Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 6481–6488

TETRAHEDRON

A convenient procedure for the synthesis of tetrathia-[7]-helicene and the selective α-functionalisation of terminal thiophene ring

Stefano Maiorana,[a,*] Antonio Papagni,[b] Emanuela Licandro,[a] Rita Annunziata,[a] Piero Paravidino,[c] Dario Perdicchia,[a] Clelia Giannini,[a] Marco Bencini,[a] Koen Clays[d] and André Persoons[d]

[a]*Dipartimento di Chimica Organica e Industriale, Universita' degli Studi di Milano, Via C. Golgi 19, 20133 Milano, Italy*
[b]*Dipartimento di Scienza dei Materiali, Universita' degli Studi di Milano 'Bicocca', Via Cozzi 53, 20125 Milano, Italy*
[c]*Isagro Ricerca (Istituto Donegani), Via Fauser 4, 28100 Novara, Italy*
[d]*Department of Chemistry, University of Leuven, Celestijnenlaan 200D, B-3001 Leuven, Belgium*

Received 7 May 2003; revised 13 June 2003; accepted 3 July 2003

Abstract—This paper describes a convenient preparation of tetrathia-[7]-helicene (TH[7]), the generation of the α-anion on the terminal thiophene ring, and the synthesis of the 2-formyl-tetrathia-[7]-helicene (2-CHO-TH[7]). The key intermediate trans-1,2-dibenzodithiophene-ethene, prepared in 97% yield by McMurry coupling of the 2-formyl-benzo[1,2-*b*;4,3-*b*′]dithiophene, was transformed into TH[7] using a known procedure. The described method affords TH[7] in 46% overall yield, which is more than four times the yield previously reported in the literature. The α-anion of TH[7], which is easily generated on the α-position of one of the terminal thiophene rings, reacts with electrophilic reagents such as D_2O and DMF. The latter reaction proved to be the best way to prepare 2-CHO-TH[7], a key intermediate for the preparation of new substituted heterohelicenes.

1. Introduction

Organic non-linear optical (NLO) materials now play a key role in developing new ultra-fast, large-scale optical data processing devices.[1] It has very recently been recognized that, in chiral materials, electric-dipole transitions alone cannot fully explain the circular and linear differences observed in even-order NLO responses, and that contributions from magnetic-dipole and/or electric-quadrupole transitions should be included.[2] Since these two transitions have different symmetry properties from those of electric-dipole transitions, even-order non-linearities are possible even in highly symmetric bulky materials. A second harmonic generation involving magnetic-dipole transitions from a racemic and centrosymmetric crystal of chiral molecules has recently been observed.[3]

Molecules with these features are extremely interesting as they may open up the possibility of developing new photo-refractive materials without resorting to poling processes. Suitable candidates are systems with large second-order non-linearity that have an intrinsic high molecular anisotropy or can be arranged in anisotropic supramolecular architectures. Strong chiral effects in second-order non-linearity have recently been observed in chiral poly(isocyanide) monolayers with a significant contribution by magnetic transition,[4] and helicenes (which are known to posses high molecular anisotropy) have been suggested as interesting substrates to study.[5]

The NLO properties of many fully carbo-helicenes, such as [7]-helicene or [6]-helicenebisquinones (HBD), have already been investigated theoretically and experimentally[6] but, to the best of our knowledge, little or nothing has been done on the corresponding heterohelicenes,[7] although some thia-helicenes were synthesized in the late 1960s and their optical properties were investigated in the early 1970s.[8]

Besides studying the optical properties and molecular crystal architecture of heterohelicenes, another aspect of interest is the use of suitably substituted derivatives as new chiral ligands for catalysts[9] and, in principle, thia-helicenes are more easily functionalised than their corresponding carbo-helicenes. For the above reasons, we concentrated on the tetrathia-[7]-helicene TH[7] **1**, which required setting up a synthetic procedure that would afford a reasonable amount of starting material.[10] Here, we describe our investigations of the significant laboratory-scale synthesis and the functionalisation of TH[7] **1** through the selective generation of the α-anion of one of the terminal thiophene rings and reaction with electrophilic reagents.

Keywords: heterohelicenes; McMurry reaction; oxidative photocyclisation; large-scale preparation; NLO properties.
* Corresponding author. Tel.: +39-02-503-14142; fax: +39-02-503-14139; e-mail: stefano.maiorana@unimi.it

0040–4020/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/S0040-4020(03)01056-1

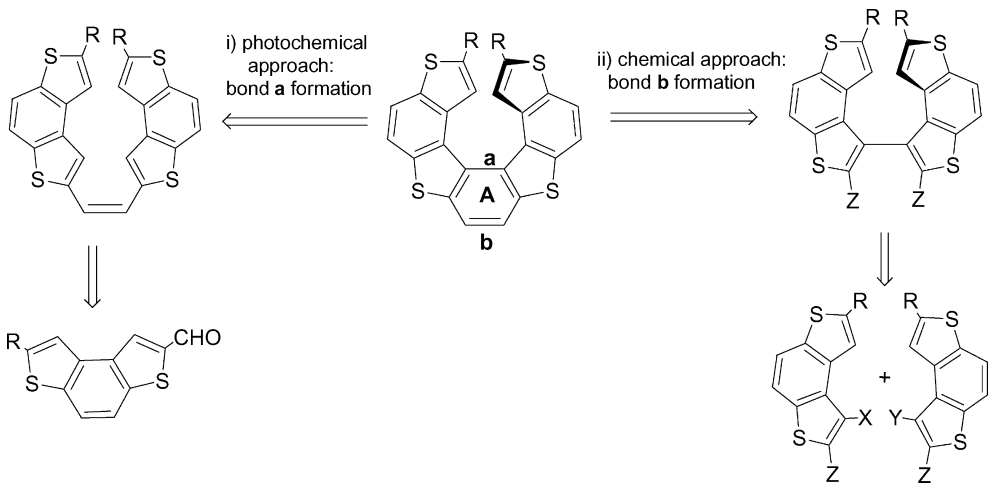


Figure 1. Synthetic approaches to tetrathia-[7]-helicenes.

