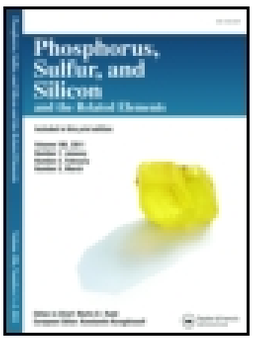


Taylor & Francis
Taylor & Francis Group

Phosphorus, Sulfur, and Silicon and the Related Elements

ISSN: 1042-6507 (Print) 1563-5325 (Online) Journal homepage: http://www.tandfonline.com/loi/gpss20

[4+2]-Cycloaddition Of Sterically Hindered Thiophene S-Oxides To Alkenes And So Extrusion Reactions Of The Cycloadducts

Thies Thiemann, Jesus Iniesta & David J. Walton

To cite this article: Thies Thiemann, Jesus Iniesta & David J. Walton (2016): [4+2]-Cycloaddition Of Sterically Hindered Thiophene S-Oxides To Alkenes And So Extrusion Reactions Of The Cycloadducts, Phosphorus, Sulfur, and Silicon and the Related Elements, DOI: 10.1080/10426507.2015.1100191

To link to this article: http://dx.doi.org/10.1080/10426507.2015.1100191

Accepted author version posted online: 20 Jan 2016.

[4+2]-CYCLOADDITION OF STERICALLY HINDERED THIOPHENE *S*-OXIDES TO ALKENES AND SO EXTRUSION REACTIONS OF THE CYCLOADDUCTS

Thies Thiemann[a,*,#], Jesus Iniesta[b,c], David J. Walton[d]

[a]Institute of Materials Chemistry, Kyushu University, Kasuga-koh-en, Kasuga-shi 816-8580, Japan

[b]Institute of Electrochemistry, University of Alicante, 03690, San Vicente del Raspeig, Alicante, Spain

[c]Physical Chemistry Department, University of Alicante, 03690, San Vicente del Raspeig, Alicante, Spain

[d]School of Health and Life Sciences, Coventry University, Priory Street, Coventry, CV1 5FB, UK

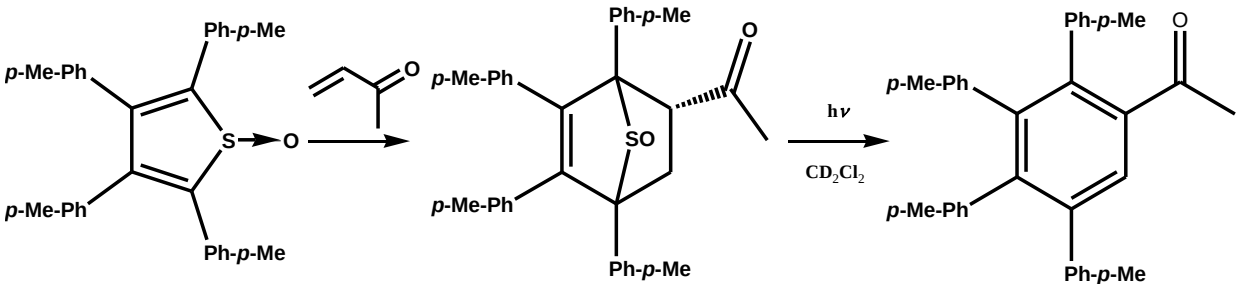
[#]current address: Department of Chemistry, United Arab Emirates University, PO Box 15551, Al Ain, Abu Dhabi, United Arab Emirates; thies@uaeu.ac.ae; thiesthiemann@yahoo.de

[*]Corresponding Author Email: thiesthiemann@yahoo.de

Abstract

Cycloaddition reactions of 2,5-di-*tert*-butylthiophene *S*-oxide and 2,3,4,5-tetrakis(*p*-tolyl)thiophene *S*-oxide with alkenes are described. The reactivity of 2,5-di-*tert*-butylthiophene *S*-oxide as diene in Diels Alder reactions is compared with 2,5-di-*tert*-butylthiophene *S*,*S*-dioxide. The thermal and photochemical SO extrusion reactions of the cycloadducts under formation of

highly substituted aromatic compounds are exemplified.



Keywords

thiophene *S*,*S*-dioxide, thiophene *S*-oxide, cycloaddition, SO extrusion

INTRODUCTION

Easy synthetic access to arenes with neighboring sterically exacting substituents is still of great interest.[1] One preparative route to arenes is via [4+2]-cycloaddition and subsequent oxidative aromatization.[2] For a more facile approach to substituted arenes via [4+2]-cycloaddition, it is advisable to introduce at least two double bonds into the constructed ring system during the cycloaddition. This can be achieved by the right selection of the dienophile in form of an acetylene,[2,3] an allene[4] or an aryne[5] in case of an areno-annelation reaction. Alternatively, the additional unsaturation can be introduced by choosing a cyclic dienophile, which would lead to a bicyclic system with a bridged 6-membered carbocycle, where the bridge would be extruded or opened in a subsequent reaction step, which simultaneously introduces the additional unsaturation into the carbocycle. Use of a cyclic diene has the advantage of a locked-in *cisoid* diene system, ideal for the cycloaddition. Typical examples of such cyclic dienes that lead to bicyclic cycloadducts with an extrusable bridge are pyrones,[6] cyclopentadienones,[7] furans[8] and thiophenes[9] and their derivatives. While furans, especially those with electron-donating substituents, are passable dienes for Diels-Alder type cycloadditions, thiophenes are not, where in fact only a handful of specifically substituted thiophenes[9] have been used successfully. Thiophenes, however, can be oxidized to thiophene oxides, and these are classical cyclic dienes. Thiophene *S,S*-dioxides[10] have been used as diene components in cycloaddition reactions for some time, while the preparation of thiophene *S*-oxides and their use as substrates in cycloaddition reactions have been studied more recently.[11,12] For the most part, thiophene *S,S*-dioxides are thermally and photochemically[13] much more stable than thiophene *S*-oxides. On the other hand, as dienes in Diels Alder type reactions, thiophene *S*-oxides have been found

generally more reactive than the corresponding thiophene *S,S*-dioxides. In the following, the authors show the reactivity of a tetraarylthiophene *S*-oxide and of 2,5-*tert*-butylthiophene *S*-oxide as diene components in Diels Alder reactions with alkenes. As contrast, comparative cycloadditions with tetraphenylcyclopentadienone (tetracyclone) and with 2,5-di-*tert*-butylthiophene *S,S*-dioxide are shown. Also, photochemically and thermally driven transformations of the 7-thia-bicyclo[2.2.1]hept-5-ene *S*-oxides as the primary cycloadducts to the corresponding substituted arenes and cyclohexadienes are exemplified. Overall, the cycloaddition of alkenes to thiophene *S*-oxides with bulky substituents at positions C2 and C5 with a subsequent SO-extrusion reaction is to be seen as an additional route to oligo-substituted arenes with bulky neighboring groups.

