/g. Longer standing of the melt formed solid produces a solid with a thermogram almost identical to that of the original ethanol recrystallized material. Eastman lists the mesophase range from 193 °C to 204 °C.

The crystallization path is as follows:

$$\begin{tikzcd}
C \arrow[r, "192.7^\circ"] & L \arrow[d, "185.3^\circ"] \\
& M \arrow[ul, "153.8^\circ"]
\end{tikzcd}$$

Cholesteryl hydrogen phthalate, unlike the diester of phthalic acid, exhibits a cholesteric and a smectic mesophase on cooling.

On heating, the ethanol recrystallized solid melts directly to the isotropic liquid at 169.0 °C and requires 17.7 cal/g. On a molar basis, this is almost identical to the molar heat of melting of the diester. On cooling, the cholesteric mesophase forms at 153.4 °C and liberates 0.15 cal/g. Further cooling produces the smectic mesophase at 89.1 °C and liberated 0.91 cal/g. The smectic mesophase supercools below 0 °C and does not reform the solid. On reheating, the smectic mesophase melts directly to form the isotropic liquid at 95.4 °C and required 1.13 cal/g. This is the only cholesteryl ester examined which produced this particular melting pattern.

$$\begin{tikzcd}
C_1 \arrow[r, "169.8^\circ"] & L \arrow[d, "153.4^\circ"] \\
M_2 \arrow[u, "?\text{ below }0^\circ"] \arrow[ur, "95.4^\circ"] & M_1 \arrow[l, "89.1^\circ"]
\end{tikzcd}$$

The smectic material, from a previous melt, recrystallized *in situ* from ethanol as the solid C_1 which then reproduced the previous solid melting pattern. This precludes decomposition as an operating factor.

Cholesteryl chloroformate does not exhibit distinguishable mesophases on heating or cooling. The alcohol recrystallized solid melts directly to the isotropic liquid at 125.2 °C. The liquid freezes directly to a less ordered solid at 94.9 °C.

Discussion

The existence of a consistent body of thermodynamic data on a broad group of cholesteryl esters permits a consideration of what molecular forces are operational in the formation of mesophases of the cholesteric type. What portion of the ester molecule participates in the various phase transformations can now be discussed on grounds other than simple geometry. For the purpose of this discussion, the total of the thermodynamic data is summarized in Table 4.