2. Results and discussion

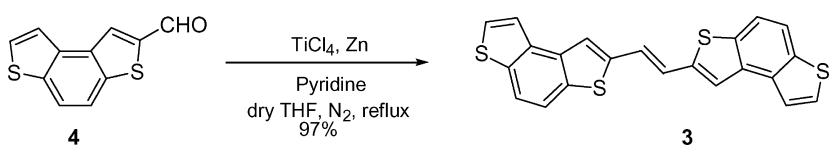
The synthesis of TH[7] **1** can be summarised by the two general strategies shown in Figure 1: (i) a photochemical approach in which the middle aromatic ring A is produced by means of the oxidative photocyclization of a 1,2-diarylethene precursor in the presence of iodine or oxygen (formation of the single bond a);[12] and (ii) a chemical approach in which ring A is built chemically (formation of the double bond b).[13]

Each approach has advantages and disadvantages. Both can be used to synthesize the parent TH[7] or its mono- or di-substituted derivatives, but the photochemical pathway is more indicated for the synthesis of unsubstituted TH[7] or TH[7] bearing substituents that do not react under photochemical conditions. It is also more straightforward, although it suffers from drawbacks such as the fact that the reaction is performed in very dilute solutions, is not compatible with acid-sensitive functional groups (HI is generated during the process), and nitro and amino groups cannot be used because their presence quenches the singlet electronic state involved in the photo-induced ring A formation step. The chemical approach is more flexible, more tolerant in terms of the substituent nature, and more suitable for preparing enantiopure TH[7]. However, at a scale of hundreds of milligrams, the preparation of precursors normally requires considerable synthetic work.

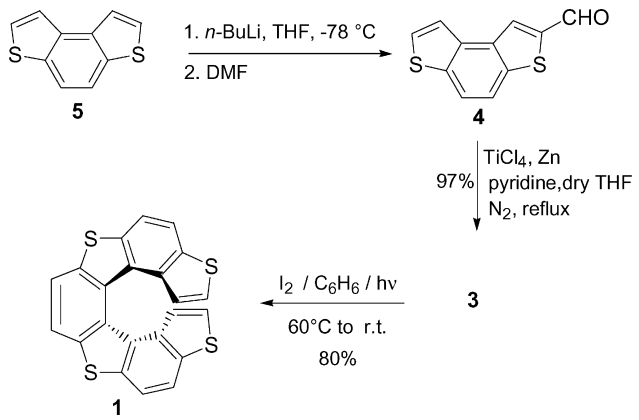
The aim of this study was to optimize the preparation of parent TH[7] **1**, and to start a systematic study of the reactivity of TH[7] (which to the best of our knowledge, has hardly been investigated), such as the selective generation of an α-anion on thiophene ring. In addition, we focused our attention on the synthesis of the 2-formyl-tetrathia-[7]-helicene (2-CHO-TH[7]) **2**, which we have identified as the key intermediate for the preparation of new heterohelicenes with the aim of achieving optical resolution, and confirming the predicted non-linear properties.[14,15]

In order to synthesize the parent TH[7] **1** on a significant laboratory scale, we carefully considered the procedures reported in the literature,[10a] particularly the possibility of increasing the yields of the key intermediate 1,2-bis-(2-benzo[1,2-*b*;4,3-*b*′]dithiophenyl) ethene **3**, which represents the crucial point in the reaction sequence because it is the direct precursor of TH[7]. In the reported synthesis,[10b] **3** is prepared in unsatisfactory yields by means of several steps from aldehyde **4**. We thought that the McMurry reaction on aldehyde **4** might be a useful, new, easy and direct entry to 1,2-bis-(2-benzo[1,2-*b*;4,3-*b*′]dithiophenyl) ethene **3** (Scheme 1). It has been previously reported for the synthesis of the alkene precursor of 5,8,11,14-tetrathia-[9]-helicene.[16]

The aldehyde **4** was initially obtained by us in 69% yield following the published procedure.[10] We subsequently found that a significant improvement in yield (86%) could be achieved by means of the electrophilic formylation of the α-anion of benzodithiophene generated with *n*-BuLi at −78°C, and DMF (Scheme 2). The aldehyde **4** was then directly transformed under standard McMurry conditions into the alkene **3** with a very high yield (97%). The alkene **3** was finally photocyclized in benzene solution to the final TH[7] **1** by means of irradiation with a medium pressure Hg lamp (150 W) at 60°C for 11 h and at 25°C for 13.5 h (Scheme 2). The high yield of the formylation reaction and McMurry coupling make it possible to obtain TH[7] **1** in an overall yield of 46% from the commercially available 2-thiophenecarboxyaldehyde, and 63% from the benzodithiophene **5**. These yields are significantly (four times)



Scheme 1. Synthesis of alkene **3** via McMurry coupling.

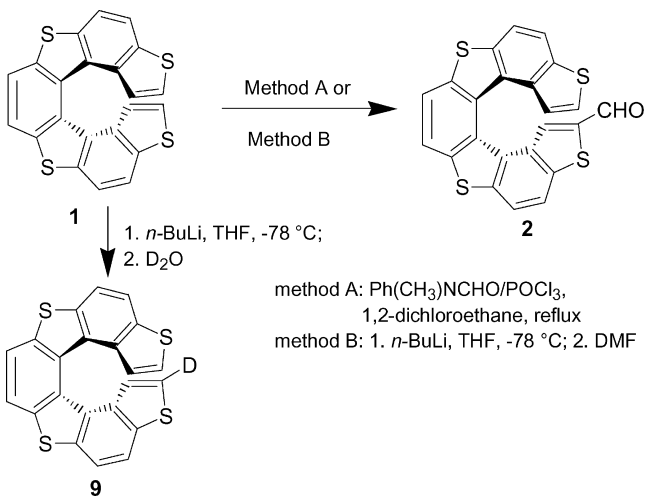


Scheme 2. Reaction sequence to tetrathia-[7]-helicene **1**.