RESULTS AND DISCUSSION

First was tested the reactivity of alkenes towards tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**), which was synthesized via reaction of thionyl chloride with tetrakis(*p*-tolyl)zirconacyclopentadiene, produced from bis(cyclopentadienyl)zirconium(IV) dichloride and bis(*p*-tolyl)acetylene, following an analogous procedure.[4,9,14] It must be noted that the cycloaddition of tetraarylthiophene *S*-oxides with alkynes has been studied previously,[4,15] but not with alkenes. Here, tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**) was reacted with a number of dienophiles in $CHCl_3$ (Scheme 1). To many of the dienophiles with two or one electron withdrawing group, tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**) already cycloadds at 50 ^{o}C in acceptable yields, although tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**) does not react well with (*E*)-1,2-dibenzoylethene (**2f**) at 50°C, so that the reaction temperature in this case had to be raised to

70 ^{o}C. Even then, the yield of the cycloadduct **3g** remained poor. **1a** itself is thermally relatively stable, although thiophene *S*-oxides are generally known to be thermally relatively labile. When heated to 70°C in chloroform for 11 h, **1a** was recovered unchanged. With maleic anhydride (**2b**) and *N*-phenylmaleimide (**2a**) at 50 ^{o}C, **1a** gave the corresponding cycloadducts **3a** and **3b** in excellent yield. **3b** was hydrolyzed to the diacid **3c** (BzlNMe$_3$OH, H$_2$O),[16] which was subsequently converted with an ethereal solution of diazomethane to diester **3d**, which was also produced directly in a cycloaddition of **1a** with dimethyl maleate (**2c**) (Scheme 1).

In all cycloaddition reactions above, the products were formed as one stereoisomer, only. This stereoselectivity has been remarked upon previously in analogous reactions, where the stereochemistry of the cycloadducts could be determined by single crystal X-ray structure analysis.[17] The reactions show *endo*-selectivity, indicating kinetic control of the product, with the lone electron pair on sulfur of the sulfoxy-bridge lying on the side of the newly formed double bond of the product. The stereoselectivity at sulfur is governed by the Cieplak effect.[18] Experimental observations in Diels-Alder reactions of dienophiles with 5-substituted cyclopentadienes have shown that the dienophiles will approach *anti* to the antiperiplanar σ-bond that is the better donor at the 5-position of the cyclopentadiene. The lone-pair electron orbital on sulfur stabilizes the vacant σ^*-orbital of the developing incipient σ-bonds better than the lone-pair electron orbitals of the oxygen of the sulfoxy moiety.

When comparing tetraarylthiophene *S*-oxides with tetraarylcyclopentadienones (tetracyclones) as dienes in cycloaddition reactions, it must be noted that tetracyclones for the most part necessitate higher reaction temperatures than their tetraarylthiophene *S*-oxide counterparts. When stirring a

mixture of tetraphenylthiophene *S*-oxide (**1b**), tetraphenylcyclopentadienone (**4a**) (or tetrakis-p-tolylthiophene-*S*-oxide (**1a**) and 3,4-bis(*p*-tolyl)-2,5-diphenylcyclopentadienone (**4b**) and *N*-phenylmaleimide (**2a**) in deuterated chloroform, only the cycloadduct **3i** (and **3a**, respectively) of the tetraarylthiophene *S*-oxide with *N*-phenylmaleimide was obtained (Scheme 2).

Tetracyclones are usually thermally much more stable than tetraarylthiophene-*S*-oxides. Nevertheless, tetracyclones are not stable at elevated temperatures under all conditions. Thus, the authors have shown that tetracyclones convert to α-pyrones when heated in aerated diphenyl ether,[19] a solvent that is frequently used as a solvent for Diels-Alder type cycloaddition reactions at higher temperatures. Also, tetracyclones have been shown to be reductants at elevated temperatures, such as in the case of the cycloaddition of tetraphenylcyclopentadienone to benzothiophene-*S*,*S*-dioxide, where excess tetraphenylcyclopentadienone reduces the sulfone moiety in the cycloadduct, in juxtaposition to the same reaction with tetraphenylthiophene *S*-oxide, where the sulfone moiety in the cycloadduct remains intact.[20] Nevertheless, cycloaddition reactions of tetracyclones under microwave irradiation[21] and under solvent free conditions[7c] have recently provided additional possibilities of preparing oligoarylbenzenes under milder conditions. Therefore, tetraarylthiophene *S*-oxides and tetracyclones can be seen as complimentary diene substrates for the preparation of oligoarylbenzenes and of generally oligosubstituted benzenes, complimentary also, as the strategy of preparation differs and, depending on the substitution, one or the other preparation may be preferred due to ease of access. Tetraarylcyclopentadienones can be prepared by Weiss reaction, which for instance would not allow an easy preparation of tetracyclones with four different aryl groups. Also, alkyl-substituted cyclopentadienones are not easily accessible[22] and often react as dienophile rather than as diene.[23] The preparation of

thiophene *S*-oxides by oxidation of the corresponding thiophenes limits the substitution pattern of the thiophene *S*-oxides to the substitution pattern of the corresponding thiophenes, where it must be ascertained that the substituents still allow for a smooth oxidation of the thiophene to the thiophene S-oxide to occur.

Next, 2,5-bis(*tert*-butyl)thiophene *S*-oxide (**1c**),[24] prepared by oxidation of 2,5-bis(*tert*-butyl)thiophene with *m*-CPBA in the presence of $BF_3{\cdot}Et_2O$,[4] was found to cycloadd to dienophiles with one electron-withdrawing substituent at 60 ^oC. Cycloadducts **5** were obtained with 60 – 65% yield, again as single isomers (Scheme 3). The *tert*-butyl ester **5c** could be hydrolyzed to carboxylic acid **5d** without affecting the SO bridge. The reaction of 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**) with *p*-naphthoquinone (**2i**) gave cycloadduct **5b** in 72% yield (Scheme 3).

The reactivity of 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**) in the cycloaddition reactions above was compared to that of 2,5-di-*tert*-butylthiophene *S*,*S*-dioxide (**6**), prepared by oxidation of 2,5-di-*tert*-butylthiophene with *m*-CPBA in the absence of $BF_3{\cdot}Et_2O$. No reaction took place between 2,5-di-*tert*-butylthiophene *S*,*S*-dioxide (**6**) and dienophiles **2** at 60 ^oC. With mono- and disubstituted acetylene dienophiles such as with benzyl propiolate, ethyl propiolate and diethyl acetylenedicarboxylate, **6** did not undergo a cycloaddition at even 100 ^oC. *p*-Naphthoquinone (**2i**) and *N*-(*p*-chlorophenyl)maleimide (**2h**) cycloadded to **6**, but at reaction temperatures of 195 ^oC and at 140 ^oC, respectively. For these reactions diphenyl ether was used as solvent. At the reaction temperatures, the SO_2 bridge of the primary cycloadducts extruded cleanly and in the case of the reaction with *p*-naphthoquinone (**2i**), 1,4-di-*tert*-butylanthraquinone (**7b**), and in the

case of the reaction with *N*-(*p*-chlorophenyl)maleimide (**2h**), a mixture of the corresponding di-*tert*-butylphthalimide (**7a**) and di-*tert*-butyldihydrophthalimide (**8a**) was obtained (Scheme 4).

