3,4-Bis(tributylstannyl)furan: a Versatile Building Block for the Regiospecific Synthesis of 3,4-Disubstituted Furans†

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By utilising an oxazole–alkyne Diels–Alder reaction, 3,4-bis(tributylstannyl)furan is prepared and its synthetic potential assessed by its conversion into several 3,4-disubstituted furans *via* Stille-type palladium-catalysed reactions.

The synthesis of polysubstituted furans[1] appears especially worthy of study because they are important building blocks for natural and non-natural product syntheses.[2] However, the propensity of furans to undergo both metallation and electrophilic reaction at carbon-2 or carbon-5[3] has inspired a persistent quest to establish sophisticated methods for producing furans with substituents at carbon-3 and carbon-4.[4] In this connection, a convenient route to prepare regiospecifically 3,4-disubstituted furans was devised as part of our continuing efforts to design novel benzenoid molecules.[5] Recent work on the conversion of trialkylstannylfurans to 3-acylfurans[4,6a,b] and 2-alkenylfuran[6c] also prompted us to disclose our own results. In this communication, we report the preparation of 3,4-bis(tributylstannyl)furan **1a** and its pivotal

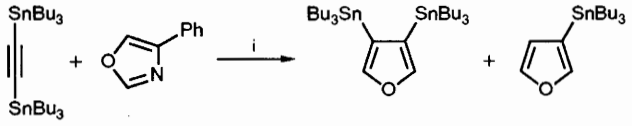
† 3,4-Disubstituted furans: Part 2. Part 1: M. S. Ho and H. N. C. Wong, *J. Chem. Soc., Chem. Commun.*, 1989, 1238.

role as a prominent starting material for 3,4-disubstituted furan synthesis.

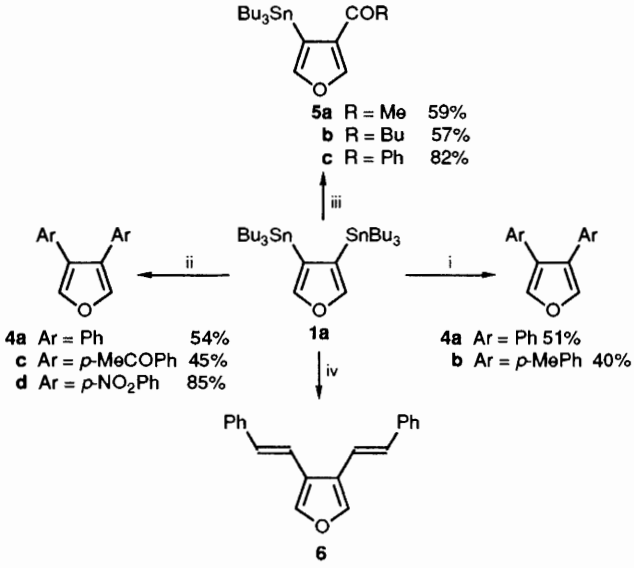
The strategy to be employed for the synthesis of **1a** was the alkyne–oxazole Diels–Alder cycloaddition.[2b,7] Thus, a solution of the commercially available bis(tributylstannyl)acetylene **2** and 4-phenyloxazole **3**[8] was thermolysed in a sealed tube at 185 °C for 6–7 days to give a separable mixture of **1a** and the known **1b**[6b] in 19 and 23% yield, respectively.‡ The structure of **1a** was assigned by ^{1}H and ^{13}C NMR spectroscopy.§ The fact that **1a** can, in practice, be obtained in multigram scale more or less compensates the apparent difficulties associated with its meagre yield.

Having secured a seemingly reliable access to **1a**, its preliminary transformations to various 3,4-disubstituted furans were, therefore, sought. As anticipated, **1a** was converted into 3,4-diarylfurans **4**[4a] in moderate yields by utilising Stille-type coupling reactions.[9] We have found that both bis(triphenylphosphine)palladium dichloride (5 mol%)[9b] and tetrakis(triphenylphosphine)palladium (4 mol%)[9c] are effective catalysts in these experiments. The configuration of **4** was substantiated spectroscopically.§

