Cross-Coupling Reactions with Acetylenic Dithiafulvenes

Katrine Qvortrup,[a,b] Asbjørn Sune Andersson,[a] Jan-Philipp Mayer,[b] Anne Sofie Jepsen,[b] Mogens Brøndsted Nielsen*[a]

[a] Department of Chemistry, University of Copenhagen, Universitetsparken 5, 2100 Copenhagen Ø, Denmark
Fax +4535320212; E-mail: mbn@kiku.dk

[b] Department of Chemistry, University of Southern Denmark, Campusvej 55, 5230 Odense M, Denmark

Received 29 July 2004

Abstract: The scope of acetylenic dithiafulvenes in palladium-catalyzed cross-coupling reactions is reported. From such reactions we have obtained a selection of new extended tetrathiafulvalenes (TTFs), based on *p*-diethynylbenzene, tri-, and tetraethynylethene cores.

Key words: alkynes, conjugation, cross-coupling, enynes, heterocycles

The development of new acetylenic building blocks based on the dithiafulvene unit has allowed ready access to alkyne-extended derivatives of the π-donor tetrathiafulvalene (TTF).[1] Compound **1** (Figure 1) presents one such building block that was recently reported by Diederich, Nielsen, and co-workers.[1a,b] Thus, subjecting **1**, after desilylation (**2**), to an oxidative Hay homo-coupling[2] affords the butadiyne-extended TTF **3**. Owing to their redox and chromophoric properties, such molecules are interesting in both materials and supramolecular chemistry.[1b,f,3] Molecular construction from acetylenic building blocks[4] benefits from the versatility and high functional group tolerance of acetylenic coupling reactions.[5] We now focus on the ability of acetylenic dithiafulvenes to undergo Sonogashira–Hagihara cross-couplings[6] with different aryl and vinyl halides. Until now only one such example has been reported, namely the coupling with 2,5-diiodothiophene which provided the extended TTF **4**.[1b]

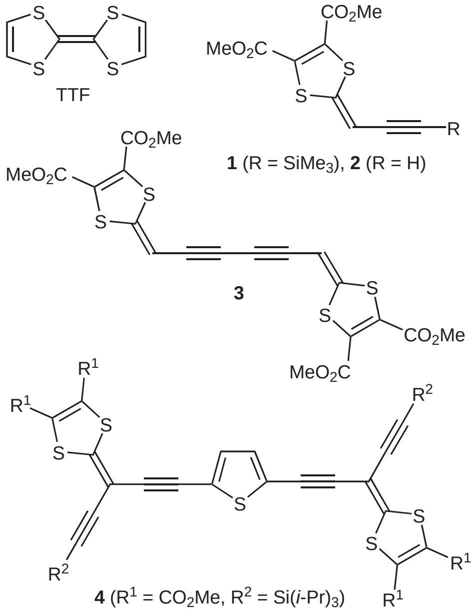
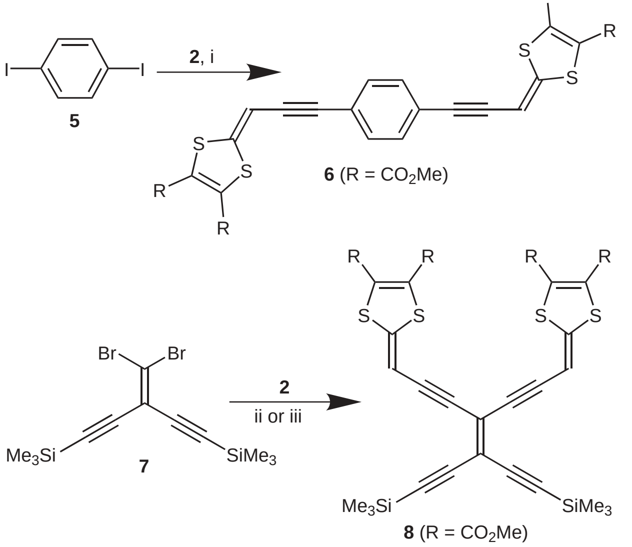


Figure 1 Acetylenic derivatives of tetrathiafulvalene (TTF).