Oxidative extrusion of the sulfoxy bridge in cycloadducts similar to **3** and **5** have been reported to have been accomplished thermally[25] or at room temperature when the reactions were run electrochemically,[26] photochemically[27] or using $KMnO_4$ as oxidant under phase transfer conditions[25]. Nevertheless, the electrochemical oxidative SO extrusion often leads to blockage of the electrodes after some time due to fouling. The oxidative extrusion with $KMnO_4$ under phase transfer conditions can lead to variable results. Thus far, the photochemical SO extrusion has been studied for two cycloadducts, only.[27]

Thermal SO-extrusion reactions with 7-thiabicyclo[2.2.1]hept-5-ene *S*-oxides occur only at relatively high temperatures. Thus, **3a** does not extrude SO even when kept at 130 °C (12 h) in diphenylether. However, when **3a** is heated in diphenylether at 160 °C for 14h, the SO-extruded and aromatized product **9a** can be isolated with 75% yield (Scheme 5). At that temperature, the extrusion reaction is still slow, so that after 4h an appreciable amount of starting material can be detected. Higher reaction temperatures (180 ^{o}C) and shortened reaction times (9h) give **9a** with slightly lower yield.

1,4-Di-*tert*-butylthiabicyclo[2.2.1]hept-5-ene *S*-oxides **5** were found to extrude SO more readily (Scheme 6). When *N*-(*p*-chlorophenyl)-1,4-di-*tert*-butyl-7-thiabicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide *S*-oxide (**5a**) was heated in diphenyl ether at 140 ^{o}C for 1 h, *N*-(*p*-chlorophenyl)-3,6-di-*tert*-butylphthalimide (**7a**) was found with 74% yield, the remainder being starting material. Raising the temperature to 170 ^{o}C did not improve the yield of **7a**, however, and

produced a small amount (5%) of *N*-(*p*-chlorophenyl)-3,6-di-*tert*-butyl-1,2-dihydrophthalimide (**8a**). Heating acetyl-1,4-di-*tert*-butyl-7-thiabicyclo[2.2.1]hept-5-ene *S*-oxide (**5e**) in diphenyl ether at 140 ^{o}C for 30 min gives 30% 2,5-di-*tert*-butylacetophenone (**7c**) with 60% of the starting material remaining (Scheme 6). After 1 h at 140 ^{o}C, 2,5-di-t*ert*-butylacetophenone (**7c**), which had been prepared previously by more tedious routes, was produced in 65% yield.[28] Again, the tetrakis-(*p*-tolyl) substituted analog **3e** required higher reaction temperatures and longer reaction times to give **9b** with 70% yield (Scheme 5).

Some years ago, the authors studied the SO-photo-extrusion at room temperature of two 7-thiabicyclo[2.2.1]hept-5-ene *S*-oxides, namely the products stemming formally from the cycloaddition of 2,5-dimethylthiophene *S*-oxide and of 2,3,4,5-tetramethylthiophene *S*-oxide with *N*-phenylmaleimide.[27] In both cases the SO bridge could be extruded photochemically to give methyl substituted *N*-phenylphthalimides as the aromatized products.[27] In the following, it was investigated whether this SO-photo-extrusion, which finds its counter-part in the photo-extusion of the CO bridge in cycloadducts of tetraarylcyclopentadienones and alkenes,[29] can be carried out with the cycloadducts prepared above. The cycloadducts were photo-irradiated in CD_2Cl_2 at $\lambda > 222$ nm without use of sensitizer. The reactions were screened for the aromatized compounds as the desired products. However no identification of potential minor side-products was carried out. The photoreactions were monitored by ^{1}H NMR spectroscopy. Photo-irradiation of tetraphenyl-7-thiabicyclo[2.2.1]hept-5-ene *S*-oxide **3i** gave a mixture of dihydrophthalimide **8b** and phthalimide **9c** (Scheme 7). It is believed that the dihydrophthalimide is an intermediate in the photo-extrusion/oxidation reaction and that the extruded sulfur monoxide (SO) oxidizes **8b** to **9c**. SO is a triplet in its ground state ($X^3\Sigma^-$) and has two excited states ($a^1\Delta$) and ($b^1\Sigma^-$), 17.6

kcal/mol and 30.0 kcal/mol above the ground state, respectively.[30] The mercury lamp used in our experiment would have sufficient energy to elevate SO from ($X^3\Sigma^-$) to ($a^1\Delta$). Nevertheless, SO ($a^1\Delta$) deactivates quickly to SO ($X^3\Sigma^-$).[31] Also SO ($X^3\Sigma^-$) has a short lifetime in solution but has been trapped in cycloaddition reactions, previously.[32] In the present case, it is not clear whether SO ($a^1\Delta$) or SO ($X^3\Sigma^-$) is responsible for the aromatization step or whether another pathway operates. In the photoreaction of **3a**, **3a** was applied to a preparative TLC plate (20 × 20 cm, silica gel 60 F_{254} 2 mm, with concentration zone, from Merck KGaA). The plate was developed with ether/hexane 1:1, until a zone of starting material separated clearly from the line of application (from the concentration zone). Then, the zone was photo-irradiated directly with a UVP-Mineralight Lamp, model UVGL-15, at λ = 254 nm. The plate was irradiated for 3 × 20 min. Once the two were well separated, the zone containing the starting material was photo-irradiated again (3 × 20 min.), where the product zone was protected from the irradiation by a cover of aluminum foil. The process was repeated one more time to give a total irradiation time of 3 h. Overall, the photo-irradiation gave phthalimide **9a** with 55% yield. Scheme 7 shows further examples of SO-photo-extrusion with 7-thiabicyclo[2.2.1]hept-5-ene *S*-oxide substrates **3** leading to the aromatized products **9**.

CONCLUSIONS

Both 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**) and 2,3,4,5-tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**) undergo cycloaddition reactions with mono- and bis-acceptor substituted alkenes furnishing highly substituted 7-thiabicyclo[2.2.1]hept-5-ene *S*-oxides **3** and **5** with acceptable yields. The reactivity difference between 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**) and 2,5-di-*tert*-

butylthiophene *S*,*S*-dioxide (**6**) is pronounced, where 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**) cycloadds to many of the electron-poor alkenes at 60 ^{o}C, while 2,5-di-*tert*-butylthiophene *S*,*S*-dioxide (**6**) needs 140 ^{o}C or more. Tetraarylthiophene *S*-oxides such as **1a** and **1b** are building blocks for oligoarylbenzenes and can be used alternatively to tetraarylcyclopentadienones (tetracyclones). Nevertheless, the SO-extrusion of the 7-thiabicyclo[2.2.1]hept-5-ene *S*-oxides **3** and **5** remains problematic, with needed temperatures of 140 ^{o}C or above. Nevertheless, the thermal extrusion yields some interesting, highly substituted aromatic compounds such as **7c** or **9e**,[33] which were not easily accessible previously. Photochemical SO-extrusion has been carried out successfully with six cycloadducts (**3a**, **3d-f**, and **3i**), although reaction times remain long.

