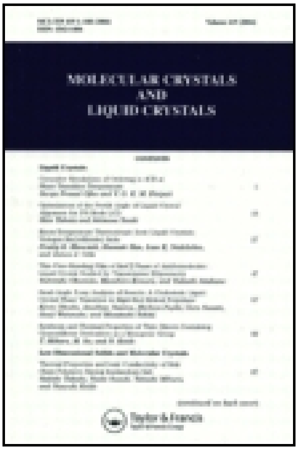

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A Convenient Synthesis of 4-(trans-4'- n-alkylcyclohexyl) Benzoic Acids

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A Convenient Synthesis of 4-(trans-4′-*n*-alkylcyclohexyl) Benzoic Acids

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A convenient method of obtaining 4-(trans-4′-*n*-alkylcyclohexyl) benzoic acids from alkanoyl chlorides, cyclohexene and benzene is described. Homologous series of above mentioned acids and their nitriles with alkyl tail 2 to 10 carbon atoms were prepared and temperatures of their phase transitions were determined.

INTRODUCTION

Ever since Schubert *et al.* described in 1975 trans-4-*n*-alkylcyclohexane-1-carboxylic acid esters[1] and Eindenschink *et al.* in 1977 trans-1-*n*-alkyl-4-(4′-cyanophenyl) cyclohexanes (PCH)[2], compounds with hydrogenated benzene, biphenyl and terphenyl rings have been the object of rapidly increasing interest.[3,4] Today that is one of the main lines of developing research as regards the synthesis of new liquid-crystalline compounds. The source of that concern lies primarily in the low viscosity of trans-1, 4-substituted hexane derivatives and to a minor degree in the low anisotropy of the refractive indeces.[3,5]

In our preliminary report we have described a convenient and simple method of obtaining 4-(trans-4′-*n*-alkylcyclohexyl) benzoic acids and their nitriles[6] which is illustrated by the scheme:

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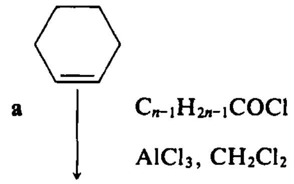

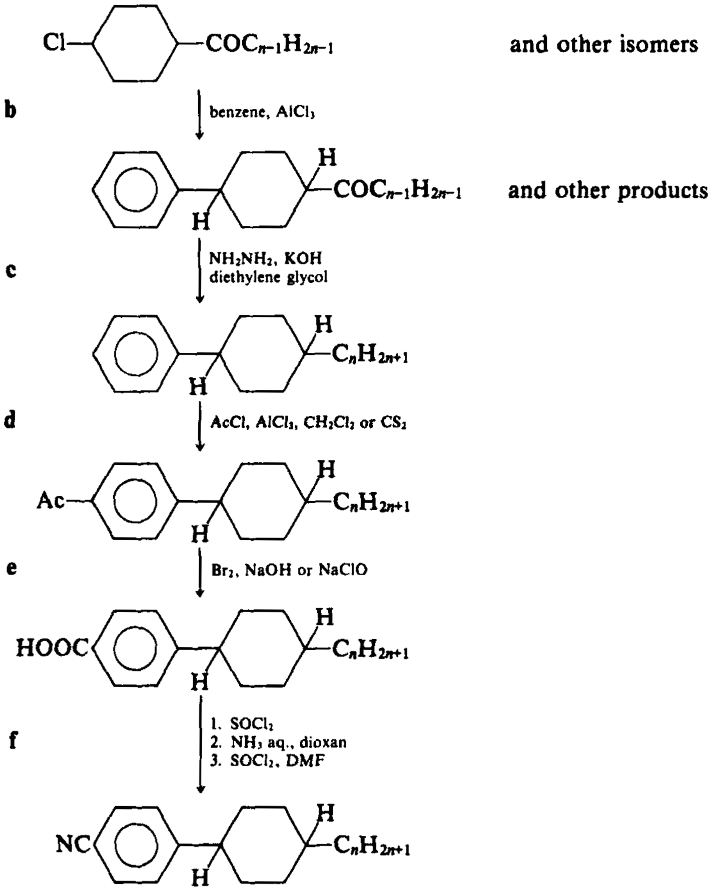

The method is based on the finding of Nenitzescu[7] who studied the reaction of cyclohexene, acetyl chloride and benzene in carbon disulfide in the presence of anhydrous $AlCl_3$ and detected among other products the presence of trans-1-acetyl-4-phenylcyclohexane.