The proton affinity of the acetylide of **2** is close to that of phenylacetylide. Thus, we find from calculations, employing the Gaussian 03 program package,[7] values of 364 and 369 kcal mol^{-1}, respectively (at 0 K).[8] In other words, the acidities of **2** and phenylacetylene are assumed to be similar if solvent effects are neglected.

The Sonogashira coupling between **2** and a simple aryl halide was first investigated. Compound **1** was desilylated by K_2CO_3 in MeOH–THF according to a standard procedure.[1b] The resulting product **2** was then treated with 1,4-diiodobenzene (**5**) and the $Pd(PPh_3)_2Cl_2$–CuI catalyst system, which gave the *p*-diethynylbenzene-extended TTF **6** in good yield (Scheme 1).[9]



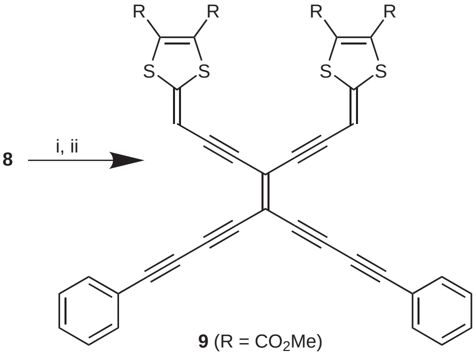
Scheme 1 Palladium-catalyzed cross-couplings with **2**. *Reagents and conditions*: i. $Pd(PPh_3)_2Cl_2$, CuI, Et_3N, THF, r.t., 2.5 h, 78%; ii. $Pd(PhCN)_2Cl_2$, $P(t\text{-}Bu)_3$, CuI, $(i\text{-}Pr)_2NH$, THF, toluene, microwave heating, 60 °C, 6 min, 38%; iii. $Pd(PhCN)_2Cl_2$, $P(t\text{-}Bu)_3$, CuI, $(i\text{-}Pr)_2NH$, THF, toluene, ultrasonification, 30 °C, 4 h; 84%.

Geminally functionalized Tetraethynylethenes (TEEs) are conviniently constructed from the vinylic dibromide **7** (Scheme 1) and arylacetylenes, which contain either electron-donating (e.g. NMe_2) or withdrawing (e.g. NO_2)

SYNLETT 2004, No. 15, pp 2818–2820
Advanced online publication: 08.11.2004
DOI: 10.1055/s-2004-835641; Art ID: D21504ST

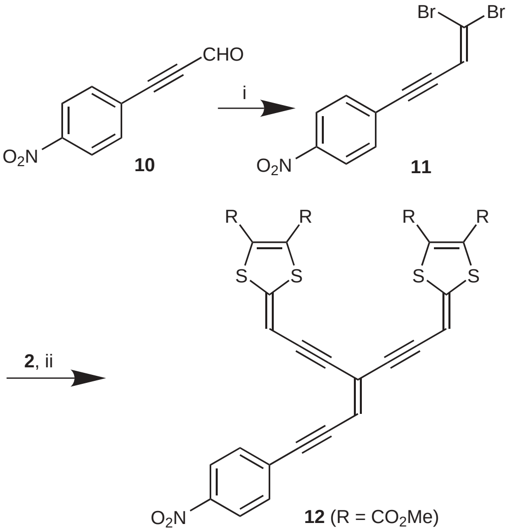
substituents, in the presence of the $Pd(PPh_3)_2Cl_2$ catalyst.[4,10] Nevertheless, treatment of **7** with **2** under these conditions failed to provide the TEE-extended TTF **8**. Many cross-couplings are enhanced by using bulky, electron-rich phosphines.[11] Recently, Hundertmark et al.[12] developed a versatile catalyst system, $Pd(PhCN)_2Cl_2$–P(*t*-Bu)$_3$, that allows room temperature Sonogashira coupling of aryl bromides with a wide variety of terminal acetylenes. We therefore turned to this catalyst and at the same time subjected the reaction mixture to microwave heating at 60 °C for six minutes. Hereby **8** was gratifyingly obtained in a yield of 38%. The yield was improved further by substituting the microwave heating with ultrasonification at 30 °C for four hours.[13] The TEE core was under these conditions constructed in yields as high as 84%. The reaction also worked at room temperature without microwave or ultrasonification, but it required much longer reaction time (up to 24 hours), and the yield varied considerably. In contrast, high yields and short reaction times are easy to reproduce when using ultrasonification. The beneficial use of ultrasonification is likely a result of the high viscosity of the reaction mixture since little solvent is employed (ca. 1 mL per 1 mmol of **2**).

