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Troublesome Alkoxythiophenes-Mesomorphic Behavior and Highly Efficient Synthesis

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The synthesis of a novel ferroelectric alkoxythiophene-containing liquid crystal is described together with the mesophase morphology of the material. The alkoxythiophene unit is introduced by a highly efficient ring closure of an appropriate γ-ketoester using Lawesson's reagent as the sulfurating agent. Our new cyclization methodology represents the most efficient synthetic pathway for the synthesis of this unit.

Keywords: ferroelectric; alkoxythiophene; cyclization; biaxiality

INTRODUCTION

Thiophene has been shown to be an efficient unit in promoting liquid crystal mesophases, and recently has been incorporated into mesogens exhibiting S_C^* phases[1-4]. Difficulties in the synthesis of certain thiophene derivatives has led to a concentration of work consisting of materials incorporating alkyl[5-7], alkylsulfanyl[8], acyl[9] and recently α,α-difluoroalkyl[10] moieties as terminal units. In this paper we report the synthesis of an alkoxythiophene derivative exhibiting the ferroelectric smectic C phase and numerous tilted subphases. The material was targeted as a match for both the McMillan and Wolf models and is a good fit with Goodby's twisted model[11] that has proven useful to chemists in structural design.

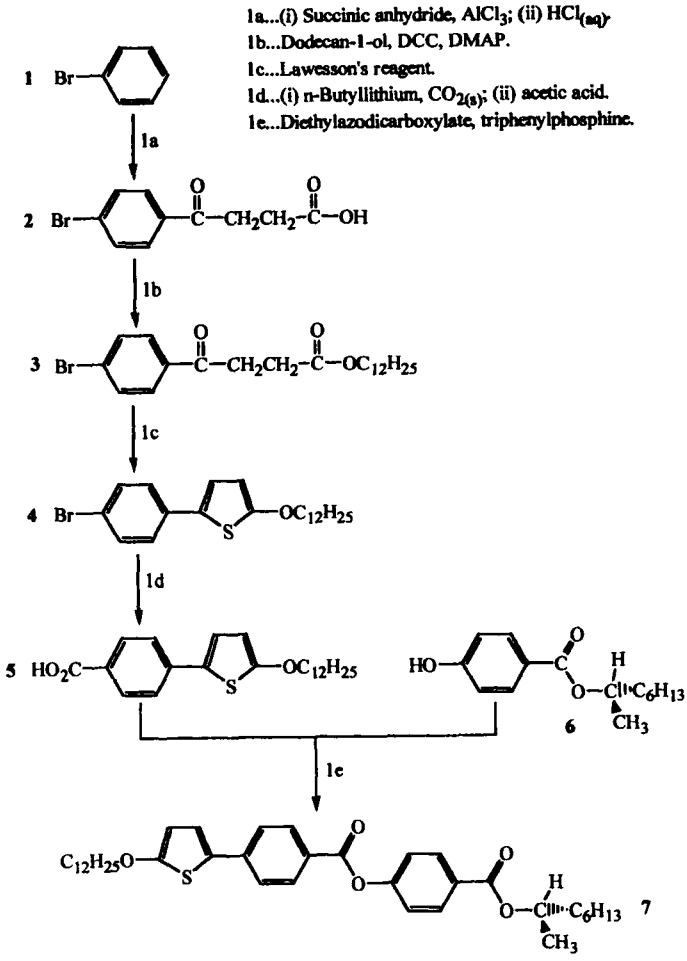
The synthesis of alkoxythiophenes has been thoroughly reviewed by Gronowitz and Hörnfeldt[12, 13]. In these reviews and numerous related papers it quickly becomes apparent that the unit is very difficult to synthesize in high yields and purity, especially when the carbon chain exceeds two carbon atoms in length. Classical methods used to obtain such derivatives include nucleophilic aromatic substitution[14], alkylation of the thien-2-one tautomers[15] and ring closure of γ-ketoesters with H_2S/HCl[16] gases and phosphorus pentasulfide. The last of these methods is not without controversy as a publication by Sagitdinov[17] reports high yields of desired products whilst more recent work by Sedavkina[18] shows unequivocally that the thienones are the major products. We attempted to repeat the work of Sagitdinov and were unsuccessful in eight attempts. However, using our method we obtained one of the materials [2-Ethoxy-5-(4'-hexylbiphenyl-4-yl)thiophene] reported by Sagitdinov and obtained the desired compound which had a very different phase sequencing from that reported.