EXPERIMENTAL

General remarks

Melting points (mp., uncorrected) were determined on a Yanaco microscope hotstage. IR spectra (υ_{max}, KBr/cm^{-1}) were measured with a JASCO IR-700 instrument. ^{1}H NMR spectra (at 270 MHz and 395.7 MHz) and ^{13}C NMR spectra (at 67.8 MHz and 99.45 MHz) were recorded with a JEOL EX-270 and a JEOL Lambda 400 FT-NMR spectrometer, respectively. The chemical shifts are relative to TMS (solvent $CDCl_3$). MS were measured with a JMS-01-SG-2-spectrometer (EI, 70 eV). Column chromatography was carried out on Wakogel C-300. For the photo-irradiation in solution, a 1 kW Tokyo Rigaku high-pressure mercury lamp was used. The photochemistry on silica gel was carried out with a UVP-Mineralight Lamp, model UVGL-15, at λ = 254 nm. PLC plates (20 × 20 cm; silica gel 60 F_{254} 2 mm from Merck KGaA) were used.

2,5-Di-*tert*-butylthiophene *S*,*S*-dioxide (**6**)[34] and 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**)[4] were prepared analogous to known procedures.

Tetrakis(*p*-tolyl)thiophene *S*-oxide (1a).

In an inert atmosphere, *n*-BuLi (1.59 M, 21.5 mL, 3.32 mmol) was added to a slurry of zirconocene dichloride (5.0 g, 17.1 mmol) and bis(*p*-tolyl)acetylene (7.5 g, 34.2 mmol) in dry THF (150 mL) at −78 ^{o}C. Subsequently, the mixture was warmed to rt. and stirred for 3 h. Next, the solution was cooled to 0 ^{o}C and thionyl chloride (2.2 g, 18.8 mmol) in hexane (10 mL) was added within 30 min. The resulting mixture was stirred at rt for 3 h. After the reaction was complete, the mixture was poured into conc. aq. $NaHCO_3$ (200 mL). The product was extracted with CH_2Cl_2 (200 mL) and the organic phase was washed with water (200 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexane/ether 1:1) to give **1a** (4.72 g, 10.2 mmol, 60%) as a pale yellow solid; mp. 110 ^{o}C. IR: 3025, 2918, 1502, 1324, 1182, 1116, 1087, 1062, 1018, 851, 832, 819, 731, 539, 519. ^{1}H NMR (270 MHz): δ 2.26 (s, 6H, 2 CH_3), 2.30 (s, 6H, 2 CH_3), 6.80 (d, 4H, ^{3}J = 8.3 Hz), 6.94 (d, 4H, ^{3}J = 7.9 Hz), 7.07 (d, 4H, ^{3}J = 7.9 Hz), 7.25 (d, 4H, ^{3}J = 8.1 Hz). ^{13}C NMR (67.8 MHz): δ 21.2, 127.9, 128.9, 129.3, 129.6, 129.7, 130.6, 137.8, 138.4, 140.8, 145.3. MS (FAB, 3-nitrobenzyl alcohol): *m/z* [MH^+] 461 (70), [M^+–O] 444 (100), [M^+–S] 428 (20), [M^+–SO] 412 (30). Calcd. for $C_{32}H_{29}OS$: 461.1939. Found: 461.1940. HRMS Calcd. for $C_{32}H_{28}$: 412.2191. Found: 412.2194. HRMS Calcd. for $C_{32}H_{28}O$: 428.2140. Found: 428.1247. Anal. Calcd. for $C_{32}H_{28}OS{\cdot}0.25\ H_2O$ (465.13); C, 82.63; H, 6.12%. Found C, 82.92; H, 6.31%.

_N_-Phenyl-3,4,5,6-tetrakis(_p_-tolyl)-7-thia-bicyclo[2.2.1]hept-5-ene-2,3-carboxamide 7-oxide (3a).

A solution of tetrakis(*p*-tolyl)thiophene *S*-oxide (**1a**, 87 mg, 0.19 mmol) and *N*-phenylmaleimide (**2a**, 40 mg, 0.23 mmol) in $CHCl_3$ (1.5 mL) was heated for 14 h at 50 ^oC. The solution was concentrated *in vacuo*, and the residue was subjected to column chromatography on silica gel (hexane/ether 1:1) to give **3a** (107 mg, 89%) as a colorless solid, mp. 296 ^oC. IR: 3026, 2918, 1716 (C=O), 1503, 1377, 1188, 1102, 799, 753, 729. ^1H NMR (270 MHz): δ 2.14 (s, 6H, 2 CH_3), 2.30 (s, 6H, 2 CH_3), 4.95 (s, 2H), 6.62 (d, 4H, ^3J = 7.9 Hz), 6.71 (d, 4H, ^3J = 7.9 Hz), 7.00 (vs, 8H), 7.24 – 7.36 (m, 5H). ^{13}C NMR (67.8 MHz): δ 21.1 50.1, 80.5, 126.1, 126.4, 128.5, 128.9, 129.1, 129.2, 130.1, 130.5, 131.8, 134.2, 137.4, 138.0, 138.3, 174.3. MS (FAB, 3-nitrobenzyl alcohol): *m/z* [MH^+] 634 (35), [M^+–SO] 585 (100), 438 (36). MS (EI, 70 eV): *m/z* [M^+–SO] 585 (100), 444 (44), 438 (41). HRMS Found: 634.2418. Calcd. for $C_{42}H$ (MH^+, FAB). Anal. Calcd. for $C_{42}H_{35}O_3NS$ (657.82); C, 79.59; H, 5.57; N, 2.21. Found C, 79.31; H, 5.66; N, 2.17%.

_N_-(_p_-Chlorophenyl)-1,4-di-_tert_-butyl-7-thiabicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide _S_-oxide (5a).

A mixture of 2,5-di-*tert*-butylthiophene *S*-oxide (**1c**, 80 mg, 0.38 mmol) and *N*-(*p*-chlorophenyl)maleimide (**2h**, 79 mg, 0.38 mmol) in $CHCl_3$ (1.5 mL) was heated for 12 h at 60 ^oC. The solution was concentrated *in vacuo*, and the residue was subjected to column chromatography on silica gel (chloroform/hexane/ether 1:1:1) to give **5a** (142 mg, 89%) as a colorless solid, mp. 213^oC. IR: 1710 (C=O). ^1H NMR (270 MHz): δ 1.32 (s, 18H, 6 CH_3), 7.11 (d, 2H, ^3J = 8.0 Hz), 7.34 (d, 2H, ^3J = 8.0 Hz). ^{13}C NMR (67.8 MHz): δ 28.7 (6C, 6 CH_3), 33.5

(2C, C_{quat}, $\underline{C}(CH_3)_3$), 48.3 (2C, CH), 80.7 (2C, C_{quat}), 127.9 (2C, CH), 129.3 (2C, CH), 129.5 (C_{quat}), 130.3 (2C, CH), 134.7 (C_{quat}), 173.9 (2C, C_{quat}, CO). MS (FAB, 3-nitrobenzyl alcohol): *m/z* [[^{37}Cl]MH^+] 422 (7), [[^{35}Cl]MH^+] 420 (17), [[^{35}Cl]M^+–SO] 371 (13), 154 (100), 136 (82). HRMS Found: 420.1396. Calcd. for $C_{22}H_{27}O_3N^{35}ClS$: 420.1400 ([^{35}Cl]MH^+, FAB).

