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Substituent Effects on the Mesophase Stability for Cholesteryl Benzoylbenzoates

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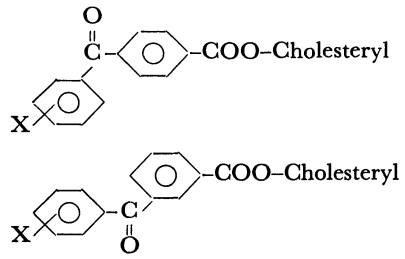
The thermal properties of cholesteryl esters of substituted benzoylbenzoic acids were examined. The substituent effects on the thermal stability of the chloesteric phase of these esters are quite striking. For cholesteryl 4-(4′-substituted benzoyl)benzoates, the Ch-I transition temperatures are slightly influenced by an electronic effect of the substituents, because the bond direction of the substituents is tilted with respect to the long molecular axis. For cholesteryl 4-(3′-substituted benzoyl)benzoates and cholesteryl 3-(4′-substituted benzoyl)benzoates, the Ch-I transition temperatures are influenced by the polarizability anisotropy of the terminal phenyl ring, which probably gives rise to a change in the ratio of the number of more-linear isomers to the number of less-linear isomers. For cholesteryl 4-(2′-substituted benzoyl)benzoates, the substituents increase the angle between the two phenyl rings, *i.e.*, the thickness of the benzophenone moiety, due to the repulsive interaction between the substituent(s) and ortho-hydrogens of the other phenyl ring, and therefore decrease the Ch-I transition temperature largely.

Recently we examined the mesomorphic properties of some cholesteryl esters of arylbenzoic acids incorporating the angular linkages, such as –CO–, –O–, –S–, and $-CH_2-$.[1,2] In spite of the angular geometry, these esters exhibit a cholesteric phase and their thermal stabilities are in the order of $-CO->-O->-CH_2->-S-$. These results indicate that the mesophase stability is strongly dependent on the electronic effect of the carboxylic acid moieties. But a replacement of the aryl ring by the cyclohexyl ring at the terminal position of cholesteryl 4-benzoylbenzoate gives rise to a depression of the Ch-I transition temperature by only 6 °C, and the replacement at the inner position enhances it by 7 °C,[2] though the replacement would decrease the electronic effect of the carboxylic acid moiety because of the reduced conjugative interactions among carbonyl and ester groups and rings. These results appear to be inconsistent. So we are interested in the role of the electronic effect of the carboxylic acid moiety on the mesophase stability. For this purpose, we have prepared two types of cholesteryl esters of substituted benzoylbenzoic acids with the following formula:



In this paper, the substituent effect on the mesophase stability will be discussed in terms of the structural features of the benzophenone moiety and the electronic effect of the substituents.

Experimental

Preparation of Materials. Substituted 4-methylbenzophenones were prepared by the Friedel-Crafts reaction[3] of toluene with the substituted benzoyl chloride, which was prepared from the substituted benzoic acid and thionyl chloride[4] or phosphorus pentachloride.[5]

3- And 4-(substituted benzoyl)benzoic acids, except for 3- and 4-(4′-alkylbenzoyl)benzoic acids, were prepared by sodium dichromate oxidation[6] of the substituted 4-methylbenzophenone.

4-(4′-Alkylbenzoyl)benzoic acids were prepared by the Friedel-Crafts reaction[3] of the alkylbenzene with terephthaloyl chloride, followed by hydrolysis.

3-(4′-Alkylbenzoyl)benzoic acids were prepared by the Friedel-Crafts reaction[3] of the alkylbenzene with isophthaloyl chloride, followed by hydrolysis.

3-(3′-Methylbenzoyl)benzoic acid was prepared by Grignard reaction[7] of dimethyl isophthalate with 3-methylphenylmagnesium bromide.