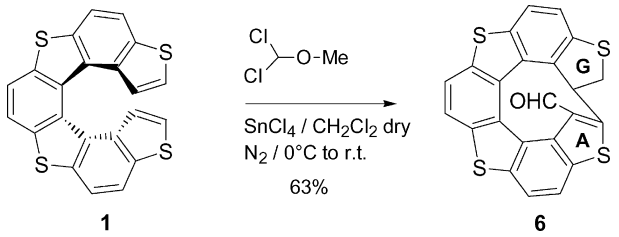
higher than those previously reported. In addition, the use of the McMurry reaction reduces the total number of steps necessary to prepare the alkene **3**.

It is worth noting that the McMurry reaction affords the alkene **3** as a *trans*/*cis* (95/5) mixture (Scheme 1), and that the *trans* isomer is almost insoluble even in benzene. This insolubility probably explains the long reaction time required for the photocyclisation, since the *trans* isomer must isomerise to the *cis* isomer before being cyclised. However, the yields are quite good, reaching 80% in TH[7] **1**. Having established an efficient protocol for the synthesis of TH[7] **1**, we undertook a systematic study of the reactivity of TH[7] in order to prepare differently substituted derivatives and, in this paper, we describe the formylation of TH[7]. 2-Formyl-tetrathio-[7]-helicene **2** was selected as a key intermediate for the preparation of new substituted heterohelicenes through the elaboration of the formyl group, for the optical resolution and for the study of NLO properties.

There are several ways of introducing the formyl group on an electron-rich aromatic ring. The Vilsmeier reaction has been successfully used on benzodithiophene **5** to give **4**[10] and, when applied to TH[7] **1**, gave the expected 2-formyl derivative **2**; however, the yield was rather low (34%) and it required quite a long reaction time (33 h at reflux) (Scheme 3, method A), and we observed widespread decomposition of the starting TH[7] **1**.



Scheme 3. α-Functionalisation of helicene **1**.



Scheme 4. Formation of **6**.

In a second experiment, we used commercially available α,α-dichloromethyl methyl ether as the formylating reagent, which has been reported to be a good formylating reagent for activated aromatic substrates.[17]

The treatment of TH[7] **1** with Cl_2CHOCH_3 in the presence of $SnCl_4$ in dry CH_2Cl_2 at 0°C, and then at room temperature, afforded an unexpected formylated product **6** in 63% yield, in which the two terminal thiophene rings **A** and **G** are linked by a carbon–carbon bond (Scheme 4).

The structure of **6** is proposed on the basis of NMR studies (Figure 2).

A complete spectroscopic investigation was necessary to establish the structure of **6**. A concerted use of several gradient-enhanced experiments, such as 2D COSY, $^1H/^{13}C$ 2D HMQC[18] (Heteronuclear Multiple-Quantum Coherence) and $^1H/^{13}C$ 2D HMBC[18,19] (Heteronuclear Multiple-Bond Correlation), provided the sequence-specific assignment of the multi-ring aromatic derivative. The 2D NOESY experiment confirms the formyl group position on the A ring and indicates the carbon atoms involved in the bond between the A and G rings.

From the $^1H/^1H$ connectivities found in 2D COSY spectra, three pairs of aromatic protons can be distinguished. To assign each pair of protons to a ring, we performed the heteronuclear direct- and multiple-bond correlations experiments: $^1H/^{13}C$ HMQC gave for all protons the direct attachment to carbons, while $^1H/^{13}C$ HMBC allowed the complete assignments of all the protons and quaternary carbons.

We can establish the correct sequence of the aliphatic carbons on the G ring (CH–CH_2–S) starting from the values of the direct $^{13}C–^1H$ coupling constant found in the

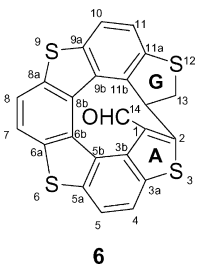
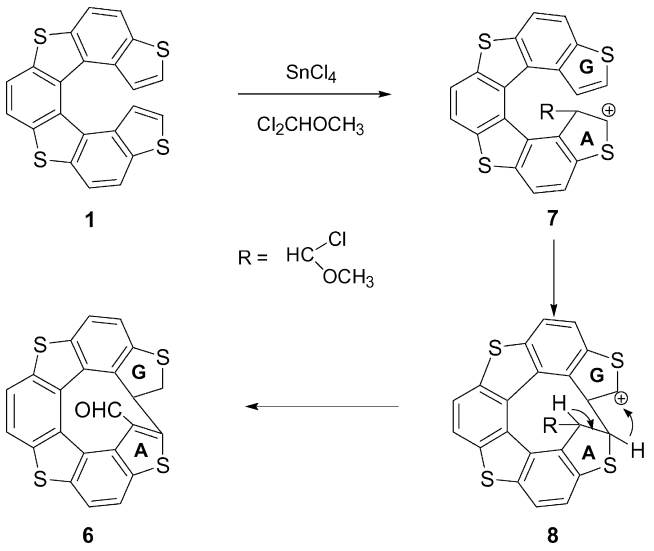


Figure 2. Structure and numbering of compound **6**.



Scheme 5. Proposed mechanism for formation of **6**.

INEPT spectrum: ^{1}J=148 Hz for the CH_2 group and 136 Hz for the CH group;[20] indeed the $^{1}J_{C-H}$ value can increase up to 148 Hz because of the presence of the sulphur atom in the α-position, as described in the literature. Moreover, the 2D NOESY spectrum showed the correlation between H-14 and H-13_B (lowfield), and between the aldehydic proton and H-13_A (highfield). These results, which are supported by the long-range coupling constant correlations between C-2 and H-13_A, H-13_B, H-14 and the proton of the formyl group, strongly suggest that the A and G rings are connected by a bond between C-2 and C-14.

