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Cyclopenta-thiophenes. VIII. Thiophene Analogues of Isoindenes *

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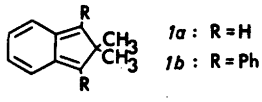
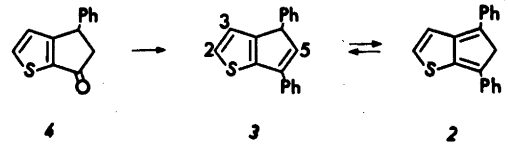
4,6-Diphenyl-5*H*-cyclopenta[*b*]thiophene (*2*), a thiophene analogue of the unknown 1,3-diphenyl-isoindene, is found to exist in equilibrium with 4,6-diphenyl-4*H*-cyclopenta[*b*]thiophene (*3*) and is shown to possess high Diels-Alder reactivity. Unexpectedly, it was found that also *3* reacts with dienophiles under mild conditions.

Considerable effort has been made in recent years on attempts to prepare isoindenes (2*H*-indenes).[2] So far only the 2,2-dimethyl derivatives *1a* and *b* have actually been isolated.[2,3] The corresponding compounds without the blocking methyl groups, exist entirely as indenes (1*H*-indenes), although isoindenes have been invoked as intermediates in some of their reactions.[4,5] This is obviously due to the facile 1,5-hydrogen shift or acid/base catalysed prototropy from the *ortho*-quinonoid structure to the more stable, aromatic system.



1a: R = H
1b: R = Ph

The pronounced tendency for the benzene moiety to retain its aromatic character in these systems, suggested to us that analogues of isoindenes where the benzene part has been replaced by the less aromatic thiophene ring, might be stable compounds. We therefore decided to synthesise the *b*-annelated thiophene analogue of 1,3-diphenylindene (*3*) and try to isomerise it to the isostructure *2* (Scheme 1).



4 *3* *2*

Scheme 1.

The known 4,5-dihydro-4-phenyl-6*H*-cyclopenta[*b*]thiophene-6-one (*4*) [6] gave the corresponding tertiary alcohol in fair yield after reaction with phenylmagnesium bromide. Dehydration was accomplished in refluxing benzene solution in the presence of catalytic amounts of *p*-toluenesulfonic acid. Already after the first trace of acid had been added, the solution became fluorescent. As fluorescence is characteristic of the corresponding isoindene, *1b*,[3] we took this as a good indication of isomerisation of the initially formed olefin, *3*, to the elusive 5*H*-cyclopenta[*b*]thiophene, *2*.

However, NMR analysis of the dehydrated product revealed only one product, which was assigned the structure 4,6-diphenyl-4*H*-cyclopenta[*b*]thiophene (*3*). The NMR spectrum shows a significant long range coupling of 1.5 Hz through the least zig-zag path between the 2- and the 5-hydrogen. This excludes the 5*H*-isomer (*2*) (which is expected to give a two-proton signal at comparatively high field). The 6*H*-isomer is expected to give a spectrum similar to the observed one. However, on the basis of previous experience with 4*H*- and 6*H*-cyclopenta[*b*]thiophenes,[7] it is highly unlikely that the initially formed 4*H*-isomer isomerises to the less stable 6*H*-isomer in this acidic medium. The stability of the 6*H*-isomer is probably, in this case, even less than in other 6*H*-isomers investigated due to steric hindrance between the 3-hydrogen and 4-phenyl ring.

* No. VII of this series, *cf.* Ref. 1. Part of No. VIII was presented at the 6th International Symposium on Organic Sulfur Chemistry in Bangor, U.K., 1974.

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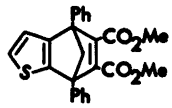

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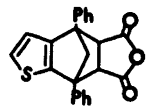

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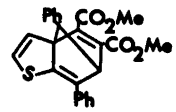

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We still felt that the strong fluorescence was due to the presence of small amounts of *5H*-cyclopenta[*b*]thiophene *2*. Expecting high reactivity of *2* towards dienophiles, dimethyl acetylenedicarboxylate, and in a second experiment maleic anhydride, was added. This instantaneously removed the fluorescence. After 4 h reflux in benzene solution, the isoadducts *5* and *6* were isolated in almost quantitative yield. The question of *exo*/*endo* isomerism in *6* is still not settled, but judging from TLC only one of the isomers is formed.

Evidently *2* exists in equilibrium with 3. When *3* was refluxed in benzene solution and then cooled to 10 °C, the amount of *2* could be determined by "titrating" with maleic anhydride in benzene. The endpoint was taken as the disappearance of the fluorescence. The amount of *2* present at equilibrium was estimated at < 8 %. This is an upper limit as it is difficult to exclude the possibility that some of *3* isomerises to *2* during the titration, even at this low temperature.

