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Synthesis and Liquid Crystalline Phases of Pyridazine Derivatives II

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Four more pyridazine compounds were synthesized. The compounds have a general structure R-X-Y-Z-R′; where Y is 3, 6 disubstituted pyridazine ring, X and Z are either *trans* cyclohexyl or phenyl rings, R and R′ are n-alkyl groups. The structure assignments were confirmed by carbon 13 NMR. Their liquid crystalline properties were evaluated. When both X and Z are cyclohexyl rings, the compounds have a single smectic b phase. However, if a phenyl ring is introduced into the system, the morphology becomes complicated.

Keywords: synthesis, pyridazine, smectic, classification

INTRODUCTION

In our previous paper,[1] we discussed the synthesis and liquid crystalline behavior of three ring center core pyridazine compounds with general structure R-X-Y-Z-R′; where X is a cyclohexyl ring, Y could either be a cyclohexyl or a phenyl ring, and Z is a pyridazine ring. We also mentioned the possibility of simplifying the smectic phase transitions by substituting the phenyl ring with another cyclohexyl ring, but we had only one example and we needed to have more compounds synthesized and evaluated before we could draw any conclusions.

It is also very interesting to see what would be the liquid crystalline behavior if the pyridazine ring were moved to the Y position. Therefore a series of compounds with the general structure R-X-Y-Z-R′, where Y is a pyridazine ring and X and Z are either cyclohexyl or phenyl rings, were synthesized and their liquid crystalline behavior evaluated.

SYNTHESIS

The synthesis method we used can be divided into three major steps:

1) The preparation of methyl ketones with the desired structure.
2) The activation of the methyl groups in order to connect them together.
3) The preparation of hydroxy diketone by aldo condensation, and its cyclization with hydrazine to make the pyridazine compound.

Using 3-(4-n-pentyl-*trans*-cyclohexyl) 6-(4-n-butyl-*trans*-cyclohexyl) pyridazine, Tek# 2119 as an example, the method is represented as follows:

1) The scheme of the preparation of 4-n-alkyl *trans*-cyclohexyl methyl ketone is described in Figure 1. The main point here is to make sure the alkyl and the carbonyl groups are at the *trans* positions. The hydrogenation of 4-alkylbenzoic acid (I) gives a mixture of *cis*- and *trans*- alkylcyclohexane carboxylic acid with *cis*-isomer as the dominating product (II). But it is easy to isomerize the *cis*-isomer into *trans*-isomer (III) by using the methods reported by I. Takashi et al.[2] The *trans* nitrile (VI) is made by dehydration of the amide. Reaction of nitriles with a grignard agent is a well known synthetic route leading to ketimines which can be easily hydrolyzed to give ketones (VII).[3]