***N*-(*p*-Chlorophenyl)-3,6-di-*tert*-butylphthalimide (7a)**.

Method A: A solution of **6** (196 mg, 0.86 mmol) and *N*-chlorophenylmaleimide (**2h**, 284 mg, 1.37 mmol) in deaerated diphenyl ether (1 g, 930 μL) was heated at 140 ^oC for 17 h. Thereafter, the cooled solution was subjected to column chromatography on silica gel (hexane to elute the solvent, then hexane/$CHCl_3$/ether 2:1:1) to give **7a** (110 mg, 35%) as a colorless solid, mp. 214 ^oC. ^1H NMR (270 MHz): δ 1.54 (s, 18H, 2 Bu^t), 7.40 (d, 2H, ^3J = 8.9 Hz), 7.48 (d, 2H, ^3J = 8.9 Hz), 7.71 (s, 2H); ^{13}C NMR (67.8 MHz): δ 30.5 (6C, 6 CH_3), 36.0 (2C, C_{quat}, $\underline{C}(CH_3)_3$), 129.0 (2C, CH), 129.7 (2C, CH), 132.1 (C_{quat}), 133.5 (2C, CH), 142.5 (C_{quat}), 150.1 (2C, C_{quat}), 157.6 (2C, C_{quat}), 188.8 (2C, C_{quat}, CO). MS (EI, 70 eV): *m/z* [[^{37}Cl]M^+] 371 (37), [[^{35}Cl]M^+] 369 (100), [[^{35}Cl]M^+–CH_3] 354 (84). HMRS Found: 369.1496. Calcd. for $C_{22}H_{24}O_2N^{35}Cl$: 369.1496 and *N*-(*p*-chlorophenyl)-3,6-di-*tert*-butyl-1,2-dihydrophthalimide (**8a**) (16 mg, 5%) as a colorless solid, mp. 200 ^oC. ^1H NMR (270 MHz): δ 1.19 (s, 18H, 2 Bu^t), 3.91 (s, 2H), 6.06 (s, 2H), 7.28 (d, 2H, ^3J = 8.6 Hz), 7.41 (d, 2H, ^3J = 8.6 Hz); ^{13}C NMR (67.8 MHz): δ 29.9 (6C, 6CH_3), 36.0 (2C, C_{quat}, $\underline{C}(CH_3)_3$), 47.4 (2C, CH), 120.8 (2C, CH), 126.7 (2C, CH), 129.6 (2C, CH), 131.1 (C_{quat}), 134.4 (C_{quat}), 139.9 (C_{quat}), 178.0 (2C, C_{quat}, CO); MS (EI, 70 eV): *m/z* [[^{37}Cl]M^+] 373 (11), [[^{35}Cl]M^+] 371 (31), [[^{35}Cl]M^+–CH_3] 356 (19), 175 (100). HRMS Found: 371.1654. Calcd. for $C_{22}H_{26}O_2N^{35}Cl$: 371.1652.

Method B: A solution of **5a** (50 mg, 0.12 mmol) in diphenyl ether (2 mL) was heated at 170 ^{o}C for 1 h. Thereafter, the cooled solution was subjected to column chromatography on silica gel (hexane to elute the solvent, then hexane/$CHCl_3$/ether 2:1:1) to give **7a** (30.6 mg, 69%) and *N*-(*p*-chlorophenyl)-3,6-bis(*tert*-butyl)-1,2-dihydrophthalimide (**8a**) (2.4 mg, 5%).

N-Phenyl-3,4,5,6-tetrakis(*p*-tolyl)phthalimide (9a).

Method A: *N*-Phenyl-1,4,5,6-tetrakis(*p*-tolyl)-7-thiabicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide *S*-oxide (**3a**, 33 mg, 0.05 mmol) in diphenyl ether (450 mg, 420 μL) was heated to 180 ^{o}C for 9 h. Thereafter, the cooled solution was subjected to column chromatography on silica gel (initially hexane, to elute the solvent diphenyl ether, then hexane/ether 1:1) to give **9a** (20 mg, 65%) as a colorless solid; IR: 2920, 1721 (C=O), 1601, 1368, 1114, 805, 763, 722. ^{1}H NMR (270 MHz): δ 2.12 (s, 6H, 2 CH_3), 2.27 (s, 6H, 2 CH_3), 6.62 (d, 4H, ^{3}J = 7.9 Hz), 6.71 (d, 4H, ^{3}J = 7.9 Hz), 7.00 (vs, 8H), 7.24 – 7.36 (m, 5H). MS (FAB, 3-nitrobenzyl alcohol): *m/z* 584 (MH^+, 49). HRMS Found: 584.2591. Calcd. for $C_{42}H_{34}O_2N$: 584.2590 (MH^+).

Method B: **3a** (19.7 mg, 0.031 mmol) was dissolved in $CHCl_3$ (2 mL) and applied to a preparative TLC plate (20 × 20 cm, silica gel 60 F_{254} 2 mm, with concentration zone, from Merck KGaA). The plate was run with ether/hexane 1:1, until a zone of starting material separated clearly from the line of application (from the concentration zone). Then, the zone was photo-irradiated directly with a UVP-Mineralight Lamp, model UVGL-15, at λ = 254 nm. The plate was irradiated for 3 × 20 min. Then, the plate was developed once more with hexane/ether 1:1, to separate the product from the starting material. Once the two were well separated, the zone containing the starting material was photo-irradiated again (3 × 20 min.), where the product zone

was protected from the irradiation by a cover of aluminum foil. The process was repeated once more to give a total irradiation time of 3 h. Thereafter, the remaining starting material was separated from the zones of product formed in the three photo-irradiation processes. The product containing silica gel was taken off the plate and transferred to a short column fitted with a cotton pad. The substance was eluted off the column with ether. The column was washed once with $CHCl_3$. The eluted fractions were concentrated *in vacuo* to give **9a** (10 mg, 55%).

