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Synthesis of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates, monomers for side chain liquid crystal polymers

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Abstract A variety of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates, which can serve as monomers for side chain liquid crystal polymers, were readily synthesized from hydroquinone. Instead of the rare and expensive 2,5-dihydroxybenzaldehyde, cheaper and readily available hydroquinone was employed as starting material in our new method. Hazardous reagents, such as highly flammable BH_3.THF employed in the reported literature, were excluded as well. Our new method uses cheaper starting materials and chemicals, which are easier to handle with less safety issues.

Graphical Abstract A variety of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates, which can serve as monomers for side chain liquid crystal polymers, were readily synthesized from hydroquinone. Instead of the rare and expensive 2,5-dihydroxybenzaldehyde, cheaper and readily available hydroquinone was employed as starting material in our new method. Hazardous reagents, such as highly flammable BH_3.THF employed in the reported literature, were excluded as well. Our new method uses cheaper starting materials and chemicals, which are easier to handle with less safety issues.

Yong Li and Yao Yuan contributed equally to this work.

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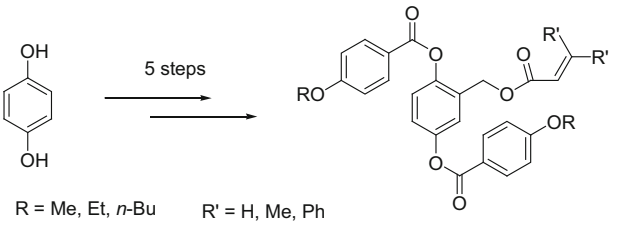


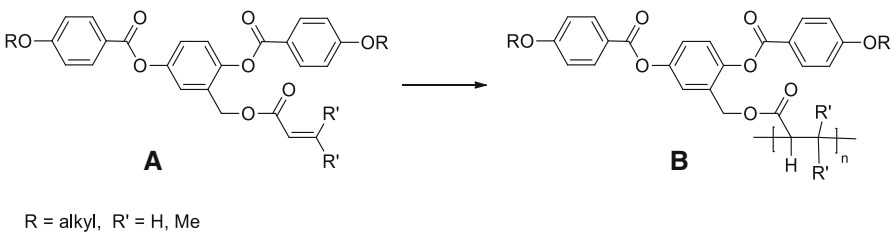
Keywords 2,5-(4-alkoxybenzoyloxy)benzyl acrylates · 2,5-(4-alkoxybenzoyloxy)benzyl cinnamates · Side chain liquid crystal polymers

Introduction

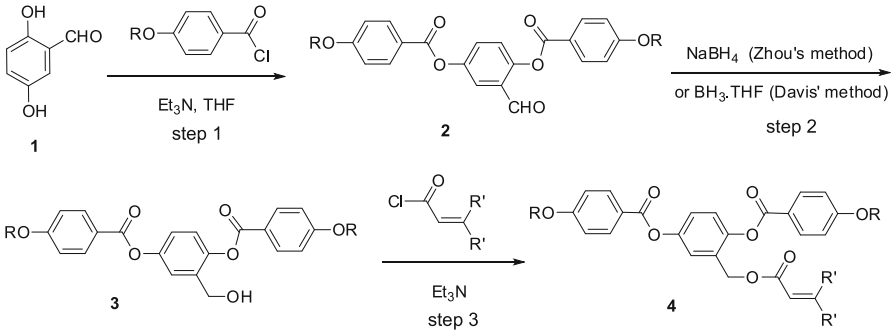
The 2,5-(4-alkoxybenzoyloxy)benzyl acrylates (Scheme 1A) are monomers of a class of side chain liquid crystal polymers [1–3] (Scheme 1 B), which exhibit liquid crystalline behaviour over a wide temperature range [3]. Many liquid crystalline copolymers and elastomers can also be prepared by copolymerisation of the 2,5-(4-alkoxybenzoyloxy)benzyl acrylates with other monomers [3].

The first synthesis of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates was reported by Zhou et al. [1] in 1987 (Scheme 2). A modification was made by Davis et al. [3] in 1996 (Scheme 2).