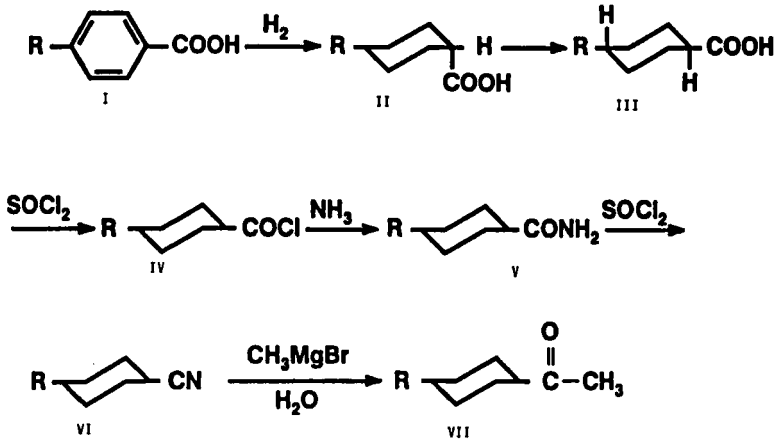

FIGURE 1

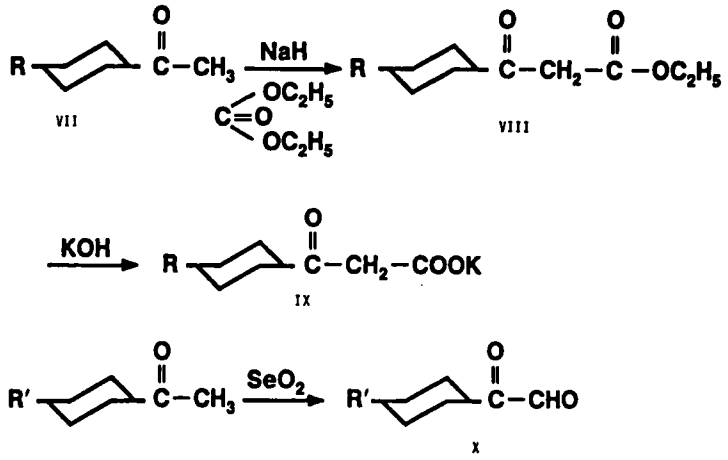

FIGURE 2

2) The processing steps for the activation of the methyl groups are represented in Figure 2. The ketoester (VIII) is obtained by condensation of the 4-alkyl-*trans*-cyclohexyl methyl ketone with diethyl carbonate in the presence of sodium hydride using a method similar to that described by S. B. Soloway and F. B. LaForge.[4] The ketoester (it's structure assignment has been confirmed by carbon 13 NMR) is hydrolyzed by potassium hydroxide in a mixture of 1:1 dioxane and water at 0°C and stirring for 3 days into a potassium salt of the ketoacid (IX).

The same (or with a different alkyl group) alkylcyclohexyl methyl ketone can be oxidized by selenium dioxide in dioxane while protected by nitrogen to form a keto-aldehyde (X)., which is extremely unstable and therefore has to be used as formed without purification.

3) The last steps of the synthesis leading to the final pyridazine compound[5] are described in Figure 3. The solution of potassium ketoester (IX) is buffered with carbon dioxide until saturation, and is mixed with the keto-aldehyde at 0°C and stirred 3 days. An adole condensation product is obtained (XI). It loses carbon dioxide when acidified with hydrochloric acid. The crude hydroxy diketone (XII) can be used directly for cyclization reaction without purification. The hydroxy diketone (XII) is reacted with hydrazine monohydrate by refluxing in toluene solution. The crude final product (XIV) is purified by preparative HPLC and recrystallized in hexane. The structure assignment was confirmed by Carbon or C 13 NMR (Figure 4) and its purity was checked by HPLC.