The long-range couplings of C-11a and C-11b with H-14 and H-13_A and, at the same time of C-11a with H-10 and of C-11b with H-11, was the key to assign the hydrogen atoms of the F ring, the attribution being supported by the correlation of C-9b with H-14 and H-10. The aromatic protons H-4 and H-5 were assigned on the basis of the correlations with C-3b and C-5b, respectively, the C-3b carbon is revealed for its simultaneous coupling with the aldehydic proton. As a consequence, the last set of aromatic protons H-7 and H-8 was attributed and their relative assignment is straightforward for the presence of a coupling between C-6b and H 7 and C-8b and H8, confirmed by the ^{4}J coupling between C-6b and H-5, which allowed us to distinguish H-7 from H-8.

A possible reaction mechanism to explain the formation of **6** is shown in Scheme 5. In the presence of the Lewis acid $SnCl_4$, Cl_2CHOMe is the electrophilic species attacking the α-position of the terminal thiophene ring B to give the cation **7** which, in turn, can act as an electrophile reacting with the terminal thiophene ring A to give **8**. Intermediate **8** is then transformed into the final product 6 through the re-aromatisation of the B ring and a hydride shift from the B ring to the positively charged carbon atom in the A ring, and hydrolysis of the chloromethoxy methyl group to the formyl group. Although the proposed mechanism finds some support in a published paper,[16] the presence of an intermediate radical or tin hydride species cannot be excluded. It is worth noting that only one diastereoisomer of compound **6** is formed, which means that the configuration of the new stereogenic centre is controlled by the helical chirality of TH[7].

We then explored the synthesis of the aldehyde **2** via electrophilic formylation of the anion in position 2 of the terminal thiophene ring of TH[7] **1** with DMF (Scheme 3, method B). The generation of the anion in position 2 in the helicene **1** has never been reported before,[21] but was an important goal since it could open up an easy entry to differently substituted TH[7]. The anion was formed by adding 1.1 equiv. of *n*-BuLi to the solution of TH[7] **1** in dry THF at −78°C, keeping the reaction mixture at −78°C under stirring for 40 min. To check the presence of the anion, D_2O was added to the reaction mixture at −78°C. After a standard work-up, the α-monodeuterated TH[7] **9** was obtained in 90% yield (Scheme 3). The structure of **9** was confirmed by the mass and ^{1}H NMR spectra.

In a second experiment, the α-anion generated in anhydrous THF as described above was treated with 2 equiv. of dry DMF at −78°C. After a standard work-up, the tetrathia-[7]-helicene-2-carbaldehyde **2** was isolated in 66% yield together with 27% of unreacted thiahelicene **1** (Scheme 3, method B). After being modified by generating the anion in the presence of TMEDA, the same procedure afforded the aldehyde **2** in comparable yields but in a purer form.

3. Conclusions

We here report a convenient synthesis of the key alkene intermediate **3**, which is now available in overall good yields and reasonable reaction times, and can be transformed into the final helicene **1** as reported by Winberg.[8] The α-anion was generated on the terminal thiophene ring of TH[7] **1**, and its reactivity with electrophiles was proven by reaction with D_2O and DMF. The latter reaction produced the corresponding previously unknown 2-formyl-TH[7] **2**. The optical resolution of **2** is currently under investigation in our laboratory.

4. Experimental

4.1. General

Reagents obtained from commercial sources were used without further purification. Before use, the THF was dried by distillation over sodium wire/benzophenone and the butyl lithium solutions were titrated. In order to monitor the progress of the reactions, thin layer chromatography (TLC) was performed using Merck silica gel 60 F254 precoated plates. Flash chromatography was performed using Merck silica gel 60, 230–400 mesh. Melting points were determined by means of a Büchi 510 apparatus and are uncorrected or with a Mettler Toledo 820 DSC. The IR spectra were recorded on a Perkin–Elmer FT-IR 1725X. High-resolution mass spectra were recorded on a Vg Analytical 7070 EQ.

Unless otherwise stated, all of the operations were performed under an inert atmosphere and using oven dried glassware.

4.2. NMR measurements

The ^1H and ^{13}C spectra were acquired on a Bruker AMX 300 spectrometer operating at 300.133 MHz (^1H) and at 75.47 MHz (^{13}C). All the experiments were carried out at room temperature (27°C), using $CDCl_3$ as solvent, except for compound **6**, which was dissolved in DMSO-d_6, not being soluble in $CDCl_3$. ^{13}C {^1H} spectra were obtained using Waltz decoupling, and were exponentially multiplied to give 0.8 Hz line broadening before Fourier transformation.

2D Spectra. All of the two dimensional experiments were acquired with a Bruker inverse 5 mm z-gradient probe. The 90° pulse widths were 9.2 μs and 13.1 μs for ^1H and ^{13}C, respectively. The gradient was shaped by a waveform generator and amplified by a Bruker B-AFPA-10. A sinusoidal gradient of 1 ms length and a recovery time of 0.1 ms was used. The 2D COSY spectra were recorded with a 1024×1024 data matrix and 512 increments of 1 scan each, in magnitude mode, with a relaxation delay of 1.0 s and a 1:1 gradient combination, then processed using zero-filling in f_1 and an unshifted sine-bell apodisation function.

The HMQC and HMBC spectra were recorded using standard Bruker software sequences of inv4gs and inv4gslplrnd, respectively. The following acquisition parameters were applied in both experiments: spectral widths in the f_1 (^{13}C) and f_2 (^1H) dimensions of 14000 and 2700 Hz respectively, a 1024×1024 data matrix, 512 time increments of 200 scans each, and a 5:3:4 gradient combination.[18,19] We set the interpulse delay for the evolution of long-range coupling as Δ_1=3.5 ms in both experiments and Δ_2=60 ms only in HMBC. The Fourier transformations were performed using a shifted sine-bell apodisation function in the f_1 dimension and an unshifted sine-bell apodisation function in the f_2 dimension.

