On the Phosphite-Mediated Synthesis of Dithiafulvenes and π -Extended Tetrathiafulvalenes

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Abstract: By phosphite-mediated couplings between functionalized benzaldehydes and 1,3-dithiole-2-thiones we have obtained a variety of π -extended tetrathiafulvalenes (TTF). In particular, this method has provided a new stilbene-extended TTF with lateral alkyne functionalities, an H-type cruciform structure. This outcome is the result of a phosphite-mediated coupling between two aldehydes.

Key words: cruciform, heterocycles, phosphite, sulfur, tetrathiafulvalene

The phosphite-mediated coupling of two 1,3-dithiole-2-(thi)ones has been employed extensively for preparing derivatives of the redox-active molecule tetrathiafulvalene (TTF, Scheme 1).¹ This method has also been employed to prepare dithiafulvenes (DTF) and π -extended TTFs via coupling between a central unit containing one, two, or three aldehyde functionalities and a 1,3-dithiole-2-(thi) $one^{2,3}$ or coupling of the latter to an anthraguinone.⁴ Very recently we prepared the cruciform structure 1 (Figure 1) that is composed of two orthogonally situated extended TTFs.³ The final step in the synthesis involved a triethylphosphite-mediated coupling of an OPE3 (oligophenyleneethynylene) containing an aldehyde group in each end. In general, π -conjugated cruciform motifs are interesting as molecular wires for organic electronics or as molecular sensors.^{3,5} Here we present an alternative synthesis of the cruciform 1 and the broader scope of the phosphite-mediated coupling; in particular, its use for preparing a stilbene unit (or OPV2, oligophenylenevinylene) as the central part of a new H-type extended TTF cruciform.

Our first objective was to prepare a simple but useful DTF building block containing an iodophenyl functionality that could subsequently be used in palladium-catalyzed cross-coupling reactions and hence be used in an alternative procedure for making the cruciform **1**. Indeed, heating a mixture of 4-iodobenzaldehyde (**2**) and the 1,3-dithiole-2-thione **3**⁶ (ratio of 1:2.5) in triethylphosphite to 110 °C for two hours produced the DTF **4** in almost quantitative yield (Scheme 2)⁷ (note: all reactions were conducted under an argon atmosphere and with triethylphosphite that had been stored under argon and

SYNLETT 2013, 24, 0231–0235 Advanced online publication: 12.12.2012 DOI: 10.1055/s-0032-1317921; Art ID: ST-2012-D0931-L © Georg Thieme Verlag Stuttgart · New York degassed with argon prior to use, but not distilled). This compound was next successfully subjected to a cross-coupling reaction with the known diethynyl compound 5^8 to furnish the cruciform 1 in a yield of 60%.⁹



Scheme 1 Phosphite-mediated couplings



Figure 1 Extended TTF cruciform molecule prepared by final phosphite-mediated couplings

Next, we investigated the possibility for generating bisand tris-DTF-substituted benzenes by phosphite couplings. Related DTF compounds were previously prereactions.10 First, pared by Wittig-Horner terephthalaldehyde (6) was treated with the thione $7,^{6}$ which gave the benzene-extended TTF 8^{11} (Scheme 3). The yield varied from 54% to 79% when increasing the molar equivalents of 7 relative to 6 from 2.2 to 4. Next, 1,3,5-triformylbenzene 9 was treated with 7 (ratio of 1:9) to generate the tris-DTF 10^{12} in a yield of 20%, corresponding to a yield of 58% for each DTF formation. The reaction was very slow as it took four days for consumption of the aldehyde starting material 9 (possibly, in part, due to the insolubility of the mono- and di-DTF adducts), while consumption of **6** only took two hours.