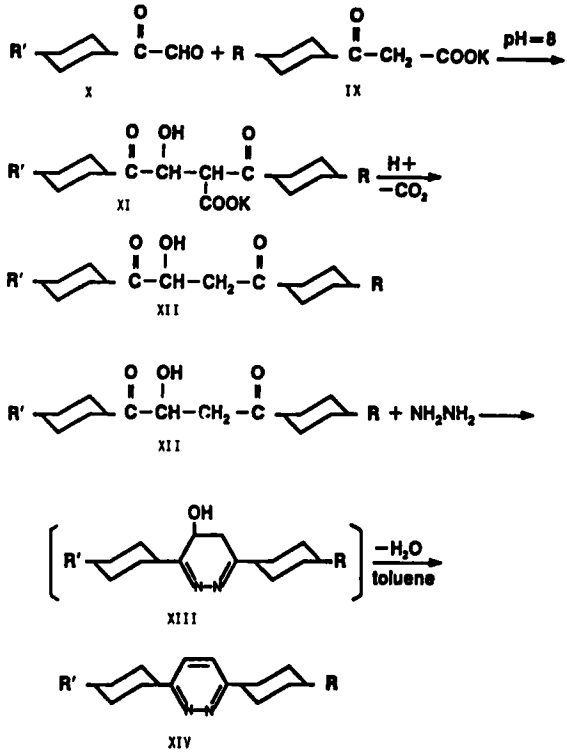

FIGURE 3

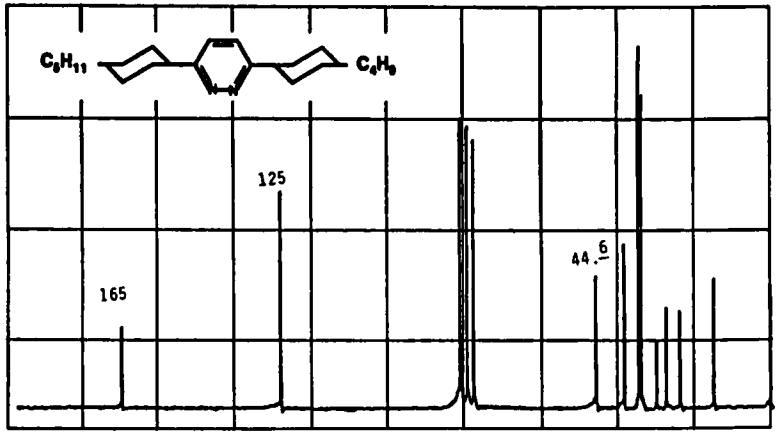

FIGURE 4

RESULTS AND DISCUSSION

Four compounds were synthesized. Their structures, phase transition temperatures and yields are presented in Table I.

Transition temperatures were determined using a differential thermal analyzer (Perkin-Elmer DTA1700 and System 7/4 controller). Temperatures interpolated from the thermograms are within ±1°C. Phase identifications were made by texture observations using a heat stage (Mettler FP80 DSC microscope stage) and an Olympus polarizing microscope.

Material 2117, 2118 and 2119 were all found to have the following morphologies:

$$\text{Cryst} \leftrightarrow \text{SmB} \leftrightarrow \text{Is}$$

Material 2122 has a more complicated morphology with two or three mesophases. Thermograms of a first heating and reheated samples are shown in Figure 5. Textures observed on cooling a reheated sample show that the first mesophase is Smectic A. Batonets appear out of the isotropic melt and quickly coalesce into a fan texture. At 165°C, transition bars appear across the fan backs. As the bars fade, a broken fan texture is left (Figure 6-b). This texture takes a few minutes to stabilize, but does not change after 24 hours at 130°C (Figure 6-c). At 60°C on cooling, a subtle texture change occurs throughout the sample (Figure 6-d); the number of faint lines breaking the fans increases slightly. Crystallization occurs at 52°C. No texture change was observed for cryst→II on heating. For a reheated sample of 2122, we propose the morphology:

$$\begin{array}{l} \text{Cryst} \rightarrow \text{I} \leftrightarrow \text{SmA} \leftrightarrow \text{Is} \\ \quad\quad\quad\quad \nwarrow \quad \swarrow \\ \quad\quad\quad\quad\ \ \text{II} \end{array}$$

TABLE I

R-X-Y-Z-R'

TEK#	R	X	Y	Z	R'	MP	MESOPHASE	CLEAR
2117	Propyl	CY	PZ	CY	pentyl	165	Sb	204
2118	Pentyl	CY	PZ	CY	Pentyl	43	Sb	179
2119	Butyl	CY	PZ	CY	Pentyl	87	Sb	173
2122	Pentyl	CY	PZ	PH	Pentyl	83	Sa, II, I	208

CY = cyclohexyl, PH = phenyl, PZ = pyridazine

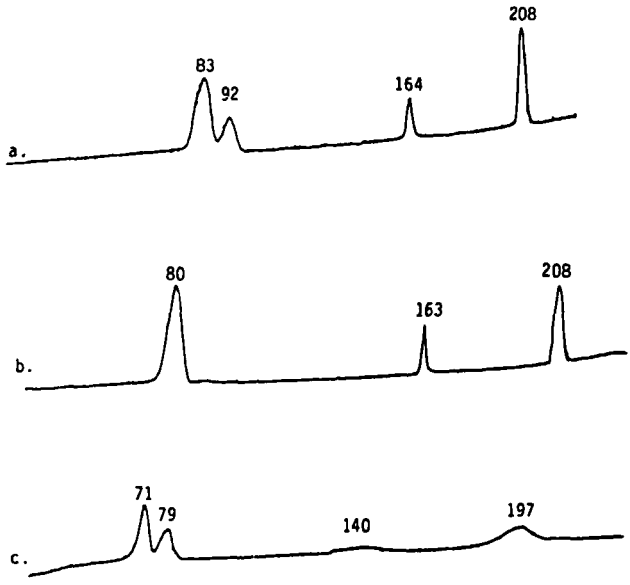

FIGURE 5 Heating Thermograms of 2122. a) First Heating; b) Sample Reheated after Cooling to room temperature; c) Sample reheated after Cooling to −20°C, (Temp. in °C).

