Studies on Electrolytic Substitution Reactions. XII.

Synthesis of 4-Alkoxy-4'-cyanobiphenyls — a Class of Liquid Crystals — *via* Anodic Cyanation of 4,4'-Dialkoxybiphenyls in Emulsion Systems

LENNART EBERSON* and BERTIL HELGÉE

Division of Organic Chemistry 1, Chemical Center, University of Lund, P.O.B. 740, S-220 97 Lund, Sweden

The anodic cyanation of 4,4'-dialkoxybiphenyls has been studied in an emulsified system consisting of dichloromethane/tetrabutylammonium sulfate, substrate and aqueous sodium cyanide. Good yields of 4'-alkoxy-4-cyanobiphenyls (among which an important class of liquid crystals is included) have been obtained, besides minor amounts of products originating from addition of cyanide ion, hydrogen substitution and coupling. The displaced alkoxy group appears as a mixture of the corresponding alcohol and aldehyde, indicating a one-electron process.

The anodic cyanation of aromatic ethers in non-nucleophilic solvents is known to give mainly products originating from substitution of either a ring hydrogen or an alkoxy group. The ratio between these types of products is dependent upon other substituents in the ring. As an example, 1,4-dimethoxybenzene mainly undergoes substitution of a methoxy group whereas 1,3-dimethoxybenzene only gives substitution of ring hydrogens.[1,2] With methanol as solvent, anodic addition of one methoxy and one cyano group across the double bond system occurs in competition with substitution.[3]

We have earlier shown that the use of an emulsified system containing aqueous sodium cyanide, dichloromethane and tetrabutylammonium sulfate is superior to other solvent supporting electrolyte systems used in anodic

cyanation reactions.[3,4] The work described in the following report was undertaken in order to demonstrate the synthetic utility of electroorganic methods in general and emulsion electrolysis in particular. The aim of the work was to synthesize 4-alkoxy-4-cyanobiphenyls. Compounds of this class have earlier been synthesized in a five-step reaction sequence, starting from 4-nitrobiphenyl, with an overall yield of 5.5 − 14 %.[5] These compounds belong to a class of substances which can form nematic liquid crystals.
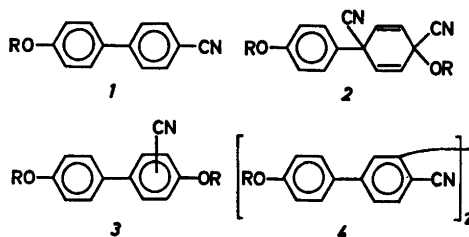
RESULTS

The emulsion electrolyses were performed as described previously,[3,4] using 4,4'-dibutoxy- or 4,4'-dioctyloxybiphenyl as substrates.

4,4'-Dibutoxybiphenyl. Products (*1−4*, R = Bu) are shown below and yields are given in Table 1. 4-Butoxy-4'-cyanobiphenyl (*1*) is formed in good material yield without any dependence on current density and degree of conversion (1.8 F/mol gives 86 % conversion of the starting material). The selectivity of the reaction is reasonably good. The ratio between butoxy-substituted product (*1*) and hydrogen-substituted product (*3*) is around 7. This ratio is usually higher for similar systems when the reaction is run in acetonitrile/tetraethylammonium cyanide.[1] Comparison with runs in this system was, however, not possible due to the low solubility of the substrate in acetonitrile.

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Table 1. Anodic cyanation of 4,4'-dibutoxybiphenyl.

Amount of substrate/mmol	Current/ A	Current density/ mA cm⁻²	Charge/ F mol⁻¹	Yield/% Current	Material[a]	Product (R = butyl)
10	0.15	1.9	1	37	66	*1*
					11	*2*
					9	*3*
10	0.15	1.9	1.8	35	64	*1*
					13	*2*
					8	*3*
					2[b]	*4*
10	0.5	6.25	1.8	29	62	*1*
					16	*2*
					9	*3*

[a] Based on consumed starting material and determined by GLC. [b] Isolated yield.

