LIQUID CRYSTALS, III

SYNTHESIS OF *N*-(ALKOXYCARBONYL-n-DECYL)-3β-CHOLESTERYL URETHANES AND THEIR POLYMORPHIC AND MESOMORPHIC PROPERTIES*

By

G. MOTIKA, P. M. AGÓCS, J. A. SZABÓ and A. I. ZOLTAI

Institute of Organic Chemistry, József Attila University, Szeged, Hungary

(Received 10th March, 1980)

Homologous series of *N*-(alkoxycarbonyl-*n*-decyl)-3β-cholesteryl urethanes have been prepared. The phase transitions have been measured with the aid of differential scanning calorimetry. The textures of the mesophases have been determined with a hot stage equipped polarizing microscope. The phase transition schemes have been described.

Introduction

In the past few years many homologous series with cholesterol skeleton have been prepared, with various functional groups at the 3β-position in ring A [1]. The phase transitions (mesomorphic and polymorphic) in these homologous series have been examined in detail. The examinations were carried out with the aims of recognizing the regularities within the homologous series, establishing the structure — property relationships and synthetizing compounds with valuable properties.

We have synthetized homologous series containing the cholesterol skeleton, in which two different bonding systems exist. On changing the distance between the two bonding systems (in our case ester and carbamate), it was observed how the variation in the number of carbon atoms alters the phase transition properties. Our model materials were *N*-(alkoxycarbonyl-*n*-alkyl)-3β-cholesteryl urethanes. The alkoxy groups were changed from methoxy to dodecyloxy. The number of carbon atoms between the two bonding systems varied from one to ten. In this publication we describe the syntheses and mesomorphic properties of compounds, produced from 11-amino-undecanoic acid. In this case ten carbon atoms exist between the NH and the carbonyl group.

* Part II: *J. A. Szabó, A. I. Zoltai, P. M. Agócs* and *G. Motika*: Acta Phys. et Chem. Szeged, in press.

Experimental

The synthesis route is shown in Fig. 1.

Cholesteryl chloroformate (V) was prepared in benzene by the reaction of cholesterol (IV) and phosgene. In the esterification of the amino acid (II) with the C_4—C_5 alcohols (I) the corresponding alcohol was used as solvent, whereas for the higher homologs an inert solvent was employed. The esterification was carried out by introducing HCl gas into the refluxing solution. The amino acid ester hydrochlorides (III) obtained and cholesteryl chloroformate (V) were coupled in benzene with the aid of triethylamine, leading to the compounds with ester and carbamate functions (VI).

After completion of the reaction, the product was purified by column-chromatography and crystallization. The analytical data of the compounds prepared are shown in Table I.

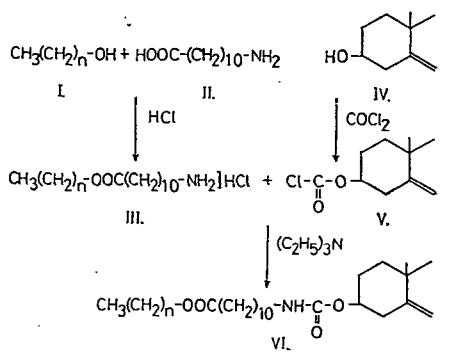

Fig. 1. Synthesis route of *N*-(alkoxycarbonyl-*n*-decyl)-3β-cholesteryl urethanes

The column-chromatographic purifications were carried out with the aid of aluminium oxide packing. For the thin-layer chromatography examinations Silicagel G (REANAL) and Kieselgel HF_{254} nach Stahl (MERCK) adsorbents and Silufol (KAVALIER, Chechoslovakia) plates were used.

Ninhydrin and 50% phosphoric acid were applied as developing reagent. The fluorescent plates were observed with a UV lamp (HANOVIA).

The calorimetric measurements were made with a PERKIN-ELMER DSC-2 calorimeter, in highly-purified nitrogen atmosphere. The weight of the samples lay in the range 3—7 mg. The heating and cooling rates were generally 10 K/min, and the sensitivity of the instrument was 5—10 mcal/s. The temperatures of the phase transitions could be reproduced with an accuracy of ± 1K.

For the measurement of the melting points and determination of the textures of the mesophases a PHMK (VEB Analytik, Dresden) apparatus and an AMPLIVAL POL-U (Carl Zeiss, Jena) polarizing microscope (equipped with a hot stage) were applied.

