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6-n-Alkoxy-3-Pyridinecarboxaldehydes: New Intermediates to Liquid Crystals. Properties of Some Derivatives

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6-n-Alkoxy-3-Pyridinecarboxaldehydes: New Intermediates to Liquid Crystals. Properties of Some Derivatives.

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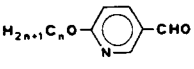
The synthesis of new intermediates to liquid crystals, a series of 6-n-alkoxy-3-pyridinecarboxaldehydes is described. The mesomorphic properties of their precursors, the 6-n-alkoxy-3-pyridinecarboxylic acids are reported. Some derivatives of the carboxaldehydes, the 6,6′-di-n-alkoxy-3,3′-dipyridylmethylenehydrazines and the 6′,6″-di-n-n-alkoxy-3′,3″-dipyridylmethylene-1,4-phenylenediamines, are described and their mesomorphic properties reported. The 1,4-phenylenediamine derivatives show greater mesomorphic stability than the azines, most of the azines being non-mesomorphic while the 1,4-phenylenediamine derivatives show smectic polymorphism with wide mesophase ranges.

INTRODUCTION

Some authors have reported mesomorphic derivatives of unsubstituted 2-, 3- and 4-pyridinecarboxaldehydes,[1] of terminally-substituted 2- and 3-aminopyridines,[2,3,4] and of terminally-substituted 2- and 3-pyridinecarboxylic acids.[5,6]

However, the 6-n-alkoxy-3-pyridinecarboxaldehydes (I), which are of interest as intermediates in the synthesis of mesomorphic compounds such as Schiff's bases, azines, stilbenes, etc., have not been reported in the literature, for the chemical instability of these compounds makes them difficult to obtain in a pure state.

In this paper we report a method of synthesis that gives some 6-n-alkoxy-3-pyridinecarboxaldehydes pure and in good yield.



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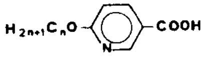

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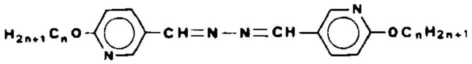

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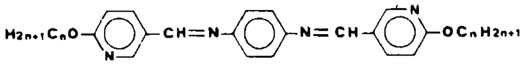


[IV]

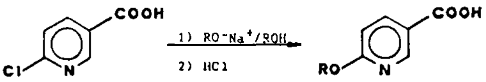
We have studied the mesomorphic properties of the 6-n-alkoxy-3-pyridinecarboxylic acids (II) which are intermediates in the synthesis of the above compounds.

We also report the properties of some derivatives of the pyridine aldehydes expected to show mesomorphic behaviour: the 6,6′-di-n-alkoxy-3,3′-dipyridylmethylenehydrazines (III) and the 6′,6″-n-alkoxy-3′,3″-dipyridylmethylene-1,4-phenylenediamines (IV).

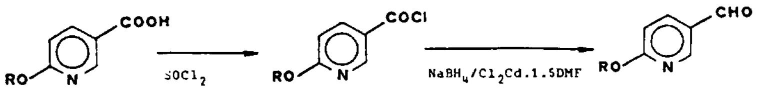
RESULTS AND DISCUSSION

1. Synthesis of the heterocyclic aldehydes

The synthesis of the 6-n-alkoxy-3-pyridinecarboxaldehydes involves two steps: 1) Obtaining the 6-n-alkoxy-3-pyridinecarboxylic acids from the 6-chloronicotinic acid



2) Catalytic reduction of the acids to aldehydes *via* the acyl chloride



The 6-n-alkoxy-3-pyridine carboxylic acids have been reported before by some authors.[5,7] In this work we have used the method reported by Pavluchenko and others,[5] which produces good yields. However we disagree to some extent with the thermal data reported by Pavluchenko.

