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Synthesis of dibromotetraalkoxybiphenyls using ferric chloride

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Abstract

Provided key reactive sites are blocked, oxidation of dialkoxy benzene derivatives can be stopped at the biphenyl stage.

Oxidative coupling of aromatic or heterocyclic compounds provides a method for creating aryl–aryl bonds which is sometimes cheaper, quicker or easier than palladium-based routes.[1–7] In our work on the synthesis of triphenylenes we have shown that a ferric chloride–dichloromethane/methanol workup protocol provides the best route to a wide range of systems.[1–4] These reactions involve a repeated cycle of one-electron oxidation, carbon–carbon bond forming and deprotonation steps and, when an excess of ferric chloride is used, the cycle continues until a highly conjugated, non-reactive cation or radical cation is formed. The methanol workup reduces this cation back to the neutral oligomer. It is an essential part of the protocol, since an aqueous workup of these cation solutions frequently results in a mixture of addition/substitution products.[5] In at least one case it has been proved that the carbon–carbon bond forming step involves the dimerisation of a radical cation[6] and this may explain why, in the case of benzene derivatives containing an amino or alkoxy substituent, coupling usually occurs *para* (less frequently *ortho*) to the substituent.

In the case of dialkoxybenzene derivatives we have shown that the extent of oligomerisation depends critically on the substitution pattern of the ring and in this paper we show that this can be modulated using bromine substituents to block key reactive sites.

Hence *meta*-dialkoxybenzenes give a polymer that is sparingly soluble in chlorinated solvents. The ^{1}H NMR spectrum of the polymer obtained from 1,3-dimethoxybenzene in $CDCl_3$ is broad and shows the presence of two aromatic protons at δ 6.6 and 7.2 with a 1:1 intergration. On this basis it is assigned the structure **2** (Scheme 1).[8]

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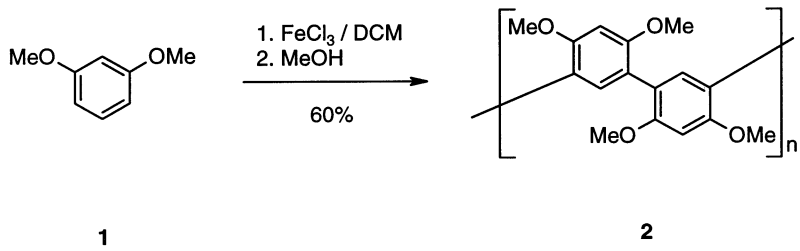
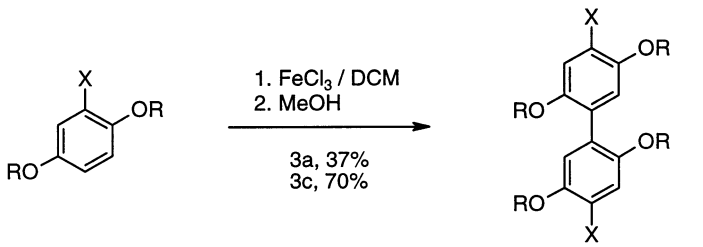


1 2

Scheme 1.

Para-dialkoxybenzene derivatives give predominantly the dimer (the biphenyl). When 1,4-dihexyloxybenzene **3a** is oxidised using ferric chloride in dichloromethane, the only isolatable low molar mass product is 2,2′,5,5′-tetrahexyloxybiphenyl **4a** (37%).[9] Similarly, Nishinaga et al.[10] had previously shown that 1,4-dimethoxybenzene **3b** gave 2,2′,5,5′-tetramethoxybiphenyl **4b** (39%) when oxidised using aluminium trichloride. Presumably the low yield of these reactions is related to the fact that the products contain free 4 and 4′ sites through which further coupling reactions can occur. When these sites are blocked with a bromine, the yield of biphenyl is much improved. Hence oxidation of 2-bromo-1,4-dimethoxybenzene **3c** using the usual ferric chloride–dichloromethane/methanol workup protocol gives the biphenyl **4c** in 70% yield (Scheme 2).[9]

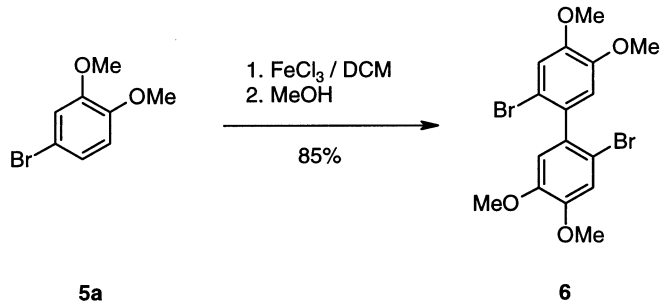


3a R = C_6H_{13}, X = H
3b R = Me, X = H
3c R = Me, X = Br

4a R = C_6H_{13}, X = H
4b R = Me, X = H
4c R = Me, X = Br

Scheme 2.

Simple *ortho*-dialkoxybenzenes give the cyclic trimer (2,3,6,7,10,11-hexaalkoxytriphenylene)[1] but, once again, blocking the 4-position with a bromine forces the reaction to stop at the biphenyl stage. Hence 4-bromo-veratrole **5a** (Scheme 3) gives the biphenyl **6** in 85% yield.[11] Analogues of **5a** with longer alkyl chains also undergo this reaction although it is accompanied by a little dealkylation and realkylation of the crude product is needed to simplify the purification and to give a good yield. Starting from 4-iodo-1,2-dimethoxybenzene, no 2,2′-diiodo-4,4′,5,5′-tetramethoxybiphenyl was obtained. However, iodine was released under the reaction conditions.