The 2D NOESY spectra were recorded using the NOESY pulse sequence and phase cycling method described by Marion and Wüthrich,[23] with a 1024×1024 data matrix and 256 increments of 96 scans each, a mixing time of 1.0 s, and a relaxation delay of 5.0 s.

4.2.1. Benzo[1,2-*b*;4,3-*b*′]dithiophen-2-carbaldehyde (4). *Method A*. Freshly distilled $POCl_3$ (3.53 g, 23.1 mmol) was added to a solution of *N*-methyl-formanilide (2.84 g, 21 mmol) in methylene chloride (5 mL) cooled to 0°C. The mixture was allowed to warm to room temperature and stirred for 30 min, and the resulting yellow–orange solution (the colour indicates the formation of Vilsmeier salt) was added dropwise to a solution of benzo[1,2-*b*;4,3-*b*′]-dithiophene (2.00 g, 10.5 mmol) in methylene chloride (15 mL). The mixture was refluxed for 19 h and the progress of the reaction was monitored by TLC (eluent: light petroleum/methylene chloride 1:1). During this period, two supplementary additions of Vilsmeier salt were needed in order to achieve the satisfactory conversion of benzo-[1,2-*b*;4,3-*b*′]dithiophene. The reaction was quenched by adding a 1 M aqueous solution of sodium acetate (200 mL) and extracted using methylene chloride (2×100 mL). The collected organic phases were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the crude material was purified by means of vacuum column chromatography (eluent: light petroleum/methylene chloride 1:1), affording 1.48 g (6.79 mmol, yield 69%) of benzo[1,2-*b*;4,3-*b*′]dithiophen-2-carbaldehyde **4**; mp 102–103°C (MeOH);[10a,b] IR (nujol) 1674 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, J=5.4 Hz, 1H), 7.70 (d, J=5.4 Hz, 1H), 7.75 (d, J=8.7 Hz, 1H), 7.91 (d, J=8.7 Hz, 1H), 8.31 (s, 1H), 10.09 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.3, 122.1, 123.3, 128.7, 132.1 (CH), 134.1, 136.3, 137.5, 140.9, 143.4 (Cq), 184.7 (CHO) ppm; EIMS *m*/*z*: 218 (M^+), 189 (22).

Method B. A *n*-BuLi 1.6 M hexane solution (4.05 mmol) was added dropwise under stirring to a solution of benzo[1,2-*b*;4,3-*b*′]dithiophene (700 mg, 3.68 mmol) in dry THF (30 mL) at −78°C. The solution was stirred for 5 min at −78°C and for 15 min at room temperature. The resulting yellow solution was cooled at −78°C, treated with dry DMF (537 mg, 7.36 mmol) and the progress of the reaction monitored by TLC (light petroleum, CH_2Cl_2 7:3). After 30 min at −78°C, the solution was warmed to room temperature (the colour of the solution changes to pale yellow), and quenched with a saturated aqueous solution of NH_4Cl (5 mL). The THF was removed under reduced pressure, the crude material was taken up with CH_2Cl_2 (60 mL) and washed with a saturated aqueous solution of NH_4Cl until pH 5 (3×25 mL). The organic phases were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the crude material was purified by means of flash column chromatography. First fraction collected with light petroleum as eluent: 71 mg (10%) of unreacted benzo[1,2-*b*;4,3-*b*′]dithiophene; second fraction collected with light petroleum/methylene chloride as 6:4 eluent: 580 mg (72%) of benzo[1,2-*b*;4,3-*b*′]dithiophen-2-carbaldehyde **4**.

4.2.2. 1,2-Bis-(2-benzo[1,2-*b*;4,3-*b*′]dithiophenyl)-ethene (3). Pure $TiCl_4$ (1.04 g, 5.48 mmol) was carefully added to dry THF (20 mL) at 0°C, thus affording a bright-yellow mixture due to the formation of $TiCl_4$.2THF complex. After stirring the mixture at 0°C for 5 min, zinc (0.673 g, 10.3 mmol) was added and the mixture was refluxed for 2 h (the colour changes from yellow to dark blue), after which pyridine (0.344 g, 4.60 mmol) was added and the refluxing continued for another 30 min. After cooling the mixture at room temperature, a solution of benzo[1,2-*b*;4,3-*b*′]dithiophen-2-carbaldehyde **4** (1.00 g, 4.60 mmol) in dry THF (8 mL) was added and the reaction mixture was refluxed for a further 7 h. The progress of the reaction was monitored following the disappearance of benzo[1,2-*b*;4,3-*b*′]dithiophen-2-carbaldehyde by TLC (eluent: light petroleum/methylene chloride 1:1). The solvent was removed under reduced pressure and the green crude mixture taken up with 35% HCl (20 mL) and ice (14 g). The resulting mixture was stirred for 1 h, and the yellow precipitate filtered off and washed with water. After drying overnight at 80°C, 0.906 g (2.24 mmol, yield 97%) of the 1,2-bis-(2-benzo[1,2-*b*;4,3-*b*′]dithiophenyl)-ethene **3** was obtained as a yellow solid (mixture of *cis*/*trans* isomers); mp 375°C; IR (nujol) 1645 cm^{-1}; UV (CH_2Cl_2; λ_{max}; (log ε)) 357 (3.90), 374 (4.21), 395 (4.37), 419 (4.29) nm; ^1H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 1H), 7.32 (s, 1H), 7.76 (s, 1H), 7.73 (s, 1H), 7.67 (d, J=9.1 Hz, 1H), 7.60 (d,

J=9.1 Hz, 1H), 7.56 (d, J=5.6 Hz, 1H), 7.47 (d, J=5.6 Hz, 1H); FABMS (positive mode) m/z:404 $[M]^+$.

