Tetrahedron 69 (2013) 207-211

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Active-alkali metal promoted reductive desulfurization of dibenzothiophene and its hindered analogues

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ARTICLE INFO

Article history: Received 14 August 2012 Received in revised form 24 September 2012 Accepted 15 October 2012 Available online 22 October 2012

Keywords: Alkali metals Reduction Desulfurization Dibenzothiophenes Biphenyls

ABSTRACT

Dibenzothiophene and some related organosulfur compounds are efficiently reductively desulfurized under mild reaction conditions, with Na and/or Li metal in the presence of a catalytic amount of tet-raphenylethylene in THF at room temperature. This simple methodology was applied to the synthesis of several substituted biphenyls, thus realizing a connection between the directing properties of the sulfur atom of dibenzothiophene and the efficiency of 1,2-dianions of tetraphenylethane as homogenous electron transfer reagents.

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1. Introduction

Reductive desulfurization of organic compounds is of importance both in organic synthesis and in industry. In the former case, a synthetic transformation utilizes a sulfur-containing directing group that can then be reductively removed in a successive step of the whole synthetic procedure.¹ Particularly, the sulfur atom in benzo- and dibenzothiophene heterocycles exerts a strong directing effect towards metallations and electrophilic aromatic substitutions.² Moreover, benzo- and dibenzothiophenes are between the most abundant sulfur-containing impurities in crude oils, and their desulfurization is a mandatory issue in the production of non polluting fuels.³

At an industrial level, catalytic hydrogenation of fuels and coals (hydrodesulfurization, HDS) is realized under relatively harsh reaction conditions (high pressures and temperatures), in the presence of heterogeneous catalysts, such as γ -Al₂O₃-supported Co, Mo, W and Ni compounds.^{4,5}

The most refractory sulfur-containing compounds present in fuels are known to be the alkyl-dibenzothiophenes, especially those substituted at the 4 and 6 positions, such as 4,6-dimethyldibenzothiophene (4,6-DMDBT, **1e**), and their low reactivity is generally attributed to the steric hindrance.⁵

Accordingly, there is an increasing interest in new methodologies to convert efficiently C–S bonds into C–H bonds including, *inter alia*, homogeneous catalytic hydrogenation,⁶ oxidative processes,⁷ Grignard-mediated catalytic desulfurizations,⁸ reductive desulfurizations with Ni-containing reagents.^{1a,9}

Despite their ready availability and high reducing power, relatively few reports concern the exhaustive reductive desulfurization of dibenzothiophene with alkali metals. Indeed, most of its reductions with alkali metals were projected to afford 2mercaptobiphenyl, in the form of the corresponding intermediate diorganometal, as the main reaction product.^{10,11} Indeed, with a noticeable exception involving the employment of alkali metals absorbed into silica gel,¹² low yields of biphenyl were obtained unless high temperatures were used.^{13–16}

Following our interest in the development of efficient alkali metal-mediated synthetic procedures¹⁷ and alternative protocols for the chemical transformation of widespread environmental contaminants,¹⁸ we wish to report here on the effectiveness of sodium and lithium metals, in the presence of catalytic amounts of tetraphenylethylene (TPE), in promoting the reductive desulfurization of dibenzothiophene, as well as of the corresponding sulfone and sulfoxide. This methodology was additionally applied to the synthesis of several substituted biphenyls, realizing a connection between the directing properties of the sulfur atom of dibenzothiophene and the efficiency of TPE to behave as a homogeneous electron shuttle, thus allowing the employment of alkali metals in highly efficient single electron transfer (SET) reductions.¹⁹





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2. Results and discussion

2.1. Starting materials

Chart 1 shows the various dibenzothiophenes examined in this work, together with the corresponding desulfurization products.

2.2. Reductive desulfurization reactions

Na and/or Li metal were activated by stirring a THF suspension of the freshly cut metal with TPE under a N_2 atmosphere for 1 h at rt. The reductions were run by the dropwise addition of a solution of the appropriate substrate to the resulting deep red mixture over



Chart 1. Formulae and acronyms of the various benzothiophenes investigated and the corresponding desulfurization products.

Dibenzothiophene (DBT, **1a**) and dibenzothiophene sulfone (DBTO₂, **1c**) are commercially available, whilst dibenzothiophene sulfoxide (DBTO, **1b**), was synthesized according to a literature procedure.²⁰

Dibenzothiophenes **1d**,^{2a} **1e**,^{2a} **1f**²¹ and **1g**^{2b} were synthesized according to literature procedures as depicted in Scheme 1, taking advantage of the directing properties of the sulfur atom of dibenzothiophene to direct metallation (for **1d** and **1e**) and electrophilic aromatic substitution (for **1f** and **1g**) reactions.