In the present work the usefulness of the method described above for obtaining 4-trans-(4′-*n*-alkyl-cyclohexyl) benzoic acids and their nitriles was tested with respect to the whole homologous series of compounds with an alkyl chain of 2–10 carbon atoms ($n = 2$ to 10), and full details of the preparative procedure being given. In the present authors' opinion the described method is more convenient than that described by Eindenschink *et al.* who used 4-*n*-alkylcyclohexanones as the initial substrates.[2] These substrates were obtained in several steps, where after the reaction with phenyl-magnesium bromide a mixture of cis- and trans-phenylalkylcyclohexanols is obtained which have to be separated chromatographically and subjected separately to hydrogenolysis under different conditions in order to remove the hydroxyl group and convert the product into trans-1-*n*-alkyl-4-phenylcyclohexane. In the procedure adopted by the present authors pure compounds of formula **4** are not isolated, but the raw product obtained in step **c** is subjected to acylations. It is only the ketones **5** that are isolated as pure compounds from advantage being taken of their low solubility. In the farther steps use was made of well known conventional methods of converting methylketones into acid and next into nitriles.

EXPERIMENTAL

Synthesis of trans-1-(4′-acetylphenyl)-4-heptylcyclohexane

(**a**) 1000 ml of dry methylene chloride and 187 g (ca 1.4 mole) of anhydrous $AlCl_3$ were mixed, cooled to about 5–10° when 178.2 g (1.2 mole) enanthoyl chloride were added dropwise. Next, the mixture was cooled to $-10°$ and at that temperature 98.4 g (1.2 mole) of cyclohexene (C_6H_{10}) were added dropwise. When this operation was terminated, cooling was interrupted and the mixture left to get heated to about 10° when it was poured onto crushed ice (2.5 kg.). The organic phase was separated and the aqueous one was extracted with 200 ml of methylene chloride. The combined organic phases were washed twice with 5% HCl, several times with water and dried over anhydrous $MgSO_4$. CH_2Cl_2 was removed on a Rotovap. The dark, oily residue was diluted in the flask with 100 ml benzene and evaporated again to remove the solvent with residual methylene chloride.

(**b**) 1000 ml of dry benzene and 187 g (1.4 mole) of anhydrous $AlCl_3$ were mixed thoroughly in a flask placed on a water bath. Next, the product of cyclohexene acylation obtained in step **a** was slowly added (1.5 hour) dropwise. Gaseous HCl was evolved and the temperature was increased automatically to about 35°. Then the mixture was heated for 4 hours at 45–50°, cooled, poured onto ice, the organic layer was separated and washed with 5% HCl, several times with water. Excess benzene was removed on a Rotovap. The resultant dark, oily liquid contains trans-1-enanthoyl-4-phenylcyclohexane.