Our new method involves the cyclization of γ-ketoesters with Lawesson's reagent whereby products are obtained in high yields after purification. We have noted that reaction time is extremely important, and constant monitoring by GLC is needed to avoid the formation of volatile by-products seen upon using extended reaction times.

SYNTHESIS

Experimental

The synthetic pathway used to obtain **7** is given in Scheme 1.



Scheme 1 Synthetic pathway used to obtain (*S*)-(+)-1-methylheptyl 4-[4-(5-dodecyloxythien-2-yl)phenylcarbonyloxybenzoate

3-(4-Bromobenzoyl)propanoic acid (2)

Anhydrous aluminum chloride (26.67 g, 0.2000 mol) was added all at once to a mechanically stirred, cooled (0 °C) mixture of succinic

anhydride (10.01 g, 0.1000 mol) and bromobenzene (96.87 g, 0.6170 mol) under dry argon. Shortly after the addition of the aluminum chloride the reaction turned from a clear-yellow to a clear-orange solution and the evolution of $HCl_{(g)}$ was observed. The reaction conditions were maintained for a period of 4 h before the mixture was allowed to warm to room temperature. The reaction was stirred for 96 h at room temperature before being poured into cooled (0 °C) dilute hydrochloric acid (250 mL, 50%) and mechanically stirred for 1 h. The precipitate was filtered off and washed with water (1 L) before being crystallized from toluene and dried *in vacuo* (P_2O_5, $CaCl_2$, 18 h) to afford white crystals. Yield 24.23 g (94%), mp 146-150 °C. ^{1}HNMR (DMSO-d_6) δ 2.59(2H, t), 3.21(2H, t), 7.88(2H, d), 7.96(2H, d), 12.19(1H, s). IR (KBr) ν_{max} 791, 840, 905, 990, 1074, 1105, 1198, 1241, 1281, 1332, 1410, 1447, 1479, 1585, 1670, 1730, 2600-3400 cm^{-1}. MS m/z 256.2(M^+), 185.1, 183.1(100%), 157.1, 155.1. Anal. Calcd for $C_{10}H_9BrO_3$: C, 46.72; H, 3.53. Found: C, 46.69; H, 3.49.

Dodecyl 3-(4-bromobenzoyl)propanoate (3)

N,N'-Dicyclohexylcarbodiimide (7.77 g, 0.0377 mol) was added all at once to a stirred solution of dodecan-1-ol (5.85 g, 0.0314 mol), compound **2** (8.50 g, 0.0331 mol), and 4-(*N,N*-dimethylamino)pyridine (1.56 g, 0.0128 mol) in anhydrous dichloromethane (300 mL) at room temperature under dry argon. The reaction mixture was stirred at room temperature overnight (TLC analysis confirmed a complete reaction) before the *N,N'*-dicyclohexylurea was filtered off and washed with dichloromethane (150 mL). The filtrate was washed with potassium hydroxide (5%, 2 x 150 mL), acetic acid (10%, 2 x 150 mL), water (2 x 200 mL) and dried ($MgSO_4$). The drying agent was filtered off and the solvent was removed *in vacuo*. The crude product was purified twice by column chromatography (silica gel / ethyl acetate : hexanes (60-80 °C), 1:5) to give a white solid which was dried *in vacuo* (P_2O_5, KOH, paraffin wax, 24 h). Yield 13.30 g (quant), mp 50-52 °C, purity (GLC) 100%. ^{1}HNMR ($CDCl_3$) δ 0.93(3H, t), 1.13-1.40(20H, m), 2.76(2H, t), 3.27(2H, t), 4.09(2H, t), 7.61(2H, d), 7.87(2H, d). IR (NaCl) ν_{max} 787, 1584, 1679, 1727, 2800-3000 cm^{-1}.