2,3,4,5-Tetrakis(*p*-tolyl)acetophenone (9b)

Method A: A solution of **3e** (50 mg, $9.4 \cdot 10^{-5}$ mol) in diphenyl ether (500 mg, 460 μL) was heated to 170 °C for 9 h. The cooled solution was subjected directly to column chromatography on silica gel (initially hexane to elute the solvent, thereafter hexane/ether 1:1) to give **9b** (31.5 mg, 70 %) as a colorless solid. IR: 3022, 2920, 2856, 1688, 1517, 111, 1029, 813. ^{1}H NMR (270 MHz): δ 1.90 (s, 3H, COC$\underline{H}_3$), 2.12 (s, 3H, CH_3), 2.14 (s, 3H, CH_3), 2.27 (s, 6H, 2 CH_3), 6.59 – 6.74 (m, 8H), 6.89 (d, 2H, ^3J = 8.1 Hz), 6.93 (d, 2H, ^3J = 8.1 Hz), 6.97 (vs, 4H); MS (EI, 70 eV): *m/z* [M^+] 480 (100), [M^+–CH_3] 465 (54), [M^+–C_2H_2O] 438 (41), 149 (29). HRMS Found: 480.2456. Calcd. for $C_{36}H_{22}O$: 480.2453.

Method B: A solution of **3e** (16.6 mg, 3.1×10^{-5} mol) in CD_2Cl_2 (0.5 mL) was photo-irradiated with a 1 kW Tokyo Rigaku high-pressure mercury lamp, with the reaction system cooled at rt. The mixture was analyzed by ^{1}H NMR spectroscopy after 30 min., 2.5 h and 4 h, after which the photo-irradiation was stopped. The mixture was subjected to column chromatography on silica gel (hexane/ether 1:1) to give **9b** (9.8 mg, 65%).

Acknowledgements

This project was supported in part by ESPRC (in UK) and J. Iniesta thanks the ESPRC for funding of a stay at Kyushu University, Fukuoka, Japan. The authors thank Ms. Y. Tanaka for carrying out the mass and high resolution mass spectroscopic measurements of the compounds. The elemental analyses were carried out at the Central Analysis Center, Hakozaki Campus, Kyushu University.

REFERENCES

[1] (a) Yoshida, K.; Horiuchi, S.; Iwadate, N.; Kawagoe, F.; Imamoto, T. *Synlett* **2007**, 1561–1562. (b) Yoshida, K.; Hayashi, A; Yanagisawa, *Org. Lett.* **2011**, *9*, 4627–4630.

[2] (a) Hilt, G.; Danz, M. *Synthesis* **2008**, 2257–2263. (b) Hilt, G.; Smolko, K. I. *Angew. Chem. Int. Ed.* **2003**, *42*, 2795–2797.

[3] (a) Horie, H.; Kurahashi, T.; Matsubara, S. *J. Chem. Soc., Chem. Commun.* **2012**, 3866–3868.

[4] Thiemann, T.; Fujii, H.; Ohira, D.; Arima, K.; Li, Y. Q.; Mataka, S. *New J. Chem.* **2003**, *27*, 1377–1384.

[5] (a) Pérez, D.; Peňa, D.; Guitián, E. *Eur. J. Org. Chem.* **2013**, 5981–6013; (b) Hayes, M. E.; Shinokubo, H.; Danheiser, R. L. *Org. Lett.* **2005**, *7*, 3917–3920.

[6] (a) Woodard, B. T.; Posner, G. H. *Advances in Cycloaddition* **1999**, *5*, 47–83. (b) Delaney, P. M.; Moore, J. E.; Harrity, J. P. A. *J. Chem. Soc., Chem. Commun.* **2006**, 3323–3325.

[7] (a) Buszek, K. R. *Tetraphenylcyclopentadienone, e-EROS Encyclopedia of Reagents for Organic Synthesis*, **2001**; (b) Hapke, M.; Gutnov, A.; Weding, N.; Spannenberg, A.; Fischer, C.; Benkhäuser-Schunk C.; Heller, B. *Eur. J. Org. Chem.* **2010**, 509–514. (c) Khazaei, A.; Zolfigol, M. A.; Manesh, A. A. *J. Chin. Chem. Soc*. **2013**, *52*, 515–518.

[8] Padwa, A.; Dimitroff, M.; Waterson, A. G.; Wu, T. *J. Org. Chem.* **1997**, *62*, 4088–4096.

[9] (a) Kumamoto, K.; Fukuda, I.; Kotsuki, H. *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 2015–2017. (b) Helder, R.; Wynberg, H. *Tetrahedron Lett.* **1972**, 605–608. (c). Kuhn, H.-J.; Gollnick, K. *Chem. Ber.* **1973**, *106*, 674–696. (d) Corral, C.; Lissavetzky, J.; Manzanares, I. *Synthesis* **1997**, 29–31.

[10] (a) Melles, J. L. *Recl. Trav. Chim. Pays-Bas* **1952**, *71*, 869–878. (b) Nakayama, J.; Hirashima, A. *J. Am. Chem. Soc.* **1990**, *112*, 7648–7653. (c) Moiseev, A. M.; Tyurin, D. D.; *Balenkova*, E. S.; Nenajdenko, V. G. *Tetrahedron* **2006**, *62*, 4139–4145. (d) Van Tilborg, W. J. M.; Smael, P.; Viser, T. P.; Louwenhoven, C. G.; Reinhoudt, D. N. *Rec. Trav. Chim. Pays-Bas*, **1975**, *94*, 85–88.

[11] (a) Li, Y. Q.; Matsuda, M.; Thiemann, T.; Sawada, T.; Mataka, S.; Tashiro, M. *Synlett* **1996**, 461–464. (b) Furukawa, N.; Zhang, S.-Z.; Sato, S.; Higaki, M. *Heterocycles* **1997**, *44*, 61–66. (c) Li, Y. Q.; Thiemann, T.; Sawada, T.; Mataka, S.; Tashiro, M. *J. Org. Chem.* **1997**, *62*, 7926–7936. (d) Nakayama, J.; Yu, T.; Sugihara, Y.; Ishii, A. *Chem. Lett.* **1997**, *26*, 499–500. (e) Furukawa, N.; Zhang, S.-Z.; Horn, E.; Takahashi, O.; Sato, S.; *Heterocycles* **1998**, *47*, 793–809. (f) Takayama, J.; Sugihara, Y.; Takayanagi, T.; Nakayama, J. *Tetrahedron Lett.* **2005**, *46*, 4165–4169. (g) Pouzet, P.; Erdelmeier, I.; Ginderow, D.; Mornon, J.-P.; Dansette, P. M.; Mansuy D. *J. Chem. Soc., Chem. Commun.* **1995**, 473–474.

[12] (a) For reviews, see: Lu, Y.; Dong, Z.; Wang, P.; Zhou, H.-B. *Top. Heterocycl. Chem.* **2015**, *39*, 227–294. (b) Thiemann, T.; Iniesta, J. *Research Trends in Heterocyclic*

Chemistry **2011**, *15*, 71–88. (c) Thiemann, T.; Gopal Dongol, K. *J. Chem. Res.* (*S*) **2002**, *26*, 303 – 308; (*M*) **2002**, 701–708. (d) Thiemann, T.; Walton, D. J.; Brett, A. O.; Iniesta, J.; Marken, F.; Li, Y. Q. *ARKIVOC* **2009**, Vol. ix, 96–113. (e) Nakayama, J. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1–17.