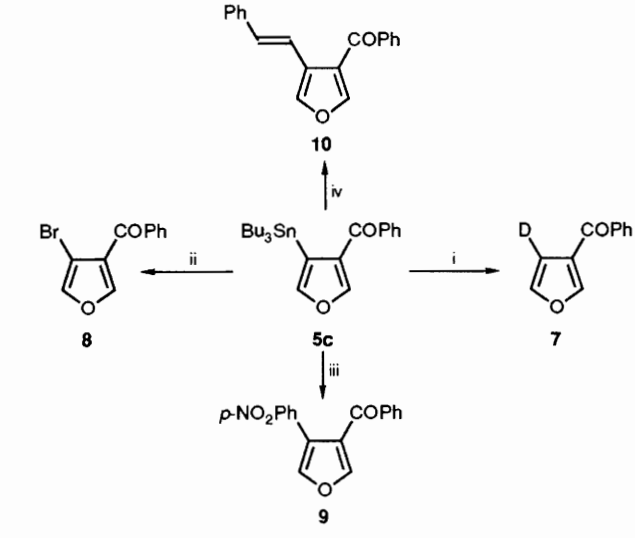
Another way in which **1a** can be converted would be its partial acylation reaction with an acid chloride in the presence of a palladium catalyst (5 mol%),[10] leading to 3-acyl-4-(tributylstannyl)furan **5**.§ On the other hand, *trans*-β-bromostyrene **1a** underwent allyl palladium chloride dimer (4 mol%) catalysed reaction to give exclusively *trans*-3,4-bis(styryl)-furan **6**§ in 69% yield.



Scheme 1 *Reagents and conditions*: i, sealed tube, 185 °C, 6–7 days



Scheme 2 *Reagents and conditions*: i, ArI, $PdCl_2[P(C_6H_5)_3]_2$, CuI, HMPA, 65 °C, 10–24 h; ii, ArBr, $Pd[P(C_6H_5)_3]_4$, HMPA, air, 65–80 °C, 10–24 h; iii, RCOCl, $PdCl_2[P(C_6H_5)_3]_2$, THF, 65–80 °C, 10–24 h; iv, *trans*-C_6H_5CH=CHBr, $[(C_3H_5)PdCl]_2$, HMPA, room temp., 1 h; HMPA = hexamethylphosphoramide, THF = tetrahydrofuran



Scheme 3 *Reagents and conditions*: i, CF_3CO_2D, CH_2Cl_2, room temp., 40 min; ii, Br_2, THF, −78 °C, 30 min; iii, *p*-$NO_2C_6H_4Br$, $Pd[P(C_6H_5)_3]_4$, HMPA, 80 °C, 23 h; iv, *trans*-C_6H_5CH=CHBr, $[(C_3H_5)PdCl]_2$, HMPA, 60 °C, 2 h

Upon treatment with either [$^2H_1$]trifluoroacetic acid,[11] or bromine,[12] the remaining tributylstannyl group of **5c** was replaced accordingly with a deuterium atom or a bromine atom, affording **7** (45 ± 2% deuterium content) and **8** in 96 and 83% yield, respectively.§ It is noteworthy that **8** in principle can be converted further into various 3,4-disubstituted furans by employing the Heck-type reactions.[13] Finally, compound **5c** also underwent smooth palladium-catalysed reaction (4–5 mol%) with *p*-nitrophenyl bromide and *trans*-β-

‡ *Experimental procedure*: A solution of bis(tributylstannyl)acetylene **2** (100 g, 165 mmol) and 4-phenyloxazole **3** (26.5 g, 182 mmol) was heated at 185 °C in a sealed tube for 6–7 days. It was then opened and the resulting benzonitrile was removed under vacuum. The residue was chomatographed on an alumina column (2.5 kg, Grade II, neutral, hexanes) to give a mixture of **1a**, **b** and unchanged **2**. Acetylene **2** was removed from the mixture by absorbing on a bed of alumina [450 g, Merck 1085 aluminum oxide H for TLC (thin layer chromatography)] overnight and was washed subsequently with hexanes to give a mixture of **1a** and **b**. Fractional distillation under vacuum gave **1b** as a colourless oil (13.7 g, 23%), b.p. 80 °C (0.01 mmHg) [lit.[6b] b.p. 109–111 °C (0.6 mmHg)]. Compound **1a** that remained as non-volatile residue was further purified on a short alumina column (100 g, Grade III, neutral, hexanes) to give **1a** (20 g, 19%) as a colourless liquid.

