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Lawrence Verbit [a] & George A. Lorenzo [a]
[a] Department of Chemistry, State University of New York at Binghamton, Binghamton, New York, 13901, U.S.A.
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Synthesis and Liquid Crystal Properties of Some Urethans†

LAWRENCE VERBIT* and GEORGE A. LORENZO

Department of Chemistry, State University of New York at Binghamton, Binghamton, New York 13901, U.S.A.

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The urethan (carbamate) linkage (—NHCOO—) has been investigated as a central group in liquid crystal systems. Cholesteryl N-*para*-substituted-phenylcarbamates exhibit cholesteric mesophases with mesophase stability roughly parallel to increasing molecular polarizability. A smectic, in addition to a cholesteric mesophase was found in the case of cholesteryl N-*n*-hexadecylcarbamate. The *n*-octyl analog has a monotropic cholesteric mesophase, while the *n*-butyl analog is not mesogenic.

The N-*para*-methoxyphenylcarbamates of cholesterol, cholestanol, stigmasterol, α-sitosterol, campesterol, and 5-androstene-3β-ol-17-one, with the exception of the latter which was not mesogenic, exhibit enantiotropic mesophases. Twentyfive other non-steroidal urethans having a wide variety of structures, as well as several urea derivatives, were prepared but none was mesogenic.

1 INTRODUCTION

The urethan (carbamate) linkage, —NHCOO—, is of potential interest in the search for new mesogenic compounds. Derivatives of carbamic acid, H_2NCOOH, urethans are chemically stable compounds. They are not ordinarily susceptible to oxidation and are relatively resistant to reduction. One of the simplest urethans, ethyl carbamate, has found use as a soporific drug while some other derivatives possess useful tranquilizing properties.

In addition to good chemical stability, some other features of the urethan function appeared of interest for the design of new liquid crystalline materials. The urethan linkage possesses π-electron density and has a

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permanent dipole oriented at an angle to the main molecular axis. Spectroscopically, it has good transparency in the ultraviolet region, absorbing below 220 nm. Another point of interest is that urethans may be formed in polymerizing systems.

The nomenclature of urethans requires a brief word. They are properly named as derivatives of carbamic acid. For example, the correct name for compound **A** is *n*-butyl N-methylcarbamate although *n*-butyl N-methylurethan also is frequently used.

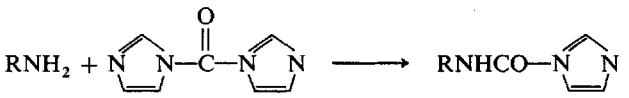
$$CH_3NHCOO\text{-}n\text{-}C_4H_9$$

A

There are three main synthetic routes for the preparation of urethans; equations 1, 2, and 3.

$$R{-}N{=}C{=}O + HOR' \longrightarrow RNHCOOR' \quad (1)$$

$$RNH_2 + ClCOOR' \longrightarrow RNHCOOR' \quad (2)$$



$$RNH_2 + \text{(carbonyldiimidazole)} \longrightarrow RNHCO{-}\text{(imidazole)} \quad (3)$$

$$RNHCO{-}\text{(imidazole)} \xrightarrow{R'OH} RNHCOOR'$$

Reactions 1 and 2 are particularly convenient where the appropriate isocyanate or chloroformate is available. Equation 3, utilizing the 1,1′-carbonyldiimidazole reagent,[1] makes possible the synthesis of a wide variety of urethans directly from the corresponding amine and alcohol.

The available literature has yielded only a single report of mesogenic urethans. Verdino and Schadendorff[2] in 1935 condensed a series of aromatic amines with cholesteryl chloroformate and reported that four of their compounds melted to give cloudy liquids which cleared upon further heating. Table I includes data for these compounds.

2 RESULTS

By the method of equation 2, we have prepared a series of cholesteryl urethans whose transition data are given in Table I. Using equations 1 and 2, a series of N-*para*-methoxyphenylurethans of several 3β-hydroxy-steroids was prepared; these data are presented in Table II. For the most part the

compounds in Table I and II exhibit twisted nematic (cholesteric) mesophases.