The yield of the addition product (*2*) increases somewhat with current density and is only little affected by an increase in the degree of conversion. Bis-cyano adducts have not earlier been found in the anodic cyanation of benzene derivatives. An analogous product, 1,2,3,5-tetraphenyl-2,5-dicyano-Δ^3-pyrroline, has been reported from the cyanation of 1,2,3,5-tetraphenylpyrrole.[6] A nitrile-isonitrile adduct was formed in the anodic addition of cyanide ion to 9,10-dialkylanthracenes.[7]

The dimer (*4*), formed in 2 % yield in one experiment, was not sought for in the other experiments given in Table 1 since it could not be analyzed by GLC.

The current yields given in Table 1 are calculated on the basis of a one-electron process. This assumption is discussed further below. The low current yields are probably due to concurrent oxidation of cyanide ion and/or water.

4,4'-Dioctyloxybiphenyl. Yields and products (*1*, R = C_8H_{17}) are given in Table 2. The influence of current density upon the product distribution is similar to that found for 4,4'-dibutoxybiphenyl. The by-products were not

isolated and their yields were estimated by assuming that their GLC response factors relative to an internal standard are the same as for the starting material.

The second experiment in Table 2 was run in a divided cell in an argon atmosphere in order to protect the products originating from the alkoxy group from being either reduced at the cathode or oxidized by oxygen from the air. As is seen in Table 2 both octanal and 1-octanol were found in the reaction mixture. The somewhat lower combined yield of these products compared to that of *1*, R = C_8H_{17} is due to the fact that a rather large volume of dichloromethane must be removed by *in vacuo* evaporation before GLC analysis can be performed. During this procedure the more volatile products, octanal and octanol, inevitably are lost to a higher extent than *1*, R = C_8H_{17}.

Structure assignments. The structures of the main products in the reaction were readily assigned from the spectroscopic data given in the experimental part.

Two of the by-products were isolated in amounts large enough for structure determination with spectroscopic methods. The main

Table 2. Anodic cyanation of 4,4′-dioctyloxybiphenyl.

Amount of substrate/mmol	Current/ A	Current density/ mA cm⁻²	Charge/ F mol⁻¹	Yield/% Current	Material[a]	Product (R = octyl)
5	0.15	1.9	1.8	36	78	*1*
					15	Other products[c]
5[b]	0.15	1.9	1.8	29	76	*1*
					20	c
					29	Octanal
					18	Octanol
5	0.50	6.25	1.8	24	70	*1*
					20	c

[a] Based on consumed starting material and determined by GLC. [b] Divided cell. [c] According to GLC/MS at least one dicyanooctyloxybiphenyl, one cyanodioctyloxybiphenyl, and one dicyano adduct.

by-product was isolated by column chromatography. MS showed the M⁺ peak at *m/e* 350 which is a parent ion equivalent to the addition of two cyano groups to 4,4′-dibutoxybiphenyl. The IR spectrum showed a nitrile band at 2240 cm⁻¹. The ¹H NMR spectrum showed two nonequivalent $-O-CH_2-$ triplets, a singlet at δ 6.15 integrating for four protons and a typical pattern of a 1,4-disubstituted benzene at δ 7.1, also integrating for four protons. This shows that the addition occurred over one of the phenyl groups, giving a cyclo-hexadiene derivative. The singlet at δ 6.15 originates from the olefinic protons and the only possible structure with four olefinic protons is the one given for product *2*. The ¹³C NMR spectrum showed four signals with high intensity in the olefinic/aromatic region originating from four pairwise equivalent carbon atoms in the aromatic ring and four pairwise equivalent carbon atoms in the cyclohexadiene ring, all carrying a hydrogen substituent. This is in accordance with structure *2*. Whether the cyano groups are situated *cis* or *trans* has not been investigated.