(**c**) 1200 ml diethylene glycol, 225 g (ca 4 moles) KOH, 310 g (ca. 5 moles) 80% hydrazine hydrate and product from step **b** were refluxed for 1 hour, the temperature was then slowly raised and the volatile components have been distilled off until the temperature in the flask achieved 220°. The distillation condenser was replaced by a reflux one and refluxing was continued for 1 hour. After cooling the mixture was diluted with water and the hydrocarbons were extracted with hexane (twice with 500 ml portions). The extract was washed with water, diluted 5% H_2SO_4 and the 75–80% H_2SO_4. During washing 80% H_2SO_4 extract was darkened and dark resinous substances were precipitate. After refining with sulfuric acid (repeated 3–4 times) the hydrocarbon **4** solution was washed with water to a neutral reaction, dried over anhydrous $MgSO_4$, then hexane was removed on a Rotovap. The residue, a yellow oily liquid in a quantity of 252 g was distilled under reduced pressure using a 40 cm Vigreux column. Three fractions were collected:

I in the range 80–122°/0.05 mm Hg: in an amount of 12 g containing about

50% trans-1-heptyl-4-phenylcyclohexane,

II in the range 122–133°/0.05 mm Hg: in an amount of 19 g containing about

55% of trans-1-heptyl-4-phenylcyclohexane,

III in the range 133–138°/0.05 mm Hg: in an amount of 130 g containing about

70% of trans-1-heptyl-4-phenylcyclohexane.

(d) The mixture of 600 ml of dry methylene chloride and 89 g (0.66 mole) of anhydrous $AlCl_3$ was cooled to 5–10° when 46 g (0.59 mole) of acetyl chloride was added dropwise. Next the temperature was lowered to 0° and 130 g of hydrocarbon **4** (IIIrd fraction obtained in step **c**) were added slowly (1.5 hour) dropwise. When the adding was concluded, mixing was continued for about 3 hours at 0°. The contents were then poured onto ice and the organic layer was separated. The aqueous phase was extracted with 100 ml of methylene chloride and the extract was added to the main fraction. The organic phase was washed with 5% HCl, water and then dried over anhydrous $MgSO_4$. CH_2Cl_2 was distilled off on a Rotovap. The yellow, solidifying oil obtained was twice crystallized from methanol: 87 g of trans-1-(4′-acetylphenyl)-4-heptylhexane were obtained in the form of white flakes, m.p. 63.5–64.5°, yield 24.1% with respect to enantoyl chloride used in step **a**.

IR (KBr), 830 cm^{-1}(intense, para- substituted benzene ring) and 1675 cm^{-1} (C═O, intense).

The acetylphenyl derivatives of other alkylcyclohexanes were obtained in a similar way. Their melting points and elementary analyses are summarized in Table I.

TABLE I

Phase transition temperatures and the results of combustion analysis of the compounds **4**, **5**, **6**

Compound	**4**		**5**					**6**				
				Combustion data					Combustion data			
				calculed %		found %			calculed %		found %	
C_nH_{2n+1}	b.p. (°C/mmHg)	% hydrocarbon **4** in fraction III	m.p. (°C)	C	H	C	H	Phase transition (°C)	C	H	C	H
C_3H_7	75–80/0.05	85	50.0–50.5	83.55	9.90	83.24	10.19	K 217 N 275 I	78.01	9.00	77.67	9.15
C_4H_9	85–90/0.05	80	72–73	83.67	10.14	83.68	10.12	K 201 N 265 I	78.42	9.29	78.41	9.27
C_5H_{11}	120–125/0.05	70	64–66	83.77	10.36	83.69	10.26	K 180 N 265 I	78.79	9.55	78.58	9.52
C_6H_{13}	122–130/0.05	80	79.5–80.5	83.86	10.56	83.76	10.72	K 169 N 258 I	79.12	9.78	79.10	9.75
C_7H_{15}	133–138/0.05	70	63.5–64.5	83.94	10.74	83.90	10.78	K 161.5 S_1 190.5 N 259 I	79.42	10.00	79.35	10.04
C_8H_{17}	140–155/0.10	80	69–71	84.01	10.90	84.02	10.98	K 147 S_1 211 N 248 I	79.69	10.19	79.64	10.25
C_9H_{19}	138–156/0.05	75	69.5–70.5	84.08	11.05	83.95	11.02	K 129 S_3 160 S_2 174 S_1 222 N 248 I	79.95	10.37	80.17	10.41
$C_{10}H_{21}$	155–165/0.10	55	76–77	84.15	11.18	84.05	11.10	K 114 S_3 161 S_2 182 S_1 218 N 241 I	80.18	10.53	80.11	10.66

