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Short Communications

Cyclopentathiophenes. X. Synthesis of 6,8-Diphenyl-7*H*- (and 6*H*) benzo[*b*]cyclopenta[*d*]thiophenes *

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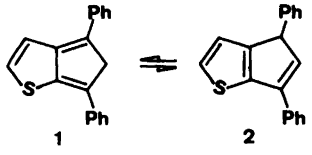
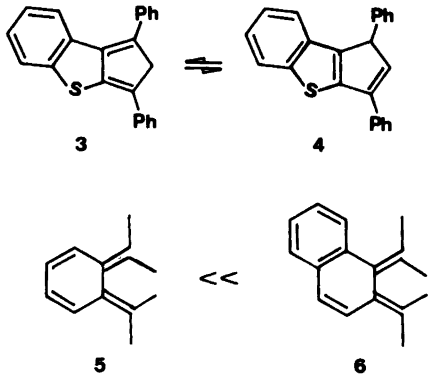
Some time ago a report from these laboratories described the synthesis of a thiophene analogue of isoindene, *1*.[2] Although *1* could be trapped using various dienophiles, it was found to be in equilibrium with the indene analogue *2*, a fact which precluded its isolation. The equilibrium concentration of *1* was less than 8 %.



1 2

In an attempt to increase the amount of isostructure at equilibrium, we found it of interest to try to annulate a benzene ring to the thiophene part of *1* and thereby obtain *3*. This would make the olefinic bond in the thiophene moiety of *1* part of an aromatic system and thus stabilize *3* relative to *1* more than *4* would be stabilized relative to *2*. There is recent evidence for this benzo-annulation effect: whereas tetramethyl *o*-xylylene *5* in solution has a half life of only some min, the benzo-annelated compound *6* is infinitely stable in the dark.[3] We describe our efforts in this field.

The synthesis of *3* was carried out according to Scheme 1. Benzo[b]thiophene was sequentially reacted with butyllithium and cinnamaldehyde to produce an alcohol which in turn was oxidized to the α-β-unsaturated ketone, (*E*?)-2-(3′-phenyl-



3 4 5 6

2′-propenoyl)benzo[*b*]thiophene, with pyridinium chlorochromate in dichloromethane. Cyclization was achieved using polyphosphoric acid. Reaction of the resulting ketone with phenylmagnesium bromide afforded a high yield of the tertiary alcohol. Elimination of water was effected upon reflux in benzene solution containing catalytic amounts of *p*-toluene sulfonic acid.

The product exhibited a strong green fluorescence in benzene solution, taken as an indication of the presence of the *ortho*-quinonoid compound *3*. We have previously shown that *1* possesses fluorescent properties. TLC showed that the reaction mixture consisted of at least two compounds. Column chromatography provided a main fraction which gave a ^{1}H NMR spectrum in *deutero*-chloroform consistent with a mixture of *3* and *4*. A 2H singlet at δ 3.87 is assigned to the methylene protons of *3* and a 1H doublet at δ 4.60 (J 2.0 Hz) is assigned to the methine proton of *4*. Integration over these signals gives 55 % of *3* and 45 % of *4*. Aromatic and vinylic protons appear as an unresolved multiplet at δ 6.6–7.8. ^{13}C NMR spectroscopy support this conclusion. Although the aromatic and vinylic part of the spectrum is poorly resolved, a signal at δ 49.6 shows coupling to two hydrogens (C7 in *3*) and a signal at δ 53.3 shows coupling to one hydrogen (C6 in *4*).

Separation of *3* and *4* by crystallization from various solvents proved impossible and also chromatography (both thin layer and column) consistently gave mixtures of the two isomers in

* Part IX, see Ref. 1.