In an original attempt to prepare a derivative of **5** containing alkylthio substituents at the DTF rings rather than ester groups, we subjected the dialdehyde 11^{13} and each of the thiones 12^{14} and 13^{14} to phosphite-mediated couplings



Scheme 2 Alternative synthesis of 1 via a new DTF building block



Scheme 3 Synthesis of benzene-extended TTF

as shown in Scheme 4 (using 3–4 mol equiv of the thiones). Surprisingly, these reactions generated the stilbene (OPV2) derivatives **14** and **15**¹⁵ in reasonable yields considering the fact that three couplings have occurred. It is noteworthy that a similar compound did not seem to form even as a byproduct in the 79% yielding synthesis of **8**, although we cannot account for the exact fate of the remaining 21% of the dialdehyde **6**. Thus, the presence of the electron-withdrawing ethynyl substituents in **11** enhances the electrophilicity of both the carbonyl carbon and its neighboring oxygen, the latter towards phosphite. For phosphite-mediated coupling of two aldehydes to an al-

kene, the oxygen of one aldehyde has to act as an electrophile towards phosphorus, and the carbon of this aldehyde thereafter becomes nucleophilic towards another electrophilic aldehyde carbon. Indeed, Ramirez et al.¹⁶ have previously shown that two molecules of o- or p-nitrobenzaldehyde, that is, an aldehyde containing an electronwithdrawing substituent, can react with trialkylphosphites at 20 °C to furnish a 2,2,2-trialkoxy-1,3,2-dioxaphospholane (Figure 2), while *m*-nitrobenzaldehyde did not undergo reaction under these conditions. In our reaction, we cannot say whether the aldehyde-aldehyde coupling occurs before or after the aldehyde-thione coupling as both the DTF and aldehyde para substituents as well as the one ortho-ethynyl substituent should allow for mesomeric delocalization of the negative charge formed at the carbonyl carbon after nucleophilic attack by phosphorus on the neighboring carbonyl oxygen (Figure 3). Competing reaction channels should thus influence the yields of 14 and 15. It should be noted that isolation of 14 was performed by pouring the reaction mixture onto methanol, resulting in precipitation of the compound. We cannot exclude that some of the originally targeted products are formed, but they were not isolated in our hands from the mother liquor after 14 had been precipitated. The only byproduct we could unambiguously assign was the TTF resulting from homocoupling of two thiones. The longer alkyl groups in 15 resulted in increased solubility and rendered purification by column chromatography necessary, and again the tetraalkylthio-substituted TTF was identified as a byproduct. As a test experiment, we subjected benzaldehyde itself to the phosphite conditions in the absence of a thione; no reaction was observed after six hours of heating in agreement with the work of Ramirez et al.¹⁶ The formation of small amounts of stilbene has, nevertheless, previously been observed when heating benzaldehyde in triethylphosphite at 220 °C in an ampul for 8.5 hours as has the formation of difurylethylene by heating furfural and triethylphosphite at 160 °C.¹⁷ We also conducted test reactions on the dialdehyde 11 with triethylphosphite in the absence of the thione at 100 °C and at room temperature. When heated, reactions occur readily giving a mixture of products. Attempts to precipitate these compounds with methanol failed, but removal of the solvents gave a solid which was highly luminescent under UV-light irradiation (also on TLC plates and in solution). At ambient temperatures, 11 was also found to react slowly with triethylphosphite; however, there were again many products observed when monitoring the reaction by ¹H NMR and ¹³C NMR spectroscopy, there were also some signals observed in ³¹P NMR spectra. However, these products were not as highly luminescent as those formed upon heating the reaction mixture. Although the exact products from these reactions were not identified, the results confirm that 11 by itself readily reacts with triethylphosphite.

