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Molecular rearrangement in the Birch reduction of dibenzothiophenes

Pavel Kukula,* Andreas Dutly, Heinz Rüegger and Roel Prins*

Institute for Chemical and Bioengineering, ETH Zurich, HCI, 8093 Zurich, Switzerland

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Abstract—A molecular rearrangement observed during the Birch reduction of dibenzothiophene and 4,6-dimethyl-dibenzothiophene was explored and a mechanism for the rearrangement has been proposed.

The Birch reduction has been a synthetically useful and powerful method for the partial reduction of aromatic rings for more than 60 years.[1] Numerous compounds have been subjected to reducing conditions that include alkali metal and ammonia and various modifications and extensions of the Birch reduction have been developed.[2] The scope of the Birch reduction also covers a variety of heteroaromatic systems such as pyridines, indoles, furans and thiophenes.[3] Recently, we have been concerned with the reduction of 4,6-dimethyl-dibenzothiophene to tetra-, hexa- and dodecahydro-4,6-dimethyl-dibenzothiophenes.[4] The Birch reduction has been tested as a possible route to the partially hydrogenated 4,6-dimethyl-dibenzothiophenes as well.

Only a few reports on the Birch reduction of dibenzothiophene and its derivatives are available[5–7] and the unresolved questions concerning the mechanism, nature of the reactive intermediates and the product distribution still remain. It is known from the literature that dibenzothiophene **1a** is reduced by alkaline metal reduction in ammonia to 1,4-dihydro-dibenzothiophene **2** as the major product (Fig. 1).[5] Other works claim over-reduction and cleavage of the C–S bond to the corresponding thiophenol **3** (position of the isolated double bond not confirmed).[6,7] A detailed study suggests that the order of the reagent addition may be critical to the product distribution, for example, the 1,4-dihydro-derivative **2** arises if a solution of substrate in ether and ethanol is added to sodium in ammonia, whereas thiophenol **3** is the major product if the metal is added last.[7]

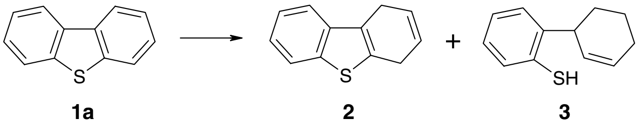

Figure 1. Birch reduction of dibenzothiophene.

In our case, we were interested in more saturated products with intact C–S bond, such as tetra- and hexahydro-4,6-dimethyl-dibenzothiophene. To investigate the possibility of further hydrogenation to more saturated products, a large excess of proton source (ethanol) and continuous addition of sodium to the reaction mixture were applied. A number of optimization experiments carried out with 4,6-dimethyl-dibenzothiophene **1b** (Fig. 2) showed that further reduction without C–S bond cleavage is possible. Reactions were carried out until full conversion of the starting material and the product composition was analyzed by GC–MS. The main products obtained were those with one fully hydrogenated benzene ring of the dibenzothiophene structure, that is, various isomers of hexahydro-dimethyl-dibenzothiophene with molecular weight 218 amu. All products appeared to have the same retention time and mass spectrum as the appropriate standards of partially hydrogenated 4,6-dimethyl-dibenzothiophenes prepared by catalytic hydrogenation.[4] The only difference was found in the mass spectrum of

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* Corresponding authors. Tel.: +41 44 633 4536; fax: +41 44 632 1162 (P.K.); e-mail addresses: pavel.kukula@chem.ethz.ch; roel.prins@chem.ethz.ch

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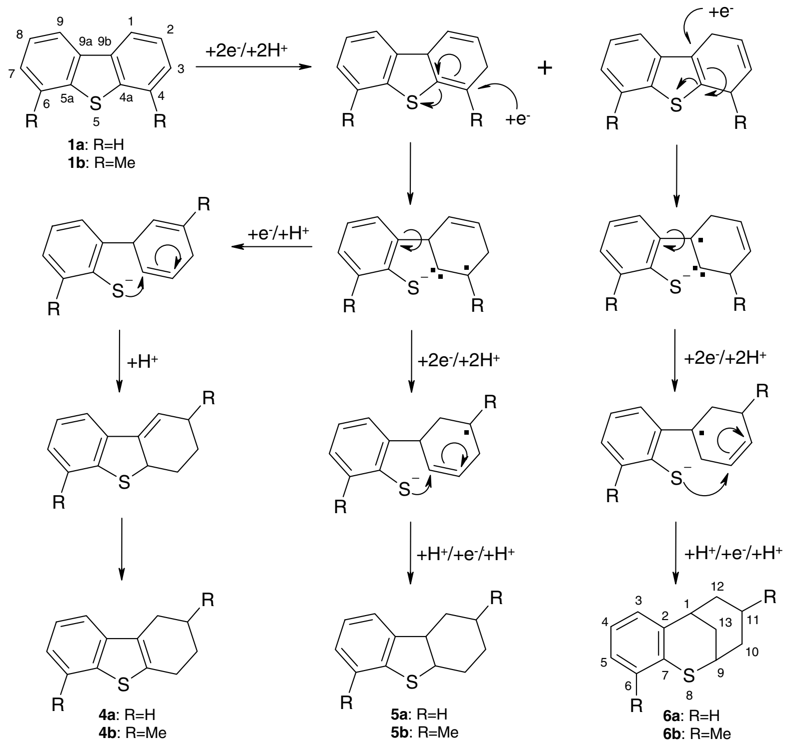

Figure 2. Mechanism of the molecular rearrangement during the Birch reduction of dibenzothiophenes.

tetrahydro-dimethyl-dibenzothiophene (cf. lit.[4] with Supplementary data). The products, isolated from the reaction mixture, were fully characterized by NMR experiments (^{1}H, ^{13}C, DEPT, COSY, HETCOR, long range HETCOR and NOE) and the X-ray crystal structure of the crystalline products **4b** and **5b** was measured (see Supplementary data). It was found that the methyl group at the hydrogenated ring of tetrahydro-dimethyl-dibenzothiophene **4b** and hexahydro-dimethyl-dibenzothiophene **5b** was shifted from position 4- to position 2- (Fig. 2). Moreover, the molecule with expanded S-containing heterocyclic ring **6b** has been identified as one of the hexahydro isomers. Similar results were obtained with **1a** (Table 1).