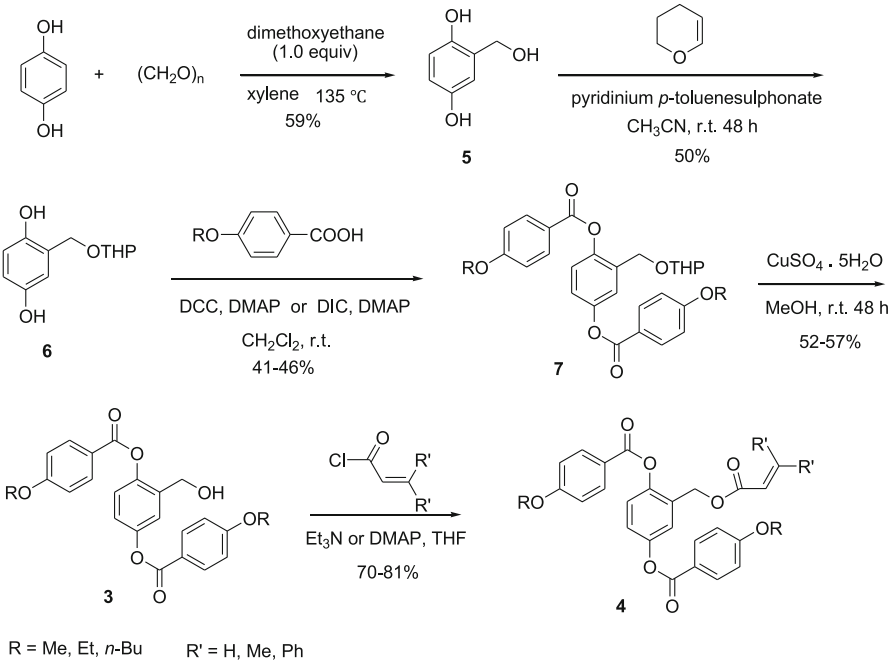
As shown in Scheme 2, the starting material 2,5-dihydroxybenzaldehyde (**1**) is rare and expensive. In step 2, it seems that the reduction of aldehyde **2** by $NaBH_4$ (Zhou's method [2, 3]) is not as successful as the authors claim [3]. Because instead of $NaBH_4$, BH_3.THF (step 2, Davis' method [3]) must be used for the reduction of aldehyde **2**. Otherwise the alcohol **3** can not be obtained while unexpected products are formed [3]. The BH_3.THF solution is highly flammable and sensitive to air or moisture. It can react violently with water and may form explosive peroxides in contact with air. As a result, Davis' method would be hazardous. On the other hand, insufficient information about the yields for preparation of aldehyde **2**, alcohol **3**, and compound **4** was reported by the literature [1–3]. Only when R=Me and R′=H the yields were given by both methods [1–3]. While R=Et or *n*-Bu, no yields were reported [2] even if the compounds were fully characterized by ^{1}H-NMR, elemental analysis, and IR.



Scheme 1 Synthesis of side chain liquid crystal polymers from 2,5-(4-alkoxybenzoyloxy)benzyl acrylates



Scheme 2 Reported methods for synthesis of 2,5-(4- alkoxybenzoyloxy)benzyl acrylates



Scheme 3 Our synthesis route to 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates

Results and discussion

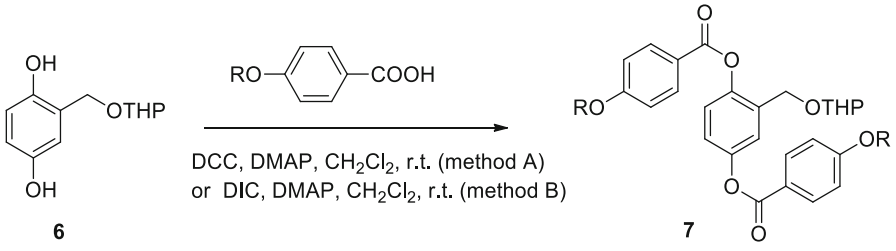
We reported herein a new method for the synthesis of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates from cheap starting materials. The new method uses chemicals which are easier to handle with less safety issues (Scheme 3).