The broken fan texture of I, and the SmA ↔ I transition enthalpy of .5Kcal/mol suggest that it may be the Smectic G phase,[6] however further study is required to confirm this.

EXPERIMENTAL

The compounds were purified on a Water 500A preparative HPLC instrument. The structures of the products were established by their carbon 13 and proton NMR spectra taken on a JEOL FX 90 Q Fourier Transform NMR spectrometer and by IR spectroscopy. The purity of the final products was checked on a Perkin-Elmer series 10 HPLC instrument.

trans-4-n-pentylcyclohexyl nitrile (VI): *trans*-4-n-pentylcyclohexan carboxylic acid (III) 5 g, which was made by the same method as I. Takashi, and 5 ml thionyl chloride was dissolved in 100 ml of toluene. The solution was boiled under reflux for three hours. It was concentrated under vacuum to remove all thionyl chloride, and redissolved in toluene. Anhydrous ammonia gas was introduced at room temperature until saturation and the mixture was put aside over night.

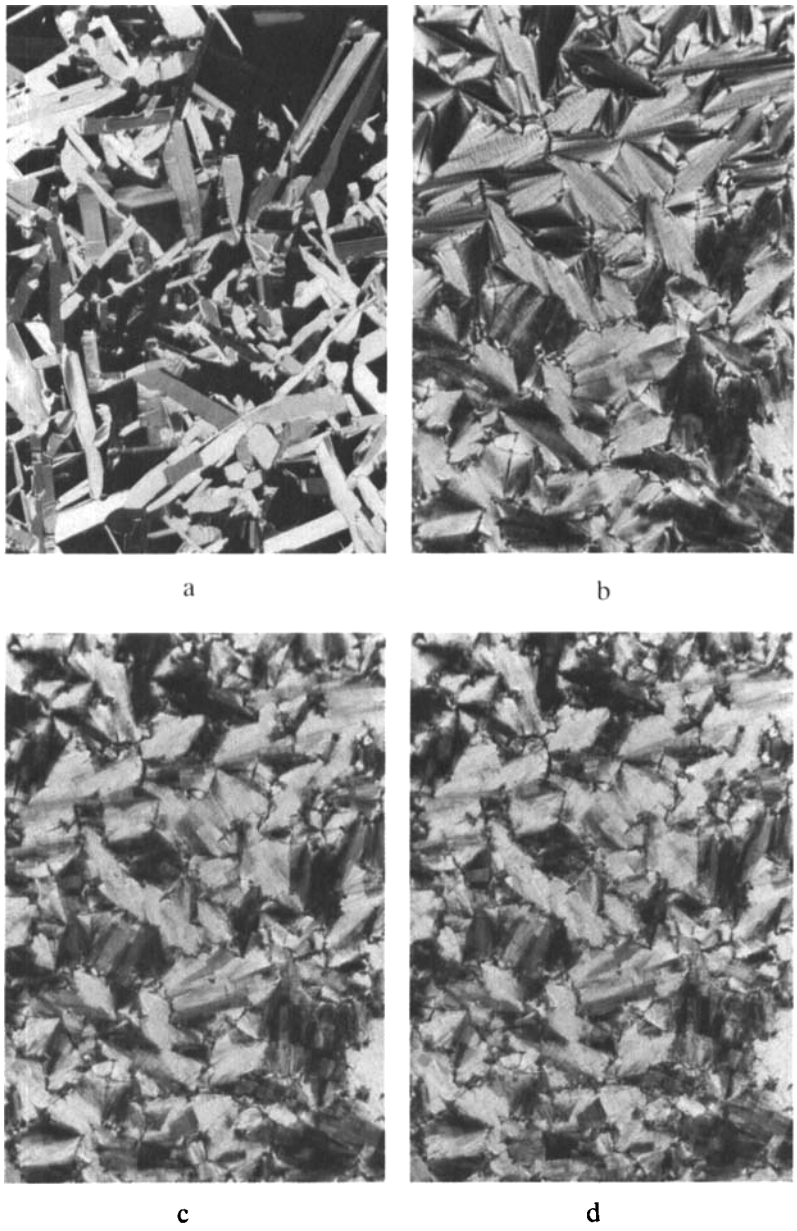

FIGURE 6 Photomixrographs of; a) SmB texture of 2119 @ 200°C, and 2122, b) Sa—I transition, 165°C, c) I after 15 minutes @ 128°C, and d) II at 51°C. All photos taken through crossed polarizers.