4.2.3. Tetrathia-[7]-helicene (1).[10a] 1,2-Bis-(2-benzo[1,2-*b*; 4,3-*b'*]dithiophenyl)-ethene **3** (142 mg, 0.351 mmol, 1 equiv.) was dissolved in benzene (250 mL) at 70°C. A 0.5% (w/v) solution of iodine in benzene (1.6 mL) was added, and the stirred solution was irradiated with a 150 W unfiltered Hg medium pressure lamp, equipped with a quartz jacket. During the first 11 h, the solution temperature was maintained at 60°C, after which it was allowed to fall to 28°C and a 0.5% (w/v) solution of iodine in benzene (1.6 mL) was added. The solution was then irradiated at 28°C for 13.5 h. The course of the reaction was followed by TLC. The reaction mixture was then extracted with a saturated Na_2SO_3 solution (2×100 mL); the aqueous phases were extracted with toluene (3×100 mL). The organic phases were collected and the solvent was removed under reduced pressure, affording 156 mg of solid residue, further purified by flash chromatography (eluent: light petroleum/methylene chloride 7:3) to give 113 mg of **1** (0.281 mmol, 80%); mp 269°C; UV (CH_2Cl_2; λ_{max}; (log ε)) 208 (4.67), 226 (4.73), 246 (4.74), 370 (4.40), 387 (4.41) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74 (d, J=5.6 Hz, 1H), 6.91 (d, J=5.6 Hz, 1H), 7.96 (d, J=8.5 Hz, 1H), 8.04 (d, J=8.5 Hz, 1H), 8.02 (s, 1H); HRMS calculated for $C_{22}H_{10}S_4$: 401.9665, found: 401.9682, EIMS m/z: 402 (M^+), 368 (28), 355 (20), 184 (14).

4.2.4. Monodeuterated-tetrathia-[7]-helicene (9). An *n*-BuLi 1.6 M hexane solution (0.171 mmol) was added dropwise under stirring to a solution of tetrathia-[7]-helicene **1** (62 mg, 0.154 mmol) in dry THF (5 mL) at −78°C. The solution was stirred for 40 min at −78°C, and the resulting pale orange solution was quenched with D_2O (0.5 mL) and allowed to warm to room temperature (the colour of the solution changes from pale orange to light yellow). The THF was removed under reduced pressure, and the crude material taken up with CH_2Cl_2 (15 mL) and washed with water (5 mL). The organic phases were dried over Na_2SO_4 and the solvent removed under reduced pressure, affording 56 mg (0.139 mmol, yield 90%) of [7]-monodeuterated-thia-heteroelicene **9** as a pale yellow solid. mp 265°C; UV (CH_2Cl_2; λ_{max}; (log ε)) 210 (4.61), 226 (4.59), 245 (4.63), 369 (4.28), 388 (4.30) nm. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (d, J=5.6 Hz, 1H), 6.83 (d, J=5.6 Hz, 1H), 6.67 (s, 1H), 7.90 (d, J=8.5 Hz, 2H), 7.96 (d, J=8.5 Hz, 2H), 7.95 (s, 2H). HRMS calculated for $C_{22}H_9DS_4$: 402.9727, found: 402.9755, EIMS m/z: 403 (M^+), 369 (35), 356 (17), 184 (16).

4.2.5. Tetrathia-[7]-helicene-2-carbaldehyde (2). *Method A*. Freshly distilled $POCl_3$ (3.53 g, 23.1 mmol) was added to a solution of *N*-methyl-formanilide (71 mg, 0.525 mmol) in DCE (0.5 mL) and cooled to 0°C. The mixture was allowed to warm to room temperature and stirred for 30 min, and the resulting yellow-orange solution (the colour indicates the formation of Vilsmeier salt) was added dropwise to a solution of tetrathia-[7]-helicene **1** (89 mg, 0.221 mmol) in DCE (2 mL). The mixture was refluxed for 33 h and the progress of the reaction was monitored by TLC (eluent: light petroleum/methylene chloride 1:1). During this period, three supplementary additions of Vilsmeier salt were needed in order to achieve a satisfactory conversion of [7]-thiaheteroelicene. The reaction was quenched by adding a 1 M water solution of sodium acetate (90 mL) and extracted with methylene chloride (2×100 mL). The collected organic phases were dried over Na_2SO_4, the solvent removed under reduced pressure and the crude material purified by flash column chromatography (eluent: light petroleum/methylene chloride 7:3 and then 1:1) affording 33 mg (0.077 mmol, yield 34%) of thia-[7]-helicene-2-carbaldehyde **2** as a yellow solid: mp 255°C; IR (CH_2Cl_2) 1667 cm−1; UV (CH_2Cl_2; λ_{max}; (log ε)) 225 (4.69), 244 (4.69), 334 (3.93), 346 (4.04), 364 (4.13), 398 (3.83) nm; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.65 (d, J=5.6 Hz, 1H), 6.95 (d, J=5.6 Hz, 1H), 7.32 (s, 1H), 7.99–8.16 (m, 6H), 9.26 (s, 1H); ^{13}C NMR (75 MHz, CDCl3) δ 118.8, 120.5, 121.1, 121.5, 121.6, 122.7, 125.1, 125.2, 135.5 (CH),129.3, 129.7, 130.0, 131.8, 134.9, 136.7, 137.1, 137.2, 137.4, 137.9, 138.2, 140.2, 140.9 (Cq), 184.0 (CHO); HRMS calculated for $C_{23}H_{10}OS_4$: 429.9614, found: 429.9676, EIMS m/z: 430 (M^+), 368 (34), 355 (17), 184 (10).