Although not an aldehyde substrate, it is worth mentioning that reductive dimerization of phthalic anhydride to biphthalyl by triethylphosphite was found to occur in yields of 65–70%.¹⁸





Scheme 4 Synthesis of H-type extended TTF cruciforms



Figure 2 2,2,2-Trialkoxy-1,3,2-dioxaphospholane products (mixture of diastereomers) formed from *p*-nitrobenzaldehyde and a trialkyl-phosphite at 20 $^{\circ}$ C.¹⁶



Figure 3 Selected resonance formulas for the intermediates (with X equal to either O or the 1,3-dithiole ring) resulting from attack of trialkylphosphite on aldehyde oxygen

The ¹H NMR spectra of cruciforms **14** and **15** showed four CH resonances in the region $\delta = 6.9-7.8$ ppm, which are assigned to the fulvenes (two identical protons), the central alkene (two identical protons), and the two different aryl protons (two identical pairs). The assignment of the central double bond to an *E* configuration seems reasonable from steric reasons, but was confirmed by X-ray crystallographic analysis of **14** as shown in Figure 4. The two 1,3-dithiole rings are not in the same plane as the central OPV2 plane; thus, the angle between the least squares plane defined by a dithiole ring and the least squares plane defined by the neighboring benzene ring is 37°.



Figure 4 Two different views of the molecular structure of 14 (CCDC 908191); crystals were grown from CH_2Cl_2 -heptane

The new extended TTFs are all strong chromophores. Figure 5 shows the absorption spectra of the benzene-extended TTF 8 and 10 and the new H-type cruciform 15 in comparison to the previously reported cruciform 1.3 Compound 15 has a lowest-energy absorption ($\lambda_{max} = 464 \text{ nm}$) that is slightly red-shifted relative to the similar absorptions of 8 (λ = 407 and 424 nm) and of 1 [λ = 402, 437 nm (shoulder)]. The intensities of these absorptions are similar for 8 and 15, but significantly lower than those of 1, in accordance to the fact that 1 has two more DTF units. In addition, compound 15 exhibits two absorptions at $\lambda =$ 276 and 313 nm (shoulder). For comparison, (E)-stilbene has absorptions at $\lambda = 295$ and 307 nm (MeCN)¹⁹ and 1,4bis(trimethylsilylethynyl)benzene has absorptions at $\lambda =$ 279, 288, and 294 nm (CHCl₃).²⁰ Compound 10 exhibits absorption maxima at $\lambda = 246$ and 371 nm. The lowest-energy absorption is thus significantly blue-shifted relative to those of the other compounds. The three DTF are in 10 positioned in *meta* positions relative to each other, which accounts for a less efficient π -electron delocalization between them.



Figure 5 UV-vis absorption spectra in CH₂Cl₂

In conclusion, by phosphite-mediated couplings we have obtained a variety of DTF/extended TTF compounds. The serendipitous formation of a stilbene-extended TTF from a diethynyl-substituted terephthalaldehyde, while terephthalaldehyde itself furnished the expected benzene-extended TTF, demonstrates how a subtle balance of electronic effects determines the outcome of phosphitemediated couplings of benzaldehyde derivatives. In this work we focused attention on triethylphosphite as reagent; it would be interesting to investigate in future work the outcome when using instead trimethylphosphite. Moreover, it is worth noting that the stilbene/H-type cruciform derivatives 14 and 15 resemble previously reported²¹ OPE/OPV H-mers without DTF units and they might indeed be interesting as functional wires for molecular electronics after further functionalization. We are currently exploring these molecules for further acetylenic scaffolding via the four ethynyl groups. Gratifyingly, preliminary experiments show that good stability of the compound is maintained after removal of the silvl protecting groups.