As shown in Scheme 3, 2-(hydroxymethyl)benzene-1,4-diol (**5**) can be obtained in 59 % yield by the reaction of hydroquinone with excess paraformaldehyde in xylene [4]. The starting materials are much more cheaper than the 2,5-dihydroxybenzaldehyde (**1**) employed in the reported methods. Compound **5** can be prepared on a multigram scale. After selective protection of the hydroxymethyl group of **5** with 3,4-dihydro-*2H*-pyran [5, 6] in the presence of pyridinium p-toluenesulphonate, **6** can be obtained in 50 % yield. Subsequently, we tried to synthesize **7**. As shown in Scheme 4, two methods were employed for the synthesis of **7**. It's worthy to noted that *N*,*N*′-Diisopropylcarbodiimide (DIC) has to be employed when preparing **7b** and **7c**. **7** can be prepared in modest yield from **6**.

With **7** in hand, we next tried to synthesize **3** by deprotection of the *THP*-group. Mild reactions have to be employed in order to prevent hydrolysis of the two ester groups of **7**. $CuSO_4.5H_2O$ [7, 8] was, therefore, employed for the *THP*-deprotection. As shown in Scheme 5, **3** can be obtained in modest to good yields.

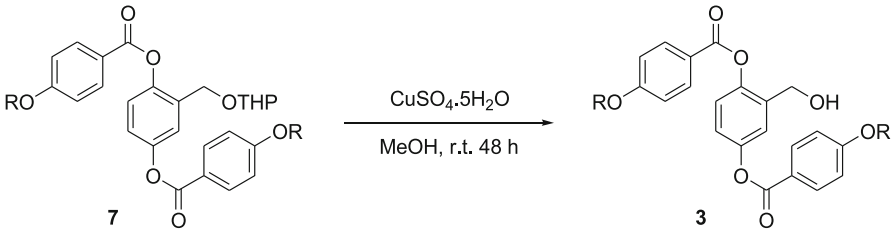
Finally, we tried to synthesize the monomer 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates **4** from **3** with appropriate acid chloride [1–3].

As shown in Table 1, various 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates **4** can be synthesized from **3** in the presence of Et_3N (entries 1, 2, 3, Table 1) or DMAP (entries 4, 5, 6, 7, Table 1) in good to excellent yields. The alkoxy groups in **4** can be the butoxy group (entries 1, 2, 3, Table 1), ethoxy group (entries 4, 5, 6, Table 1) or methoxy group (entry 7, Table 1). The groups attached by in the olefinic bond of **4** can be only H atoms (entries 1, 4, Table 1), a methyl group (entries 2, 3, 5, Table 1) or a phenyl group (entries 6, 7, Table 1). The methyl group attached in the olefinic bond of **4** can be in the terminal of the olefinic bond (entry 3, Table 1) or adjacent to the carbonyl group (entries 2, 5, Table 1). The



7a, R = *n*-Bu, yield = 46%. method A
7b, R = Et, yield = 41%, method B
7c, R = Me, yield = 43%, method B

Scheme 4 Synthesis of **7** from **6**



3a, R = *n*-Bu, yield = 57%., **3b**, R = Et, yield = 52%, **3c**, R = Me, yield = 55%

Scheme 5 Synthesis of **3** by deprotection of **7**

diverse monomers **4** could be employed for synthesis of versatile side chain liquid crystal polymers.

In summary, a variety of 2,5-(4-alkoxybenzoyloxy)benzyl acrylates and cinnamates **4** which could serve as monomers for side chain liquid crystal polymers were readily synthesized from hydroquinone. Instead of the rare and expensive 2,5-dihydroxybenzaldehyde, cheaper and readily available hydroquinone was employed as starting material in our new method. Hazardous reagents such as highly flammable BH_3.THF employed in the reported literature were excluded as well. The new method uses chemicals, which are easier to handle with less safety issues. The preparation of monomers **4** on a multigram scale by our new method is under research in our lab. This part of the work will be reported in due course.