The major product of **1a** as well as of **1b** reduction was the hexahydro-isomer with the five-membered heterocyclic ring **5a** and **5b**. The hexahydro-isomers with the six-membered heterocyclic ring (thiane derivatives) **6a** and **6b** were produced to a lower extent. The 5:6 ratio was significantly higher in the case of methylated dibenzothiophene, probably because of steric requirements of the methyl group on the cyclohexane ring. Only small concentrations of tetrahydro-dibenzothiophenes **4a** and **4b** were observed. The rearrangement proceeded with almost total selectivity since we did not observe formation of partially hydrogenated 4,6-dimethyl-dibenzothiophenes. The amount of by-products did not exceed 10 wt %. The Birch reduction of **1a** was more difficult than that of **1b** and a higher amount of sodium together with longer reaction time had to be applied in order to reach the same conversion as with **1b**.

Table 1. Product distribution of the Birch reduction of **1a** and **1b**

	4 (%)	**5** (%)	**6** (%)	By-products[a] (%)	Time[b] (h)
1a	8	56	27	9	3.5
1b	5	71	18	6	1.5

[a] Amount of by-products.

[b] Time to reach 95% conversion.

The molecular rearrangement, which takes place during the reduction of **1a** and **1b**, can be explained by cleavage of the C-4a S-5 bond, rotation of the partially reduced benzene ring around the C-9a C-9b bond, and subsequent addition of the thiophenolate anion to the partially reduced benzene ring (Fig. 2).

The first step in the rearrangement is the partial reduction of one benzene ring of the dibenzothiophene structure. The 3,9b-dihydro isomer is formed preferentially, because of the prevailing effect of the electron-donating S-atom (electron-donating groups stabilize ortho and meta electron density in the radical anion and thus the main reduction product will have the least number of electron-donating and highest number of electron-withdrawing groups at the bridge heads).[8] In the next step, an electron is added to C-4 or C-9b, which results in the splitting of the C-4a S-5 bond into a carbene and a thiophenolate anion, the repulsive interaction of which induces rotation around the C-9a C-9b bond. The carbene is immediately saturated by the addition of two protons and two electrons. The existence of a carbene intermediate under Birch reduction conditions has already been proposed in the literature.[9] The thiophenolate nucleophile then adds to the double bond of the partially reduced ring[10] and the heterocyclic ring closes in position C-1 or C-2 depending on the dihydro-dibenzothiophene structure. A five- or six-membered heterocyclic ring is thus formed and its further reduction results in compound **5** or **6**, respectively.

Tetrahydro-4,6-dimethyl-dibenzothiophene **4** can be formed by reaction of the carbene radical formed from 3,9b-dihydro-4,6-dimethyl-dibenzothiophene. The carbene may react with the radical to a double bond, followed by immediate reduction by an electron and a proton. The final tetrahydro product **4** is formed by addition of the thiophenolate nucleophile to the double bond of the partially reduced ring, protonation and isomerization of the double bond under the basic conditions to the more stable C-4a C-9b position.

Our results demonstrate that dibenzothiophenes can be reduced to tetra- and hexahydro-derivatives by the Birch reduction. Although C–S bonds are still present in the final product molecules, the observed methyl group shift and extension of the S-heterocycle, which takes place during the Birch reduction of dibenzothiophenes, indicate that a molecular rearrangement has taken place, which can only occur by C–S bond breaking and reclosing.

Typical experimental procedure for the Birch reduction. The reaction was carried out in a two-neck 100 ml flask equipped with a thermometer and reflux cooler. The liquid ammonia (80 ml) was condensed in a pre-cooled flask kept at −78 °C in a suspension of dry ice and *i*-PrOH. 4,6-Dimethyl-dibenzothiophene **1b** (2 g, 9.4 mmol) was added at once, followed by ethanol (6.0 ml, 0.1 mol) and sodium (1 g, 43 mmol). The mixture was stirred vigourously with a magnetic stirrer and the stirring was continued until all the sodium had dissolved and a blue solution was obtained. After about 10 min the blue colour disappeared and a new portion of sodium (100 mg, 4.3 mmol) was added. The blue colour of the reaction mixture was kept by adding new portions of sodium for about 2 h. The total amount of sodium added was 1.7 g (73 mmol). When the blue colour of the reaction mixture had disappeared, solid ammonium chloride (1 g, 18.7 mmol) was added while stirring and the solution cleared up. The ammonia was allowed to evaporate and 50 ml water was cautiously added. The mixture was extracted three times with 50 ml CH_2Cl_2, the extracts were evaporated under vacuum, dried with sodium sulfate and analyzed by GC–MS. Yield 90%, typical product composition: **4b** (5%), **5b** (71%), **6b** (18%) and by-products (6%).

Supplementary data

Complete experimental and spectroscopic data for this Letter were submitted as Supplementary data. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.06.026.

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