When *3* (*2* removed by iso-adduct formation) was kept with an excess of dimethyl acetylenedicarboxylate at 10 °C for 3 h and a further 3 h at room temperature, a new adduct (*7*), could be isolated in almost quantitative yield. The NMR spectrum is in full accord with this structure, showing an interesting long-range coupling between the former 2- and 5-hydrogen of 1 Hz.

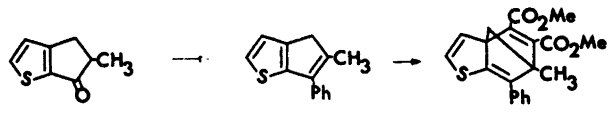
This adduct is interesting as it shows that one of the double bonds in the thiophene ring of *3* can be considered as part of a cyclopentadiene system possessing Diels-Alder reactivity. A similar reaction has previously been observed for 2-vinylthiophene under much more vigorous conditions.[8]

Although these results show that the two phenyl rings in *2* and *3* are not sufficient to make the iso-structure predominant at equilibrium, it is predictable that properly substituted aryl groups will do so by extending the conjugation.

On the other hand, the presence of only *one* phenyl ring is clearly insufficient to make the iso-structure detectable even with trapping reagents. This was demonstrated by the following experiment (Scheme 2):

The known ketone *8* [6] was treated with phenylmagnesium bromide and the resulting tertiary alcohol dehydrated by refluxing in benzene solution with *p*-toluenesulfonic acid to the indene analogue *9*. The NMR spectrum of the product corresponds well with the proposed structure. *9* does not show fluorescence. As shown in Scheme 2, *9* reacts with dimethyl acetylenedicarboxylate in refluxing benzene solution to produce exclusively the adduct *10*, which is analogoues to *7*. As expected the NMR spectrum of *10* lacks the long-range coupling of 1 Hz observed for *7* due to the presence of the methyl group.

Neither do the *two* phenyl rings in 1,3-diphenylindene make the iso-structure sufficiently stable to allow reaction with dienophiles. This was demonstrated by refluxing 1,3-diphenylindene with dimethyl acetylenedicarboxylate or maleic anhydride in benzene solution for 40 h and recovering all the starting material unchanged. This again indicates the reluctance of the benzenoid indene system to adopt an *ortho*-quinonoid structure.



8 9 10

Scheme 2.

EXPERIMENTAL

*4,5-Dihydro-4,6-diphenyl-6*H*-cyclopenta*[b]*-thiophene-6-ol.* The Grignard reagent from bromobenzene and magnesium (25 mmol of each) was placed in an ice bath and *4* (2.40 g, 11 mmol) in dry ether (80 ml) was added dropwise. After the addition was complete, the mixture was stirred an additional 30 min at room temperature and then poured onto ice. The ether phase was separated, washed with water and dried ($MgSO_4$). From the filtered ether phase 1.50 g (46 %) of the title compound, m.p. 98–100 °C, was isolated. ^{1}H NMR (60 MHz, C_6D_6): δ 2.1 (1 H, s), 2.6 (1 H, dd, J 13.8 and 6.2 Hz), 3.1 (1 H, dd, J 13.8 and 8.4 Hz), 4.0 (1 H, dd, J 8.4 and 6.2 Hz), 6.4 (1 H, d, J 4.9 Hz), 6.8 (1 H, d, J 4.9 Hz), 7.1–7.3 (10 H, m).

*4,6-Diphenyl-4*H*-cyclopenta*[b]*thiophene (3).* 4,5-Dihydro-4,6-diphenyl-6*H*-cyclopenta[*b*]thiophene-6-ol (1.75 g. 10 mmol) was refluxed for 2 h in dry benzene (50 ml) with a small amount of *p*-toluenesulfonic acid in nitrogen atmosphere. The water from the reaction was collected with a Dean-Stark separator. The fluorescent solution was washed with water and dried ($MgSO_4$). After filtration and evaporation of the benzene, the crude product was taken up in ether. 1.34 g (82 %) of the title compound was obtained as large colourless crystals from ether m.p. 88.0–91.5 °C. ^{1}H NMR (60 MHz, C_6D_6): δ 4.3 (1 H, d, J 2.2 Hz), 6.4 (1 H, dd, J 2.2 and 1.5 Hz), 6.6 (1 H, d, J 5.0 Hz), 6.8 (1 H, dd, J 5.0 and 1.5 Hz), 7.0–7.8 (10 H, m).