30 min. Reaction mixtures were stirred at the same temperature for the appropriate time (see Table 1), and quenched with H₂O. Workup with ethyl acetate or diethyl ether led to a mass recovery typically \geq 90%, and the crude mixtures were analyzed by ¹H and ¹³C NMR, IR spectroscopy and GC/MS analysis.

It is worth noting that we found no evidence for the formation of significant amounts of the corresponding 2-mercaptobiphenyls. Reaction conditions and yields are reported in Table 1.



Scheme 1. Synthesis of dibenzothiophenes 1d–g, according to literature procedures: Ref. 2b, EAS: Br₂, CHCl₃, 0 °C to rt; Ref. 2b, cross coupling: PhB(OH)₂, Pd(PPh₃)₄, K₂CO₃, DME/ H₂O, 85 °C; Ref. 2a, R¹=H, R²=CH₃: *n*-BuLi, hexane/THF, -78 °C, then CH₃I; Ref. 2a, R¹=R²=CH₃: *n*-BuLi, hexane, TMEDA, -78 °C, then CH₃I; Ref. 21: *n*-BuLi, hexane/Et₂O, 0 °C, then CH₃I. EAS=Electrophilic aromatic substitution.

 Table 1

 Desulfurization of compounds 1 with alkali metals and catalytic amounts of TPE^a

Entry	Substrate	Reductant	Cat (% mol)	Metal/ 1 M ratio	Product	Yield ^b
1	1a	Na/TPE	20	10	2a	>90
2	1a	Na/TPE	10	10	2a	>90
3	1b	Li/TPE	10	8	2a	90
4	1c	Na/TPE	20	10	2a	72 ^c
5	1c	Na/TPE	20	13	2a	>90 ^d
6	1d	Na/TPE	20	10	2b	60 ^e
7	1d	Na/TPE	20	15	2b	>90
8	1e	Na/TPE	20	15	2c	<5
9	1e	Na/Li/TPE	20	$20^{\rm f}$	2c	>90
10	1e	Na/Li/TPE	20	12 ^g	2c	>90
11	1f	Na/TPE	20	10	2c	>90
12	1g	Li/TPE	15	8	2d	90

 a All reactions were run in dry THF, under $N_{2}, \, \text{for 14} \ h \ \text{at rt, unless otherwise}$ indicated.

^b As determined by ¹H NMR analyses of the crude reaction mixtures.

^c 28% of **1a** was also recovered.

^d Reaction run for 26 h at rt.

e 40% of 1a was also recovered.

^f Reaction run with 10 equiv of Na and 10 equiv of Li.

^g Reaction run with 5 equiv of Na and 7 equiv of Li.

We first investigated in some details the reductive desulfurization of dibenzothiophene (**1a**, DBT). After several attempts, we found that the reaction of **1a** with an excess of Na metal and a catalytic amount (20% mol) of TPE resulted, after 14 h at rt, in complete conversion of the starting material, with almost quantitative formation of biphenyl **2a**. A minor amount of 1,1,2,2tetraphenylethane, i.e., the reduction product of TPE, was also recovered. Interestingly, a comparable result was obtained in the presence of a reduced amount (10% mol) of TPE (Table 1, entries 1 and 2).

A similar reaction run in the absence of TPE led to complete consumption of the starting material, but afforded a somewhat more complex reaction mixture containing, besides the desired biphenyl, **2a**, minor amounts of products of reduction of the aromatic ring(s), most probably formed by further reaction of the main reaction product with the excess of the metal (not reported in Table 1). Additionally, it is worth noting that previously reported Na mediated exhaustive conversions of **1a** into **2a** were carried out in the presence of a large excess of Na metal in tetradecane at 150 °C during 24 h,¹⁴ or employing an excess of an almost 1:1 mixture of Na and Li as reducing agent in refluxing dioxane.¹³

From a mechanistic point of view, these results indicate that TPE acts as an electron shuttle through the formation of a *vic*-diorganometallic derivative,¹⁹ able to promote an effective electron transfer from the metal to the substrate under homogeneous and mild conditions, as schematically outlined in Scheme 2 where, for simplicity, only dianionic intermediates are reported. Indeed, the exhaustive desulfurization most probably proceeds via the intermediate formation of several different intermediates, including radical anions, monoanions and neutral species, the latest species probably forming via hydrogen atom abstraction or protonation reactions.^{22,23}