Experimental

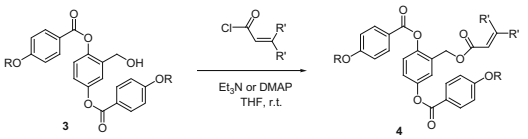
General

All commercially available reagents were used without further purification. Column chromatography was performed on silica gel (200–300 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded in $CDCl_3$ or $(CD_3)_2SO$ at 400 MHz on a Bruker NMR spectrometer. All chemical shifts are reported in ppm downfield from TMS and peak multiplicities are referred to as singlet (*s*), doublet (*d*), quartet (*q*), and multiplet (*m*).

Synthesis of 5

2-(hydroxymethyl)benzene-1,4-diol (**5**) can be synthesized in 59 % yield by the reaction of hydroquinone with excess paraformaldehyde in xylene according to the reported method [4]. Compound **5** can be prepared on a multigram scale. IR (neat): 3752, 2840, 2368, 1728, 1704, 1648, 1620, 1524, 1332, 1288 cm^{-1}. ^{1}H-NMR ($(CD_3)_2SO$): δ 8.59 (s, 1H), 8.57 (s, 1H), 6.75–6.74 (m, 1H), 6.56–6.54 (m, 1H), 6.44–6.41 (m, 1H), 4.94–4.91 (m, 1H), 4.41 (d, $J = 4.8$ Hz, 2H). ^{13}C-NMR ($(CD_3)_2SO$): δ 150.2, 146.8, 129.8, 115.5, 114.4, 113.7, 58.7. HRMS (FAB) calcd

Table 1 Synthesis of **4** from **3**



Entry	Substrate **3**	Acid chloride/Base	Product **4**	Yield[a]
1	**3a**	/ Et_3N	**4a**	**81%**
2	**3a**	/ Et_3N	**4b**	**79%**
3	**3a**	/ Et_3N	**4c**	**75%**
4	**3b**	/ DMAP	**4d**	**79%**
5	**3b**	/ DMAP	**4e**	**70%**
6	**3b**	Ph / DMAP	**4f**	**80%**
7	**3c**	Ph / DMAP	**4g**	**76%**

[a] Isolated yield

for $C_7H_8O_3$ (MH+): 140.0473; found: 140.0476. Elemental analysis: calc 59.99 % C, 5.75 % H; found 59.88 % C and 5.65 % H.

Synthesis of 6

2-(hydroxymethyl)benzene-1,4-diol (**5**) (100 mg, 0.71 mmol) was dissolved in 10 mL CH_3CN. To the solution, pyridinium p-toluenesulphonate (178 mg, 0.71 mmol) was added. To the mixture a solution of 3,4-dihydro-*2H*-pyran (60 mg, 0.71 mmol) in 10 mL CH_3CN was added. The mixture was stirred at r.t. for 48 h. After removal of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, PE/EtOAc = 1:1) to afford compound **6** (80 mg, yield: 50 %). IR (neat): 3306, 3035, 2870, 1613, 1455 cm^{-1}. ^{1}H-NMR ($(CD_3)_2SO$): δ 8.71 (s, 1H), 8.65 (s, 1H), 6.70 (d, $J = 2.8$ Hz, 1H), 6.60–6.55 (m, 1H), 6.49–6.46 (m, 1H), 4.67–4.66 (m, 1H), 4.56 (d, $J = 12.4$ Hz, 1H), 4.36 (d, $J = 12.4$ Hz, 1H), 3.83–3.77 (m, 1H), 3.49–3.45 (m, 1H), 1.76–1.72 (m, 1H), 1.68–1.62 (m, 1H), 1.53–1.47 (m, 4H). ^{13}C-NMR ($(CD_3)_2SO$): δ 150.1, 147.4, 125.7, 115.9, 115.3, 114.7, 97.8, 63.8, 61.6, 30.7, 25.5, 19.5. HRMS (FAB) calcd for $C_{12}H_{16}O_4$ (MH+): 224.1049; found: 224.1051. Elemental analysis: calc 64.27 % C, 7.19 % H; found 64.20 % C and 7.10 % H.