Adduct formation between 2 *and dimethyl acetylenedicarboxylate.* Dimethyl acetylenedicarboxylate (0.99 g, 7 mmol) in benzene (100 ml) was added dropwise during 1 h to a solution of *3* (1.92 g, 7 mmol) in benzene (50 ml) under nitrogen. The mixture was then refluxed for 4 h. After evaporation of the benzene, ether was added and a yellowish powder precipitated. This crude product was recrystallized from methanol to give 2.5 g (86 %) of the iso-adduct *5*, m.p. 145.0–147.5 °C. Anal. $C_{25}H_{20}O_4S$: C, H. MS[IP 70 eV; *m/e* (% rel. int.)]: 416 (34, M), 357 (33, [M – CO_2CH_3]), 297 (100, [M – $CH_3O_2C-C{\equiv}C-CO_2CH_3$]). ^{1}H NMR (60 MHz, C_6D_6): δ 2.9 (1 H, d, J 7.3 Hz), 3.1 (3 H, s), 3.2 (3 H, s), 3.3 (1 H, d, J 7.3 Hz), 6.5 (1 H, d, J 5 Hz), 7.0 (1 H, d, J 5 Hz), 7.0–7.5 (10 H, m).

Adduct formation between 2 *and maleic anhydride.* With the same procedure as for the adduct formation above, about 90 % of crystalline *6* was obtained, m.p. 192–197 °C. Anal. $C_{23}H_{16}O_3S$: C, H. MS [IP 70 eV; *m/e* (% rel. int.)]: 274 (100, [M – maleic anhydride]). ^{1}H NMR (60 MHz, $(CD_3)_2CO$): δ 2.9 (2 H, s), 4.6 (2 H, s), 6.8 (1 H, d, J 5 Hz), 7.2–8.0 (11 H, m).

Adduct formation between 3 *and dimethyl acetylenedicarboxylate.* Dimethyl acetylenedicarboxylate (1.42 g, 10 mmol) in benzene (100 ml) was added dropwise with stirring to *3* (2.74 g, 10 mmol) in benzene (50 ml) under nitrogen at 10 °C. After the addition was completed, the mixture was stirred for 3 h at 10 °C and then 3 h at room temperature. The crude product was purified by treatment with charcoal and recrystallized from ethyl acetate/hexane and from methanol. This gave 3.5 g (84 %) of *7* as strongly yellow crystals, m.p. 105.5–110.5 °C. Anal. $C_{25}H_{20}O_4S$: C, H, S. MS [IP 70 eV; *m/e* (% rel. int.)][: 357 (100, [M – CO_2CH_3]), 297 (13), 295 (16). ^{1}H NMR (60 MHz, C_6D_6): δ 3.4 (3 H, s), 3.5 (3 H, s), 4.2 (1 H, d, J 2 Hz), 4.9 (1 H, dd, J 2 and 1 Hz), 5.9 (1H, d, J 6 Hz), 6.1 (1 H, dd, J 6 and 1 Hz), 6.8–7.6 (10 H, m).

*5-Methyl-6-phenyl-4*H*-cyclopenta*[b]*thiophene* 9. Starting from the known 4,5-dihydro-5-methyl-6*H*-cyclopenta[*b*]thiophene-6-one [6] and phenylmagnesium bromide according to the procedure described above for the synthesis of 4,5-dihydro-4,6-diphenyl-6*H*-cyclopenta[*b*]-thiophene-6-ol, the tertiary alcohol, 4,5-dihydro-6-phenyl-5-methyl-6*H*-cyclopenta[*b*]thiophene-6-ol, was prepared in almost quantitative yield. This alcohol was used directly in the dehydration step which was performed as described for the preparation of *3*. In this way *9* was obtained in 75 % yield from the ketone as white flakes from methanol, m.p. 70–71 °C. ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.1 (3 H, s), 3.2 (2 H, s), 6.9 (1 H, d, J 5 Hz), 7.0 (1 H, d, J 5 Hz), 7.1–7.7 (5 H, m).

Adduct formation between 9 *and dimethyl acetylenedicarboxylate.* A mixture of *9* (2.1 g, 10 mmol) and dimethyl acetylenedicarboxylate (1.4 g, 10 mmol) was refluxed for 5 h in benzene solution (50 ml). After evaporation of the solvent, 3.0 g (86 %) of *10* crystallized from methanol as yellow crystals, m.p. 115–117 °C. MS [IP 70 eV; *m/e* (% rel. int.)]: 354 (39, M), 212 (100, [M – $CH_3O_2C-C{\equiv}C-CO_2CH_3$]). ^{1}H NMR (60 MHz, C_6D_6): δ 1.6 (3 H, s), 2.0 (1 H, d, J 7 Hz), 2.4 (1 H, d, J 7 Hz), 3.3 (3 H, s), 3.4 (3 H, s), 6.1 (1 H, d, J 6 Hz), 6.2 (1 H, d, J 6 Hz), 7.0–7.8 (5 H, m).

The melting points are uncorrected. The NMR spectra were recorded on a Varian A 60 A (with TMS as an internal standard). The MS data were collected with an AEI MS 902 spectrometer. The elemental analysis were carried out by Ilse Beetz, Mikroanalytisches Laboratorium, Kronach, Germany.

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