Twenty-five other urethans were prepared by the synthetic routes of equations 1 and 3, but mesomorphic behavior was not observed. The data for these compounds are given in Tables III and IV. In addition, several urea derivatives were prepared in a search for mesogenicity in this system, but without success. The data for these aryl urea derivatives are given in Table V.

3 DISCUSSION

The cholesteryl urethans are arranged in Table I in order of increasing mesophase-to-isotropic temperature, the so-called clearing point. At this temperature, the long-range intermolecular forces responsible for the ordered liquid are overwhelmed by thermal energy effects and the mesophase is destroyed. The clearing point is thus a useful measure of the thermal stability of the mesophase. Note that with respect to thermal stability, it does not matter whether the clearing point lies above or below the crystal-to-liquid point, i.e., whether the mesophase is enantiotropic or monotropic.

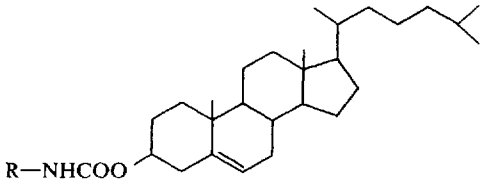
The data in Table I reveal that, with one exception, all the urethans have crystal-to-mesophase points above 100° and exhibit the twisted nematic (cholesteric) phase. The lowest melting urethan, **2** ($R = C_{16}H_{33}$), is also the only one to possess a smectic phase. In many mesogenic systems, smectic behavior is found in compounds having terminal alkyl groups longer than heptyl or octyl.[4] However, the corresponding *n*-octyl urethan, **1**, possesses only a monotropic cholesteric phase with a clearing point of 76°, while the *n*-butyl and cyclohexyl analogs, **13** and **15**, respectively, are non-mesogenic. These latter two compounds, with melting points of 125° and 159°, respectively, could not be supercooled very far. By analogy with **1** and **2**, one might expect to find a mesophase below *ca.* 80° for the cholesteryl N-alkyl urethans.

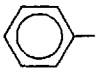
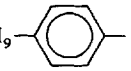
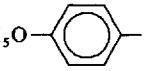
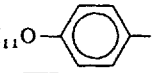
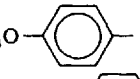
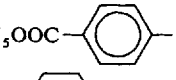
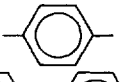
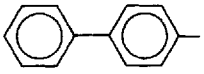
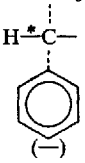
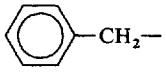
Consideration of the clearing points of compounds **1–11** indicates a correlation of mesophase stability with increasing molecular polarizability. The alkyl urethans **1** and **2** have the lowest mesophase stability as measured by the clearing point. The N-substituted benzene ring, **3**, with its polarizable π-electrons raises the clearing point some 65°. Addition of groups possessing unshared electrons to the *para*-position of the aromatic ring, compounds **5–11**, increases the polarizability of the π-system and results in clearing points some 35 to 90° higher than the parent benzene compound, **3**. In line with this reasoning, a *para-n*-butyl group, **4**, having no unshared electrons to contribute to the π-system, has only a slight effect on the clearing point.

The absence of mesogenic behavior in the α-phenylethyl and benzyl urethans, **12** and **14**, indicates the profound effect of a saturated carbon

TABLE I

Transition temperature data for some N-substituted Cholesteryl Carbamates, in order of increasing clearing point[a]



Compound No.	R[b]	Phase transitions and temperatures[c]
1	C_8H_{17}—	K 104 I (76 C)
2	$C_{16}H_{33}$—	K 60 S 79 C 81 I
3		K 170 I (146 C)[d]
4	C_4H_9— 	K 150 I (149 C)
5	C_2H_5O— 	K 140 C 180 I[e]
6	$C_5H_{11}O$— 	K 164 C 180 I
7	Br— 	K 182 C 186 I[e]
8	CH_3O— 	K 155 C 194 I
9	C_2H_5OOC— 	K 191 C 194 I[e]
10	O_2N— 	K 202 C 208 I[e]
11		K 185 C 235 I
12		m.p. 122–123
13	C_4H_9—	m.p. 124–125
14		m.p. 145–146
15	*cyclo*-C_6H_{11}—	m.p. 158–159

[a] All compounds gave satisfactory elemental analyses.