TABLE 4 Thermal Data on Some Cholesteryl Esters

Compound	Mol. Wt.	Extended Chain Length (Å)	Solid → Mesophase			Mesophase → Isotropic Liquid			Graphical Code[a]
			T_m(°C)*	ΔH(kcal/Mole)	ΔS(cal/Mole/°K)	T_m(°C)	ΔH(kcal/Mole)	ΔS(cal/Mole/°K)	
Cholesteryl Formate (4)	414.6	4.20	97.0	5.24	14.2	97.1**	0.0827**	0.248**	1
Cholesteryl Acetate (4)	428.70	4.80	110.9	4.59	12.0	-	-	-	2
Cholesteryl n-Propionate (4)	442.7	5.90	101.6	5.76	15.4	115.2	0.102	0.263	3
Cholesteryl Butyrate (5)	456.77	7.37	98.6	5.52	14.8	112.5	0.126	0.327	4
Cholesteryl n-Valerate (5)	470.75	8.85	92.6	6.04	16.5	91	0.127**	0.349	5
Cholesteryl n-Caproate (4)	484.78	10.2	120.4	7.27	18.5	98.7	0.150**	0.403	6
Cholesteryl n-Heptylate (4)	498.8	11.5	116.0	8.48	21.8	← Not Resolved →			7
Cholesteryl Caprylate (5)	512.83	12.9	112.7	9.69	25.1	92.7	0.23**	0.628	8
Cholesteryl Nonate (4)	526.9	14.3	80.7	5.32	15.0	93.0 66.0**	0.12 0.057**	0.33 0.17	9
Cholesteryl n-Decylate (4)	540.9	15.8	87.2	7.19	19.9	91.4 68.5**	0.15 0.097**	0.41 0.28	10
Cholesteryl Laurate (5)	568.93	18.4	99.0	9.96	26.8	87.4** 80.7**	0.49 0.40	1.36 1.13	11
Cholesteryl Myristate (4)	597.05	21.0	73.6	11.2	32.3	80.0 85.6	0.31 0.24	0.88 0.67	12
Cholesteryl Palmitate (4)	625.08	24.0	79.6	14.2	40.3	70.0** 64.0**	0.28 0.36	0.82 1.07	13
Cholesteryl Stearate (4)	653.1	26.5	85.0	16.5	46.1	71** ← Not Resolved →	0.35**	1.01 -	14
Cholesteryl Anisoate	520.76	10.1	179.2	8.44	18.7	264.9	0.29	0.54	15
Dicholesteryl Adipate	883.29	9.4	195.5	7.00	14.9	225.5	0.87	1.75	16
Cholesteryl Cinnamate	516.81	11.0	162.6	6.87	15.8	215.2	0.17	0.35	17
Cholesteryl Benzoate (6)	490.77	8.5	145.8	5.30	12.7	180.7	0.17	0.38	18
Cholesteryl Crotonate	454.72	8.0	112.8	5.91	15.31	162.0	0.30	0.69	19
Dicholesteryl Sebacate	939.49	16.0	179.1	10.6	23.4	175.8**	0.88**	1.96	20
Dicholesteryl Phthalate	903.38	9.5	186.4	9.48	20.6	-	-	-	21
Cholesteryl Heptafluorobutyrate	582.66	8.5	114.2	6.35	16.4	-	-	-	22
Cholesteryl p-Phenylazobenzoate	599.83	15.5	192.4	7.08	15.2	185.3	0.36	0.79	23
Cholesteryl Hydrogen Phthalate	534.78	9.6	169.8***	9.78***	22.0***	153.4** 89.1**	0.080 0.49	0.19 1.35	24
Cholesteryl Chloroformate	449.12	4.5	120.6	6.34	16.1	-	-	-	25

*Temperature of Endothermal Minimum on Second Heating.
**From Cooling Data, Mesophase Does Not Form on Heating.
***From First Heating. Sample Does Not Crystallize Completely from the Melt.
[a] Graphical Code Refers to Figures.

The first transition to consider is the thermally large event—the transition from solid to mesophase or isotropic liquid. Since it has been shown that some significant differences can exist between alcohol and melt recrystallized solids, the melt recrystallized solid has been taken as a standard state in this discussion and in Table 4. When the entropies of fusion of the normal saturated esters are plotted as a function of ester molecular weight, Fig. 1, two lines result. A sharp break occurs between C_8 and C_9 carbon chains. A satisfactory correlation cannot be obtained for the other cholesteryl esters if ester molecular weight is used as one of the axes. The chain length of the acid in Å is a much more satisfactory basis. The lines were constructed using the normal saturated acid points.[5] The acid chain lengths were estimated by measuring the extended length of Fisher–Hershfelder models. This sort of plot permits cholesteryl heptafluorobutyrate to be plotted near the location where cholesteryl butyrate appears. The molar heat of fusion of the heptafluorobutyrate ester is in