3- And 4-(substituted benzoyl)benzoyl chlorides were prepared from the 3- and 4-(substituted benzoyl)benzoic acid and phosphorus pentachloride.[5]

Cholesteryl esters were prepared from the 4- and 3-(substituted benzoyl)benzoyl chloride and chloesterol.[8] All esters were purified by column chromatography on silica gel, followed by recrystallization from a suitable solvent. The elemental analyses are listed in Table 3.

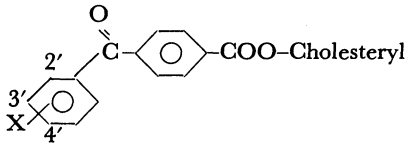
Physical Measurement. Identification of the mesophase and determination of the transition temperatures were made using a Nikon polarizing microscope in conjunction with a Mettler FP 52 heated stage and control unit. Transition enthalpies were determined using a Daini Seikosha differential scanning calorimeter, model SSC-560. Entropy values were calculated using the equation, $\Delta S=\Delta H/T$.

Results and Discussion

The thermal properties of cholesteryl 4-(substituted benzoyl)benzoates and cholesteryl 3-(substituted benzoyl)benzoates are summarized in Tables 1 and 2, respectively.

Cholesteryl 4-(4′-Substituted benzoyl)benzoates. Generally, terminal groups with a small, compact structure such as cyano, halogen, methoxy, nitro, methyl, raise the N-I or Ch-I transition temperature relative to hydrogen because of increased polarizability anisotropy.[9,10] As is evident from Table 1, although the melting points appreciably change by introduction of the substituent at the 4′-position of **1**, the effect on the Ch-I transition temperature is remarkably small. Generally, introduction of methyl or methoxyl groups at the terminal position of a molecule gives rise to an increase in the N-I or Ch-I transition temperature

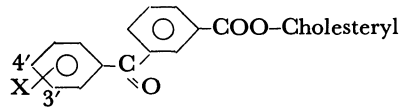
Table 1. Thermodynamic properties of cholesteryl 4-(substituted benzoyl)benzoates



Graphical code	X	T_{MP} °C	$T_{Ch\text{-}I}$ °C	$\Delta H_{Ch\text{-}I}$ kJ mol^{-1}	$\Delta S_{Ch\text{-}I}$ J K^{-1} mol^{-1}
1[a]	H	134.2	210.3	0.51	1.01
2[b]	4′-CH_3	158.3	205.9	0.52	1.09
3	4′-C_2H_5	179.0	193.1	0.40	0.86
4	4′-C_3H_7	174.3	(169.2)	—	—
5	4′-F	154.2	227.1	0.52	1.04
6	4′-Cl	175.4	206.4	0.43	0.90
7	4′-Br	182.6	214.6	0.38	0.78
8	4′-CH_3O	158.5	205.4	0.44	0.92
9	4′-NO_2	200.1	215.6	0.54	1.11
10	3′-F	142.4	219.6	0.53	1.08
11	3′-Cl	165.0	213.8	0.44	0.90
12[c]	3′-NO_2	175.1	233.0	1.01	2.00
13[d]	3′,5′-Cl	161.0	194.4	0.56	1.18
14	2′-F	154.1	168.6	0.38	0.86
15	2′-Cl	157.7	[90]	—	—
16	2′,4′-Cl	151.3	[90]	—	—
17	2′,6′-Cl	185.6	[−10]	—	—

a) This compound underwent a change in crystal form at 119.5 °C. b) This compound also underwent a change in crystal form at 150.1 °C. c) This compound showed a smectic A phase ($T_{S_A\text{-}Ch}$=156.5 °C). d) This compound also underwent a change in crystal form at 149.1 °C. ( ): Monotropic transition. [ ]: "Virtual" transition temperature.

Table 2. Thermodynamic properties of cholesteryl 3-(substituted benzoyl) benzoates



Graphical code	X	T_{MP} °C	$T_{Ch\text{-}I}$ °C	$\Delta H_{Ch\text{-}I}$ kJ mol^{-1}	$\Delta S_{Ch\text{-}I}$ J K^{-1} mol^{-1}
18	H	149.6	(71.7)[a]	0.15	0.44
19	4′-CH_3	141.4	(89.0)	0.64	1.77
20	4′-C_3H_7	144.0	(85.0)	—	—
21	3′-CH_3	153.3	(43.4)	0.16	0.51

a) ( ): Monotropic transition.

