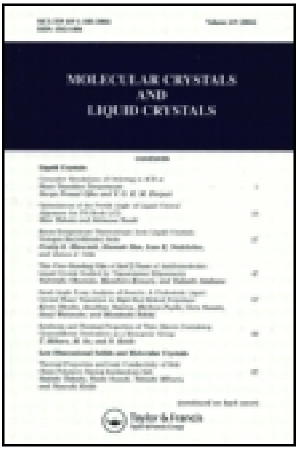

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A Convenient Method of Obtaining 2-Cyano-4-Alkylphenols, 4-Cyanophenol and 4-Cyanoaniline

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A Convenient Method of Obtaining 2-Cyano-4-Alkylphenols, 4-Cyanophenol and 4-Cyanoaniline

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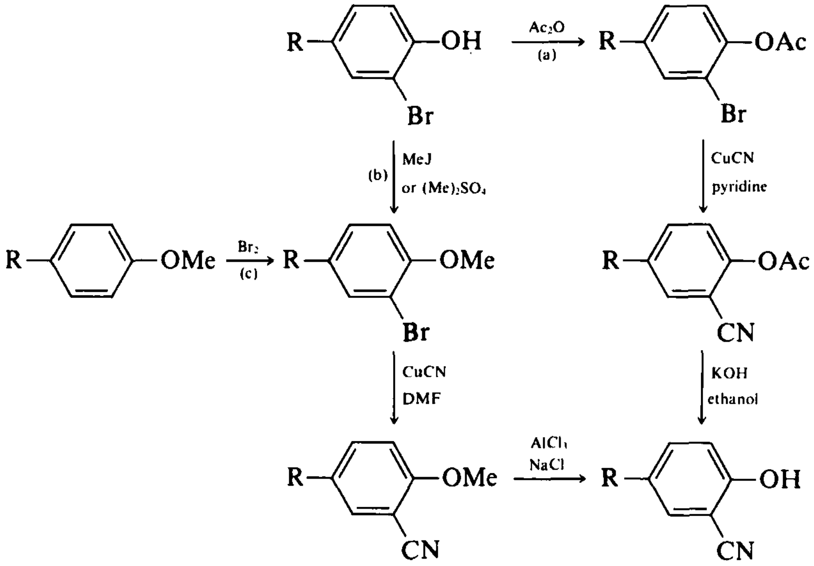
A convenient method is described of obtaining 2-cyano-4-alkylphenols and 4-cyanophenol by substituting bromine atom for the cyano group in the respective bromoanisoles and demethylation of the cyanoalkylanisoles. It is suggested to prepare 4-cyanoaniline by reduction of 4-cyanonitrobenzene with aqueous hydrazine solutions.

INTRODUCTION

4-Cyanoaniline is a substrate for obtaining many important liquid-crystalline Schiff bases,[1-3] azo and azoxy compounds,[4-7] whereas 4-cyanophenol serves for obtaining esters[1,5,8] with a high positive dielectric anisotropy. Alkyl derivatives of 2-cyanophenol have found application in the synthesis of liquid-crystalline compounds with negative anisotropy.[9]

RESULTS AND DISCUSSION

The simplest known method of obtaining 2-cyano-4-alkylphenols[10] is presented by the reaction scheme sequence as given on the following page. The substitution of bromine atom for the cyano group in 2-bromo-4-alkylphenol acetates does not proceed in high yield. The reaction products contain many byproducts which hinder the isolation of 2-cyano-4-alkylphenol acetates. In contrast the method of obtaining 2-cyano-4-alkylphenols presented in the reaction sequence (b) or (c) proves unusually efficient; the latter variant is more suitable in the case of *n*-alkyl derivatives with a large alkyl radical, since 4-*n*-alkylanisoles are more easily obtained than 4-alkylphenols. The former are obtained in excellent yields by successive acylation of anisole



and Huang–Minlon reduction of the resulting ketone. Substitution of bromine for the cyano group in 2-bromo-4-alkylanisole proceeds in a high yield.