Method B. A *n*-BuLi 1.6 M hexane solution (0.171 mmol) was added dropwise under stirring to a solution of tetrathia-[7]-helicene (62 mg, 0.155 mmol) in dry THF (5 mL) at −78°C. The solution was stirred for 40 min at −78°C, and the resulting pale orange solution was treated with dry DMF (24 mg, 0.329 mmol). The progress of the reaction was monitored by, TLC (light petroleum/CH_2Cl_2 1:1). After 17.5 h at −78°C, the solution was warmed to room temperature (during this period the colour changes from orange to dark red) and quenched with a saturated aqueous solution of NH_4Cl (5 mL). The THF was removed under reduced pressure, and the crude was taken up with CH_2Cl_2 (15 mL) and washed with water (5 mL), saturated water solution of NH_4Cl until pH 5. The organic phases were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the crude material was purified by flash column chromatography (eluent: light petroleum/methylene chloride 7:3 and then 1:1, 4:6, finally 2:8) affording 44 mg (0.102 mmol, yield 66%) of [7]-thiaheterohelicen-2-carbaldehyde **2** as a yellow solid.

Method C. An *n*-BuLi 1.6 M hexane solution (0.533 mmol) was added dropwise under stirring to a solution of tetrathia-[7]-helicene (195 mg, 0.485 mmol) in dry THF (13.5 mL) at −78°C, followed by the addition of freshly distilled (over CaH_2) TMEDA (62 mg, 0.534 mmol). The solution was stirred for 40 min at −78°C, and the resulting pale orange solution was treated with dry DMF (24 mg, 0.329 mmol). The progress of the reaction monitored by TLC (light petroleum/CH_2Cl_2 1:1). After 17.5 h at −78°C, the solution was warmed to room temperature (during this period the colour changes from orange to dark red) and quenched with a saturated water solution of NH_4Cl (5 mL). The solvent was removed under reduced pressure, and the crude was taken up with CH_2Cl_2 (15 mL) and washed with water (5 mL) saturated water solution of NH_4Cl until pH 5. The organic phases were dried over Na_2SO_4 and the solvent removed under reduced pressure; the crude material was purified by flash column chromatography (eluent: light petroleum/methylene chloride 7:3 and then 1:1, 4:6, finally 2:8) affording 115 mg (0.267 mmol, yield 55%) of tetrathia-[7]-helicene-2-carbaldehyde as yellow solid.

4.2.6. Compound (6). A 1 M solution of $SnCl_4$ in CH_2Cl_2 (65 mg, 0.250 mmol) was carefully added dropwise under stirring to a solution of tetrathia-[7]-helicene (77 mg, 0.192 mmol) in dry CH_2Cl_2 (6 mL) cooled to 0°C. The solution was kept under stirring at 0°C for 45 min, and then the α,α-dichloromethyl methyl ether (29 mg, 0.253 mmol) was added and the solution was kept under stirring at 0°C for 45 min. The reaction was monitored by, TLC (light petroleum/CH_2Cl_2 1:1). The solution was allowed to warm to room temperature and stirred for 45 min. The reaction was quenched with ice (15 mL), and the mixture was stirred for 1 h and then filtered on celite and extracted with CH_2Cl_2 (20 mL). The collected organic phases were dried over Na_2SO_4, the solvent was removed under reduced pressure, and the crude material was purified by flash column chromatography (eluent: light petroleum/methylene chloride 1:1 and then 2:8) affording 52 mg (0.121 mmol, yield 63%) of **6** as an orange solid: mp 301°C; IR (nujol) 1645 cm^{-1}; UV (CH_2Cl_2; λ_{max}; (log ε)) 206 (4.39), 219 (4.50), 222 (4.49), 248 (4.55), 339 (4.01), 357 (4.05) nm; ^1H NMR (300 MHz, DMSO) δ 3.80 ($H13_A$), 4.10 ($H13_B$), 6.20 (H14), 8.0 (H10), 8.03 (H4), 8.11 (H7), 8.22 (H5), 8.34 (H8), 11.09 (CHO), ^{13}C NMR (75 MHz, DMSO) δ 50.0 (C13), 55.5 (C14), 121.3 (C4), 121.9 (C7), 123.1 (C11), 124.1 (C8), 124.1 (C10), 124.3 (C5), 130.0 (C6b), 131.8 (C5b), 132.8 (C8b), 134.0 (C5a), 135.0 (C11b), 135.3 (C9a), 136.9 (C11a), 138.1 (C6a), 138.5 (C3b), 139.0 (C9b), 139.2 (C1), 139.6 (C8a), 140.1 (C3a), 146.9 (C2), 189.4 (CHO); HRMS calculated for $C_{23}H_{10}OS_4$ 429.9614, found: 429.9608, FABMS (positive mode) *m/z*: 430 $[M]^+$.

Acknowledgements

The authors gratefully acknowledge joint financial support from the Ministero dell'Istruzione, dell'Università e della Ricerca Scientifica (MIUR), Rome, and the University of Milan (National project 'Stereoselezione in Sintesi Organica. Metodologie e Applicazioni'); they also acknowledge the CNR (Rome). The work was also supported in the framework of a EU COST Chemistry programme (D14/0008/99).