The isolated dimeric product was, according to MS, a dimer of 4-butoxy-4′-cyanobiphenyl. The ¹H NMR spectrum showed two groups of signals in the aromatic region, one typical pattern of a 1,4-disubstituted benzene and one multiplet. The multiplet is shifted down-field upon addition of Eu(fod)₃, which can bind either to the cyano group or to the oxygen on the butoxy group. By comparing the effect of Eu(fod)₃ on 4-methylbenzonitrile and 4-

methoxytoluene it was established that the ring protons of 4-methylbenzonitrile were more strongly influenced than the ring protons of 4-methoxytoluene.* This demonstrates that the multiplet in the spectrum of the dimer originates from the rings with the cyano substituent and the bond between the two monomeric units. The ¹³C NMR spectrum showed ten signals in the aromatic region indicating that the product was one of the two symmetrically coupled isomers. The signals were assigned by comparison between the experimental shifts and shifts calculated from literature data on substituted benzenes.[8] The 3,3′-coupled isomer was the only one giving a good correspondence between calculated and experimental shifts. Hence the isolated dimer was assigned the structure of 4,4′″-dibutoxy-4′,2″-dicyano-1,1′:3′,1″:5″,1′″-quadriphenyl (*4*).

DISCUSSION

It has earlier been postulated[1] but not proved that the substitution of a methoxy group for a cyano group in the anodic cyanation of methoxybenzenes proceeds *via* loss of formaldehyde and a proton from a cyclohexadienyl cation, as exemplified by the formation of 4-methoxy-benzonitrile from 1,4-dimethoxybenzene (route *b*, Scheme 1, R′ = CH₃O, R = H).

The results given above show that apart from the expected aldehyde, the corresponding alcohol is also formed in the cyanation of

* This is contrary to what has been found for aliphatic ethers and nitriles with Eu(DPM)₃.[9]
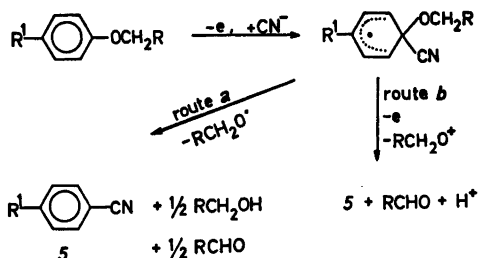
Scheme 1.

4,4'-dioctyloxybiphenyl. This result does not fit with the two-electron mechanism depicted in route *b*, Scheme 1. In order to rationalize our results we instead suggest the mechanism shown in route *a*. The initially formed radical cation reacts as usual with cyanide ion to form a cyclohexadienyl radical, which then loses an alkoxy radical with formation of the cyano substitution product. The alkoxy radical undergoes a disproportionation reaction to give alcohol and aldehyde. This means that the conversion of 4,4'-dialkoxybiphenyl to 4-cyano-4'-alkoxybiphenyl is a one-electron process. The fact that more aldehyde than alcohol is formed indicates that the leaving radical to some extent is further oxidized to the cation which gives rise to the excess of aldehyde. A control experiment showed that 1-octanol cannot be oxidized to octanal under the experimental conditions used in the cyanation reaction.

A case where an alkoxy radical is cleaved off from a radical cation has been described by Utley et al.[10] When dibenzyl ether was oxidized the radical cation formed was cleaved to give a benzyl cation and a benzyloxy radical. The radical then underwent disproportionation to give the corresponding alcohol and aldehyde.

Finally, it should be noted that displacement of alkoxy by cyano groups in biphenyl derivatives can also be effected photochemically *via* a radical cation mechanism. As an example, photolysis of 4,4'-dimethoxybiphenyl in *t*-BuOH/water (1:3) in the presence of cyanide (0.1 M) gave *1*, R = CH₃ and 4,4'-dicyanobiphenyl in 28 and 15 % yield, respectively.[11]

EXPERIMENTAL

General. IR spectra were recorded with a Perkin-Elmer Model 257 grating spectrometer. ¹H NMR spectra were recorded with either

a Varian A 60 spectrometer or a Jeol MA 100 spectrometer. ¹³C NMR spectra were recorded with a Jeol FX 60 spectrometer. Mass spectra were recorded with an LKB 9000 spectrometer coupled to a gas chromatograph. GLC analysis was performed using a Hewlett-Packard 5830 GLC system equipped with either a 1.5 m × 3 mm 3 % OV-1 column or a 2 m × 3 mm OV-17 column.

Chemicals. Solvents, reagents, and supporting electrolytes used in this work were commercially available reagent grade chemicals.