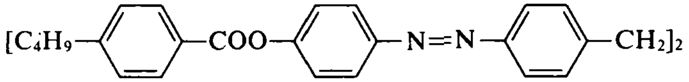
This method for preparing cyanoanisoles was also used to obtain 4-cyanophenol from 4-bromoanisole in a high yield. In our opinion, the latter method of obtaining this compound is more convenient than those described previously, i.e. from 4-aminophenol by the Sandmayer method,[11] by dehydration of 4-hydroxybenzaldoxime[12,13] or of 4-hydroxybenzamide.[14–17] Another method, consisting in heating sodium *p*-hydroxybenzoate with adiponitrile under conditions described in Ref. 18, in our opinion does not give 4-cyanophenol in a very good yield. We repeated this synthesis and found by gas chromatography that there is only 10% cyanophenol in the tarry reaction products.

Previously, 4-cyanoaniline has been obtained by reduction of 4-nitrobenzonitrile with zinc,[19] tin,[20] iron,[21] stannous chloride[22] or Raney nickel,[23] from 4-aminoacetanilide in the Sandmayer reaction,[24] from 4-bromoaniline by reaction with CuCN[25] or as result of dehydration of 4-aminobenzaldoxime.[26] We have found that the most efficient and simple method is the reduction of 4-nitrobenzonitrile with aqueous hydrazine solutions. After the reaction has been initiated by heating, the temperature of the reaction mixture increases rapidly to the boiling point accompanied by vigorous evolution of nitrogen; usually after 5–20 min the reduction is complete. At high hydrazine concentrations (80%) the reaction proceeds very violently. Hydrazine concentrations in the range 60–80% were found to be optimal, giving a reduction which proceeds rapidly and smoothly. Hydrazine solutions of greater dilution can also be used, but with concentrations lower than 40%, it is advantageous to add potassium or sodium carbonate in order to maintain a short reaction time.

EXPERIMENTAL

Materials and procedures

All reagents were obtained commercially with the exception of 4-cyanonitrobenzene that prepared after the manner of Ref. 27. GLC analysis was performed on a PYE Unicam GCV aparatus with flame ionization detector. A glass column was used (4 mm i.d. and 1 m long) filled with 2%



on Chromosorb W AW DMCS (0.15–0.2 mm). This liquid-crystalline stationary phase was used because it is convenient for benzene isomer separations with higher b.p.[28]

The temperature of the column was 200° and that of the detector 230°, feeder 300°, argon was the carrier gas, and the flow rate was 25 ml/min.

Spectral analyses were obtained using following instruments: Specord 71 IR; Tesla BS 487 (H^1 nmr, in CCl_4 with TMS internal standard).

4-n-Alkanoylanisoles A mixture of 293,7 g (2.2 mole) anhydrous $AlCl_3$, 223,6 g (2.1 mole) butyryl chloride in 1.5 l CCl_4 was cooled to temperature between −5° and 0°, and then 216 g (2 mole) anisole was added dropwise in 4 hr with vigorous stirring. This reaction mixture was stirred at 0° for 2 hr and then poured onto ca 1500 g ice.

The CCl_4 layer was washed with water, dried over anhydr. $MgSO_4$, the solvent removed (Rotovap) and the residue distilled at 111°/1.1 mm to give 288 g (81%); Ref. 29 b.p. 162–163°/20 mm; IR (neat, film) 845 cm^{-1} (intense, para substituted Ar) and 1690 cm^{-1} (C=O, intense); nmr, Figure 1, δ 7.80 (d, 2, ortho to COC_3H_7), δ 6.80 (d, 2, ArH ortho to OCH_3), δ 3.79 (s, 3, OCH_3), δ 2.70 (t, 2, $COCH_2$), δ 1.69 (m, 2, CH_2), δ 0.96 (t, 3, CH_3).

The nmr spectra showed a symmetrical aromatic proton pattern which is strong evidence for the 4-isomer, (Figure 1); the purity detected GLC ca 97%. 4-*n*-pentanoylanisole was prepared in the same manner to give 334 g (87%), b.p. 130°/0.6 mm; Ref. 29 b.p. 165–167°/14 mm.