11-amino-undecanoic acid ester hydrochlorides (III)

Method A: In the case of C_1-C_4 alcohols the corresponding alcohol was applied as solvent. 2 g (0.01 mole) 11-amino-undecanoic acid (II) was refluxed in 25 ml C_1-C_4 alcohol, while HCl gas was introduced into the solution during 6—8 h. After evaporation, the product was washed with acetone and dried. Yield: ~80%.

Method B: For the higher alcohol homologs an inert solvent was employed. 2 g (0.01 mole) 11-amino-undecanoic acid (II) and 0.02 mole of the appropriate alcohol were dissolved in 50 ml chlorobenzene, and HCl gas was introduced under

Table I

Physical data of N-(alkoxycarbonyl-n-decyl)-3β-cholesteryl urethanes

No.	Alkoxy group	Mol. formula	Mol. weight	Analysis (%) Found	Calc.
VI/1	Methoxy	$C_{40}H_{69}NO_4$	628,00	C=75,72 H=10,86	C=76,50 H=11,07
VI/2	Ethoxy	$C_{41}H_{71}NO_4$	642,03	C=77,04 H=11,05	C=76,70 H=11,15
VI/3	Propyloxy	$C_{42}H_{73}NO_4$	656,05	C=75,62 H=11,26	C=76,90 H=11,22
VI/4	Butyloxy	$C_{43}H_{75}NO_4$	670,08	C=76,95 H=11,04	C=77,08 H=11,28
VI/5	Pentyloxy	$C_{44}H_{77}NO_4$	684,11	C=76,50 H=11,01	C=77,25 H=11,34
VI/6	Hexyloxy	$C_{45}H_{79}NO_4$	698,13	C=77,61 H=11,67	C=77,42 H=11,41
VI/7	Heptyloxy	$C_{46}H_{81}NO_4$	712,16	C=77,33 H=11,78	C=77,58 H=11,46
VI/8	Octyloxy	$C_{47}H_{83}NO_4$	726,19	C=77,10 H=11,68	C=77,74 H=11,52
VI/9	Nonyloxy	$C_{48}H_{85}NO_4$	740,22	C=77,41 H=11,50	C=77,89 H=11,57
VI/10	Decyloxy	$C_{49}H_{87}NO_4$	754,24	C=79,87 H=11,43	C=78,03 H=11,63
VI/11	Undecyloxy	$C_{50}H_{89}NO_4$	768,27	C=77,77 H=11,40	C=78,17 H=11,68
VI/12	Dodecyloxy	$C_{51}H_{91}NO_4$	782,30	C=77,99 H=11,76	C=78,30 H=11,72

reflux during 5—8 h. The reaction mixture was evaporated to dryness under reduced pressure. The product was washed with acetone and dried. Yield: ~60%.

Cholesteryl chloroformate (V)

38.6 g (0.1 mole) cholesterol (IV) was dissolved in 350 ml abs. benzene and phosgene was introduced during stirring until the reaction was complete. The reaction mixture was allowed to stand overnight at room temperature, and then flushed out with nitrogen to remove the phosgene. The solution was washed with water, dried over anhydrous sodium sulfate and evaporated to dryness. Yield: ~90%.

N-(alkoxycarbonyl-n-decyl)-3β-cholesteryl urethanes (VI)

0.01 mole 11-amino-undecanoic acid ester hydrochloride (III) and 0.02 mole triethylamine were dissolved in 50 ml abs. benzene under stirring, and 4.5 g (0.01 mole) cholesteryl chloroformate (V) in 50 ml abs. benzene was added during 15—20