Synthesis of 4-(trans-4'-n-heptylcyclohexyl) benzoic acid

(e) 800 g of ice were added to the solution of 192 g (4.8 moles) NaOH in 190 ml water cooled to room temperature. Next 192 g (1.2 mole) Br_2 were added dropwise with strong agitation. A solution of 87 g (0.29 mole) of methylketone **5**, obtained previously, in 350 ml dioxane were added dropwise to the cold solution of sodium hypobromite. The mixture was strongly agitated for about 5 hours when the temperature gradually increased and the contents assumed the form of whipped cream. The mixture is then heated on a water bath to 60–65° and next cooled to room temperature. Excess hypobromite was removed by adding 60 ml of 40% $NaHSO_3$ solution and acidifying the mixture to an acid reaction with hydrochloric acid. The precipitate of acid **6** was filtered, washed several times with water and recrystallized without drying from ethyl alcohol. The procedure yielded 78 g of the acid with phase transition temperatures: K 156–158° N 252° I. A small sample was twice recrystallized from ethanol.

The compound obtained: K 161.5 S_1 190.5 N 259 I. The yield with respect to the ketone was 88.9%.

IR: (KBr), 1650 cm^{-1} (C═O) and 2200–3000 cm^{-1} (broad, —OH).

The phase transition temperatures and elementary analyses of all the acids obtained are summarized in Table I.

(f) 46 g (0.155 mole) of the above obtained acid **6** were refluxed with 42 g (0.35 mole) $SOCl_2$ and a drop of DMF for 2.5 hours. Excess $SOCl_2$ was distilled off and the remainder was diluted with 100 ml of dry dioxane: the solution obtained was added dropwise to 300 ml of 25% aqueous ammonia cooled to 0°. The obtained 45 g of the amide were treated with 38 ml (0.48 mole) $SOCl_2$ in 250 ml of dry DMF. The mixture heats itself and the amide is dissolved. In order to conclude dehydration the solution was further heated for 3 hours at 80° when it was poured into 800 ml of cold water, and the product was extracted with benzene (3X with 200 ml). The extract was washed with water, 5% $NaHCO_3$ and again water. After drying over anhydrous $MgSO_4$ the solution was filtered through a dozen or so centimeter thick layer of silica gel, and the column was washed with benzene.

The eluates were concentrated on a vacuum evaporator, the oil obtained was dissolved in about 300 ml of methanol at 30° and the solution was filtered to remove a small amount of precipitate. The solution was cooled to −20°, the crystals filtered, again dissolved in methanol and heated with a small amount of activated carbon for a dozen or so minutes at the boil. After filtering off the carbon and cooling, 32.5 g of compound **7** were obtained in the form of white needles. The phase

TABLE II

Phase transition temperatures for compounds 7

	Phase transition temperatures (°C)					
	according to Ref. 5			this work		
C_nH_{2n+1}	K → N	S → N	N → I	K → N	S → N	N → I
n-C_3H_7	36		46	42[a]		46
	42[b]		45			
n-C_4H_9	41		40.5			
n-C_5H_{11}	30		55	30		55
n-C_6H_{13}	42		47			
n-C_7H_{15}	30		59	29.5		59
n-C_8H_{17}				36		54.5
n-C_9H_{19}				44		59.0
n-$C_{10}H_{21}$				49	(31.5)	57.5

[a] After distillation the compound melts at 36°, and further crystallization does not affect that temperature.

[b] According to patent (Ref. 9).

transition temperatures were: K 30° N 59° I. The yield with respect to the acid used was 75%. The phase transition temperatures of the remaining compounds obtained of the same homologous series are summarized in Table II.