Then it was concentrated under vacuum to remove ammonia, and thionyl chloride 5 ml and 70 ml of toluene were added. The mixture was boiled under reflux for 5 hours. It was concentrated under vacuum and about 4.2 g of yellow oil was obtained, IR 2230 (—CN), carbon 13 NMR 122 (—CN), 37, 36, 32, 2*31, 2*29.5, 27.5, 25.5, 22, 13.5 ppm. It was not pure, but could be used directly for the next step. The same method was used for the preparation of 4-n-*trans*butyl-cyclohexane carbonitrile.

4-n-pentylcyclohexyl methyl ketone (VII): methyl magnesium bromide ether solution (Aldrich 2.85 M) 10 ml was added dropwise to the ether solution of 4-n-pentyl-cyclohexane carbonitrile. The mixture was stirred over night under nitrogen. Water was added to decompose the magnesium complex followed by diluted hydrochloric acid until a pH = 1 was achieved. The mixture was then extracted by ether and the ether solution was washed with water and dried over magnesium sulfate. The solution was concentrated and the residue purified by preparative liquid chromatography (normal phase, 25% ethyl acetate in hexane as solvent). About 4 g methyl ketone was obtained, carbon 13 NMR 211.8 (carbonyl), 51.8, 37.2, 3*32.6, 32.2, 2*28.5, 27.8, 26.5, 22.7, 14 ppm. n-Butylcyclohexyl methyl ketone was prepared by the same method.

Ethyl 4-n-pentylcyclohexyl carboxoacetate (IIX): A mixture of 6.5 g sodium hydride, 13 ml diethyl carbonate and 50 ml ether was heated to reflux under nitrogen. A solution of 4-pentylcyclohexyl methyl ketone 5.5 g in 20 ml ether was slowly dropped in over a period of 3.5 hours. The mixture was boiled under reflux for three more hours, cooled down and stirred over night at room temperature. Acetic acid was added until acidic, then water was added. The mixture was then extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. It was then decolorized by charcoal and concentrated. The residue was purified by preparative chromatography (normal phase, 25% ethyl acetate in hexane as solvent). A slightly yellow colored liquid 5.2 g was obtained, carbon 13 NMR 205.8 (ketone), 167.4 (ester). 61.2, 51.3, 47.5, 37.2, 2*32.4, 32.2, 2*28.3, 26.5, 22.7, 14.1 ppm.

3-(4-n-*trans*-butylcyclohexyl) 6(4-n-*trans*-pentylcyclohexyl) pyridazine (XIV): Selenium 0.56 g water 2 ml and 20 ml dioxane were mixed, stirred and heated until the white crystals dissolved. 4-butyl-cyclohexyl methyl ketone 1 g was added. The mixture was boiled under reflux for three hours under nitrogen. After the mixture was cooled, it was diluted with 50 ml dioxane and mixed with the solution of potassium 4-pentyl cyclohexyl carboxo acetate (made from 1.2 g

ethyl pentyl-cyclohexyl carboxo acetate, 0.6 g potassium hydroxide, 5 ml water and 15 ml dioxane. The mixture was hydrolyzed for 3 days at 0–5°C and then saturated by carbon dioxide). The reaction mixture was kept at 0–5°C for four days, then 20% hydrochloric acid 5 ml was added and it was concentrated to remove the dioxane. The residue was dissolved in 50 ml toluene, the toluene solution was washed twice with water and dried over magnesium sulfate. Hydrazine monohydrate 1 ml was added to the toluene filtrate and the mixture boiled under reflux for three hours. The toluene solution was washed twice with water, dried over magnesium sulfate and concentrated. The residue was purified by preparative liquid chromatography (normal phase, 30% ethyl acetate in hexane as solvent). The compound was recrystallized from hexane. About 0.3 g pure materials was obtained, Carbon 13 NMR, 2*165.3, 2*124.8, 44.6, 37.3, 37.2, 37, 4*33.3, 4*32.7, 32.2, 29.2, 26.6, 23, 22.7, 2*14 ppm.

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