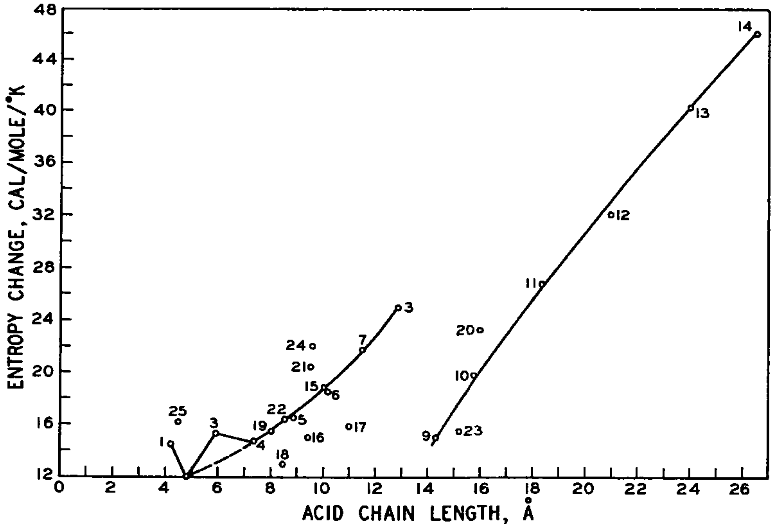


Figure 1. Effect of alkyl chain length on the entropy of the major endothermal event for a group of cholesteryl esters (Numbers refer to Graphical Code in Table 4).

good agreement with that of its neighbors on the chain length plot. In order to bring all the data into some regular relationship, it was necessary to add the solid → solid phase transitions (if any) to the solid → mesophase transition in Fig. 1. This operation is valid in entropy comparisons.[12]

There is no even–odd effect apparent in Fig. 1 such as exists with the acids alone. There is a large break between the curve ending with cholesteryl caprylate and beginning with cholesteryl nonanoate. Even–odd alternation occurs only to a small extent with the ethyl and methyl esters of these acids.[13] The esters of cholesterol fall into two distinct and separate groups as a function of entropy of fusion and acid chain length. The first group between 4 Å and 13 Å chain length contains the saturated normal acids from the formate to the caprylate (octanoate) and most of the higher esters including the dibasic acid esters. Only the anisoate and *p*-phenyl azobenzoate esters appear to belong to the nonanoate to stearate ester group. These two exceptions are interesting since these two acids belong to another series of dipolar liquid crystal-forming materials which have higher entropies of fusion than the cholesteryl esters. The heats of solid → mesophase transition are very close to the molar heats of the methyl acid esters alone.[13]

From Fig. 1, it is evident that the thermally large event is regulated by the acid chain length and little affected by the presence of the massive and probably immobile cholesterol rings. The molar heats and entropy of fusion of cholesterol hydrogen phthalate and the diester (Nos. 21 and 24) are almost identical. This would be expected if only the acid chains were important. Although the authors are unable to explain the break between C_8 and C_9 acids, it indicates a change in geometrical packing of the acid chain brought about by some critical length effect. The displacement of the anisoate and *p*-phenyl azobenzoate esters indicates that the chain packing must be such that dipole interactions can occur.

A similar compilation of the mesophase → mesophase and mesophase → liquid transitions, given in Fig. 2, also shows an

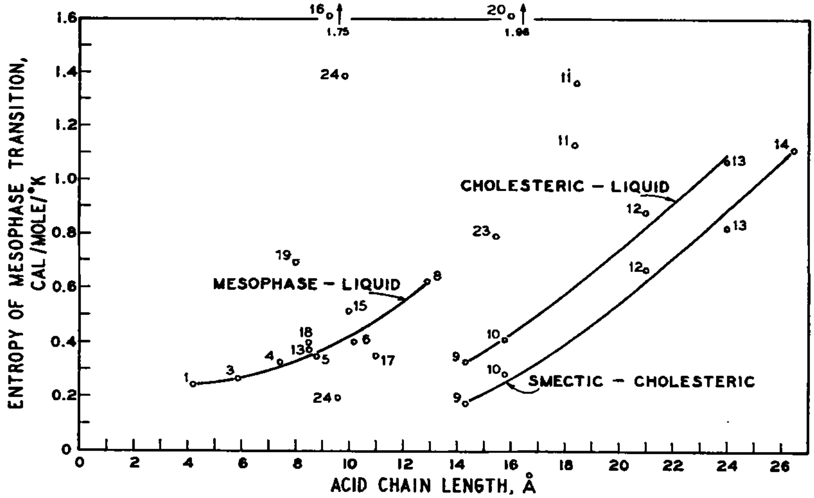


Figure 2. Effect of alkyl chain length on mesophase transition entropy for a group of cholesteryl esters (Numbers refer to Graphical Code in Table 4).