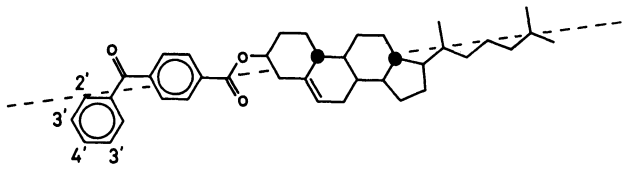


Fig. 1. Structural model of cholesteryl 4-benzoylbenzoates. The dotted line represents the long molecular axis.

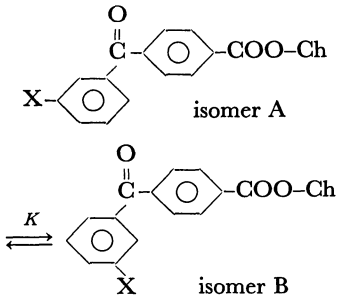
by more than 50 °C.[11] For **1**, this trend is absent. Furthermore, when the number of the carbon atoms in the alkyl chain at the 4′-position is increased (**1**—**4**), the Ch-I transition temperatures decrease steeply without any distinct alternation between odd and even members.[12] These characteristics are quite striking and should be related to the angular geometry of the benzophenone moiety.

The molecular structure of cholesteryl 4-benzoylbenzoates is illustrated in Fig. 1. The valence angle between the C–C bonds linking two phenyl rings is *ca.* 120°.[13] Then, the substituent, X, located at the 4′-position contributes in two ways to the mesophase stability. One is that it increases the molecular breadth as well as the molecular length. These structural characteristics should depress the Ch-I transition temperature due to an action similar to that of the lateral substituents for ordinary mesogenic compounds. According to Gray's studies, the depression of the clearing points has a good correlation with the molecular diameter.[14] The efficiency order is reported to be H>F>CH_3>Cl>Br>NO_2. The other effect is to produce changes in conjugative interactions within the molecule, thus affecting factors such as polarizability and dipolarity. For example, the longitudinal substituent effect on the mesophase stability for cholesteryl benzoates is reported to be CN($T_{Ch\text{-}I}$=287.0 °C)>CH_3O(267.0 °C)>Cl(252.8 °C)>Br(251.6 °C)>CH_3(241.1 °C)>F(193.1 °C)>H(179.9 °C).[15] The dominant effect for the substituents is attributable to the increase in polarizability and dipolarity due to conjugation between aryl group and substituent. For cholesteryl 4-benzoylbenzoates, the substituent at the 4′-position also increases the molecular polarizability and dipolarity due to conjugative interactions between aryl and carbonyl groups. However, the anisotropy of these terms along the long molecular axis indicated by the dotted line in Fig. 1 should be smaller than that for cholesteryl benzoates, because the C–X bond is tilted by *ca.* 60° from the long molecular axis.

As is evident from Table 1, the Ch-I transition temperature in this series isn't very susceptible to changes in the effect of substituent, and the efficiency order is quite different from that for cholesteryl benzoates. Supposing that a methyl group at the 4′-position lowers the Ch-I transition temperature by 50 °C due to a steric repulsion similar to that from the methyl group at 3-position of cholesteryl benzoate,[16] and enhances it by 63 °C due to the electronic effect similar to that from the methyl group at the 4-position of cholesteryl benzoate,[15] we can expect the Ch-I transition temperature for **2** to be 223 °C. The observed Ch-I transition temperature for **2** appears to be considerably lower than the calculated one. The trend is also recognized in **6**—**9**. These facts indicate that the electronic effect of the substituent at the 4′-position isn't so large, compared with that for ordinary mesogens, because the directions of the polarizability and dipolarity arising from the terminal benzoyl portion including substituent intersect the long molecular axis.