[13] (a) Arima, K.; Ohira, D.; Watanabe, M.; Miura, A.; Mataka, S.; Thiemann, T.; Iniesta, J.; Walton, D. *Photochem. Photobiol. Sci.* **2005**, *4*, 808-816; (b) Nakayama, J.; Hiraiwa, S. Fujihara, T. *Sulfur Chem.* **2008**, *29*, 243–250; (c) Heying, M. J.; Nag, M.; Jenks, W. S. *J. Phys. Chem. Org.* **2008**, *21*, 915–924.

[14] Jiang, B.; Tilley, T. D. *J. Am. Chem. Soc.* **1999**, *121*, 9744–9745.

[15] Suzuki, S.; Segawa, Y.; Itami, K.; Yamaguchi, J. *Nature Chemistry* **2015**, *7*, 227–233.

[16] Landini, D.; Rolla, F. *J. Org. Chem.* **1982**, *47*, 154–157.

[17] (a) Li, Y. Q.; Thiemann, T.; Mimura, K.; Sawada, T.; Mataka, S.; Tashiro, M. *Eur. J. Org. Chem.* **1998**, 1841–1850. (b) Thiemann, T.; Li, Y. Q.; Thiemann, C.; Sawada, T.; Ohira, D.; Tashiro, M.; Mataka, S. *Heterocycles* **2000**, *52*, 1215–1230.

[18] (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540–4552. (b) Cieplak, A. S.; Tait, B. D.; Johnson, C. R. *J. Am. Chem. Soc.* **1989**, *111*, 8447–8462. (c) Cieplak, A. S. *Chem. Rev.* **1999**, *99*, 1265–1336.

[19] Thiemann, T.; Iniesta, J.; Walton, D. *J. Chem. Res.* **2008**, *32*, 173–180.

[20] Iniesta, J.; Matsumoto, T.; Thiemann, T. *J. Chem. Res.* **2008**, *32*, 119–114.

[21] (a) Fogel, Y.; Zhi, L.; Rouhanipour, A.; Andrienko, D.; Räder, H. J.; Műllen, K. *Macromolecule*s, **2009**, *42*, 6878–6884. (b) Englert, J. M.; Malig, J.; Zamolo, V. A.; Hirsch, A.; Jux, N. *J. Chem. Soc., Chem. Commun.* **2013**, *49*, 4827–4829.

[22] (a) Luo, Q.; Wang, C.; Zhang, W.-X.; Xi, Z. *J. Chem. Soc., Chem. Commun.* **2008**, 1593–1595; (b) Xi, Z.; Song, Q. *J. Org. Chem.* **2000**, *65*, 9157–9159.

[23] Harmata, M.; Gomes, M. G. *Eur. J. Org. Chem.* **2006**, 2273–2277.

[24] Mock, W. L., *J. Am. Chem. Soc.* **1970**, *92*, 7610–7612.

[25] Li, Y. Q.; Thiemann, T; Sawada, T.; Tashiro, M. *J. Chem. Soc., Perkin Trans. 1*, **1994**, 2323–2329.

[26] Thiemann, T.; Sa e Melo, M. L.; Campos Neves, A. S.; Li, Y. Q.; Mataka, S.; Tashiro, M.; Geiβler, U.; Walton, D. *J. Chem. Res.* **1998**, *22*, 346–347.

[27] Thiemann, C.; Thiemann, T.; Li, Y. Q.; Sawada, T.; Nagano, Y.; Tashiro, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1886–1893.

[28] (a) Nightingale, D. V.; Hucker, H. B. *J. Org. Chem.* **1953**, *48*, 1529–1537. (b) Kagechika, H.; Kawachi, E.; Hashimoto, Y.; Shudo, K. *J. Med. Chem.* **1988**, *31*, 2182–2192. (c) Sudha, S.; Palanichamy, M.; Balasubramanian, V. V.; Arabindoo, B.; Murugesan, V. *J. Mol. Catal. A* **2006**, *255*, 220–229. (d) Dhami, K. S.; Stothers, J. B.; *Tetrahedron Lett.* **1964**, 631–639. (e) Dhami, K. S.; Stothers, J. B. *Can. J. Chem.* **1965**, 479–497.

[29] Fuchs, B. *Isr. J. Chem.* **1968**, *6*, 517–520.

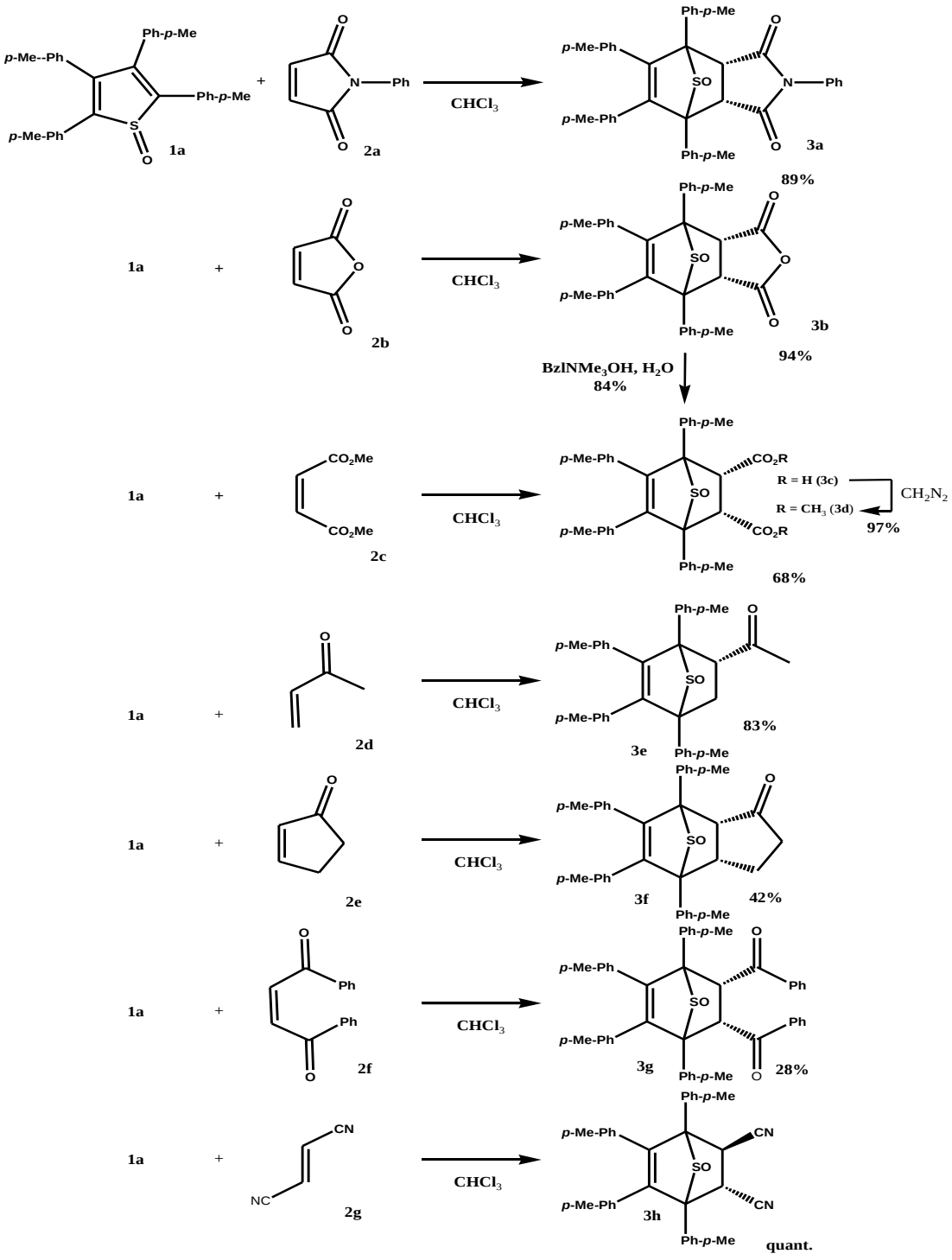
[30] Swope, W. C.; Lee, Y.-P.; Schaefer III, H. F. *J. Chem. Phys.* **1979**, *71*, 3761–3769.

