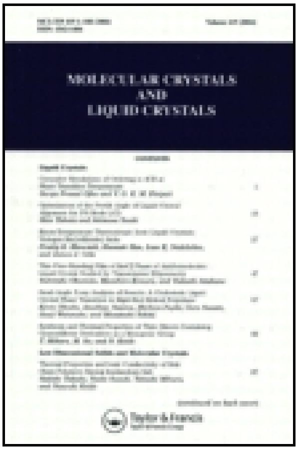

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A New Simple Method for Obtaining 4-*n*-Alkyl-4′-Cyanobiphenyls

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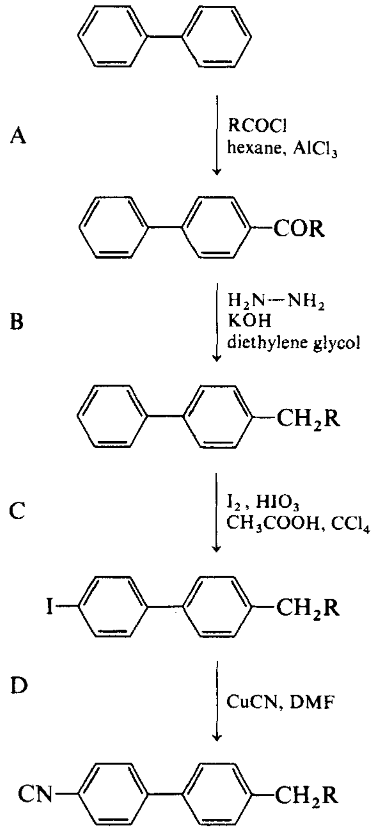
A new method is described of obtaining 4-*n*-alkyl-4′-cyanobiphenyls from biphenyl. First biphenyl is acylated and the resulting ketone is reduced in conditions of the Huang-Minlon reaction; next the obtained 4-*n*-alkylbiphenyl is converted to 4-*n*-alkyl-4′-iodobiphenyl which readily reacts with copper cyanide giving the required nitrile with a good yield.

INTRODUCTION

The 4-*n*-alkyl-4′-cyanobiphenyls were first obtained by Gray.[1] The overall yield obtained by that author, taking account of all the successive steps of the reaction (i.e. acylation of 4-bromobiphenyl, reduction and substitution of the bromine atom for the cyanide group) is low and amounts to 10 to 20% of theory. Isolation of the pure final product especially on a larger scale, is also troublesome in view of the necessity of conducting the separation on a chromatographic column. In a successive work[2] Gray modified the conditions of synthesis achieving as a result shorter reaction time and higher conversion to 4-*n*-alkyl-4′-cyanobiphenyl. Jawdosiuk[3] following Gray's reaction scheme increased the yield of alkylbromobiphenyl by isolating 4-acyl-4′-brombiphenyl hydrazide and decomposing it subsequently with sodium tert-butoxide. Another procedure of obtaining 4-alkyl-4′-cyanobiphenyls was used by Pavluchenko *et al.*[4] Those authors nitrated acylbiphenyl and after isolating 4-acyl-4′-nitrobiphenyl from the isomer mixture containing a considerable quantity of the 2′-isomer, they reduced the nitro compound to the amine by the standard Huang-Minlon method. The amine was subsequently converted to 4-alkyl-4′-cyanobiphenyl via diazonium tetrafluoroborate, here also the total yield is small (10–17% theor.).

RESULTS AND DISCUSSION

The procedure developed in our laboratory is, compared with the above described methods of obtaining 4-*n*-alkyl-4′-cyanobiphenyl, simple and yields a product of high purity. Our procedure can be represented by the following scheme:



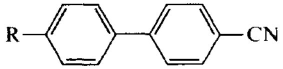
The advantage of this method of obtaining cyanobiphenyl is the ease with which the particular steps are realized and the availability of the substrates (biphenyl and acyl chlorides). The final product is obtained with a good yield and its isolation does not require the use of column chromatography. The method seems also very useful for obtaining chiral 4-alkyl-4′-cyanobiphenyls. A desirable feature of our method is that iodination of 4-*n*-alkylbiphenyl (step C) is very selective as compared with bromination and yields a 4′-substituted product. Since iodine is more reactive than bromine in the 4-position, the cyano group quantitatively displaces it under standard reaction conditions, i.e. by acting with copper cyanide in DMF solution. When the reaction is conducted in concentrated DMF solutions, the side reaction of hydrolysis of the nitrile to the amide proceeds in a minimum extent. The 4-*n*-alkylbiphenyl intermediate products are easily obtained by successive acylation of biphenyl and reduction of the ketone via the Huang–Minlon reaction conditions. These products are liquids or low-melting solids which can easily be distilled under reduced pressure. Distilled alkylbiphenyl is of fairly high purity and can be manufactured on a fairly large scale. Acylation can be conducted with an excellent yield in hexane or carbon tetrachloride instead of nitrobenzene, as recommended in the preceding works,[1,4] since the use of nitrobenzene as solvent is not very convenient. Table I is a summary of our work with comparisons to the yields reported earlier. The method advanced in the present paper can also be used for obtaining 4-alkyl-4′-cyano-*p*-terphenyls, but then the yields are lower, owing to the fact that acylation of *p*-terphenyl leads in a large extent to the diacyl derivative. Moreover the substitution of the iodine for the cyanide group is not as effective in 4-alkyl-4′-iodo-*p*-terphenyl as it was in 4-alkyl-4′-iodobiphenyl.

The purities of the intermediate products and the final product were tested by gas chromatography. The columns on which the separations were conducted were filled with Chromosorb W NAW containing the liquid-crystalline stationary phase BH × BT[N,N′-*bis*(hexyloxybenzylidene)α,α'-*bi*-*p*-toluidine] with the mesophase range 127–274° described by Janini.[5] This material allowed us to conduct the separations at high temperatures. It is characteristic of liquid-crystalline stationary phases that they allow separation of position isomers of compounds which have even identical boiling points;[6–10] for instance the separations of the isomers of different *o*-, *m*- and *p*-derivatives of benzene and biphenyl are excellent. The liquid-crystalline stationary phases are particularly useful for testing the purity of most intermediates used for the production of liquid crystals and the liquid crystals themselves if only their vapour pressures are sufficiently high.

It was found that the purity of 4-alkyl-4′-cyanobiphenyls obtained by us is very high and exceeds 99.5% by gas chromatography. This was also confirmed by the high clearing point (see Table I). In our preliminary work[12] we thought that the purity was even greater. However, we did not use these chromatographic columns with a liquid crystalline stationary phase. For these compounds we detected the presence of such contaminants as biphenyl or higher or lower members of the same homologous series. For example in PCB we found <0.5% of 4-heptyl-4′-cyanobiphenyl, and in 4-heptyl-4′-cyanobiphenyl the presence of hexyl-4′-cyanobiphenyl. The reason for that was the use of alkylcarboxylic acid chlorides containing small quantities of the neighboring members (<2%) which remain in the intermediate and final products though in decreasing amounts.

TABLE I

Yield and transition temperatures of 4-*n*-alkyl-4′-cyanobiphenyls



Compound R	Transition temperatures (°)						Yield of total synthesis (% theor.)			Yield of cyanotion (% theor.)		
	Ref. (4)		Ref. (1)		This work		Ref. (4)	Ref. (1)	This work	Ref. (4)	Ref. (1)	This work
	T_{mp}	T_{cp}	T_{mp}	T_{cp}	T_{mp}	T_{cp}						
n-pentyl	22–23	35	22.5	35	23 22.5–23[a]	37.2 35.5[a]	16.4	15.4	42.4	52	53	90.5
n-hexyl	16.7–17.5	30–30.5	13.5	27	14	30.5	11.4	12.4	46.7	43	30	80.7
n-heptyl	30–31.5	42.4	28.5	42	29	44	—	23.5	31.4	43.7	48	84.5

[a] Variant synthesis consisting in successive transformation of 4-*n*-alkylbiphenyl into 4-*n*-alkylbiphenyl carboxylic acid, its chloride, amide and nitrile.

EXPERIMENTAL

4-n-Pentanoylbiphenyl In a three-necked flask was placed 154 g (1mole) of biphenyl, 160 g (1.2 mole) anhydrous $AlCl_3$, 1000 ml of *n*-hexane, and was added slowly dropwise with mixing 120.5 g (1 mole) of valeryl chloride (allowing the temperature to rise to 45°). Mixing was continued for 2 hours, the contents of the flask being kept at a gentle boil. The flask was then emptied onto 1.5 kg of crushed ice and 50 ml of concentrated hydrochloric acid were added. After the complex was decomposed, the *n*-hexane was removed and unreacted biphenyl removed by steam distillation. After cooling, the aqueous solution was separated from the frozen pentanoylbiphenyl, which was reduced without further purification. A small sample was recrystallized from *n*-hexane, m.p. 76.5–78° (78–79° according to Ref. 11).