4-n-Alkylanisoles A mixture of 356 g (2 mole) 4-*n*-butanoylanisole, 250 g (4 mole) 80% hydrazine hydrate and 224 (4 mole) KOH in 1.5 l diethylene glycol was refluxed for 3 hr and then distilled slowly until the temperature in pot was

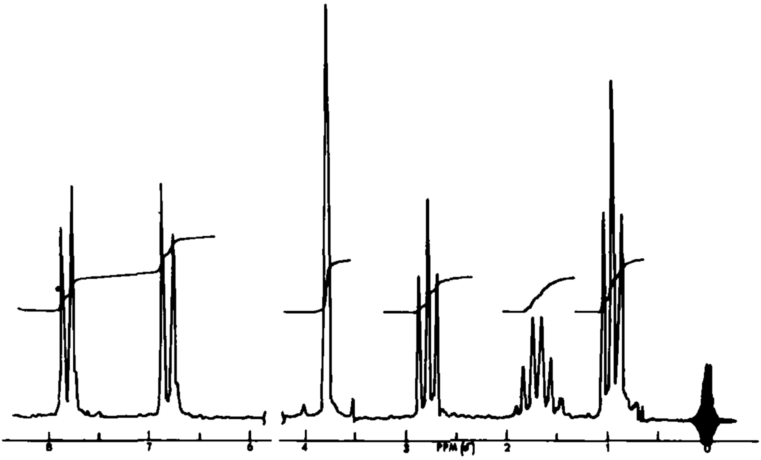


FIGURE 1 NMR spectrum for 4-*n*-butanoylanisole.

raised to 240°. The distillate was diluted water (3 1) and then extracted with hexane and the organic layer washed with water, 5% hydrochloride acid solution and once more water, dried over anhydr. $MgSO_4$, the filtrate evaporated (Rotovap) and the residue distilled 104°/16 mm to give 262 g (83%) 4-*n*-butylanisole; Ref. 29 b.p. 122–123°/20 mm; IR, band of the carbonyl group was absent; nmr, δ 7.23 (d, 2, ortho to butyl), δ 6.92 (d, 2, ArH ortho to OCH_3), δ 3.69 (s, 3, OCH_3), δ 2.51 (t, 2, CH_2Ar), δ 0.8–1.6 (m, 7, propyl); the purity ca 98%. 4-*n*-Pentylanisole was prepared in the same manner, yield 75%, b.p. 123°/13 mm; Ref. 29 b.p. 124–125°/14 mm.

2-Bromo-4-n-alkylanisoles In a 3-neck, 2 1 flask was placed 164 g (1 mole) of 4-*n*-butylanisole, 90.2 g of sodium acetate, 1.3 liter of acetic acid and 400 ml of methanol. The contents were cooled to 0° when a solution of 160 g (1 mole) of bromine in 200 ml of acetic acid was added dropwise in 3 hr. Mixing was continued for 3 hr and then the mixture was poured into 4 1 water. The insoluble oil was extracted into hexane, washed with water and sodium sulphite solution. After drying over anhydrous magnesium sulphate the hexane was removed (Rotovap) and the residue distilled at 114–115°/0.7 mm to give 211.4 g (87%) of 2-bromo-4-*n*-butylanisole. GLC analysis revealed impurities below 1%; IR (neat, film) 815 cm^{-1} and 885 cm^{-1} (1,2,4-substituted Ar), 1030 cm^{-1} and 1060 cm^{-1} (O—Me, this splitting is owing to presence of the bromine atom in ortho position); nmr spectra showed a characteristic aromatic proton pattern for 1,2,4-substitution, when 2-substituent is a strong steric hindrance, (Figure 2); δ 7.27, 72.4 (2s, 1, ArH ortho to Br, calcd δ 7.22), δ 6.95, 6.92 (2d, 1, ArH ortho to butyl, calcd δ 7.00), δ 6.66 (d, 1, ortho to O—Me, calcd δ 6.65),

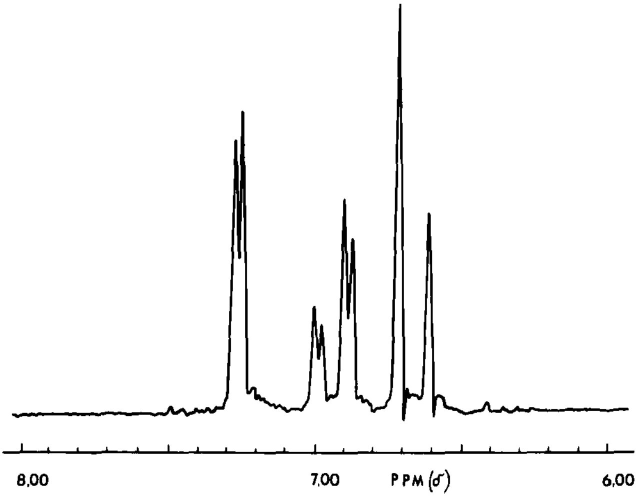


FIGURE 2 NMR spectrum for 2-bromo-4-*n*-butanoylanisole, aromatic proton pattern.