2-(4-Bromophenyl)-5-dodecyloxythiophene (4)

A stirred mixture Lawesson's Reagent (4.56 g, 11.3 mmol) and compound **3** (4.00 g, 9.40 mmol) in dry toluene (130 mL), under dry argon, was heated under reflux for 48 h. The reaction mixture was allowed to cool to room temperature and the solvent was removed *in*

vacuo to afford a yellow residue, which was immediately purified by column chromatography [silica gel / hexanes (bp 60-80 °C)] and crystallized from hexanes to afford a white fluffy solid. Yield 3.74 g (94%), mp 76-77 °C, purity (GLC) 99.9%. ^{1}HNMR ($CDCl_3$) δ 0.83(3H, t), 1.22(16H, br s), 1.40(2H, quint), 1.75(2H, quint), 4.01(2H, t), 6.14(1H, d), 6.90(1H, d), 7.31(2H, d), 7.41(2H, d). IR (NaCl) ν_{max} 775, 822, 1202, 1261, 1501, 1548, 2800-3000 cm^{-1}. MS m/z 422.14(M^+), 255.93(100%), 253.95, 57.08, 55.06. Anal. Calcd for $C_{22}H_{31}BrOS$: C, 62.40; H, 7.38. Found: C, 62.44; H, 7.33.

4-(5-Dodecyloxythien-2-yl)benzoic acid (5)

n-Butyllithium (2.7 mL, 2.5M in hexanes, 6.8 mmol) was added dropwise to a stirred, cooled (-78 °C) solution of compound **4** (2.60 g, 6.14 mmol) in dry THF (410 mL). The reaction conditions were maintained for a further 2 h (GLC analysis confirmed a complete reaction) before the reaction mixture was poured into a slurry of solid carbon dioxide and dry THF and was left to stir overnight. The solvent was removed *in vacuo* and the salt was dissolved in hot glacial acetic acid (250 mL). Ice was added to the solution and the product was filtered off, washed with water (1 L) and dried *in vacuo* (P_2O_5, paraffin wax, 48 h) to afford a white solid. The crude product was purified by column chromatography [silica gel / hexanes (60-80 °C)] to afford a white solid. Yield 0.87 g (36%), mp 199-201 °C. ^{1}HNMR (DMSO-d_6) δ 0.83(3H, t), 1.21-1.40(20H, br s), 4.09(2H, t), 6.37(1H, d), 7.39(1H, d), 7.55(2H, d), 7.87(2H, d), the carboxylic acid proton was not observed. IR (NaCl) ν_{max} 765, 849, 962, 1536, 1601, 1678, 2800-3000, 3100-3500 cm^{-1}.

(*S*)-(+)-1-Methylheptyl 4-[4-(5-dodecyloxythien-2-yl]phenylcarbonyloxy benzoate (7)

Compound **7** was prepared as described for the preparation of compound **3** using the quantities stated: *N,N'*-dicyclohexylcarbodiimide (0.463 g, 2.24 mmol), compound **6** (0.469 g, 1.87 mmol), compound **5** (0.749 g, 1.93 mmol), and 4-(*N,N*-dimethylamino)pyridine (0.093 g, 0.76 mmol). The crude product was purified twice by column chromatography [silica gel / hexanes (60-80 °C) : ethyl acetate, 20:1] before being crystallized twice from a mixture of hexanes (60-80 °C) and ethyl acetate (280:1) to afford a white, fluffy solid. Yield 0.48 g (40%). ^{1}HNMR ($CDCl_3$) δ 0.84(6H, t), 1.16-1.36(18H, br s), 1.30(3H, d), 1.42(4H, m), 1.57(2H, m), 1.71(2H, quint), 1.78(4H, quint), 4.02(2H, t), 5.13(1H, sext), 6.19(1H, d), 7.11(1H, d), 7.26(2H, d),