4-n-Pentylbiphenyl The 4-*n*-pentanoylbiphenyl (about 0.9 mole) was placed in a three-necked flask with 120 g of 80% hydrazine hydrate, 112 g KOH and 900 ml of diethylene glycol. The contents were heated with mixing to 130° for 3 hours, the excess water was removed via distillation, the pot temperature being gradually raised to 220°. When nitrogen ceased evolving heating was interrupted and the contents of the flask were diluted with water. The *n*-pentylbiphenyl was extracted with benzene. The benzene solution was washed with dilute hydrochloric acid, water, 60% and 98% sulphuric acid, twice with water and dried over anhydrous Na_2CO_3. Benzene was distilled off, and the residue was distilled under vacuum (4 hPa or 3 mm Hg), the fraction boiling at 142° being collected.

145.6 g of 4-*n*-pentylbiphenyl was obtained (what corresponds to 65% of the yield calculated in terms of biphenyl), which is a liquid at ambient temperature and has a melting range of 9.5–10.5°. The chromatogram on a liquid crystal shows that the purity is of about 98%, the main contaminants being biphenyl, heptylbiphenyl and dipentylbiphenyl. Analogously 4-*n*-hexylbiphenyl (solid with melting range 24.5–28°) was obtained with a yield of 61%, and 4-*n*-heptylbiphenyl (solid with melting range 28–33°) with a yield of 62%.

4-n-Pentyl-4′-iodobiphenyl In a three-necked 1 liter flask, 76.2 g (0.3 mole) of 4-*n*-pentylbiphenyl was heated with mixing to reflux at 80° in 210 ml of acetic acid with 57 ml of water, 9 ml of 98% H_2SO_4, 12 g (0.06 mole) HIO_3, 30.6 g (0.12 mole) I_2, 24 ml CCl_4. After heating for 10 hours the unreacted iodine was removed by adding dropwise a 10% sodium pyrosulphate aqueous solution. After the solution was discolored the contents of the flask were cooled and, the precipitate was filtered off and recrystallized from methanol and hexane. 75 g (71.9% yield) of 4-*n*-pentyl-4′-iodobiphenyl was obtained with melting range 112.5–113°.

The IR spectrum reveals characteristic bands unsymmetrically *p*-substituted benzene rings (805 and 835 cm^{-1}). The electron spectrum in hexane has the longest wave maximum at 262 nm, log = 4.482, and is characteristic for the benzene chromophore coupled with the lone electron pair of the iodine atoms.

Analogously, we obtained 4-*n*-hexyl-4′-iodobiphenyl with a 95.5% yield (melting range 112–114°) and 4-*n*-heptyl-4′-iodobiphenyl with a 60% yield (melting range 113–115°).

4-n-Pentyl-4′-cyanobiphenyl In a round-bottomed flask was heated 104 g (0.3 mole) of 4-*n*-pentyl-4′-iodobiphenyl, 31 g (0.35 mole) of CuCN and 340 ml of DMF for 6 hours at the reflux. After cooling 100 ml of 25% ammonia solution were added and the contents shaken. The isolated oil was extracted with *n*-hexane, the extract was washed with water, dilute hydrochloric acid and again with water. After drying over $MgSO_4$ the extract was filtered through a 5 cm layer of silica gel, concentrated and distilled, the 154° (0.05 mm Hg) fraction being collected. On recrystallization from dry *n*-hexane 67 g of the product (90.5% yield) were obtained, which after heating under vacuum at a temperature higher than the clearing point is characterized by the following mesophase range: $T_{\mathrm{cryst}\rightarrow \mathrm{N}}23°$, $T_{\mathrm{N}\rightarrow \mathrm{I}}37.2°$.

By an analogous procedure we obtained 4-hexyl- and 4-heptyl-4′-cyanobiphenyl. The phase transition temperatures and yields are summarized in Table I. The purity of the intermediate products and liquid crystals was ascertained by gas chromatography.

The tests were performed on a PYE Unicam 6 CV apparatus with flame-ionization detector. A glass column was used 4 mm I.D. and 1.5 m long filled with 1% BH × BT on Chromosorb W NAW (0.15–0.20 mm). The temperature of the column was 230° and that of the detector 180°, feeder 310°, argon was the carrier gas, and the flow rate was 25 ml/min.

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