Synthesis of 7a (method A)

To a mixture of 4-butoxybenzoic acid (110 mg, 0.57 mmol) and DCC (120 mg, 0.58 mmol) in 3 mL CH_2Cl_2 was added a solution of **6** (40 mg, 0.18 mmol) and DMAP (70 mg, 0.57 mmol) in 3 mL CH_2Cl_2. The mixture was stirred at r.t. for 12 h. After removal of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, PE/EtOAc = 5:1) to afford compound **7a** (51 mg, yield: 46 %).IR (neat): 2640, 2360, 1728, 1720, 1660, 1644, 1468, 1392, 1164, 1072 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 8.18–8.16 (m, 4H), 7.42 (d, $J = 2.4$ Hz, 1H), 7.28–7.20 (m, 2H), 7.01–6.99 (m, 4H), 4.80 (d, $J = 12.8$ Hz, 1H), 4.68 (t, $J = 3.2$ Hz, 1H), 4.55 (d, $J = 12.8$ Hz, 1H), 4.08 (t, $J = 6.4$ Hz, 4H), 3.85–3.79 (m, 1H), 3.50–3.45 (m, 1H), 1.87–1.80 (m, 5H), 1.68–1.43 (m, 9H), 1.02 (t, $J = 7.6$ Hz, 6H). ^{13}C-NMR ($CDCl_3$): δ 164.8, 164.5, 163.6, 163.5, 148.6, 146.1, 132.3, 132.3, 132.2, 123.3, 122.2, 121.6, 121.2, 114.3, 114.3, 97.9, 68.0, 63.7, 61.8, 31.1, 30.3, 25.4, 19.2, 19.1, 13.8. HRMS (FAB) calcd for $C_{34}H_{40}O_8$ (MH+): 576.2723; found: 576.2720. Elemental analysis: calc 70.81 % C, 6.99 % H; found 70.64 % C and 6.87 % H.

Synthesis of 7b (method B)

To a mixture of **6** (151 mg, 0.67 mmol) and DMAP (246 mg, 2.01 mmol) in 15 mL CH_2Cl_2 DIC (255 mg, 2.02 mmol) was added. The mixture was stirred for 10 min. To the mixture, a solution of 4-ethoxybenzoic acid (336 mg, 2.02 mmol) in 15 mL CH_2Cl_2 was added. The mixture was stirred at r.t. for 12 h. After removal of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, PE/EtOAc = 5:1) to afford compound **7b** (153 mg, yield: 41 %). IR (neat): 2640,

2360, 1728, 1720, 1660, 1644, 1468, 1392, 1316, 1164, 1072, 1036 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 8.16–8.13 (m, 4H), 7.39 (d, $J = 2.4$ Hz, 1H), 7.24–7.17 (m, 2H), 6.98–6.96 (m, 4H), 4.77 (d, $J = 12.8$ Hz, 1H), 4.66 (t, $J = 3.2$ Hz, 1H), 4.52 (d, $J = 12.8$ Hz, 1H), 4.13 (q, $J = 6.8$ Hz, 4H), 3.82–3.76 (m, 1H), 3.47–3.42 (m, 1H), 1.88–1.73 (m, 2H), 1.69–1.53 (m, 2H), 1.48–1.45 (m, 8H). ^{13}C-NMR ($CDCl_3$): δ 168.3, 167.0, 164.8, 163.4, 148.6, 146.1, 132.3, 132.3, 132.2, 123.3, 122.2, 121.6, 121.5, 121.3, 114.3, 114.3, 97.9, 63.8, 63.7, 61.8, 30.3, 25.4, 19.1, 14.7. HRMS (FAB) calcd for $C_{30}H_{32}O_8$ (MH+): 520.2097; found: 520.2091. Elemental analysis: calc 69.22 % C, 6.20 % H; found 69.14 % C and 6.13 % H.