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Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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 (7) (a) Synthesis of 4
- A suspension of 4-iodobenzaldehyde (2, 1.005 g, 4.34 mmol) and the thione 2 (3.303 g, 10.85 mmol) in dry degassed P(OEt)₃ (12.5 mL) was heated to 110 °C under an atmosphere of Ar. During the heating, the solid dissolved, and the color of the solution was a brown yellow color. Monitoring the reaction by TLC revealed that the reaction was complete after 2 h. The solvent was removed under reduced pressure. The brown-yellow colored residue was washed with PE to remove any excess P(OEt)₃. The residue was dissolved in minimal CH_2Cl_2 and purified by flash column chromatography (SiO₂, PE–CH₂Cl₂ = 1:4); the first yellow fraction gave the desired compound as a yellow oil or as a fine pale yellow crystalline material (2.043 g, 96%), which darkens over time; mp 97-100 °C. ¹H NMR (500 MHz, CDCl₃): $\delta = 7.67$ (d, J = 8.4 Hz, 2 H), 6.93 (d, J = 8.4Hz, 2 H), 6.42 (s, 1 H), 3.12–3.04 (m, 4 H), 2.79–2.71 (m, 4 H). ¹³C NMR (125 MHz, CDCl₃): $\delta = 137.77$, 135.23. 131.27, 128.65, 127.85, 125.02, 117.60, 117.54, 115.54, 91.53, 31.15, 31.13, 19.07, 19.02. IR (ATR): v = 2995 (m), 2870 (m), 2926 (m), 2246 (m, CN), 1738 (s), 1679 (m), 1571 (s), 1543 (s), 1491 (m), 1478 (s), 1407 (s), 1391 (s) cm⁻¹. MS-FAB: $m/z = 487 [M]^+$. Anal. Calcd (%) for C₁₆H₁₃IN₂S₄: C, 39.34; H, 2.68; N, 5.74. Found: C, 39.41; H, 2.54; N, 5.63.
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- (9) Synthesis of 1
- To a mixture of the dialkyne **5** (50 mg, 0.072 mmol), thione **4** (105 mg, 0.214 mmol), PdCl₂(PPh₃)₂ (5 mg, 0.0072 mmol), and CuI (1.4 mg, 0.0072 mmol) was added a degassed solution of THF (7 mL) and Et₃N (0.1 mL). The reaction was stirred for 2 d during which time a red colored precipitate formed. The solvent was removed, and the residue was purified by flash column chromatography (SiO₂) initially with CH₂Cl₂ as eluent to remove some impurities and unreacted **4**, then a gradient of 1–20% EtOAc was added to the eluent mixture to get the major orange/red band, which afforded **1** as an orange-red colored solid (61 mg, 60%). Characterization data are in accordance to previously reported data.³
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- (11) Synthesis of 8
 - A mixture of terephthalaldehyde **6** (100 mg, 0.74 mmol), thione **7** (673 mg, 2.98 mmol), and P(OEt)₃ (4 mL) was

heated to 100 °C under an argon atmosphere for 2 h. The reaction mixture was then allowed to cool to r.t., and the yellow precipitate was isolated and washed thoroughly with MeOH (100 mL) to provide the product as yellow crystals (286 mg, 79%); mp 164–165 °C. ¹H NMR (500 MHz, CDCl₃): δ = 7.20 (s, 4 H), 6.45 (s, 2 H), 2.44 (s, 6 H), 2.43 (s, 6 H). ¹³C NMR (125 MHz, CDCl₃): δ = 133.88, 131.87, 127.50, 127.06, 124.54, 114.66, 19.19, 19.07. MS (MALDI): *m/z* = 490 [M⁺]. Anal. Calcd (%) for C₁₈H₁₈S₈: C, 44.04; H, 3.70. Found: C, 44.02; H, 3.57.

(12) Synthesis of 10

A mixture of **9** (80.2 mg, 0.49 mmol) and thione **7** (1.01 g, 4.45 mmol) in dry degassed P(OEt)₃ (5 mL) was stirred at 110 °C for 4 d. The mixture was then concentrated under reduced pressure. The residue was subjected to dry column vacuum chromatography (SiO₂, heptane to heptane–EtOAc = 4:1, 5% increase per fraction) to provide the product as a brown solid (68 mg, 20%). ¹H NMR (500 MHz, CDCl₃): δ = 6.85 (s, 3 H), 6.46 (s, 3 H), 2.44 (s, 18 H). ¹³C NMR (125 MHz, CDCl₃): δ = 136.85, 133.22, 127.20, 124.71, 122.70, 114.50, 19.29, 19.08. HRMS (ESI⁺): *m/z* calcd for C₂₄H₂₄S₁₂⁺: 695.8521; found: 695.8496 [M⁺].