effect due to ester chain length. The break between C_8 and C_9 exists in this case as well. Esters below C_8 do not exhibit a smectic mesophase, only a cholesteric. This indicates a relationship between the ability to form a smectic mesophase and the critical chain length of the acid. That the separation of the cholesteryl plates is also important is demonstrated by the dibasic acid esters which show anomalously high values for the molar entropy and heat of transition. It is possible that some stearic effect inhibits mesophase formation in dicholesteryl phthalate under dynamic conditions. The anomalously high heats of the cholesteryl laurate smectic → cholesteric and cholesteric → isotropic liquid cannot be explained at present. As previously mentioned, this ester shows other unusual behavior.[5]

The thermodynamic data agree well with the optical model given by Chistyakov[3,7] and others.[1,14,15] The solid phase, three-dimensional order is held rigid by ester chain–chain interaction. A 4 Å chain is sufficient. When sufficient energy, between 4.5 and 9.6 kcal/mole for one arrangement and 5.3 and 16.5 +

kcal/mole for another arrangement, is present, these chains separate; and the molecules swarm or rotate into a new configuration—that of a helix stacked around the flat cholesterol ring. The degree of symmetry (entropy) in the stack is regulated by the chain length. For some chain lengths (above 14.3 Å for normal saturated esters) and shapes, an intermediate planar arrangement involving a weak interaction of acid chains in different cholesterol stacks is possible. This is the smectic phase. The smectic phase is loosely ordered in the x, y, and z directions. The cholesteric phase is ordered only about the z coordinate. On further addition of heat, the cholesteric helical stack separated; and the isotropic liquid forms. When cholesteric swarms are cooled, the weak planar intereaction can set in to produce a smectic three-dimension array. On shearing the smectic, a cholesteric texture has been observed.[16] Solid formation from the cholesteric or smectic phase involves rearranging the cholesteric or smectic helix set to bring about ester chain three-dimensional interaction.

This rearrangement hypothesis accounts for: the unusual monotropic transitions, the usual disorder of the solid phase formed from the melt, the sharpness of mesophase formation on cooling, the difference in appearance of the cholesteric mesophase when formed from the melt or from the solid, the supercooling of the solid phase, and the lack of a mesophase in pure cholesterol and epicholestanyl esters, as well as many optical phenomena observed in the past such as streaming, flashing, and flow birefringence in the isotropic liquid near a transition.

Parallels exist between the cholesteryl esters reported here and a series of *p*-*n*-alkoxy benzoic acids studied by A. J. Herbert.[17] These acids exhibit, in dimerized form, both smectic and nematic mesophases. The existence of one or both of these mesophase types is a function of alkyl chain length and molecule width. The *p*-*n*-octyl oxybenzoic acid exhibits both smectic and nematic forms. However, with these materials an even–odd effect is noticeable in the molar heats of fusion as carbon number increases. The values of total heat of fusion for many members of the *p*-*n*-alkoxy benzoic acids are very near those of the cholesteryl esters—

for example, the cholesteryl esters of the nC_{18}, C_{16}, and C_{14} acids are 16.5, 14.2, and 11.2 kcal/mole, respectively, and the *n*-*p*-alkoxy benzoates are 16.2, 13.9, and 11.9 kcal/mole.[17] This similarity is too close to be coincidental. The similarities between these two homologous series vanish in the mesophase, the heats of transition of the cholesteryl esters in the smectic and cholesteric mesophases increase with chain length, and the corresponding smectic and nematic heats of the *p*-*n*-alkoxy benzoates stay almost constant as chain length increases. Further comparisons with the benzoates and naphthoates may be very helpful in understanding the molecular order of cholesteryl esters.

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