δ 3.78 (s, 3, O—Me), δ 2.47 (t, 2, CH_2—Ar; one well defined triplet suggested that rotation about the Ar—C bond is not hindered), δ 1.8–0.8 (m, 7, unresolved).

Anal. Calcd for $C_{11}H_{15}OBr$: C-54.33%, H-6.22%, Br-32.86%.
Found: C-54.56%, H-6.16%, Br-32.70%

2-Bromo-4-*n*-pentylanisole was obtained by the same manner in a weight 183 g, b.p. 109°/0.2 mm.

Anal. Calcd for $C_{12}H_{17}OBr$: C-56.03%, H-6.67%, Br-31.07%
Found: C-56.51%, H-6.50%, Br-31.38%

Cyanoanisoles A mixture of 243 g (1 mole) of 2-bromo-4-*n*-butylanisole and 104.1 g (1.16 moles) CuCN in 250 ml DMF was refluxed for 5 hr and then cooled to room temperature. Concentrated aq. NH_4OH (300 ml) was added with vigorous shaking. This was extracted with hexane and the organic layer washed with water, dried over anhydr. $MgSO_4$, the filtrate evaporated (Rotovap) and the residue distilled at 116°/0.04 mm to give 114 g (62%) of 2-cyano-4-*n*-butylanisole.

IR (neat, film), 1030 cm^{-1} (O—Me, singlet band), 2250 cm^{-1} (CN); nmr, δ 7.30 (d, ArH ortho to butyl, partly covered with following signal), δ 7.25 (s, ArH ortho to CN), δ 6.9 (d, 2, ArH ortho to O—Me), δ 2.54 (t, 2, CH_2—Ar);

Anal. Calcd for $C_{12}H_{15}ON$: C-76.15%, H-8.00%, N-7.41%;
Found: C-76.20%, H-7.91%, N-7.41%.

2-Cyano-4-methylanisole[70%, b.p. 160°/15 mm; Ref. 30 b.p. 270°/760 mm], 2-cyano-4-*n*-pentylanisole [65%, b.p. 126°/0.04 mm] and 4-cyanoanisole [68%, b.p. 125°/13 mm, m.p. 56–57.5°; Ref. 18 m.p. 56–57°] were prepared in the same manner except that 4-cyanoanisole was extracted into ether. In all cases the purity detected by GLC was better than 99%.

Cyanophenols In an Erlenmayer flask (2 l) with an air condenser protected with a calcium chloride tube was placed 94.5 g (0.5 mole) of 2-cyano-4-*n*-butylanisole, 30 g of NaCl and 135.5 g (1 mole) anhydrous $AlCl_3$. The contents were heated on a Woods metal bath until the reaction was initiated. After the exothermic reaction had ceased, the mixture kept at temperature 130° for 40 min. The melt was cooled to RT and treated with mixture: 500 ml water, 500 g ice and 750 ml chloroform. The organic layer was washed with water, dried over $MgSO_4$ and the chloroform evaporated (Rotovap). The residue was distilled at 151°/2 mm to give a solid on cooling which was crystallized twice from a hexane:benzene mixture (4:1), to give 56 g (64%) of 2-cyano-4-*n*-butylphenol: m.p. 57–59° Ref. 10, m.p. 60.5°. Not many impurities (<1%) were detected by GLC.

IR (KBr pellet) 2250 cm^{-1} (CN), 3280 cm^{-1} (OH, broad intense); 1030 cm^{-1} absent; nmr (acetone-d_6), δ 7.2–7.4 (s, d, 2, ArH ortho to butyl), δ 7.0 (d, 1, ortho to OH), δ 3.8 (OH, broad), δ 2.56 (*t*, 2, CH_2—Ar). 2-Cyano-4-*n*-pentylphenol [65%, m.p. 80–81° lit. m.p. 81° Ref. 10, recrystallized 2x from hexane-benzene (4:1)], 2-cyano-4-methylphenol [70%, m.p. 98–99°, lit. m.p. 100–101° Ref. 31, recrystallized 2x from methanol] and 4-cyanophenol [80%, m.p. 111–112°, lit. m.p. 110–111° (Ref. 14), recrystallized 2x from benzene].