In order to obtain the aldehydes we used the method of reduction reported by Johnstone and others,[8] which gives yields of 80–90% in relation to the starting acyl chlorides. This method which uses sodium borohydride as a reducing agent and $CdCl_2 \cdot 1.5$ DMF as a catalytic agent, gave us yields of 40–60% in relation to the starting 6-n-alkoxy-3-pyridinecarboxylic acids. The operative method used by us which varies slightly from the one outlined in Johnstone's paper is described in the experimental section.

The aldehydes obtained are liquid at room temperature and decompose before boiling. Therefore we have determined the melting points of the 2,4-dinitrophenylhydrazone derivatives. These are listed in Table I, with the mass spectrometry data for the aldehydes. Since the U.V., I.R., and ^{1}H-N.M.R spectra of all the compounds are closely similar, only the data corresponding to 6-n-hexyloxy-3-pyridinecarboxaldehyde are given in the experimental section.

TABLE I

Mass spectrometric data for 6-n-alkoxy-3-pyridinecarboxaldehydes and melting points of 2,4-dinitrophenylhydrazones.

n	*m/e* (percentage)	Melting point ± 0.2 °C
2	151(57), 150(11), 137(12), 136(100), 123(36), 122(67), 107(29), 106(6), 95(6), 94(8)	203.0
4	179(13), 178(9), 150(16), 149(18), 139(17), 136(23), 124(42), 123(100), 122(76), 107(21), 106(15), 95(23), 94(29)	191.3
6	207(9), 206(12), 178(5), 177(11), 136(16), 124(53), 123(100), 122(36), 107(8), 106(7)	176.9
8	235(21), 234(7), 167(23), 139(20), 124(40), 123(80), 122(26), 95(11), 94(19), 78, 69, 67, 66, 55, 43, 41(100)	168.1
10	263(33), 262(26), 233(14), 124(28), 123(45), 122(9), 105(11), 93, 56, 55, 43, 42, 41(100)	165.1

2. 6-n-alkoxy-3-pyridinecarboxylic acids

The thermal and thermodynamic data for the intermediate 6-n-alkoxy-3-pyridinecarboxylic acids are listed in Table II.

The much higher melting points when the alkoxy chain is methoxy or ethoxy in comparison with the other homologues deserve attention, for the decrease in the melting points upon increasing the terminal chain length makes it possible for mesomorphism to take place. Nematic behaviour is obtained when the terminal chain contains four or more carbons atoms (except the pentyloxy homologue, which is non-mesomorphic). The higher homologues exhibit smectic behaviour of type C.

All the heterocyclic acids show lower transition temperatures than the analogous 4-n-alkoxybenzoic acids.[5,9] The lower crystal-mesophase and mesophase-isotropic transition temperatures obtained by replacing a benzene with a pyridine ring are due to the lesser degree of symmetry in the dimers responsible for the mesomorphism in the pyridine compounds compared with the benzene analogues. Also the existence of H---N hydrogen bonds in the pyridine compounds would be expected to disrupt their liquid crystalline order.[5]

TABLE II

Transition temperatures and enthalpies for 6-n-alkoxy-3-pyridinecarboxylic acids. (Structure II).

n	Transition	Temperature °C	ΔH Kcal/mole
1	C-I	174.6	7.05
2	C-I	186.4	8.57
4	C_1-C_2	92.5	1.04
	C_2-I	99.8	5.23
	I-N^a	90.0	
5	C_1-C_2	86.6	0.94
	C_2-I	96.8	4.89
6	C_1-C_2	76.2	0.98
	C_2-I	92.8	4.77
	I-N^a	90.6	
8	C_1-C_2	71.6	0.99
	C_2-N	88.0	5.52
	N-I	94.2	0.44
	N-S_C^a	87.3	
10	C_1-C_2	70.7	1.65
	C_2-S_C	87.2	5.71
	S_C-I	95.1	1.30

3. 6, 6′-Di-n-alkoxy-3, 3′-dipyridylmethylenehydrazines

The thermal and thermodynamic data for the phase transitions of these compounds are listed in Table III.