The above reported procedure was further extended to the reductive cleavage of the oxidized dibenzothiophenes **1b** and **1c**. In contrast with what was observed with **1a**, we were unable to get clean desulfurization of dibenzothiophene-5-oxide (**1b**, DBTO) by reacting it with Na and TPE under different reaction conditions (experiments not reported in Table 1). Better results were obtained employing a Li/TPE reducing system, leading to complete conversion of the starting material into biphenyl **2a** (Table 1, entry 3). It is however worth noting that the Na/TPE reducing system proved effective in the desulfurization of dibenzothiophene sulfone (**1c**, DBTO₂), although complete conversion of the starting material required a quite long reaction time and the presence of an excess of the metal (Table 1, entries 4 and 5).



Scheme 2. A simplified mechanism for the TPE-catalyzed reductive desulfurization of DBT, **1a**; M=Li or Na.

We next investigated the reductive cleavage of several substituted dibenzothiophenes to check the feasibility to apply our procedure to the regioselective synthesis of substituted biphenyls.

The reaction of 4-methyldibenzothiophene (**1d**, 4-MeDBT) with metallic Na in a 1:10 M ratio and in the presence of 20% mol of TPE, afforded the desired 3-methylbiphenyl, **2b**, in 60% yield, along with some unreacted starting material (Table 1, entry 6). Complete conversion of 4-MeDBT, **1d**, into biphenyl **2b** was realized by simply increasing the relative amount of metal (Table 1, entry 7).

More complex results were obtained in the reductive desulfurization of 4,6-dimethyldibenzothiophene (**1e**, 4,6-Me₂DBT), a substrate, which is known for its particularly low reactivity under HDS reaction conditions;⁵ in agreement with these antecedents, 4,6-Me₂DBT, **1e**, proved completely unreactive under the reaction conditions employed to desulfurize 4-MeDBT, **1d** (Table 1, entry 8). However, taking advantage of the observation of Farmer et al. on the synergistic effect of Na used in conjunction with Li in the reductive desulfurization of dibenzothiophenes **1a**–**c**,¹³ we successfully achieved an almost quantitative conversion of 4,6-Me₂DBT, **1e**, into the corresponding biphenyl derivative **2c**, by reacting the starting material with an excess of a Na/Li/TPE reducing system (Table 1, entries 9 and 10).

As a comparison, it is worth noting that the isomeric 2,8dimethyldibenzothiophene (**1f**, 2,8-Me₂DBT) was readily desulfurized with the Na/TPE reducing system (Table 1, entry 11), an observation further highlighting the correlation between low reactivity and steric hindrance generated by the alkyl groups near the sulfur atom.⁵

On the other side, the presence of phenyl substituents greatly enhanced the reactivity of 2,8-diphenyldibenzothiophene (**1g**, 2,8-Ph₂DBT) towards our reductive desulfurization procedure. Indeed, reduction of **1g** with the Na/TPE reducing system under different conditions led to complete conversion of the starting material as well as to the formation, besides the expected *m*-quaterphenyl, **2d**, of relevant amounts of *m*-terphenyl as well as of products of reduction of the aromatic ring(s), as identified by GC/MS analyses of the crude mixtures (not reported in Table 1). Better results were obtained by performing the reduction with an excess of Li metal and a catalytic amount of TPE (Table 1, entry 12).

Finally, we investigated the reductive desulfurization of benzothiophene (**1h**, BT) under the above reported reaction conditions. Indeed BT is a known contaminant of many fuels and several papers report its desulfurization to afford styrene¹⁴ or ethylbenzene,^{1a} depending upon the reaction conditions.

Although the Na/TPE reducing system proved unreactive, we were able to achieve complete desulfurization of **1h** by employing

a more effective Na/Li/TPE reducing system (6/10/0.2 M ratio) with an overall metal/**1h**=16:1 M ratio (Scheme 3).



Scheme 3. Reductive desulphurization of benzothiophene, 1h.