Cholesteryl 4-(3′-Substituted benzoyl)benzoates. The effect of a substituent at the 3′-position on the

mesophase stability exhibits some interesting trends. Generally, a meta-substituent (lateral substituent) increases the molecular breadth, giving rise to a decrease in the lateral interaction. However, the substituent at 3′-position slightly enhances the Ch-I transition temperatures and the di-substitution gives rise to a depression of the Ch-I transition temperature (**13**). This unusual behavior should be related to the angular geometry of the benzophenone moiety. Let's consider the conformational equilibrium, as shown below:



The energy of both isomers will be quite similar under usual conditions, such as in an isotropic medium ($K=1$). The substituent X in isomer A will elongate the molecular length and enhance a local polarizability arising from the C–X bond along the long molecular axis. The substituent X in isomer B, on the other hand, will increase the molecular breadth, causing the Ch-I transition temperature to decrease. Certainly, **11** and **12** exhibit higher Ch-I transition temperature than **6** and **9**, whereas the substituents are located at the meta-position with respect to the carbonyl group. Temperature differences for the transition between **5** and **10**, **6** and **11**, and **9** and **12** are −7.5 °C, 7.4 °C, and 17.4 °C, respectively. These tend to increase with increasing the bond polarizabilities, 0.5, 2.5, and 4.0 Å^3.[17] This fact indicates that polarizability and/or dipolarity of the C–X bond tends to move the equilibrium point toward isomer A in the mesophase. However, this contribution should be small, since we can't recognize it in the entropy change for the Ch-I transition. On the other hand, the disubstituted compound, **13**, exhibits a lower Ch-I transition temperature than that for **10**—**12**. This is caused by one of chlorine atoms inevitably occupying the unfavorable site in isomer B.

Cholesteryl 4-(2′-Substituted benzoyl)benzoates. As is evident from Table 1, the substituent effect at the 2′-position on the Ch-I transition temperature is striking. The 2′-substituted compounds, **15**—**17**, show no mesophase. So-called "virtual" Ch-I transition temperatures were determined from binary phase diagrams, as shown in Fig. 2. By mixing **15** with known amounts of **1**, and determining the Ch-I transition temperatures of the mixtures, a phase diagram for the binary system was constructed. The "virtual" Ch-I transition temperature for **15** was found, by extrapolation, to be 90 °C. Similar phase diagrams were constructed for **16** and **17**, the "virtual" ones being 90 and −10 °C, respectively. As one can assume from the structural model (Fig. 1), introduction of the substituent at 2′-position will increase not the molecular breadth but the thickness of the carboxylic acid moiety due to

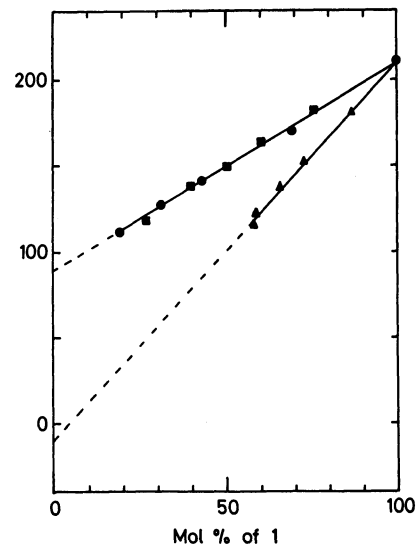


Fig. 2. Ch-I transition lines in the binary phase diagrams for (a) **1** and **15** (●), (b) **1** and **16** (■), and (c) **1** and **17** (▲).