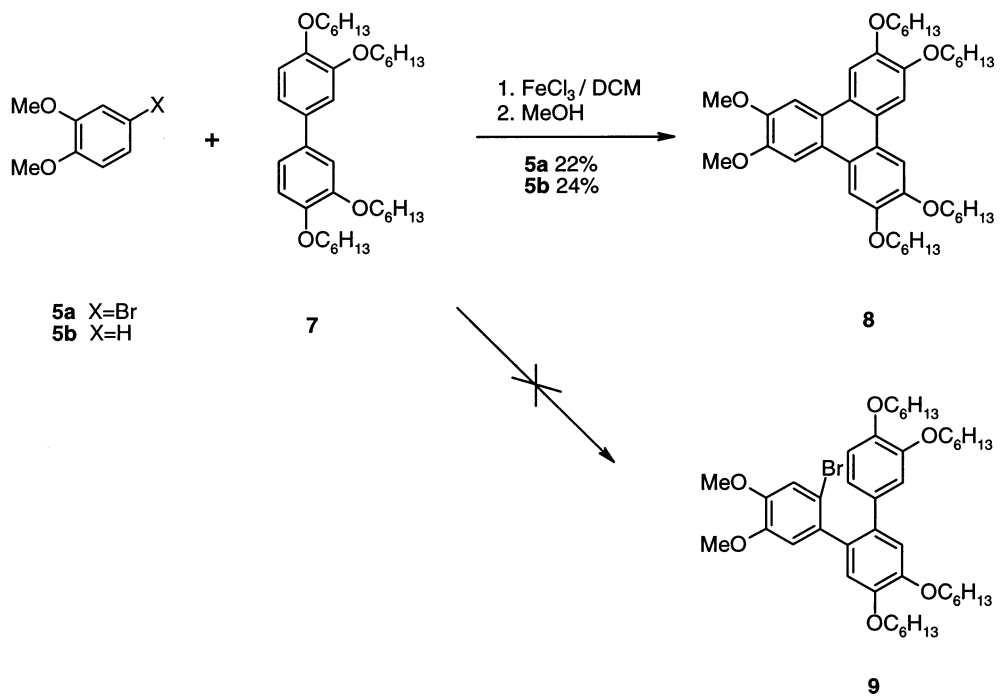


5a **6**

Scheme 3.

Dihalodialkoxybiphenyls of the type made here (**4** and **6**) have proved important intermediates in the synthesis of liquid crystals,[2] molecular magnets[13] and heterocyclic systems[14] and these new ferric chloride based routes represent a very substantial improvement on the routes previously employed.[12–15] It should be possible to generalise the 'bromine blocking group' principle to use the ferric chloride–dichloromethane/methanol workup procedure in the synthesis of many other systems.

Oxidative coupling is not limited to the production of symmetrical dimers. Provided the oxidation potentials are correctly matched, oxidation of a mixture of aromatic compounds A and B can give specifically the mixed product (A–B) with no accompanying self-coupling products (A–A or B–B). Using the ferric chloride–dichloromethane/methanol workup protocol, compound **5b** (on its own) gives a trimer[2] and compound **7** (on its own) gives a dimer. When a 1:1 mixture of **5b** and **7** is treated with ferric chloride/methanol, however, none of these self-coupling products are detected: only the desired cross-coupling product **8**[1,2] (Scheme 4). By



Scheme 4.

using 4-bromoveratrole **5a** we hoped that we could extend the bromine blocking group principle to obtain a good yield of the *meta*-terphenyl **9**.

Ferric chloride was added to the solution of 3,3′,4,4′-tetrahexyloxybiphenyl **7** in dichloromethane and after 30 min 1.5 equiv. of 4-bromoveratrole was added, and the mixture left overnight and worked-up with methanol. No bromo-substituted terphenyl was observed. The only isolatable product was 2,3-dimethoxy-6,7,10,11-tetrahexyloxytriphenylene **8** in 24% yield.[16]

Acknowledgements

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8. ^{1}H NMR data of compound **2** (300 MHz, $CDCl_3$); δ 7.2 (2H, s, Ar*H*, 6,6′), 6.6 (2H, s, Ar*H*, 3,3′), 3.74 (6H, s, ArOCH_3). Mp>250°C.
9. ^{1}H NMR data of compound **4a** (300 MHz, $CDCl_3$); δ 7.08 (2H, s, Ar*H*, 6,6′), 7.05 (2H, d, *J* 8 Hz, Ar*H*, 4,4′), 6.92 (2H, d, *J* 8 Hz, Ar*H*, 3,3′), 3.90 (8H, m, ArOCH_2), 1.2–2.2 (32H, m, CH_2), 0.88 (12H, t, *J* 6.7 Hz, CH_3). ^{1}H NMR data of compound **4c** (300 MHz, $CDCl_3$); δ 7.17 (2H, s, Ar*H*, 3,3′), 6.82 (2H, s, Ar*H*, 6,6′), 3.85 (6H, s, ArOCH_3, 5,5′), 3.73 (6H, s, ArOCH_3, 2,2′).
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11. ^{1}H NMR data of compound **6** (300 MHz, $CDCl_3$); δ 7.11 (2H, s, Ar*H*, 6,6′), 6.76 (2H, s Ar*H*, 3,3′), 3.92 (6H, s, ArOCH_3, 5,5′), 3.87 (6H, m, ArOCH_3, 4,4′).
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16. ^{1}H NMR data of compound **8** (300 MHz, $CDCl_3$); δ 7.83 (4H, s, Ar*H*), 7.78 (2H, s, Ar*H*), 4.24 (8H, t, *J* 6.7 Hz, ArOCH_2), 4.15 (6H, s, ArOCH_3), 1.99 (8H, m, CH_2), 1.40–1.60 (24H, m, CH_2), 0.94 (12H, t, *J* 6.7 Hz, CH_3).