Synthesis of 7c (method B)

To a mixture of **6** (150 mg, 0.67 mmol) and DMAP (246 mg, 2.01 mmol) in 15 mL CH_2Cl_2 DIC (255 mg, 2.02 mmol) was added. The mixture was stirred for 10 min. To the mixture, a solution of 4-methoxybenzoic acid (305 mg, 2.00 mmol) in 15 mL CH_2Cl_2 was added. The mixture was stirred at r.t. for 12 h. After removal of the solvent under vacuum, the residue was purified by column chromatography (SiO_2, PE/EtOAc = 5:1) to afford compound **7c** (152 mg, yield: 43 %). IR (neat): 2640, 2360, 1728, 1720, 1660, 1644, 1468, 1392, 1164, 1064, 1036 cm^{-1}. ^{1}H-NMR ($CDCl_3$): δ 8.20–8.18 (m, 4H), 7.43–7.42 (m, 1H), 7.27–7.21 (m, 2H), 7.03–7.00 (m, 4H), 4.80 (d, $J = 12.8$ Hz, 1H), 4.68 (s, 1H), 4.54 (d, $J = 12.8$ Hz, 1H), 3.92 (s, 6H), 3.85–3.79 (m, 1H), 3.49–3.46 (m, 1H), 1.83–1.76 (m, 1H), 1.74–1.56 (m, 5H). ^{13}C-NMR ($CDCl_3$): δ 164.8, 164.5, 164.0, 163.9, 148.6, 146.1, 132.3, 132.3, 132.2, 123.3, 122.2, 121.7, 113.9, 113.8, 97.9, 63.7, 61.8, 55.5, 30.3, 25.4, 19.1. HRMS (FAB) calcd for $C_{28}H_{28}O_8$ (MH+): 492.1784; found: 492.1791. Elemental analysis: calc 68.28 % C, 5.73 % H; found 68.20 % C and 5.68 % H.

General procedure for the synthesis of 3

To a solution of 7 in MeOH, excess $CuSO_4.5H_2O$ was added. The mixture was stirred at r.t. for 48 h. The solvent was removed under vacuum. The residue was diluted with water and extracted by EtOAc. The combined organic layer was dried over Na_2SO_4. After filtration, the filtrate was concentrated under vacuum, and the residue was purified by column chromatography (SiO_2, PE/EtOAc = 2:1) to afford **3** in 52–57 % yield.

General procedure for the synthesis of 4

Compound **3** and base (Et_3N or DMAP) were dissolved in THF. To the mixture, a solution of appropriate acid chloride in THF was added dropwise at 0 °C. After stirred at 0 °C for 4 h, the mixture was diluted with water and extracted by EtOAc. The combined organic layer was dried over Na_2SO_4. After filtration, the filtrate was concentrated under vacuum, and the residue was purified by column chromatography (SiO_2, PE/EtOAc = 2:1) to afford **4** in 70–81 % yield.

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References

1. Q.-F. Zhou, A.-M. Li, X.-D. Feng, Macromolecules **20**, 233–234 (1987)
2. Q.-F. Zhou, A.-M. Li, X.-D. Feng, Mol. Cryst. Liq. Cryst. **155**, 73–82 (1988)
3. E.A. Whale, F.J. Davis, G.R. Mitchell, J. Mater. Chem. **6**, 1479–1485 (1996)
4. G. Casiraghi, G. Casnati, G. Puglia, G. Sartori, Synthesis **1980**, 124–125 (1980)
5. D.M. Pore, U.V. Desai, R.B. Mane, P.P. Wadgaonkar, Synth. Commun. **34**, 2135–2142 (2004)
6. V. Kumbaraci, D. Ergunes, M. Midilli, S. Begen, N.J. Talinli, Heterocycl. Chem. **46**, 226–230 (2009)
7. T.K. Abu, H.C. Lokman, G. Subrata, Tetrahedron Lett. **45**, 7891–7894 (2004)
8. Z. Li, B. Liu, W.-B. Duan, L. Zhu, Synth. Commun. **45**, 2740–2747 (2015)