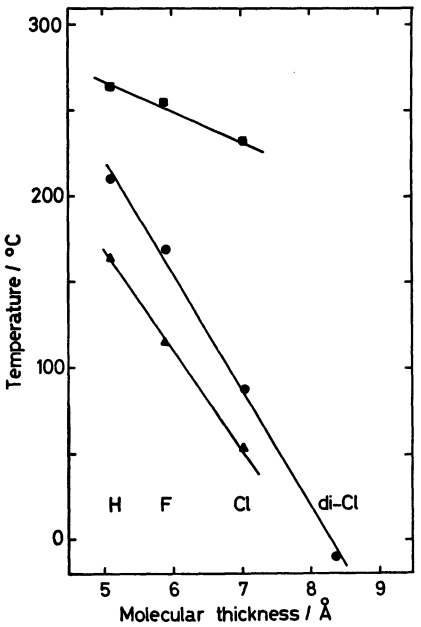


Fig. 3. A plot of molecular thickness of the benzophenone moiety[18] against the $T_{Ch\text{-}I}$ of cholesteryl 4-(2′-substituted benzoyl)benzoates (●), the $T_{N\text{-}I}$ of 2-substituted 4-*p*-(octyloxy)benzylideneaminobiphenyls (▲),[19,20] and the $T_{N\text{-}I}$ of 3′-substituted 4′-(octyloxy)biphenyl-4-carboxylic acids (■).[21]

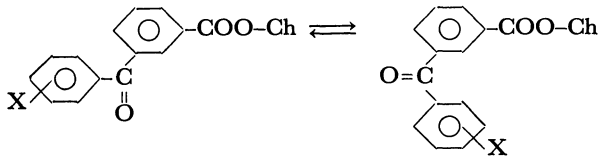
increased interaction between the substituent(s) and ortho-hydrogens at the other ring, and also will decrease the molecular polarizability arising from the resonance between both aryl and carbonyl groups. Then, the Ch-I transition temperatures for **1** and **15**—**17** are plotted against the molecular thickness of the carboxylic acid moieties[18] (Fig. 3). Similar to the other cases, these exhibit linear correlation. The slope is close to that for 2-substituted 4-*p*-(octyloxy)benzylideneaminobiphenyls[19,20] rather than 3′-substituted 4′-(octyloxy)biphenyl-

Table 3. Elemental analyses of cholesteryl esters

Graphical code	Molecular formula	Calculated(%) C	Calculated(%) H	Found(%) C	Found(%) H
1	$C_{41}H_{54}O_3$	82.78	9.15	82.48	9.14
2	$C_{42}H_{56}O_3$	82.85	9.27	82.75	9.34
3	$C_{43}H_{58}O_3$	82.90	9.39	82.83	9.49
4	$C_{44}H_{60}O_3$	82.97	9.50	82.72	9.64
5	$C_{41}H_{53}FO_3$	80.35	8.72	80.17	8.80
6	$C_{41}H_{53}ClO_3$	78.25	8.49	78.09	8.53
7	$C_{41}H_{53}BrO_3$	73.09	7.93	72.98	7.87
8	$C_{42}H_{56}O_4$	80.73	9.03	80.55	8.91
9	$C_{41}H_{53}NO_5$	76.96	8.35	77.21	8.59
10	$C_{41}H_{53}FO_3$	80.35	8.72	80.33	8.70
11	$C_{41}H_{53}ClO_3$	78.25	8.49	78.18	8.58
12	$C_{41}H_{53}NO_5$	76.96	8.35	76.90	8.24
13	$C_{41}H_{52}Cl_2O_3$	74.19	7.90	73.94	7.88
14	$C_{41}H_{53}FO_3$	80.35	8.72	80.53	8.65
15	$C_{41}H_{53}ClO_3$	78.25	8.49	77.99	8.41
16	$C_{41}H_{52}Cl_2O_3$	74.19	7.90	74.02	7.94
17	$C_{41}H_{52}Cl_2O_3$	74.19	7.90	74.09	8.02
18	$C_{41}H_{54}O_3$	82.78	9.15	82.75	9.13
19	$C_{42}H_{56}O_3$	82.85	9.27	82.67	9.24
20	$C_{44}H_{60}O_3$	82.96	9.50	82.81	9.77
21	$C_{42}H_{56}O_3$	82.85	9.27	82.91	9.20

4-carboxylic acids,[21] indicating that an increased molecular thickness due to repulsion between the substituent(s) and the ortho-hydrogens is the major cause of rapid depression of the Ch-I transition temperatures.