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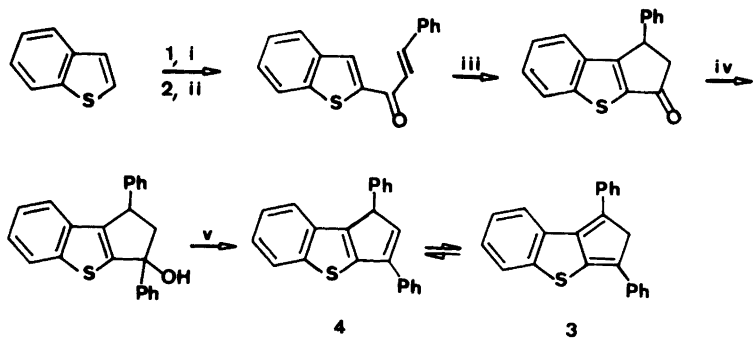
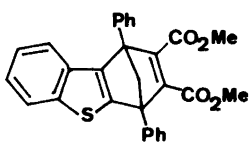


Scheme 1. Synthesis of 6,8-diphenyl-6*H*-benzo[*b*]cyclopenta[*d*]thiophene (*4*) and 6,8-diphenyl-7*H*-benzo[*b*]cyclopenta[*d*]thiophene (*3*). Reaction conditions: 1. BuLi, PhCH=CHCHO; ii. Pyridinium chlorochromate/CH_2Cl_2; iii. Polyphosphoric acid; iv. PhMgBr; v. H^+, C_6H_6, Δ.

approximately the same (thermodynamic?) proportion. We therefore decided to carry out a trapping experiment by adding dimethyl acetylenedicarboxylate as dienophile. In the trapping of *1* and *2*[2], reaction conditions could be chosen so that only one of the adducts was formed at a time. This turned out to be impossible in the case of *3* and *4*. When dimethyl acetylenedicarboxylate was added to the mixture of *3* and *4*, two adducts were isolated by column chromatography and their structures unequivocally established by spectroscopy (IR, NMR and MS). The major component was *7* and the minor was *8*. This shows that both *3* and *4* possess dienic reactivity and that they undergo Diels-Alder reactions.



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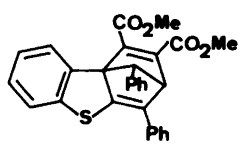

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The interesting feature is that *4* seems to have almost the same high reactivity as the ortho-quinonoid structure *3*. This conclusion is reached on the basis of the indication that *3* and *4* are in rapid equilibrium (*vide supra*) and the fact that the adducts *7* and *8* are formed in almost the same proportion as the relative amounts of *3* and *4* at equilibrium.

Another interesting observation was made during the determination of the melting point of the adduct *8*. This compound first melts in the range 165.5–171.5 °C, but after cooling and solidification new melting occurs at 93–100 °C. The structure of this assumed new compound has not been determined, but it is reasonable to suggest that *8* undergoes a similar thermal rearrangement as has been established for the corresponding adduct between *2* and dimethyl acetylenedicarboxylate.[1]

Experimental. The MS spectra were recorded on an AEI 902 and VG Micromass 7070 F. The NMR spectra were obtained with Varian HA 100 and 60 A (^1H) and with Jeol FX 60 (^{13}C). The IR spectra were obtained with Perkin-Elmer 281 and Jasco IRA 1. The melting points which are not corrected were measured using a Reichert Thermopan melting point microscope.

(E?)-2-(3'phenyl-2'propenoyl)benzo[b]*thiophene.* Butyllithium (67.7 mmol) in hexane (50 ml) was added dropwise to benzo[*b*]thiophene (8.25 g, 61.5 mmol) in dry ether (60 ml) under nitrogen at 0 °C. After stirring for 30 min, cinnamaldehyde (8.6 g, 67 mmol) in dry ether (50 ml) was added slowly. When the addition was complete, the colour changed from violet to yellow. After stirring for another 1 h, the reaction mixture was hydrolyzed with ice-water containing ammonium chloride. Part of the product precipitated out and was filtered off. The water phase was extracted several times with ether and the combined ether phases were dried ($MgSO_4$) and filtered. After evaporation, the combined products were crystallized from ethanol to give 15.6 g (95 %) of *(E)-2-(3'-phenyl-2'-propen-1'-hydroxy)-benzo*[b]*thiophene,* m.p. 122.0–124.5 °C, which was used directly in the next step. Pyridinium chlorochromate (18.3 g, 80.3 mmol) and sodium acetate (1.32 g, 16.1 mmol) were suspended in methylene chloride with stirring. The above alcohol (14.3 g, 53.5 mmol) was then dissolved in dry dichloromethane (500 ml) and with efficient stirring added slowly to the suspension. The stirring was continued for $2\frac{1}{2}$ h, the methylene chloride was

then evaporated and the product taken up in ether. Small amounts of extraneous matter were removed by treating the ether phase with charcoal. After evaporation of the ether, the title compound crystallized from methanol to give 6.3 g (44 %) of yellow crystals, m.p. 101–103 °C.