7.58(2H, d), 8.09(4H, 2 x d). ^{13}CNMR ($CDCl_3$) δ 14.291, 14.348, 20.318, 22.815, 22.913, 25.631, 26.067, 29.327, 29.384, 29.508, 29.573, 29.746, 29.795, 29.861, 29.877, 31.971, 32.144, 36.299, 72.152, 74.255, 106.314, 121.917, 123.330, 124.471, 126.639, 128.454, 128.709, 131.131, 131.336, 140.353, 154.749, 164.628, 165.704, 167.272 ppm. IR (KBr) ν_{max} 685, 725, 754, 843, 881, 1015, 1072, 1114, 1159, 1186, 1215, 1264, 1408, 1466, 1512, 1553, 1603, 1704, 1734, 2850, 2918, 3075 cm^{-1}. MS m/z 620.3(M^+), 372.2, 371.2(100%), 203.0(73.69), 202.0(16.30). Anal. Calcd for $C_{38}H_{52}O_5S$: C, 73.51; H, 8.44. Found: C, 73.49; H, 8.57.

Experimental Discussion

Compound **2** was obtained using a modification of the procedure used by Fieser *et al.*[19] which gave considerably higher yields and enhanced regioselectivity. Esterification[20] of **2** with dodecan-1-ol gave **3**, which was then subjected to cyclization with Lawesson's reagent. The same reaction carried out over a 24 h period gave a 61% yield (with starting material as the only other material), and over 72 h a 69% yield was obtained with at least ten volatile by-products being present in the reaction mixture. We have carried out this reaction on a wide variety of γ-ketoesters and we have found that the formation of volatile by-products can be kept to a minimum by careful GLC observation of the reaction. Initially we thought that the Lawesson's reagent might have been reacting with the product to give the by-products. However, we carried out a test reaction and found that we could reflux the pure product and Lawesson's reagent under our standard reaction conditions without observing any significant reaction. This test was carried out over a period of 14 days and we must conclude that the oxidized Lawesson's material is responsible for the side-reactions. Compound **4** underwent halogen-metal exchange followed by carboxylation to give **5**. The low yield of **5** was due to significant quantities of moisture present in the dry ice. Finally, **5** was esterified with **6** to give the product **7**.

RESULTS AND DISCUSSION

The transition temperatures of **7** are given in Table 1 where they are compared with the analogous compounds **9** and AS620 (**8**).

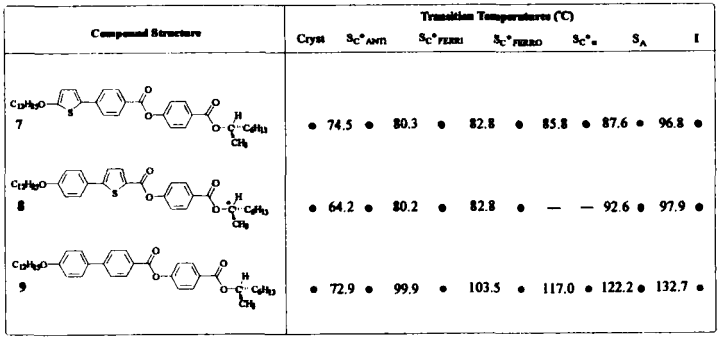


Table 1 Transition temperatures of the alkoxythienyl and the analogous phenylene and 2,5-dithienyl derivatives.

Thiophene-containing materials are often found to have lower melting points than their phenyl counterparts due possibly to the angular nature of the thiophene ring disrupting the molecular packing. However, **7** surprisingly has a higher melting point than the phenyl and thienyl analogs **9** and **8** respectively.