4,4'-Dialkoxybiphenyl. 4,4'-Biphenol (0.01 mol) was dissolved in DMF (100 ml) and pulverized potassium hydroxide (0.03 mol) was added. The mixture was stirred for 10 min before the alkyl bromide (0.03 mol) was added. After stirring for 2.5 h identical amounts of potassium hydroxide and alkyl bromide were added in the same fashion. The mixture was stirred overnight. The white precipitate formed was collected. The mother liquor was diluted with water and yielded a second crop of crystals. The combined crystal fractions were washed with water and dried. The product was recrystallized from ether.

4,4'-Dibutoxybiphenyl. Yield 93 %, m.p. 152−153 °C. ¹H NMR: δ 1.0 (6 H, t), 1.7 (8 H, m), 4.0 (4 H, t), 7.25 (8 H, typical pattern of 1,4-disubstituted benzene). MS [*m/e* (% rel. int.)]: 299 (14), 298 (59), 242 (16) 187 (13), 186 (100), 185 (17). (Found: C 80.0; H 8.78. Calc. for C₂₀H₂₆O₂: C 80.5; H 8.72).

4,4'-Dioctyloxybiphenyl. Yield 91 %, m.p. 116−117 °C. ¹H NMR: δ 0.8−2.0 (30 H, m), 4.0 (4 H, t), 7.2 (8 H, typical pattern of 1,4-disubstituted benzene).

MS [*m/e* (% rel. int.)]: 411 (31), 410 (100), 298 (14), 187 (89), 185 (18). (Found: C 81.8; H 10.2. Calc. for C₂₈H₄₁O₂: C 81.9; H 10.31).

Electrolysis equipment. Electrolyses were carried out in a water-jacketed vessel, 800 ml in volume, equipped with a platinum foil anode (80 cm²) and either a stainless steel rod or a platinum wire cathode. The electrodes were arranged concentrically. An Ultra-Turrax [12] type high-speed stirring device was placed "behind" the cathode. Constant current was maintained with either a Radiak or a Philips power supply.

General electrolysis procedure. Substrate amounts, current and charge passed are given in Tables 1 and 2. The electrolyte consisted of substrate, dichloromethane (230 ml), 1 M sodium cyanide (230 ml) and neutralized tetrabutyl-ammonium hydrogen sulfate (20 mmol) dissolved in water (15 ml). A given amount of charge was passed at constant current. When the electrolysis was started the stirrer had to be turned on for a few seconds and then turned off and left for 30 s and then turned on again. After this procedure the potential drop over the cell increased from around 4 V to 7−15 V. This behavior is probably due to a wetting phenomenon.

Work-up procedure. I. The two phases were allowed to separate and the organic layer was evaporated to dryness. The residue was taken up in ether and the ether solution washed twice with water to remove the supporting electrolyte. Ten percent of the ether solution was used for yield determination by GLC and the remaining 90 % was used for the isolation of products. The remaining starting material was precipitated by cooling the solution in Dry Ice/acetone and filtered off. The mother liquor was then evaporated to dryness and the residue was boiled with pentane leaving an insoluble tarry residue. The pentane extract was reduced in volume and chromatographed on a silica column with pentane/ether (95/5) as eluent.

II. An alternative route to isolate the main product was to cool the pentane solution in Dry Ice/acetone and collect the precipitate formed.

4,4′-Butoxycyanobiphenyl. (*1*, R = Bu). The product was isolated by column chromatography and recrystallized from pentane, yield 37 %, calculated on the basis of unrecovered starting material, m.p. 77–78 °C.
¹H NMR: δ 1.0 (3 H, t), 1.6 (4 H, m), 4.0 (2 H, t), 7.3 (4 H, typical pattern of a 1,4-disubstituted benzene), 7.7 (4 H, s). The signal at δ 7.7 was shifted downfield and split into the typical pattern of a 1,4-disubstituted benzene upon addition of Eu(fod)₃.
¹³C NMR [15.0 MHz, CDCl₃]: 145.0 (C1), 128.2 (C2), 132.3 (C3), 118.9 (C4), 131.0 (C1′), 126.9 (C2′), 114.9 (C3′), 159.7 (C4′), aliphatic carbons 67.7 (C8′), 31.2 (C9′), 19.2 (C10′), 13.8 (C11′). IR: 2220 cm⁻¹. MS [*m/e* (% rel. int.)]: 252 (4), 251 (22), 196 (14), 195 (100). Anal. $C_{17}H_{17}NO$: C, H, N.