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- (15) (a) Synthesis of 14

Compounds **11** (0.30 g, 0.92 mmol) and **12** (0.92 g, 3.62 mmol) were dissolved in P(OEt)₃ (5 mL, 29 mmol). The mixture was stirred under argon at 100 °C for 6 h. The mixture was allowed to cool to r.t. and was then poured into MeOH (100 mL). The product **14** precipitated and was collected on a filter as a red solid (130 mg, 27%); mp 150–170 °C (decomp.). ¹H NMR (500 MHz, CDCl₃): δ = 7.82 (s, 2 H), 7.63 (s, 2 H), 7.39 (s, 2 H), 6.91 (s, 2 H), 2.90 (q, *J* = 7.4 Hz, 4 H), 2.88 (q, *J* = 7.4 Hz, 4 H) 1.36 (t, *J* = 7.4 Hz, 6 H), 1.34 (t, *J* = 7.4 Hz, 6 H), 0.36 (s, 18 H), 0.28 (s, 18 H). ¹³C NMR (125 MHz, CDCl₃): δ = 136.62, 136.03, 135.98, 128.79, 128.70, 128.48, 126.75, 125.09, 122.66, 121.52, 111.52, 103.11, 103.07, 101.81, 101.25, 30.72, 30.47, 15.20,

15.10, 0.23, 0.09. IR (ATR): v = 2958 (s), 2923 (m), 2151 (s, C=C), 1694 (w), 1558 (vs), 1494 (s), 1474 (m), 1445 (m), 1402 (m), 1374 (m) cm⁻¹. HRMS (ESI⁺): *m/z* calcd for $C_{50}H_{65}S_8Si_4^+$: 1033.1924; found: 1033.1901 [MH⁺]. (b) Synthesis of 15

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Compounds 11 (0.22 g, 0.69 mmol) and 13 (0.64 g, 2.06 mmol) were dissolved in dry degassed P(OEt)₃ (4 mL, 18 mmol). The mixture was stirred under argon at 100 °C for 5 h and then allowed to cool to r.t. The solvent was removed under reduced pressure at 60 °C, and the crude residue was subjected to flash column chromatography (SiO2, 10% toluene in heptane) to give the product 15 as a red solid (67 mg, 17%); mp 188-190 °C (slight color change from ca. 110 °C). ¹H NMR (500 MHz, CDCl₃): δ = 7.82 (s, 2 H), 7.63 (s, 2 H) 7.39 (s, 2 H) 6.91 (s, 2 H) 2.85 (t, J = 7.4 Hz, 4 H), 2.85 (t, J = 7.4 Hz, 4 H), 1.68–1.61 (m, 8 H), 1.47 (q, J = 7.4 Hz, 4 H), 1.44 (q, J = 7.4 Hz, 4 H), 0.94 (t, J = 7.4 Hz, 6 H), 0.94 (t, J = 7.4 Hz, 6 H), 0.35 (s, 18 H), 0.27 (s, 18 H). ¹³C NMR (125 MHz, CDCl₃): δ = 136.57, 136.14, 135.84, 128.65, 128.53, 128.43, 126.62, 125.04, 122.59, 121.40, 111.36, 103.03, 103.00, 101.74, 101.19, 36.16, 35.89, 31.94, 31.85, 21.84, 21.82, 13.81, 13.77, 0.20, 0.06. IR (ATR): v = 2957 (vs), 2928 (s), 2871 (m), 2150 (s, C=C), 1696 (w), 1672 (w), 1553 (vs), 1492 (s), 1464 (m), 1402 (m), 1340 (vw) cm⁻ . HRMS (ESI⁺): m/z calcd for C₅₈H₈₁S₈Si₄⁺: 1145.3176; found: 1145.3116 [MH⁺]. Anal. Calcd (%) for $C_{58}H_{80}S_8Si_4$: C, 60.78; H, 7.04. Found: C, 60.26; H, 6.94.

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