MS[IP 70 eV, *m/e* (% rel.int.)]: 264 (100, M), 263 (93, [M–H]), 235 (41, [M–CHO]), 161 (62, [M–PhCH=CH]), 133 (27, [M–PhCH=CH–C=O]), 131 (29, PhCH=CH–C=O), 103 (45, PhCH=CH, 89 (56, C_7H_5), 77 (47, Ph).

^{1}H NMR (60 MHz, $CDCl_3$): δ 7.1–8.1 (m). ^{13}C NMR (15 MHz, CS_2): δ 120.8 (C9), 122.7 (C7), 124.7 (C4), 125.6 (C5), 126.9 (C6), 127.6 (C3), 128.3 (C12, C16), 128.7 (C13, C15), 130.1 (C14), 134.6 (C2), 139.0 (C3a, C7a), 143.3 (C10), 180.8 (C8); *J* (C9, H9) 157.7 Hz, *J* (C7, H7) 165.5 Hz, *J* (C4, H4) 160.6 Hz, *J* (C5, H5) 163.1 Hz, *J* (C6, H6) 163.5 Hz, *J* (C3, H3) 171.9 Hz, *J* (C12, H12)=*J*(C16, H16) 153.3 Hz, *J* (C13, H13)=*J* (C15, H15) 160.2 Hz, *J* (C14, H14) 160.2 Hz, *J* (C10, H10) 156.3 Hz. IR (KBr): 1660 (s) cm^{-1}.

6-Phenyl-6,7-dihydro-8H-benzo[b]*cyclopenta*-[d]*thiophene-8-one.* Polyphosphoric acid (200 g) was placed in a reaction vessel and stirred using a strong electric motor. 2-(3′-Phenyl-2′-propenoyl)-benzo[*b*]thiophene (3.0 g, 11 mmol) was added and the temperature was increased to 70 °C. After 7 h at this temperature, the reaction mixture was cooled and hydrolyzed using ice-water. The product was extracted with ether (5×100 ml) and the combined ether extracts washed once with water (100 ml). After treatment with charcoal and drying ($MgSO_4$), the ether was evaporated and the product crystallized from peth.ether (60–80 °C) to give 1.1 g (36 %) of the title compound, m.p. 165.0–166.5 °C.

MS[IP 70 eV, *m/e* (% rel. int.)]: 264 (100, M), 235 (87, [M–CHO]), 221 (20, [M–C_2H_3O]), 115 (19, C_9H_7), 77 (24, Ph), 51 (20, C_4H_3).

^{1}H NMR (98 MHz, $CDCl_3$): δ 2.82 (1H, dd, *J* 19 and 3.0 Hz), 3.43 (1H, dd, *J* 19 and 7.5 Hz), 4.55 (1H, dd, *J* 7.5 and 3.0 Hz), 6.9–7.4 (8H, m) 7.67 (1H, d, *J* 9 Hz).

^{13}C NMR (15 MHz, CS_2): δ 42.6 (C6), 50.6 (C7), 124.2 (C3,C4), 130.3 (C5a,C5b), 133.7 (C1a, C8a), 141.4 (C9), 148.3 (C5a, C5b, C1a) 164.1 (C8). *J* (C6, H6) 131.8 Hz, *J* (C7, H7) 132.1 Hz, *J* (C3, H3 and C4, H4) 162.6 Hz, *J* (C2, H2) 161.2, *J* (C5, H5) 172 Hz. IR (KBr): 1720 (s) cm^{-1}.

6,8-Diphenyl-6,7-dihydro-8H-benzo[b]*cyclopenta*[d]*thiophene-8-ol.* Magnesium (8.1 g, 4.0 mmol) was added to bromobenzene (0.59 g, 3.8 mmol) in dry tetrahydrofuran (20 ml) under nitrogen. The mixture was refluxed for 2 h and then cooled to 0 °C in an ice-bath. The ketone (*vide supra*) (0.50 g, 1.9 mmol) in dry THF (20 ml) was then added dropwise. After stirring for 10 min. at 0 °C and for 3 h at 67 °C, the mixture was hydrolyzed with ice-water containing ammonium chloride. The product was worked up in the usual way by extraction with ether. Crystallization from methanol gave 0.56 g (87 %) of the title compound, m.p. 130–133 °C.