Only the n-butyloxy derivative shows a monotropic nematic mesophase, whereas the other homologues are non-mesomorphic. However, all the compounds of the series show crystalline polymorphism. Compared with the benzene analogues,[10] the introduction of a hetero-atom does not modify appreciably the melting points; however, an important decrease in the mesophase stability is produced. Thus, while all the azines derived from 4-n-alkoxybenzaldehydes show mesomorphic behaviour, only a monotropic nematic mesophase in the heterocyclic azine derived from 6-n-butyloxy-3-pyridinecarboxaldehyde is observed by optical microscopy.

This reduction in mesophase stability when the benzene is replaced by the pyridine ring could be due to three effects:

Firstly, the introduction of the hetero-atom produces a decrease in the molecular symmetry[3,4,11] without increasing the molecular dipole moment since the dipole contributions of both nitrogen atoms are in opposition.

Secondly, an increase in the molecular electronic polarizability is not produced, since the 3-position of the heterocycle is the least

TABLE III

Transition temperatures and enthalpies for 6, 6′-di-n-alkoxy-3, 3′-dipyridylmethylenehydrazines. (Structure III).

n	Transition	Temperature °C	ΔH Kcal/mole
2	C_1-C_2	125.2	2.01
	C_2-I	173.4	11.10
4	C_1-C_2	74.5	2.62
	C_2-I	126.4	8.84
	I-N[a]	124.0	
6	C_1-C_2	78.6	1.25
	C_2-C_3	103.1	4.01
	C_3-I	131.6	8.57
8	C_1-C_2	92.3	3.30
	C_2-I	130.9	10.13
10	C_1-C_2	112.1	0.54
	C_2-I	121.7	12.81

a) Monotropic transition.

favorable for conjugation between the lone pair of electrons of the hetero-atom and the rest of the molecule.[7,15]

Finally, there may be forces of repulsion between the lone pair of electrons of the pyridine nitrogen atom and those of the oxygen atoms of alkoxy chains in neighbouring molecules.[7]

4. 6′,6″-Di-n-alkoxy-3′,3″-dipyridylmethylene-1,4-phenylenediamines

The thermal and thermodynamic data for these compounds are listed in Table IV.

The occurrence of smectic behaviour in all the compounds studied is noteworthy for this reveals the existence of strong lateral forces of attraction. The wide range of mesophase stability (100° on average) is also remarkable (see Figure 1).

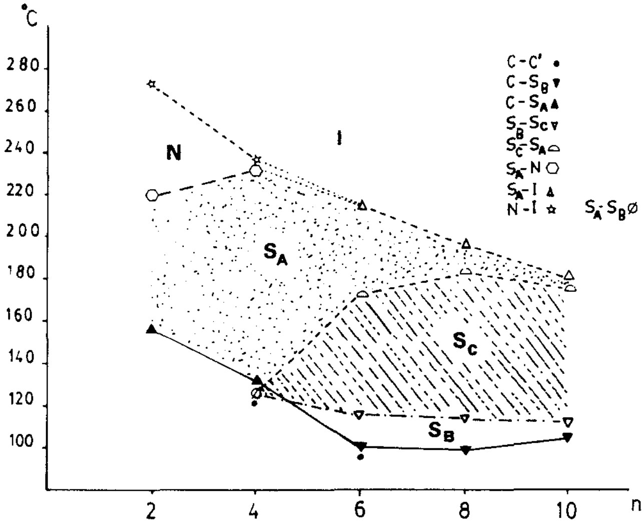
TABLE IV

Transition temperatures and enthalpies for 6′,6″-di-n-alkoxy-3′,3″-dipyridylmethylene-1,4-phenylenediamines. (Structure IV).