[b] Alkyl groups are normal unless otherwise indicated.

[c] The linear notation is described in ref. 3.

[d] G. L. O'Connor and H. R. Nace [*J. Amer. Chem. Soc.*, **75**, 2118 (1953)] report only m.p. 168.5–169° for this compound.

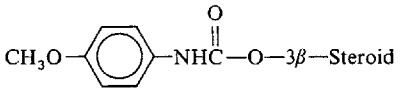
[e] Ref. 2.

atom in introducing conformational flexibility, an effect which has been noted in other systems.[5,6]

In order to examine the effects on mesogenicity of structural variations of the steroid moiety in the present series, the N-*para*-methoxyphenylurethans of the following steroids were prepared. The data are given in Table II.

TABLE II

Phase transition data for N-*para*-methoxyphenylcarbamates of some 3β-steroids[a]

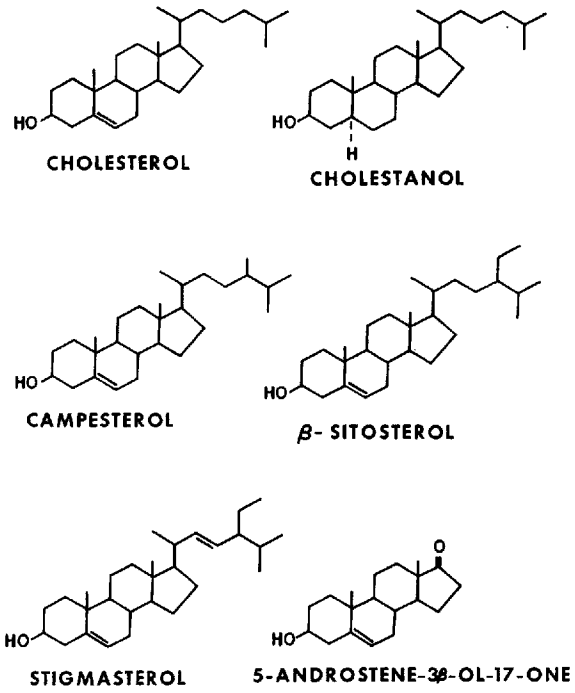


Compound No.	Steroid moiety	Transition data[b]	Cholesteric range, Δt, °C
8	Cholesterol	K 155 C 194 I	39
16	Cholestanol	K 136 C 176 I	40
17	Stigmasterol	K 150 C 155 I	5
18	β-Sitosterol	K 141 C 143 I	2
19	Campesterol	K 122 C 126 I	4
20	Dehydroepian-drosterone (5-Androstene-3β-ol-17-one)	m.p. 195–197	0

[a] All compounds gave satisfactory elemental analyses.
[b] The linear notation is described in ref. 3.

The steroids utilized all possess a 3β-hydroxyl group and, with the exception of cholestanol, all have the basic cholesterol ring geometry. Cholesterol differs from cholestanol only by the absence of the 5,6-double bond in the latter. It is a striking coincidence that the loss of the 5,6-double bond on going from the cholesteryl urethan, **8**, to the cholestanyl analog, **16**, results in a lowering of both the crystal-to-cholesteric and cholesteric-to-isotropic phase transitions, Table II, by essentially equal amounts, *ca.* 20°, so that the breadth of mesomorphic ranges are almost identical. This is in general agreement with the findings of Wiegand[7] for a series of *para*-substituted benzoates of these two steroids. The presence or absence of the 5,6-double bond does not seem to be crucial for mesophase formation.