4-Cyanoaniline a) A mixture of 21.9 g (0.15 mole) of 4-cyanonitrobenzene in 52.5 ml 80% hydrazine hydrate was heated until the reaction was initiated. After the vigorous evolution of nitrogen ceased, the reaction mixture was refluxed for ~15 min and then cooled to room temperature. The precipitate was collected by filtration, washed with water and dried to give 16 g (89%) of *p*-cyanoaniline: m.p. 85–96% recrystallized once from 50% MeOH in H_2O, lit. m.p. 85–86% (Ref. 24).

b) A mixture of 21.9 g (0.15 mole) 4-cyanonitrobenzene and 15 g K_2CO_3 in 53 ml of 17% hydrazine hydrate was refluxed for 1/2 hr. The reaction was worked up as in (a) to give 65% of 4-cyanoaniline, m.p. 85–86%.

Acknowledgments

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References

1. S. Ignasiak and M. I. Rafuse, *Mol. Cryst. Liq. Cryst.*, **30**, 125 (1975).
2. J. Billard, J. C. Dubois and A. Zann, *J. Phys.* (*Paris*), **36**, C1, 355 (1975).
3. V. V. Titov, E. I. Kovshev, L. A. Karamysheva, G. V. Purvaneckas and V. K. Daukshas, *Khim. Geterocykl. Soyed.*, *1364* (1975).
4. V. V. Titov, E. I. Kovshev, A. I. Pavluchenko, V. T. Lazareva and M. F. Grobenkin, *J. Phys.* (*Paris*), **36**, C1, 387 (1975).
5. V. T. Lazareva, V. V. Titov, K. V. Roytman, *Zhur, Org. Khim.*, **12**, 194 (1976).
6. R. Dabrowski, M. Milowski, R. Zakrzewski and J. Zielinski, *Biul. WAT*, **29**, No. 1, 109 (1980).
7. G. Adamska, R. Dabrowski, M. Ptaszyńska and Z. Witkiewicz, *Biul. WAT*, **26**, No 7, 105 (1977).
8. USA Pat., 3 795 436 (1974); CA: **80**, 114 009 s.
9. J. P. van Meter, R. T. Klingbel and D. J. Genova, *Solid State Comm.*, **16**, 315 (1975).
10. Ger. Offen., 2 240 864 (1974); CA: **81**, 25 404 v.
11. F. Ahrens, *Ber.*, **20**, 2954 (1887).
12. Neth. App., 6 610 638 (1967); CA: **67**, 90 557 x.
13. O. Brady and R. Truszkowski, *J. Chem. Soc.*, **127**, 1033 (1927).
14. Jap. Pat., 6 829 944 (1968); CA: **70**, 67 965 g.
15. G. Brit. Pat., 1 220 386 (1971); CA: **74**, 87 653 q.
16. J. Kahaoka, F. Kuga and K. Tanizawa, *Chem. Pharm. Bull.*, **18**, 398 (1970).
17. Ger. Offen., 2 020 866 (1971); CA: **76**, 59 257 m.
18. Ger. Offen., 2 047 160 (1971); **75**, 140 523 w.
19. C. Engler, *Ann.*, **149**, 297 (1869).
20. A. Fricke, *Ber.*, **7**, 1321 (1874).
21. D. Libermann, N. Rist, Fr. Grumbach, S. Cals, M. Moyeux and A. Ronaix, *Bull. Soc. Chim. France*, 702 (1958).
22. M. Bogert and L. Kohnstamm, *J. Am. Chem. Soc.*, **25**, 478 (1903).
23. H. Kazmirowski, H. Landmann, D. Walsmann, *Pharmazie*, **24**, 378 (1969).
24. USA Pat., 2 575 036 (1951); CA: **46**, 5617 h.
25. L. Friedmann and H. Shechter, *J. Org. Chem.*, **26**, 2522 (1961).
26. E. Vowinkel and J. Bartel, *Chem. Ber.*, **107**, 1221 (1974).
27. R. Dabrowski, S. Dwojacki and M. Miłowski, *Biul. WAT*, **29**, No 3, 29 (1980).
28. Z. Witkiewicz and R. Dabrowski, unpublished results.
29. S. Skraup, F. Nietev, *Ber.*, **57**, 1300 (1924).
30. L. Limpach, *Ber.*, **22**, 351 (1889).
31. O. Goldbeck, *Ber.*, **24**, 3658 (1891).