TEE **8**, containing two silyl-protected acetylene groups, is an interesting module for further acetylenic scaffolding. We present here our first efforts. The trimethylsilyl protecting groups were removed by K_2CO_3 in THF–MeOH, and the desilylated compound was hereafter subjected to an oxidative Hay coupling[2] with an excess of phenylacetylene (Scheme 2). This cross-coupling provided the large conjugated chromophore **9** in 18%. The rather low yield is partly due to significant decomposition of the desilylated intermediate. We have experienced similar stability problems in the deprotection step of related acetylenic scaffolds, such as diethynylethene-extended TTFs.[1e]



Scheme 2 Acetylenic scaffolding with **8**. *Reagents and conditions*: i. K_2CO_3, THF, MeOH; ii. phenylacetylene, CuCl, TMEDA, CH_2Cl_2, air; 18%. TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine.

One way of circumventing the stability issue is to attach the dithiafulvene units in the final step. In particular, we target novel donor–acceptor chromophores with good NLO properties. Recent studies have revealed that acetylenic scaffolds containing dithiafulvene donor groups and *p*-nitrophenyl acceptor groups exhibit good third-order nonlinearities.[1b] In the quest for new NLO candidates, we prepared a donor–acceptor chromophore with a central triethynylethene (enetriyne) core (Scheme 3). First the aldehyde **10**[14] was subjected to a Corey–Fuchs dibromoolefination,[15] which gave the vinylic dibromide **11** containing a *p*-nitrophenylacetylene substituent. A cross-coupling reaction between **2** and **11** [employing Pd(PhCN)$_2$Cl$_2$–P(*t*-Bu)$_3$ with ultrasonification] afforded **12** in a yield of 30%. For comparison, **12** is only obtained in a yield of 10% with the $Pd(PPh_3)_2Cl_2$ catalyst.



Scheme 3 Synthesis of donor–acceptor chromophore. *Reagents and conditions*: i. CBr_4, PPh_3, Zn, CH_2Cl_2, r.t., 72%; ii. $Pd(PhCN)_2Cl_2$, P(*t*-Bu)$_3$, CuI, (*i*-Pr)$_2$NH, THF, toluene, ultrasonification, 30 °C, 2.5 h, 30%.

In conclusion, we have devised methods for performing cross-coupling reactions between the acetylenic dithiafulvene **2** and a variety of halides, which have allowed the preparation of several new extended tetrathiafulvalenes with acetylenic cores. These chromophores are currently investigated for their linear and nonlinear optical properties, as well as redox properties.

Acknowledgment

The Danish Technical Research Council (STVF, Research project # 26-01-0033), Carlsbergfondet, and Direktør Ib Henriksens Fond are gratefully acknowledged for financial support.

References

(1) (a) Nielsen, M. B.; Moonen, N. N. P.; Boudon, C.; Gisselbrecht, J.-P.; Seiler, P.; Gross, M.; Diederich, F. *Chem. Commun.* **2001**, 1848. (b) Nielsen, M. B.; Utesch, N. F.; Moonen, N. N. P.; Boudon, C.; Gisselbrecht, J.-P.; Concilio, S.; Piotto, S. P.; Seiler, P.; Günter, P.; Gross, M.; Diederich, F. *Chem.–Eur. J.* **2002**, *8*, 3601. (c) Nielsen, M. B. *Synlett* **2003**, 1423. (d) Kumagai, T.; Tomura, M.; Nishida, J.-i.; Yamashita, Y. *Tetrahedron Lett.* **2003**, 6845. (e) Nielsen, M. B.; Gisselbrecht, J.-P.; Thorup, N.; Piotto, S. P.; Boudon, C.; Gross, M. *Tetrahedron Lett.* **2003**, *44*, 6721. (f) Qvortrup, K.; Jakobsen, M. T.; Gisselbrecht, J.-P.;

Boudon, C.; Jensen, F.; Nielsen, S. B.; Nielsen, M. B. *J. Mater. Chem.* **2004**, *14*, 1768.

(2) Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320.