On the other hand, the effects of relatively small structural perturbations in the steroid side chain have profound effects on mesophase formation. The β-sitosteryl and campesteryl urethans, **18** and **19**, differ structurally from the cholesteryl derivative, **8**, only by the presence of an ethyl group (β-sitosterol) and a methyl group (campesterol) at C-24. The configuration



at this carbon is **R** in both steroids. The clearing points of **18** and **19** are, respectively, 51° and 69° below that of the corresponding cholesteryl urethan. Also, their cholesteric ranges are quite narrow, 2° and 4°, respectively. An interesting comparison, whose origin is presently obscure, may be made. Unlike cholesterol, the closely related β-sitosterol and campesterol are not metabolized by the higher animals even though they have the same stereochemical configuration at all the ring carbons and differ in structure only near the end of the 17β-side chain.

Introduction of a double bond at C-22 in the β-sitosterol skeleton gives stigmasterol. The stigmasteryl urethan, **17**, has a clearing point some 12° higher than the β-sitosteryl analog, **18**, and a cholesteric range of 5°, compared to 2° for **18**. A double bond in an aliphatic side chain introduces two factors simultaneously; polarizable π-electron density and rigidity, both of which are well known to enhance mesophase formation. Pohlmann, Elser, and Boyd[8–11] have reported several elegant studies of structural alterations on the 17β-side chain of aliphatic esters of cholesterol. Our data in Table II for the steroidal urethans are too limited to allow firm conclusions to be drawn about structural effects in this system. However, many of the comparable compounds show similar trends in mesophase

stability to those studied by Pohlmann, Elser, and Boyd. We also find that mesogenic character is lost when the 17β-side chain is replaced by a keto function[9] as in the 5-androstene-3β-ol-17-one urethan, **20**. However, in contrast to the alkyl esters,[8,10] we observe for the steroidal N-*para*-methoxyphenyl urethans, only enantiotropic cholesteric phases for the stigmasterol, β-sitosterol, and campesterol derivatives.

Synthesis of other urethans and of some urea derivatives

The urethan linkage as a central group in mesogenic compounds, in addition to the steroid series described above, was explored by the preparation of twenty-five urethans excompassing a fairly broad spectrum of molecular structures. By analogy with the structures of known mesogens containing the ester, acetylenic, azomethine, azoxy, etc. linkages, we expected to observe mesomorphic behavior in at least some of the derivatives but none was found. The data are given in Tables III and IV.

Several urea derivatives were also synthesized in a brief search for mesogenicity in this system but only relatively high melting compounds were obtained. The data are given in Table V.

Experimental section

Chemical purity is an extremely important factor affecting mesophase formation, particularly in the case of steroids which are isolated from natural sources. The purity of starting materials and derivatives were determined by both thin layer and vapor phase chromatography.

TLC. Two-dimensional TLC was found to afford good separation of the steroidal urethans. The sample was applied to one corner of a 20 × 20 cm plate of silica gel GF 254 and developed first with ethyl acetate-heptane (1.8:1) and in the second direction with aceton-heptane (1.3:1). Visualization was obtained by spraying with acetic anhydride-sulfuric acid (1:1) and heating.

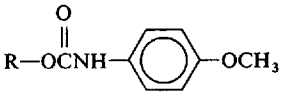
VPC. The instrument used was a Hewlett-Packard Model 5750 with flame ionization detector, modified for on-column injection. The columns were 1 m × 4 mm stainless steel. The liquid phase was OV-1, 3% on 100/120 Gas Chrom Q (Applied Science Laboratories, State College, Pa.).