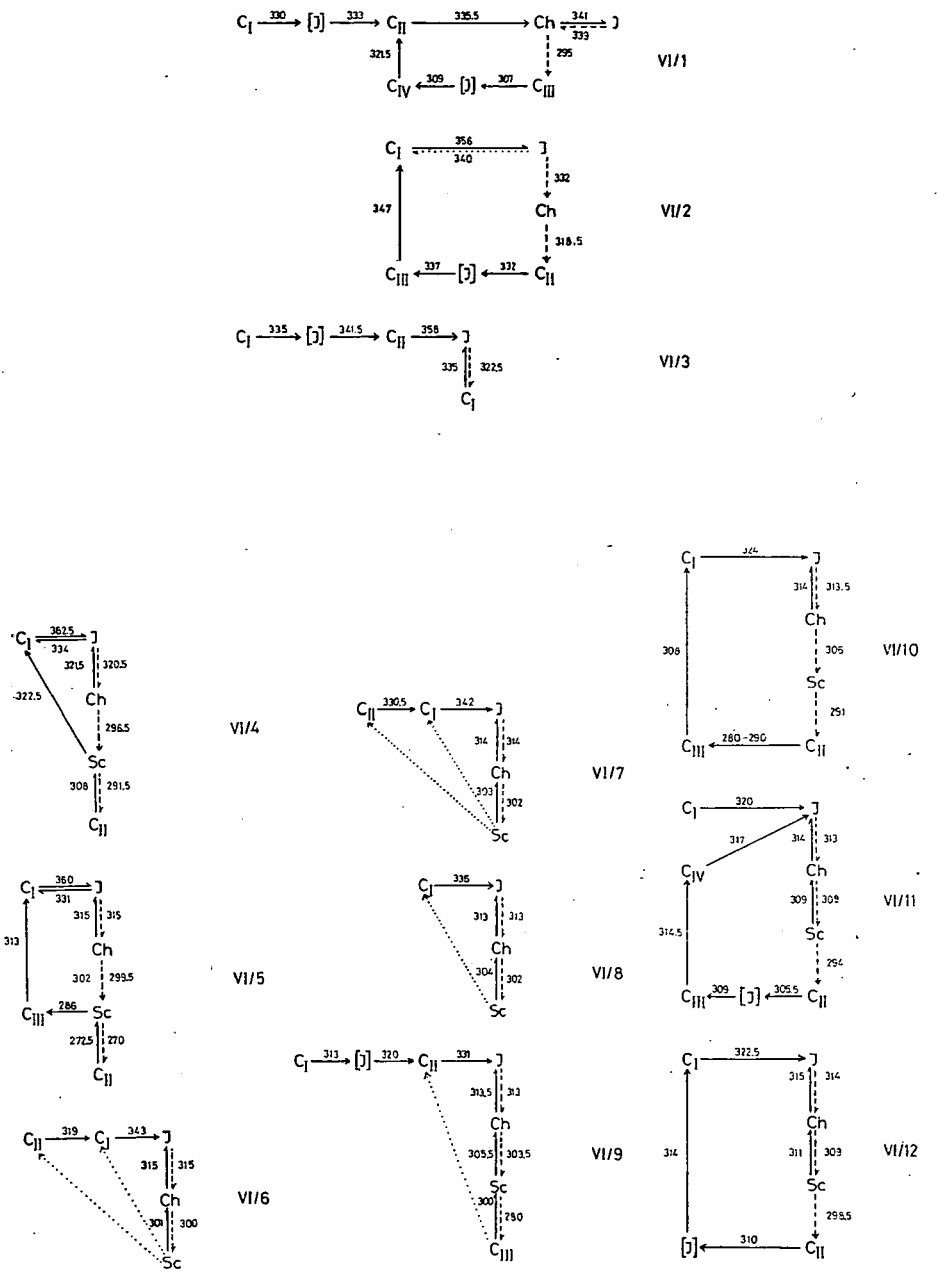

Fig. 2. Phase transition schemes of *N*-(alkoxycarbonyl-*n*-decyl)-3β-cholesteryl urethanes

min. Strirring was continued for 4—5 h, and the reaction was followed by thin-layer chromatography. When the reaction was complete, the benzene solution was washed with cold dilute hydrochloric acid and water, and dried over anhydrous sodium sulfate. The benzene was distilled off, and the crude product was purified by column-chromatography and finally crystallized from a benzene — ethyl alcohol mixture. Yield: ~50%.

Results and discussion

The phase transition schemes are shown in Fig. 2. The abbreviations are as follows:

I = isotropic liquid
Ch = cholesteric mesophase
S_c = smectic C mesophase
C_I, C_{II}, ... = crystalline modifications

The heating direction is indicated with a continuous line, the cooling direction with a broken line, and the transitions after thermostating with a dotted line.

With three exceptions, all compounds show cholesteric and smectic C liquid crystalline phases. One compound (VI/3) shows no mesophase, and in two cases (VI/1 and VI/2) only the cholesteric mesophase exists.