(3) (a) Williams, J. M.; Ferraro, J. R.; Thorn, R. J.; Carlson, K. D.; Geiser, U.; Wang, H. H.; Kini, A. M.; Whangbo, M.-H. *Organic Superconductors (Including Fullerenes): Synthesis, Structure, Properties, and Theory*; Prentice Hall: Englewood Cliffs / New Jersey, **1992**. (b) Roncali, J. *J. Mater. Chem.* **1997**, *7*, 2307. (c) Nielsen, M. B.; Lomholt, C.; Becher, J. *Chem. Soc. Rev.* **2000**, *29*, 153.

(4) For a recent account on acetylenic modules for acetylenic scaffolding, see: Nielsen, M. B.; Diederich, F. *Synlett* **2002**, 544.

(5) Siemsen, P.; Livingston, R. C.; Diederich, F. *Angew. Chem. Int. Ed.* **2000**, *39*, 2632.

(6) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627. (c) Sonogashira, K. In *Metal-Catalyzed Cross-Coupling Reactions*; Diederich, F.; Stang, P. J., Eds.; Wiley-VCH: Weinheim, **1998**, 203–229.

(7) Gaussian 03, Revision B.03, Frisch, M. J. et al., Gaussian Inc., Pittsburg PA, **2003**.

(8) The acetylene and acetylide structures were geometry optimized at the semiempirical PM3 level. Frequencies were calculated to verify that the calculated structures are local minima on the potential energy surface and to correct for zero-point kinetic energies. Single-point energy calculations were performed on the optimized structures at the B3LYP/6-311++G(2d,p) level.

(9) All new compounds were fully characterized by ^{1}H NMR and ^{13}C NMR spectroscopy, elemental analysis and/or HRMS.

(10) Tykwinski, R. R.; Schreiber, M.; Carlón, R. P.; Diederich, F.; Gramlich, V. *Helv. Chim. Acta* **1996**, *79*, 2249.

(11) For a recent review on electron-rich phosphines in organic synthesis, see: Valentine, D. H. Jr.; Hillhouse, J. H. *Synthesis* **2003**, 2437.

(12) Hundertmark, T.; Littke, A. F.; Buchwald, S. L.; Fu, G. C. *Org. Lett.* **2000**, *2*, 1729.

(13) **Experimental Procedure for Preparation of 8:** Compound **1** (418 mg, 1.27 mmol) was desilylated to form **2** as previously described (ref.^{1b}). To a mixture of CuI (3.5 mg) and Pd(PhCN)$_2$Cl$_2$ (20 mg) under argon was added argon-degassed THF (0.5 mL), toluene (0.5 mL), HN(*i*-Pr)$_2$ (0.17 mL). Then P(*t*-Bu)$_3$ (10% in hexane, 0.125 mL) was added and hereafter dibromide **7** (156 mg, 0.413 mmol), which resulted in a dark brown mixture. This mixture was transferred via a syringe to the flask containing solid **2**. The mixture was subjected to ultrasonification at 30 °C for 4 h, whereupon it was filtered through a plug of silica (eluent: CH_2Cl_2). Column chromatography (SiO_2, $CH_2Cl_2 \rightarrow CH_2Cl_2$–EtOAc 10:1) afforded **8** as a red-brown solid (253 mg, 84%). Mp 143–146 °C (decomp.). UV/Vis ($CHCl_3$): λ (ε/M^{-1}cm^{-1}): 294 (15200), 333 (15300), 378 (14500), 454 (39000) nm. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.23$ (s, 18 H), 3.83 (s, 6 H), 3.84 (s, 6 H), 5.65 (s, 2 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -0.2$, 53.4 (two overlapping), 92.7, 96.1, 97.4, 101.8, 105.2, 112.5, 118.6, 130.6, 132.2, 148.0, 159.3, 159.7 ppm. MALDI-TOF-MS (matrix: 2,5-dihydroxybenzoic acid): *m/z* = 728 [M$^+$]. Anal. Calcd for $C_{32}H_{32}O_8S_4Si_2$ (729.03): C, 52.72; H, 4.42. Found: C, 52.96; H, 4.82.

(14) The aldehyde **10** was prepared according to a literature procedure: Tretyakov, E. V.; Tkachev, A. V.; Rybalova, T. V.; Gatilov, Y. V.; Knight, D. W.; Vasilevsky, S. F. *Tetrahedron* **2000**, *56*, 10075.

(15) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.