Under these conditions, we observed formation of 1,4diphenylbutane **2e** as the main reaction product, as well as formation of minor amounts of 1,1,2,2-tetraphenylethane (see above) and diphenylmethane. From a mechanistic point of view, 1,4diphenylbutane should derive by the reductive dimerization of styrene, formed after the sulfur extrusion, and favoured by the excess of the alkali metal present in the reaction mixture. Moreover, the formation of diphenylmethane, also occasionally detected in very low amounts in some of the previously described reaction mixtures, can be rationalized taking into account the already described reaction of tetraphenylethane with an alkali metal.²⁴

3. Conclusions

The results reported above represent a significant improvement with respect to previously reported reductions of dibenzothiophenes mediated by bulk alkali metals. Indeed, the employment of TPE as an electron shuttle,²⁵ i.e., the set up of homogeneous reaction conditions, provides the means to realize the exhaustive desulfurization reaction under particularly mild reaction conditions. The effectiveness of our protocol is highlighted by the results obtained in the reductive cleavage of substituted dibenzothiophenes, thus allowing their employment as readily available starting materials in the regioselective synthesis of substituted biphenyls.

Finally, and in agreement with the findings obtained by Farmer et al.¹³ under heterogeneous reaction conditions, it is worth noting that Na, used in conjunction with Li, led to the generation of a particularly reactive reducing system even under homogeneous conditions, as evidenced by the results obtained in the desulfurization of 4,6-Me₂DBT **1e** a substrate usually considered highly unreactive under HDS reaction conditions, as well as of BT **1h**.

4. Experimental

4.1. General

Starting materials were of the highest commercial quality and were purified by distillation or recrystallization immediately prior to use. Na metal (chunks) was 99% purity. Lithium metal (dispersion (30% w/w)) in mineral oil, was washed three times with dry THF before use. THF was distilled from Na/K alloy under N2 immediately prior to use. GC/MS analyses were carried out using a Hewlett Packard 5890 GC-MS system operating in the EI mode at 70 eV, using HP-5 capillary column (30 m×0.25 mm, film thickness $0.25 \,\mu\text{m}$) working at 80 °C (3 min) to 220 °C (1 min) at 15 °C/min and from 220 °C to 300 °C (1 min) at 25 °C/min; injector and detector temperatures 250 °C. He was used as the carrier gas; flow rate 1 mL/ min; split ratio=1:10. The identification of the different reaction products was performed by comparison of their retention time and mass fragmentation pattern with those of pure authentic samples and/or by consulting of NIST (National institute of Standards and Technology) library. ¹H NMR spectra were recorded at 300 MHz and ¹³C NMR spectra were recorded at 75 MHz in CDCl₃ on a Varian VXR 300 spectrometer using TMS as a reference. IR spectra were recorded on a FTIR Jacso 680 P. TLC analyses were performed on Macherey–Nagel silica gel pre-coated plastic sheets (0.20 mm).

4.2. Starting materials

Dibenzothiophene, **1a**, dibenzothiophene sulfone, **1c**, and benzothiophene, **1h**, are commercially available and were used without further purification; dibenzothiophene-5-oxide, **1b**,²⁰ 4methyldibenzothiophene, **1d**,^{2a} 4,6-dimethyldibenzothiophene, **1e**,^{2a} 2,8-dimethyldibenzothiophene, **1f**,²¹ and 2,8-diphenyldibenzothiophene, **1g**,^{2b} were synthesized according to literature procedures.

4.3. Reductive desulfurization procedure

Deep red suspensions of Na, Li or Na and Li metals in the presence of a catalytic amount of TPE (Na/TPE, Li/TPE or Na/Li/TPE; for the relative molar ratios, see Table 1) were prepared by vigorously stirring the freshly cut metal in dry THF (10 mL) during 1 h at rt. To this mixture, a solution of the appropriate dibenzothiophene, **1**, (2 mmol) dissolved in dry THF (5 mL) was added dropwise within 30 min. The reaction mixture was vigorously stirred at rt during 14 h, after which time it was quenched by slow dropwise addition of H₂O (15 mL). The organic solvent was evaporated in vacuo and the resulting mixture was extracted with Et₂O or AcOEt (3×10 mL) and the organic phases were collected, washed with H₂O (10 mL), brine (10 mL), and dried (Na₂SO₄). After evaporation of the solvent, the resulting mixtures were analyzed by GC/MS, and the reaction products **2a**,²⁶ **2b**,²⁶ **2c**,²⁷ **2d**²⁸ and **2e**²⁹ were characterized by ¹H, ¹³C NMR and IR spectroscopies, and by comparison with literature data.

Acknowledgements

Financial support from the Università di Sassari (Fondo di Ateneo per la Ricerca) is gratefully acknowledged. M.P. acknowledge financial support from the Regione Autonoma della Sardegna (Italy), trough the project 'Promozione della Ricerca Scientifica e dell'Innovazione Tecnologica in Sardegna'.

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