DISCUSSION AND RESULTS

Synthesis of the compounds

Synthesis method proposed in the present work is simple, and involves easily available and cheap substrates. The intermediates do not have to be of high purity. The compounds with longer and shorter alkyl chains are equally easy to obtain. Process development presents no difficulties. In steps **b** and **c** crude, nonpurified reaction products are used. In step **d** an enriched by distillation hydrocarbon fraction containing on the average 70–85% of trans-1-*n*-alkyl-4-phenylcyclohexane was used with a very good result. Also satisfactory results were obtained when poorer fractions, containing up to 50% of the product **4** were used. Acylation of cyclohexene (step **a**) is best to conduct in methylene chloride or carbon disulfide. In the latter powdered $AlCl_3$ should be used as otherwise more side products are formed due to the insolubility of $AlCl_3$ complexes with acid chlorides in this solvent. The advantage of using CS_2 is the possibility of conducting both steps of the reaction (**a** and **b**) in the same vessel. As soon as step **a** is terminated, benzene is added directly to the mixture and the mixture is heated. The mixture of hydrocarbons obtained in step **c** as a result of reduction of ketones **3** with hydrazine contains several to a dozen or so different compounds in quantities varying from a fraction of percent to a dozen or so percent. This mixture is very difficult to separate, and we did not succeed to separate neither pure trans-1-*n*-alkyl-4-phenylcyclohexane nor any other components by distillation. For isolation of the fraction enriched in trans-1-*n*-alkyl-4-phenylcyclohexane a 40 cm Vigreux column was used, and the distillation was conducted very slowly. Hydrocarbons with alkyl chains longer than C_8 to C_{10} were distilled from the postreaction mixture without using the Vigreux column. In all cases a considerable amount of poorly volatile substances remained in the flask. The first pure substance was obtained after the mixture obtained in step **c** was acylated. Pure trans-1-(4′-acylphenyl)-4-*n*-alkylcyclohexanes are obtained by crystallizing the product obtained in step **d** from methanol or ethanol. In all cases the methylketones **5** were obtained with a yield of 20–25% with respect to the acid chloride used for reaction in step **a**.

Mesomorphic properties

All the methylketones of formula **5** obtained in the present work are nonmesomorphic, however, the acids derived from them reveal such properties (Table I and Figure 1b). The melting points and clearing points observed for the studied homologous series of the 4-(trans-4′-*n*-alkylcyclohexyl) benzoic acids are similar to those observed for the 4-*n*-alkylphenylbenzoic acid homolgous series,[8] but the abilities to form smectic phases are different in both series of acids. The 4-(4′-*n*-alkylphenyl) benzoic acids are stronger smectogenous: the smectic phase is observed for the compound with C_4 alkyl: for the compound with C_5 alkyl, which was repeatedly tested, two smectic phases were observed (K 176° S_2 205° S_1 258° N 268 I†) and they exist in a wide temperature range. In the 4-(trans-4′-*n*-alkylcyclohexyl) benzoic acid homologous series the smectic phase exists only for the compound with C_7 alkyl and higher: for compounds with C_9 and C_{10} alkyls three different smectic phases were observed, the transition $S_2 \rightarrow S_1$ being best visible. The textures observed under a polarizing microscope are not very characteristic so it is difficult to conclude about the kind of the observed smectic phase, and for their identification X-ray studies are more suitable.

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† According to (8) the phase transition temperatures for that compound are K 176 S 243 N 268 I.