1-Butoxy-4-[4-butoxyphenyl]-1,4-dicyano-2,5-cyclohexadiene. (*2*, R = Bu). The substance was isolated by column chromatography and recrystallized from pentane, yield 1 %, m.p. 79–80 °C.
¹H NMR: δ 0.9 (6 H, m), 1.5 (8 H, m), 3.65 (2 H, t), 3.9 (2 H, t), 6.15 (4 H, s), 7.1 (4 H, typical pattern of a 1,4-disubstituted benzene).
¹³C NMR [15.0 HMz, CDCl₃]: 42.0 (C1), 130.9 (C2), 123.6 (C3), 65.6 (C8), 31.7 (C9), 19.2 (C10,10′), 13.8 (C11,11′), 126.4 (C1′), 127.5 (C2′), 115.2 (C3′), 159.5 (C4′), 67.9 (C8′), 31.2 (C9′), 117.6 (C$_{CN}$), 116.8 (C$_{CN}$).
IR: 2240 cm⁻¹. MS [*m/e* (% rel. int.)]: 351 (2), 350 (69), 294 (19), 277 (13), 238 (32), 222 (17), 221 (100), 220 (16), 211 (30), 183 (13).

4,4′-Dibutoxycyanobiphenyl. (*3*, R = Bu). A few mg were isolated by column chromatography and recrystallized from pentane. GLC analysis of this product showed only one peak. M.p. 71–72 °C. IR: 2220 cm⁻¹. MS [*m/e* (rel. int. %)]: 324 (12), 323 (45), 267 (23), 220 (13), 212 (14), 211 (100).

4,4′′′-Dibutoxy-4′,2′′-dicyano-1,1′:3′,1′′:5′′,1′′′-quadriphenyl. (*4*, R = Bu). This dimer was isolated from the tarry residue that was insoluble in pentane. The tarry material was

boiled with methanol in which the dimer was insoluble and could be filtered off. Recrystallization from ether gave 100 mg of crystals, m.p. 156–157 °C. IR: 220 cm⁻¹ (s).
¹H NMR: δ 0.9 (6 H, t), 1.6 (8 H, m), 4.0 (4 H, t), 7.3 (8 H, typical pattern of 1,4-disubstituted benzene), 7.8 (6 H, m). The multiplet at 7.8 ppm is shifted downfield upon addition of Eu(fod)₃.
¹³C NMR [15.0 MHz, CDCl₃]: δ 130.7 (C1), 126.9 (C2), 115.1 (C3), 160.0 (C4), 145.4 (C1′), 128.6 (C2′), 142.0 (C3′), 118.1 (C4′), 134.0 (C5′), 128.6 (C6′), aliphatic carbons 67.7 (C8), 31.2 (C9), 19.2 (C10), 13.9 (C11).
MS [*m/e* (% rel. int.)]: 502 (8), 501 (29), 500 (78), 445 (6) 444 (16), 389 (29), 388 (100) 387 (16). Anal. $C_{34}H_{32}N_2O_2$: C, H, N.

4-Cyano-4′-octyloxybiphenyl. (*1*, R = C₈H₁₇). The compound was isolated according to work-up procedure II and recrystallized from pentane. The isolated yield from an electrolysis on the 10 mmol scale was 35 %, based on consumed starting material. Anal. $C_{21}H_{25}NO$: C, H, N.
¹H NMR: δ 0.82 (3 H, t), 1.3 (12 H, m), 4.0 (2 H, t), 7.0 (2 H, d), 7.5 (2 H, d), 7.65 (4 H, s). The singlet at 7.65 is shifted downfield and split into two doublets upon addition of Eu(fod)₃. IR: 2220 cm⁻¹ (s). MS: [*m/e* (% rel. int.)]: 308 (6), 307 (19), 196 (16), 195 (100), 166 (5).

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