The transition temperatures of **7** are remarkably similar to those of the thiophene analog **8**. Both compounds display smectic A, ferro, ferri and anti phases, and **7** appears to have an alpha phase (currently we are verifying this by electrooptic evaluation) based on the observation of a transient schlieren like texture at the S_A-$S_C^*_\alpha$ phase transition (also seen in **9** where the $S_C^*_\alpha$ phase has been verified).

We have successfully converted γ-ketoesters into alkoxythiophenes using Lawesson's reagent in a highly efficient synthesis. The material presented is the first example of a chiral alkoxythiophene-containing liquid crystal with ferroelectric properties.

References

[1] A. J. Seed, M. Hird, P. Styring, H. F. Gleeson, and J. T. Mills, *Mol. Cryst. Liq. Cryst.*, **299**, 19–25, (1997).

[2] A. Matharu, R. Wilson, and C. Grover, *Mol. Cryst. Liq. Cryst.*, **332**, 303–311, (1999).

[3] J. Mills, R. Miller, H. Gleeson, A. Seed, M. Hird, and P. Styring, *Mol. Cryst. Liq. Cryst.*, **303**, 145–152, (1997).

[4] J. T. Mills, H. F. Gleeson, J. W. Goodby, M. Hird, A. Seed, and P. Styring, *J. Mater. Chem.*, **8**, 2385–2390, (1998).

[5] G. Koβmehl and D. Budwill, *Z. Naturforsch*, **38b**, 1669–1677, (1983).

[6] G. Koβmehl and D. Budwill, *Z. Naturforsch* **40b**, 1199–1213, (1985).

[7] G. Koβmehl and D. Budwill, *Z. Naturforsch*, **41b**, 751–761, (1986).

[8] A. J. Seed, K. J. Toyne, and J. W. Goodby, *J. Mater. Chem.*, **5**, 653–661, (1995).

[9] D. J. Byron, A. S. Matharu, I. McSherry, and R. C. Wilson, "The synthesis and mesomorphic behavior of a new series of antiferroelectric liquid crystals containing the thiophene nucleus," presented at 10th Annual British Liquid Crystal Conference, Exeter, 1995.
[10] A. A. Kiryanov, P. Sampson, and A. J. Seed, *Mol. Cryst. Liq. Cryst.*, **328**, 237–244, (1999).
[11] J. W. Goodby, *Mol. Cryst. Liq. Cryst.*, **292**, 245–263, (1997).
[12] S. Gronowitz and A.-B. Hörnfeldt, 1986, 'Syntheses, physical properties and reactions of compounds containing thiophene-oxygen bonds.' in *Thiophene and its derivatives.*, 44, *The chemistry of heterocyclic compounds*, edited by S. Gronowitz. (New York, John Wiley and Sons), pp. 1–133.
[13] A.-B. Hörnfeldt, *Svensk. Kem. Tidskr.*, **80**, pp. 343–356, (1968).
[14] R. A. Parker, T. Kariya, J. M. Grisar, and V. Petrow, *J. Med. Chem.*, **20**, 781–791, (1977).
[15] E. B. Pedersen and S.-O. Lawesson, *Tetrahedron*, **27**, 3861–3868, (1971).
[16] J. Brunet, D. Paquer, and P. Rioult, *Phosphorus and sulfur*, **3**, 377–379, (1977).
[17] I. A. Sagitdinov and H. Schubert, *Russ. J. Org. Chem. (Engl. Transl.)*, **14**, 988–992, (1978).
[18] V. A. Sedavkina, N. A. Morozova, A. Y. Egorova, and I. G. Ostroumov, *Khim. Geterotsikl. Soedin.*, 377–380, (1987).
[19] L. F. Fieser and A. M. Seligman, *J. Am. Chem. Soc.*, **60**, 170–176, (1938).
[20] A. Hassner and V. Alexanian, *Tett. Lett.*, **19**, 4475–4478, (1978).