n	Transition	Temperature °C	ΔH Kcal/mole
2	C_1-S_A	156.8	11.77
	S_A-N	219.4	0.22
	N-I	272.9	0.22
	C_2-S_A[a]	148.6	6.25
4	C_1-C_2	122.2	0.56
	C_2-S_A	132.1	9.50
	S_A-N	232.4	0.91
	N-I	236.2	0.37
	S_A-S_B[b]	125.5	
	C_3-S_B[a]	117.4	
6	C_1-C_2	97.1	5.87
	C_2-S_B	99.6	
	S_B-S_C	116.5	0.86
	S_C-S_A	171.0	
	S_A-I	214.0	1.62
8	C_1-C_2	62.0	
	C_2-S_B	98.3	6.72
	S_B-S_C	114.5	0.98
	S_C-S_A	184.0	
	S_A-I	195.8	1.58
10	C-S_B	105.0	8.52
	S_B-S_C	112.7	1.08
	S_C-S_A	176.7	
	S_A-I	180.7	1.52

[a] Transition relating to the crystalline modification formed after cooling of the mesophase.

[b] Monotropic transition.



Replacing the benzene by the pyridine ring produces a lowering in the melting points (55° on average), as well as in the clearing points (45° on average).[12,13] At the same time, there is an increased tendency to smectic behaviour. While in the carbocyclic dianils, smectic behaviour is only observed with hydrocarbon chains with at least six carbon atoms, in the heterocyclic analogues smectic behaviour is observed in all the compounds studied irrespective of the length of the hydrocarbon chain.

As is well known, this smectogenic tendency is due to the existence of a strong dipole moment transverse to the molecular axis, which favours the lateral forces of attraction rather than the terminal ones.[3] The decreased transition temperatures, as in the pyridinic azines, are due to the lower molecular symmetry as well as to the repulsive forces between the lone pair of electrons of the pyridine nitrogen and those of the oxygen atoms of neighbouring molecules.

EXPERIMENTAL

Transition temperatures and enthalpies were determined using a Perkin-Elmer DSC-2 Differential Scanning Calorimeter. Melting points of 2,4-dinitrophenylhydrazones were determined in capillary tubes using a Mettler PF-61. Optical observations were made using a Reichert-Thermovar HT1 B11 polarizing microscope equipped with a heating stage. The characterization of products was carried out by the usual spectroscopic methods: U.V. (Perkin-Elmer 200), I.R. (Perkin-Elmer 283), N.M.R. (Perkin-Elmer R-12-B) and mass spectrometry (Hewlett-Packard 5943 A). The purity of all products was checked by the above-mentioned techniques and by elemental analysis.

The mesophase textures were observed using thin films of the samples mounted between a glass slide and a cover slip in a polarizing microscope. The mesophase textures were identified because of their similarity to the descriptions of these textures made by Demus and Richter.[16]

6-n-alkoxy-3-pyridinecarboxylic acids

Freshly cut sodium (2.3 g, 100 mmole) was added with stirring to the appropriate alcohol (300 ml). When dissolution was complete, 6-chloronicotinic acid (4.725 g, 30 mmole) was added and the mixture stirred in an oil bath at 110°C for 24 h. After cooling, the mixture was poured into dilute HC1 and extracted several times with ether. The solvents were removed under reduced pressure. The solid residue was dissolved in ethanol, precipitated with water, collected and recrystallized from hexane. Yield: 60–80%.

6-n-alkoxy-3-pyridinecarboxaldehydes

A solution of the appropriate 6-n-alkoxy-3-pyridinecarboxylic acid (20 mmole) in thionyl chloride (7 ml, 100 mmole) was heated under reflux for 4 h. After removing the thionyl chloride under reduced pressure, the liquid residue of 6-n-alkoxy-3-pyridinecarbonyl chloride was ready for use.