Cholesteryl 3-(Substituted benzoyl)benzoates. Although **18** has a low Ch-I transition temperature relative to **1**, its derivatives exhibit an apparent substituent effect on the mesophase stability, *i.e.*, the substituent at the 4'-position enhances the Ch-I transition temperature, and that at the 3'-position depresses it. These trends are in contrast with the substituent effect for **1**. These results can be accounted for by considering the conformational models shown below:



isomer C isomer D

The energy of these two isomers will be also equivalent in the isotropic state. For preservation of the parallel arrangement in the mesophase, isomer C will be preferable to isomer D, because the former is less wide than the latter. Furthermore, the substituent at the 4'-position in isomer C will increase the molecular length and anisotropy of polarizability along the long molecular axis. Then, the role of the substituent seems to be analogous to that of the substituent at the 3'-position in isomer A for **1**. The substituents at both 3'- and 4'-position in isomer D, on the other hand, give rise to an increase in molecular breadth. Then, the enhanced Ch-I transition temperatures for **19** and **20** must indicate that the position of the conformational equilibrium for **18** slightly inclines toward the left side, as the substituent is introduced at the 4'-position. We could recognize it in the entropy data (**18** and **19**). On the contrary, methyl group at the 3'-position is assumed to be inevitably unfavorable for the mesophase stability. **21** shows that case.

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References

1) M. Koden, S. Takenaka, and S. Kusabayashi, *Chem. Lett.*, **1980**, 471.
2) M. Koden, S. Takenaka, and S. Kusayashi, to be published.
3) E. D. Hughes, C. K. Ingold, and N. A. Taher, *J. Chem. Soc.*, **1940**, 949.
4) B. Herferrich and W. Schaefer, *Org. Synth.*, Coll. Vol. I, 147 (1941).
5) R. Adams and R. L. Jenkins, *Org. Synth.*, Coll. Vol. I, 394 (1941).
6) O. Kamm and A. O. Matthews, *Org. Synth.*, Coll. Vol. I, 392 (1941).
7) D. S. Noyce and P. A. Kittle, *J. Org. Chem.*, **30**, 1896 (1965).
8) G. W. Gray, *J. Chem. Soc.*, **1956**, 3733.
9) G. W. Gray, "The Molecular Physics of Liquid Crystals," ed by G. R. Luckhurst and G. W. Gray, Academic Press, London, New York, San Francisco (1979), Chap. 1.
10) W. H. de Jeu and J. van der Veen, *Mol. Cryst. Liq. Cryst.*, **40**, 1 (1977).
11) D. Demus, H. Demus, and H. Zaschke, "Flüssige Kristalle in Tabellen," VEB Deutscher Verlag für Grundstoff Industrie, Leipzig (1974).
12) M. Koden, T. Yagyu, S. Takenaka, H. Terauchi, and S. Kusabayashi, *Chem. Lett.*, **1981**, 269.
13) E. B. Fleischer, N. Sung, and S. Hawkinson, *J. Phys. Chem.*, **72**, 4311 (1968).
14) G. W. Gray, *Mol. Cryst.*, **1**, 333 (1966).
15) M. J. S. Dewar and A. C. Griffin, *J. Chem. Soc., Perkin Trans. 2*, **1976**, 713.
16) Unpublished result for our laboratory.
17) J. van der Veen, *J. de Phys.*, **36**, Cl-375 (1975).
18) F. Zuccarello, S. Millelieri, and S. Trovato, *Can. J. Chem.*, **54**, 226 (1976).
19) G. W. Gray, J. B. Hartley, A. Ibbotson, and B. Jones, *J. Chem. Soc.*, **1955**, 4359.
20) D. J. Byron, G. W. Gray, A. Ibbotson, and B. M. Worrall, *J. Chem. Soc.*, **1963**, 2246.
21) G. W. Gray and B. M. Worrall, *J. Chem. Soc.*, **1959**, 1545.