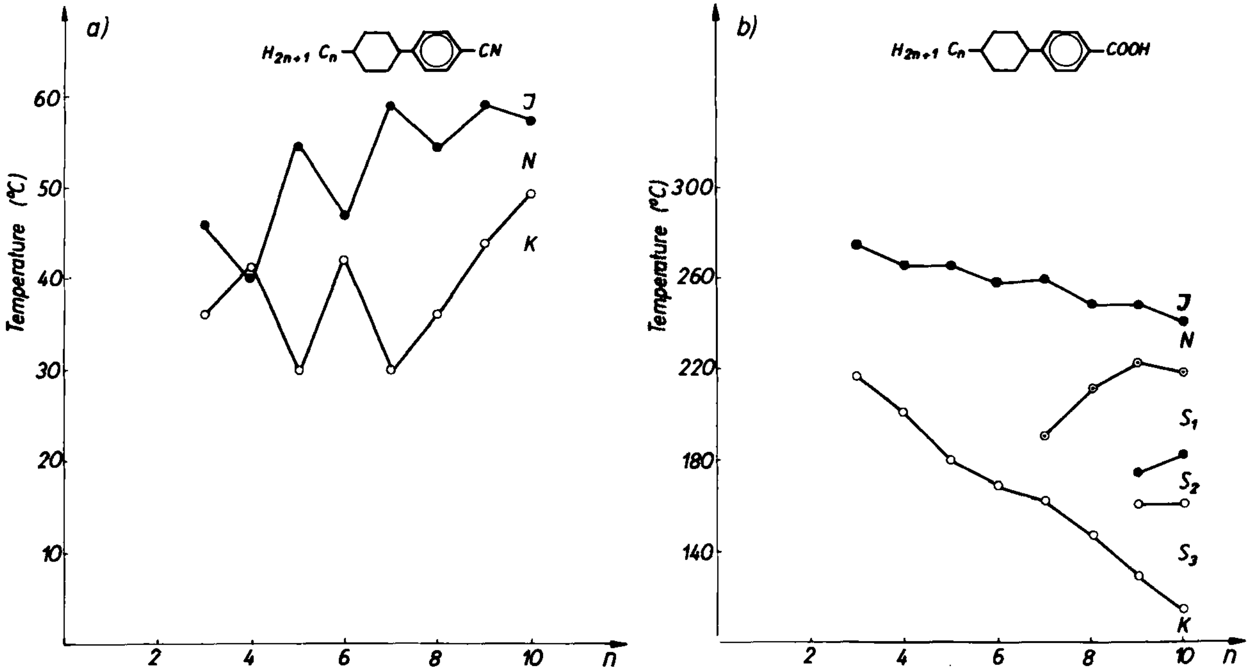

FIGURE 1 Plot of transition temperatures against alkyl chain length (*n*) for trans-1-*n*-alkyl-4-(4′-cyanophenyl) cyclohexanes (a) and 4-(trans-4′-*n*-alkylcyclohexyl) benzoic acids (b).
K = crystal, S_3, S_2, S_1 = smectic, N = nematic and I = istropic phase.

The lower smectogenic ability of molecules containing at the same time a benzene ring and a cyclohexane one as compared to molecules with two benzene rings finds also confirmation in the properties of compounds of the trans-4-(4′-cyanophenyl) alkylcyclohexane homologous series. The melting and clearing points of compounds with C_3, C_5 or C_7 alkyl obtained by the above described method are in agreement with those given in Refs. 2, 5, and 9, whereas the monotropic transition to the smectic phase in the compound with C_7 alkyl prepared by us has not been observed.

A monotropic transition to the smectic phase was observed by us for the compound with the C_{10} alkyl radical (Table II, Figure 1a). In 4-alkyl-4′-cyanobiphenyl the monotropic smectic phase exist for C_7, for C_8 an enantiotropic smectic phase is observed, and for C_{10} only the smectic phase exists,[10] since trans-4-(4′-cyanophenyl)-decylcyclohexane is a nematic only with a monotropic smectic phase. Probably the benzene-cyclohexane system of rings affects in a greater degree the regularity of the liquid-crystalline molecule than the benzene-benzene ring system. Intermolecular forces are weaker in the former compounds so the smectic phases are formed with greater difficulty. Both kinds of compounds can also differ as regards the structure and stability of the dimers formed. That conclusion finds justification also in the lower viscosity of phenylcyclohexane derivatives as compared with the biphenyl ones.

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