$CdCl_2 \cdot 1.5$ DMF (3.65 g, 12.5 mmole)[†] was added to a solution of sodium borohydride (0.76 g, 20 mmole) in acetonitrile (250 ml) and hexamethylphosphoramide (12.5 ml), and the mixture cooled in an ice-salt bath for 5 min. 6-n-Alkoxy-3-pyridinecarbonyl chloride (20 mmole) was added and stirred for 5 min. Dilute HC1 was added slowly and the reaction product extracted several times into hexane. The organic extracts were combined, washed twice with saturated $NaHCO_3$ solution, once with water and dried over $CaCl_2$. The solvent was removed and the reaction product purified by column chromatography using methylene chloride as eluent. Yield: 40–60%.[‡]

[†] $CdCl_2 \cdot 1.5$ DMF was prepared by the recrystallization of hydrated cadmium chloride ($CdCl_2 \cdot 2.5\ H_2O$) *from dimethylformamide.*[14]

[‡] 2, 4-dinitrophenylhydrazones were prepared by stirring a solution of 6-n-alkoxy-3-pyridinecarboxaldehyde, an excess of 2, 4-dinitrophenylhydrazine and a few drops of glacial acetic acid in ethanol at room temperature followed, by recrystallization of the resulting precipitate from acetonitrile.

Spectroscopic data (for $R = n - C_6H_{13}$):

U.V. (n-pentane), λ_{max}nm($\log\epsilon$): 290 (3.8), 283^{sh}, 279 (4.0), 273^{sh}, 252 (4.2).

I.R. (neat), $\bar{\nu}$ cm^{-1}: 2960, 2930, 2860, 2730, 1703, 1608, 1570, 1495, 1470, 1410, 1360, 1320, 1265, 1220, 1120, 1020, 940, 840, 710, 675.

^{1}H-N.M.R. (CCl_4), δ: 9.87 (*s*, 1H), 8.55 (*d*, 1H, $J = 2.2$ Hz), 7.98 (dd, 1H, $J_1 = 8.8$ Hz, $J_2 = 2.2$ Hz), 6.76 (*d*, 1H, $J_1 = 8.8$ Hz), 4.36 (*t*, 2H, $J = 6.7$ Hz), 0.8–1.9 (*m*, 11H).

6,6′-di-n-alkoxy-3,3′-dipyridylmethylenehydrazines

A solution of 6-n-alkoxy-3-pyridinecarboxaldehyde (2 mmole), hydrazine hydrate (50 mg, 1 mmole) and a few drops of glacial acetic acid in absolute ethyl alcohol (25 ml) was stirred at room temperature for 1 h. The precipitate was collected, washed with ethyl alcohol and recrystallized several times from the appropriate solvent. Yield: 45–55%.

6′,6″-di-n-alkoxy-3′,3″-dipyridylmethylene-1,4-phenylene-diamines

A solution of 6-n-alkoxy-3-pyridinecarboxaldehyde (2 mmole), 1,4-phenylenediamine (108 mg, 1 mmole) and a few drops of glacial acetic acid in absolute ethyl alcohol (25 ml) was stirred at room temperature for 1 h. The precipitate was collected, washed with ethyl alcohol and recrystallized several times from an appropriate solvent. Yield: 50–60%.

CONCLUSIONS

The 6-n-alkoxy-3-pyridinecarboxaldehydes are of interest as precursors of mesomorphic compounds. A method of synthesis has been developed which allows them to be obtained in good yields.

The intermediate 6-n-alkoxy-3-pyridinecarboxylic acids are mesomorphic, although their mesophases stability ranges are narrower than those of the analogous 4-n-alkoxybenzoic acids, owing to the lower symmetry of the dimers responsible for mesomorphism.

In the azines, the greater lowering of the clearing points than the melting points is responsible for the disappearance of mesomorphism in most cases.

In the 1,4-phenylenediamine derivatives, the higher extension of the electronic conjugation, owing to the presence of an additional benzene ring in the central core, allows an enhancement of mesophase stability, and these compounds show wide ranges of smectic polymorphism.

Compared with benzene analogues, the presence of the heteroatom lowers the transition temperatures in most of the derivatives studied.

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