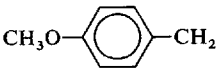
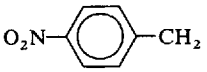
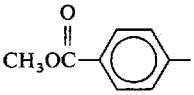
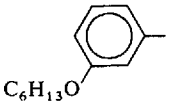
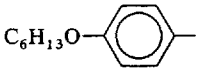
Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

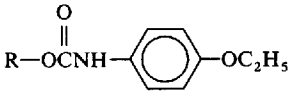
Mesophases were determined with a 100-power AO Spencer polarizing microscope equipped with a variable temperature stage designed in these

TABLE III

Non-mesogenic urethans prepared in the present study[a]



R	m.p., °C
	93–94
	137–139
	145–147
	94–95
	146–148



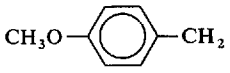
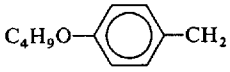
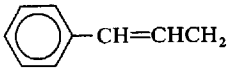
R	m.p., °C
	94–96
	109–110
	121–122

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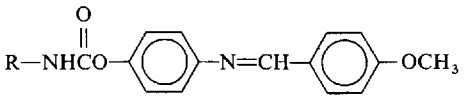
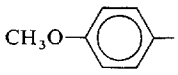
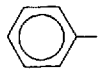
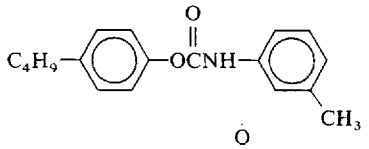
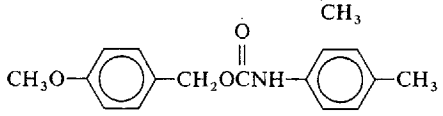
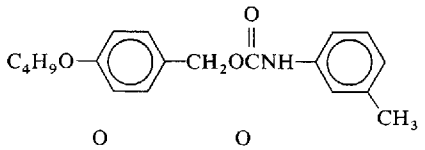
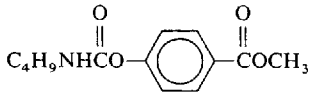
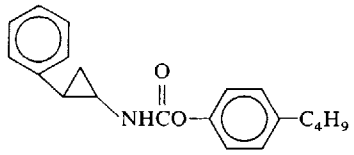
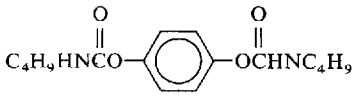
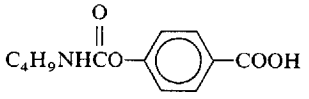
TABLE III (*Continued*)

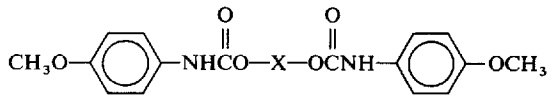


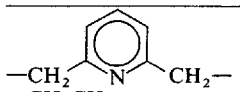
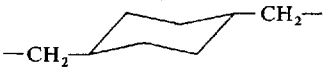
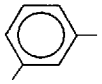
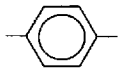
R	m.p., °C
C_8H_{17}—	106–108
	143–145
	143–145
	75–77
	87–88
	88–90
	95–96
	121–123
	195–197
	225–227

[a] All compounds gave satisfactory elemental analyses. Alkyl groups are normal.

TABLE IV

Non-mesogenic *Bis*-urethans prepared in the present study[a]



X	m.p.,°C
	170–172
$-CH_2CH_2-$	172–173
$-CH_2C{\equiv}CCH_2-$	184–186
	218–220
	224–226
	240–242
	240–242

[a] All compounds gave satisfactory elemental analyses.

laboratories.[12] For mesogenic compounds, the temperatures reported are those at which the solid or mesophase has just disappeared. Temperatures are corrected.

Purification of steroids

Cholesterol Purified by formation of the 5α,6β-dibromide and subsequent regeneration of cholesterol by Zn dust in refluxing ether,[13] m.p. 148–149°.

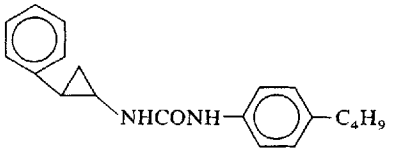
Cholestanol Prepared from the above purified cholesterol by hydrogenation in acetic acid over platinum oxide.[14] After drying *in vacuo* at 100°, the cholestanol had m.p. 141.5–142°.