References

1. (a) In *The Principles of Non-linear Optics*; Shen, Y. R., Ed.; Wiley: New York, 1984. (b) In *Introduction to Non-linear Optical Effects in Molecules and Polymers*; Prasad, P. N., Williams, D. J., Eds.; Wiley: New York, 1991. (c) In *Principles and Applications of Non-linear Optical Materials*; Munn, R. W., Ironside, C. N., Eds.; Chapman and Hall: London, 1993. (d) In *Molecular Non-linear Optics*; Zyss, J., Ed.; Academic: London, 1994. (e) In *Photonic Polymer Systems: Fundamentals, Methods and Applications*; Wise, D. L., Wnek, G. E., Trantolo, D. J., Cooper, T. M., Gresser, J. D., Eds.; Marcel Dekker: New York, 1998. (f) In *Non-linear Effects and Materials*; Gunter, P., Ed.; Springer: Berlin, 2000.
2. (a) Pershan, P. S. *Phys. Rev.* **1963**, *130*, 919–929. (b) Terhune, R. W.; Maker, P. D.; Savage, C. M. *Phys. Rev. Lett.* **1962**, *8*, 404–406. (c) Bethune, D. S.; Smith, R. W.; Shen, Y. R. *Phys. Rev. Lett.* **1976**, *37*, 431–434. (d) Kauranen, M.; Verbiest, T.; Persoons, A. *Int. J. Non-linear Opt. Phys.* **1999**, *8*, 171–189.
3. Mejer, E. W.; Havinga, E. E.; Rikken, G. L. J. A. *Phys. Rev. Lett.* **1990**, *65*, 37–39.
4. Kauranen, M.; Verbiest, T.; Meijer, E. W.; Havinga, E. E.; Teerenstra, M. N.; Schouten, A. J.; Nolte, R. J. M.; Persoons, A. *Adv. Mater.* **1995**, *7*, 641–644.
5. Ashitaka, H.; Yokoh, Y.; Shimizu, R.; Yokozawa, T.; Morita, K.; Suehiro, T.; Matsumoto, Y. *Mol. Cryst. Liq. Cryst. S&T, Sect. B: Non-linear Opt.* **1993**, *4*, 281–297.
6. (a) Verbiest, T.; Vanelshocht, S.; Kauranen, M.; Hellemans, L.; Snauwaert, J.; Nuckolls, C.; Katz, T. J.; Persoons, A. *Science* **1998**, *282*, 913–915. (b) Sioncke, S.; Van Elshocht, S.; Verbiest, T.; Persoons, A.; Kauranen, M.; Phillips, K. E. S.; Katz, T. J. *J. Chem. Phys.* **2000**, *113*, 7578–7581. (c) Belijonne, D.; Shuai, Z.; Brédas, J. L.; Kauranen, M.; Verbiest, T.; Persoons, A. *J. Chem. Phys.* **1998**, *104*, 1301–1304. (d) Minuti, L.; Taticchi, A.; Marrocchi, A.; Gacs-Baitz, E.; Galeazzi, R. *Eur. J. Org. Chem.* **1999**, 3155–3163. (e) Soon Choi, H.; Kim, K. S. *J. Phys. Chem. B* **2000**, *104*, 11006–11009.
7. Ashitaka, H.; Sasabe, H. *Non-linear Opt.* **1995**, *14*, 81–89.
8. (a) Winberg, H.; Groen, M. B. *J. Am. Chem. Soc.* **1968**, *90*, 5339–5341. (b) Winberg, H.; Groen, M. B. *J. Am. Chem. Soc.* **1970**, *92*, 6664–6665. (c) Groen, M. B. *J. Am. Chem. Soc.* **1971**, *93*, 2968–2974, and references cited therein.
9. (a) Terfort, A.; Görls, H.; Brunner, H. *Synthesis* **1997**, 79–86. (b) Reetz, M. T.; Beuttenmüller, E. W.; Goddard, R. *Tetrahedron Lett.* **1997**, *38*, 3211–3214.
10. TH[7] **1** was first prepared by Winberg in 1971 using two different methods: the first led to yields of about 18% from the commercially available 2-methylbenzothiophene, the second yielded 22% from benzothiophene. Caronna[11] has recently substantially followed the Winberg procedure to synthesize TH[7] **1** (a) Lehman, P. G.; Winberg, H. *Recueil* **1971**, 1113–1118. (b) Groen, M. B.; Schadenberg, H.; Winberg, H. *J. Org. Chem.* **1971**, *36*, 2797–2809.
11. Caronna, T.; Catellani, M.; Luzzati, S.; Malpezzi, L.; Meille, S. V.; Mele, A.; Richter, C.; Sinisi, R. *Chem. Mater.* **2001**, *13*, 3906–3914, and references therein.
12. Mallory, F. B.; Mallory, C. W. *Organic Reactions*; Wiley: New York, 1984; Vol. 30, p 1.
13. Tanaka, K.; Suzuki, H.; Osuga, H. *J. Org. Chem.* **1997**, *62*, 4465–4470, and references therein.
14. The theoretical calculations (Fribourg University, Professor Claude Daul) are currently in progress. β-Measurements were performed by one of the authors by means of hyper-Rayleigh scattering technique.[15]
15. Clays, K.; Wostyn, K.; Persoons, A.; Maiorana, S.; Papagni, A.; Daul, C. A.; Weber, V. *Chem. Phys. Lett.* **2003**, *372*, 438–442.
16. Larsen, J.; Bechgaard, K. *Acta Chem. Scand.* **1996**, *50*, 71–76.
17. Meier, H.; Kretzschmann, H.; Kolshorn, H. *J. Org. Chem.* **1992**, *57*, 6847–6852.
18. Hurd, R. E.; John, B. K. *J. Magn. Reson.* **1991**, *91*, 648–653.
19. (a) Ruiz-Cabello, J.; Vuister, G. W.; Moonen, C. T. W.; van Gelder, P.; Cohen, J. S.; van Zijl, P. C. M. *J. Magn. Reson.* **1992**, *100*, 282–302. (b) Wilker, W.; Leibfritz, D.; Kerssebaum, R.; Bermel, W. *Magn. Reson. Chem.* **1993**, *31*, 287–292.
20. Kalinowski, H. O.; Berger, S.; Braun, S. Carbon-13 NMR Spectroscopy, Wiley, New York, 1998.

21. The synthesis of [5]-thiaheterohelicene-2-aldehyde has been reported using the same protocol.[22]
22. Yamada, K.; Ishii, R.; Nakagawa, H.; Kawazura, H. *Tetrahedron: Asymmetry* **1996**, *7*, 737–746.
23. Marion, D.; Wüthrich, K. *Biochem. Biophys. Res. Commun.* **1983**, *113*, 967–974.