Compounds VI/1, VI/3 and VI/9 display the $C_I \rightarrow I \rightarrow C_{II}$ transitions only in the first heating, and these do not reappear on subsequent heating even after thermostating for several days.

In several cases (VI/2, VI/11 and VI/12) the polymorphic crystal transitions take place only over an isotropic phase in the second and subsequent heating cycles. The reason for this is presumably that the crystal nuclei required for the new crystal modifications can be formed only from the isotropic phase.

On recooling, the crystallization of compounds VI/6, VI/7 and VI/8 is extremely slow, no crystalline form being obtained after standing at 290 K for several hours. For VI/9 the crystalline C_{II} modification resulted only after several days at 290 K. Depending on the duration of the thermostating period, in the case of compounds VI/6 and VI/7 a crystalline C_{II} phase is obtained besides the crystalline C_I modificaton.

Fig. 3 shows a plot of the liquid crystal transition temperatures against the number of methylene groups *(n)* in the ester alkyl chain.

Fig. 3 reveals that the I → Ch phase transition temperatures gradually decrease but from $n=4$ remain at approximately the

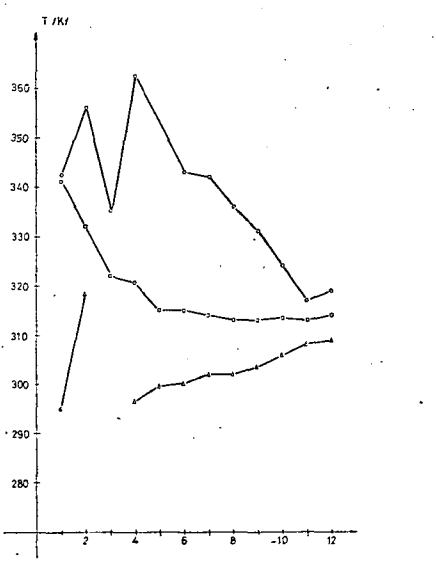

Fig. 3. Transition temperatures of *N*-(alkoxycarbonyl-*n*-decyl)-3-*β*-cholesteryl urethanes

same level. The temperatures of the Ch → S_c transitions appeared first for the *n*-pentyl ester (VI/5) and successively increase. In this way the temperature interval of the cholesteric mesophase gradually narrows. This tendency is observed with many other homologous series [2].

Only compound VI/1 formed an enantiotropic cholesteric mesophase. All other compounds show a monotropic cholesteric mesophase: on heating, the crystalline materials are transformed into the isotropic liquid.

To summarize, we may conclude that the prepared compounds exhibit a mesomorphic phase. Only cholesteric and smectic *C* mesophase are formed. The temperature interval for the existence of the cholesteric mesophase tends to decrease with the increase of the length of the alkyl chain.

Acknowledgements

The authors thank OMFB (Hungarian Technical Development Committee) for the generous technical gift and REANAL Chemical Factory, Budapest for the financial support.

Thanks are expressed to Mrs. Dr. G. Bartók—Bozóki and Mrs. Éva Gács—Gergely for the combustion analyses and to Mr. A. Gajdacsi for the technical assistance.

References

[1] *Brown, G. H.:* Advances in Liquid Crystals. Vol. II. Academic Press Inc., New York—San Francisco—London, 1976.

[2] *Demus, D., Demus, H., Zaschke H.:* Flüssige Kristalle in Tabellen. VEB Deutscher Verlag für Grundstoffindustrie, Leipzig, 1974.

ЖИДКИЕ КРИСТАЛЛЫ, III. СИНТЕЗ *N*-(АЛКОКСИКАРБОНИЛ-Н.-ДЕЦИЛ)-3β-ХОЛЕСТЕРИЛ УРЕТАНОВ И ИЗУЧЕНИЕ ИХ ПОЛИМОРФНЫХ И МЕЗОМОРФНЫХ СВОЙСТВ

Г. Мотика, П. М. Агоч, И. А. Сабо и А. И. Золтаи

Синтетизирован гомологический ряд *N*-(алкоксикарбонил-н.-децил)-3β-холестерил уретанов. Определены фазовые превращения синтетизированных веществ методом дифференциально-сканирующей калориметрии. Структура мезофаз определялась с помощъю высокотемпературного поляризационного микроскопа. Предложены схемы протекания фазовых превращений.