β-Sitosterol β-Sitosterol (Sigma Chemical Co.) was purified through the acetate as described by Pohlmann.[8] After recrystallization from ethanol and drying *in vacuo* at 100°, the β-sitosterol had m.p. 137.5–139°. It was identical in all respects to a sample kindly supplied by Dr. Pohlmann.

Campesterol The purified steroid was a generous gift from Dr. Pohlmann,[10] m.p. 157–158°.

TABLE V

Non-mesogenic urea derivatives prepared in the present study[a]

R	m.p.,°C
$C_8H_{17}OC(=O)-$	140–142
$C_2H_5(CH_3)\overset{*}{C}HCH_2OC(=O)-$	152–154
C_4H_9-	198–200
$C_2H_5(CH_3)\overset{*}{C}HCH_2OC(=O)-C_6H_4-NHCONH-C_6H_4-OCH_3$	129–131
$H_3C-C_6H_3(-NHCONH-C_6H_4-C_4H_9)$	138–141
	146–148

[a] All compounds gave satisfactory elemental analyses. Alkyl groups are normal.

Stigmasterol Stigmasterol (Sigma Chemical Co.) was recrystallized repeatedly from ethanol. After drying *in vacuo* at 100°, it had m.p. 168–170°. Typical preparations according to equations 1, 2, and 3 (Introduction) are given below.

Campesteryl N-*para-methoxyphenylcarbamate* (**19**) Campesterol (2.00 g, 5 mmol) was dissolved in 30 ml of dry benzene in a 100-ml flask equipped with a magnetic stirrer, reflux condenser, and $CaCl_2$ drying tube. Two drops of pyridine and a slight excess of *para*-methoxyphenylisocyanate (Eastman Kodak, 0.90 g, 6 mmol) was added and the mixture was refluxed for 5 hr. The solvent was then removed on the rotary evaporator, the residue taken up in 15 ml of hot $CHCl_3$, treated with decolorizing charcoal, filtered,

and the filtrate reduced to *ca.* 1 ml. The concentrated solution was diluted with 20 ml of ligroin (60–70°) and allowed to crystallize. A second recrystallization from ligroin yielded white crystals of **19**, 1.45 g, 53% yield, K 122 C 126 I.[3]

Anal Calc. for $C_{36}H_{55}O_3N$: C, 78.64; H, 10.08; Found: C, 78.49; H, 9.98.

Cholesteryl N-*para-n-butylphenylcarbamate* (**4**) Freshly distilled *para-n*-butylaniline (Eastman Kodak, 1.49 g, 10 mmol) was dissolved in 50 ml of dry benzene containing 1.0 g pyridine (12 mmol) in a 125-ml flask equipped with a pressure-equalizing dropping funnel, magnetic stirrer, and $CaCl_2$ tube. A solution of cholesteryl chloroformate (Aldrich, 4.49 g, 10 mmol) in 25 ml of benzene was added dropwise and the mixture was then stirred at room temperature for 20 hr. The solution was filtered and the filtrate washed with two 25 ml portions of water and then dried over Na_2SO_4. The solvent was then removed on the rotary evaporator and the residue recrystallized from hexane to give **4** as a white solid, 3.68 g, 66% yield, K 150 I (149 C).

Anal Calc. for $C_{38}H_{59}O_2N$: C, 81.23; H, 10.58; Found: C, 80.95; H, 10.49.