MS [IP 70 eV, *m/e* (% rel. int.)]: 324 (100, [M–H_2O]), 323 (26, [M–H_2O–H]), 320 (12), 246 (19, [M–H_2O–H–Ph]), 161 (6), 154 (8).

^{1}H NMR (60 MHz, acetone-d_6): δ 2.7–3.6 (2H, m), 4.60 (1H, t, *J* 12 Hz), 5.27 (1H, s), 7.0–7.9 (9H, m). IR (KBr): 3400 (s) cm^{-1}.

6,8-Diphenyl-7H- (and 6H) benzo[b]*cyclopenta*[d]*thiophene 3 and 4.* The above alcohol (0.56 g, 1.6 mmol) was dissolved in benzene (75 ml) and warmed to reflux under nitrogen. When a small amount of *p*-toluene sulfonic acid was added, the solution immediately acquired a strong green fluorescence and water appeared in the reflux condenser. The water was removed with a Dean-Stark water separator. The reaction mixture was stirred at reflux for 2 h and then cooled. Ater rapid washing with one portion of water (25 ml), the benzene solution was dried ($MgSO_4$). After evaporation of the solvent, the product, 0.50 g (90 %), was shown by ^{1}H NMR to consist of two components. Attempts to separate them by crystallization from benzene, methanol or acetone failed. Neither did we succeed in achieving separation of the products by column or thin layer chromatography.

^{1}H NMR (100 MHz, $CDCl_3$): 3.87 (2H, s, H7 in *3*), 4.60 (1H, d, *J* 2.0 Hz H6 in *4*), 6.5–7.8 (14–15H, m).

^{13}C NMR (15 MHz), CS_2): 49.6 (C7 in *3*), 53.3 (C6 in *4*).

Formation of Diels-Alder adducts between 3 *and* 4 *and dimethyl acetylene dicarboxylate.* The crude mixture of *3* and *4* (0.40 g, 1.2 mmol) was dissolved in benzene (50 ml) and heated to reflux under nitrogen. Dimethyl acetylene dicarboxylate (0.17 g, 1.2 mmol) in benzene (50 ml) was then added dropwise for 1 h. After further 2 h, the solution was cooled and the solvent evaporated. TLC showed the presence of two products which were separated by column chromatography (Silica Merck 9385, 0.040–0.063 mm and light pethroleum–ethyl acetate 3:1). The same two adducts were obtained when the addition was conducted by rapid mixing of the reagents in benzene solution at room temperature and keeping the solution at this temperature for 48 hrs. The two products were identified as *dimethyl 6,9-diphenyl-6,9-methano-6,9-dihydro-dibenzo*-[b,d]*thiophene-7,8-dicarboxylate* (*7*), m.p. 199–202 °C. MS[IP 70 eV, (% rel. int.)]: 466

(22, M), 407 (58, [M−CH_3C=O]), 374 (29, [M−C_7H_8]), 346 (57), 323 (100, [M−$C_6H_6O_4$−H], 271 (26), 247 (38), 172 (29).

^{1}H NMR (98 MHz, $CDCl_3$): δ 3.18 (1H, d, J 7.4 Hz), 3.46 (3H, s), 3.51 (3H, s), 7.0–7.7 (14H, m), and *dimethyl 9,10-diphenyl-5b,8-methano-5b,8-dihydro-dibenzo*[b,d]*thiophene-6,7-dicarboxylate* (*8*), m.p. 165.5–171.5 °C, MS[IP 70 eV, (% rel. int.)]: 466 (2, M), 407 (100, [M-CH_3C=O]), 375 (4,[M−C_7H_7]) 348 (7, [M-2CH_3C=O]), 346 (13), 344 (14), 329 (3), 287 (5), 270 (7), 259 (4).

^{1}H NMR (98 MHz, $CDCl_3$): δ 3.44 (3H, s), 3.70 (3H, s), 4.51 (1H, s), 4.94 (1H, s), 6.6–7.5 (14H, m).

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