§ All the reported yields are isolated yields and have not been optimised. *Selected spectroscopic data*: Compound **1a**: ^{1}H NMR ($CDCl_3$): δ 0.81–1.65 (m, 54H), 7.36 (s, 2H); ^{13}C NMR ($CDCl_3$): δ 10.09, 13.57, 27.38, 29.23, 29.38, 119.32, 148.09. Compound **4b**: m.p. 105–107 °C (from MeOH) [lit.[4a] m.p. 106–107 °C]; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 6H), 7.06–7.16 (br.s, 8H), 7.51 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 21.11, 125.99, 128.46, 129.09, 129.33, 136.64, 140.45.

Compound **5c**: ^{1}H NMR ($CDCl_3$) δ 0.84–0.90 (t, *J* 7.2 Hz, 9H), 1.08–1.15 (t, *J* 8.5 Hz, 6H), 1.25–1.39 (sextet, *J* 7.3 Hz, 6H), 1.48–1.61 (quintet, *J* 6.8 Hz, 6H), 7.26 (s, 1H), 7.42–7.54 (m, 3H), 7.80–7.83 (d, *J* 7.0 Hz, 2H), 7.95 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 10.56, 13.59, 26.72, 27.19, 29.19, 116.93, 128.42, 128.62, 131.08, 131.94, 139.61, 148.71, 149.66, 190.45. Compound **6**: ^{1}H NMR ($CDCl_3$) δ 6.88 (d, *J* 16.3 Hz, 2H), 6.99 (d, *J* 16.3 Hz, 2H), 7.22–7.48 (m, 10H), 7.58 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 118.11, 123.36, 126.30, 127.58, 128.69, 130.38, 137.41, 140.64. Compound **7**: ^{1}H NMR ($CDCl_3$) δ 6.91 (s, 0.6H), 7.46–7.58 (m, 4H), 7.82–7.87 (d, *J* 7.6 Hz, 2H), 7.91 (s, 1H).

Compound **8**: ^{1}H NMR ($CDCl_3$) δ 7.44–7.65 (m, 4H), 7.76 (d, *J* 1.4 Hz, 1H), 7.82 (d, *J* 1.4 Hz, 1H), 7.85 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 100.15, 124.79, 128.49, 129.20, 132.90, 138.19, 143.06, 148.43, 187.83.

Compound **9**: m.p. 106–108 °C (from hexane); ^{1}H NMR ($CDCl_3$) δ 7.42–7.52 (m, 2H), 7.53–7.65 (m, 3H), 7.71 (d, *J* 1.6 Hz, 1H), 7.86 (d, *J* 1.6 Hz, 1H), 7.89 (d, *J* 1.6 Hz, 2H), 8.15–8.21 (dt, *J* 6.8, 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 123.49, 124.61, 125.75, 128.23, 128.58, 129.33, 133.08, 137.83, 138.49, 142.37, 147.29, 149.83, 189.28.

Compound **10**: m.p. 72–73 °C (from MeOH); ^{1}H NMR ($CDCl_3$) δ 6.94–7.01 (d, *J* 16.6 Hz, 1H), 7.20–7.64 (m, 9H), 7.76–7.80 (m, 2H), 7.84–7.89 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 117.69, 124.51, 124.86, 126.53, 127.63, 128.54, 128.55, 129.07, 131.06, 132.52, 137.29, 139.35, 140.56, 149.80, 190.34.

bromostyrene to afford 3-benzoyl-4-*p*-nitrophenylfuran **9** and 3-benzoyl-4-*trans*-phenylethenylfuran **10** in 81 and 82% yield, respectively.§

In conclusion, we have prepared stannane **1a** and have shown that at this stage it serves competently as a versatile starting material for 3,4-disubstituted furans, the only limiting factor being the synthetic capacity of the well-established Stille-type coupling reactions. Nonetheless, a shortcoming of this programme is the separation problem‡ of **1a**, which was isolated in a disappointingly low yield. In the light of a recent report on the reverse-phase chromatography of organostannanes,[14] we believe that the yield of **1a** can be improved in due course. A thorough exploration of the synthetic potential of **1a** is being undertaken in our laboratories.

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