Bis-1,4-phenylene N-*para-methoxyphenylcarbamate* A solution of *para*-anisidine (Eastman Kodak, 0.62 g, 5 mmol) in 20 ml of dry THF was added dropwise to a stirred solution of 1,1′-carbonyldiimidazole (Aldrich, 0.81 g, 5 mmol) in 40 ml THF. After stirring for 1.5 hr at room temperature, a white ppt appeared. A solution of 0.27 g of hydroquinone (2.5 mmol) in 20 ml THF was then added dropwise and the mixture stirred for an additional 40 hr. The mixture was filtered, the filtrate diluted with 30 ml of benzene, washed with water and dried (Na_2SO_4). After removal of the solvent on the rotary evaporator, the residue was recrystallized from benzene-ethanol to give *bis*-1,4-phenylene N-*para*-methoxyphenylcarbamate, 0.84 g, 40% yield, m.p. 240–242°.

Anal Calc. for $C_{22}H_{20}O_6N_2$: C, 64.70; H, 4.94; Found: C, 64.50; H, 4.91.

1,3-(*para*-Octyloxycarbonylphenyl)urea

n-octyl para-aminobenzoate The ester was prepared by refluxing a solution of 33 g (0.25 mol) of *n*-octanol, 13.7 g (0.10 mol) of *para*-aminobenzoic acid, 7 g of concentrated H_2SO_4 in 150 ml of dry benzene until the theoretical amount of water had been collected (Dean–Stark trap). The benzene solution was then poured into 100 ml of water and made basic with Na_2CO_3. The

benzene layer was separated, dried over Na_2SO_4, and the solvent removed. The solid ester was recrystallized from hexane, yield 21.2 g (85%), m.p. 67–68°.

Anal Calc. for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30; Found: C, 72.07; H, 9.18.

The above aminoester (2.49 g, 10 mmol) in 25 ml of dry THF was added dropwise to a solution of 1,1′-carbonyldiimidazole (Aldrich, 0.81 g, 5 mmol) in 50 ml of THF. The mixture was stirred overnight at room temperature and the solvent then evaporated to give a solid which was taken up in benzene, washed with water, dried (Na_2SO_4), and the solvent removed under vacuum. The resulting white solid was recrystallized from benzene to give 1,3-(*para*-octyloxycarbonylphenyl)urea, 1.9 g (36% yield), m.p. 140–142°.

Anal Calc. for $C_{31}H_{44}O_5N_2$: C, 70.96; H, 8.45; Found: C, 71.22; H, 8.59.

Acknowledgement

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References

1. H. A. Staab, *Angew. Chem. Int. Edit. English*, **1**, 351 (1962); A. H. Staab and W. Rohr, *Newer Methods of Preparative Organic Chemistry*, **5**, 61 (1968).
2. A. Verdino and E. Schadendorff, *Monatsh. Chem.*, **65**, 141 (1935).
3. L. Verbit, *Mol. Cryst. and Liq. Cryst.*, **15**, 89 (1971).
4. G. W. Gray, *Molecular Structure and the Properties of Liquid Crystals*, Academic Press, New York, N.Y., 1962, chapter 8.
5. Ref. 4, chapter 9.
6. L. Verbit and R. L. Tuggey, *Mol. Cryst. and Liq. Cryst.*, **17**, 49 (1972).
7. C. Wiegand, *Z. Naturf.*, **4B**, 249 (1949).
8. J. L. W. Pohlmann, *Mol. Cryst. and Liq. Cryst.*, **8**, 417 (1969).
9. J. L. W. Pohlmann, W. Elser and P. R. Boyd, *Mol. Cryst. and Liq. Cryst.*, **13**, 243 (1971).
10. W. Elser, J. L. W. Pohlmann and P. R. Boyd, *Mol. Cryst and Liq. Cryst.*, **13**, 255 (1971).
11. J. L. W. Pohlmann, W. Elser and P. R. Boyd, *Mol. Cryst. and Liq. Cryst.*, **13**, 271 (1971).
12. L. Verbit and T. R. Halbert, *J. Chem, Educ.*, **48**, 773 (1971).
13. L. F. Fieser, *Org. Syn.* Coll. Vol. **4**, 195 (1963).
14. W. F. Bruce and J. O. Ralls, *Org. Syn.* Coll. Vol. **2**, 191 (1943).