[31] Beckenridge, W. H.; Miller, T. A, *J. Chem. Phys.* **1972**, *56*, 465–474.

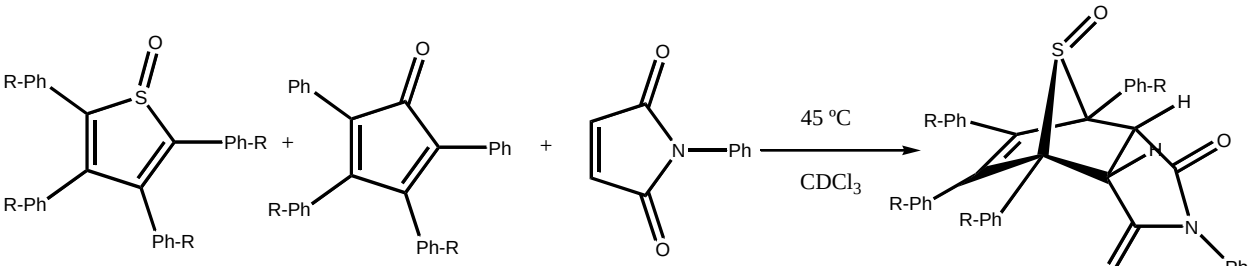
[32] Chao, P.; Lemal, D. M. *J. Am. Chem. Soc.* **1973**, *95*, 920–922.

[33] Tong, L.; Lau, H.; Ho, D. M.; Pascal, Jr., R. A. *J. Am. Chem. Soc.* **1998**, *120*, 6000–6006.

[34] Van Tilborg, W. J. M. *Synth. Commun.* **1976**, *6*, 583–589.



Scheme 1



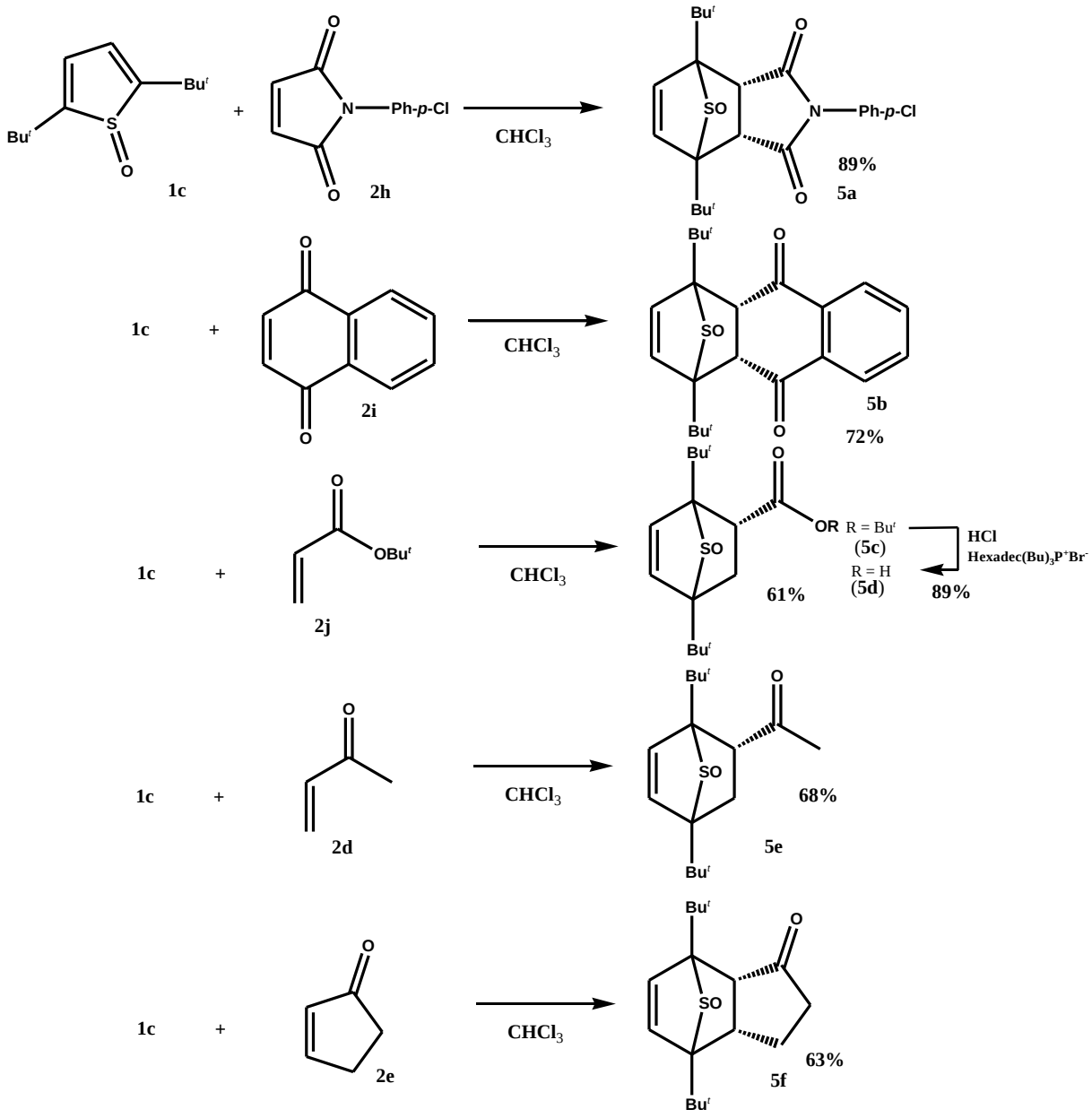
1 eq. 1 eq. 2 eq.

1b: R = H **4a**: R = H **2a**

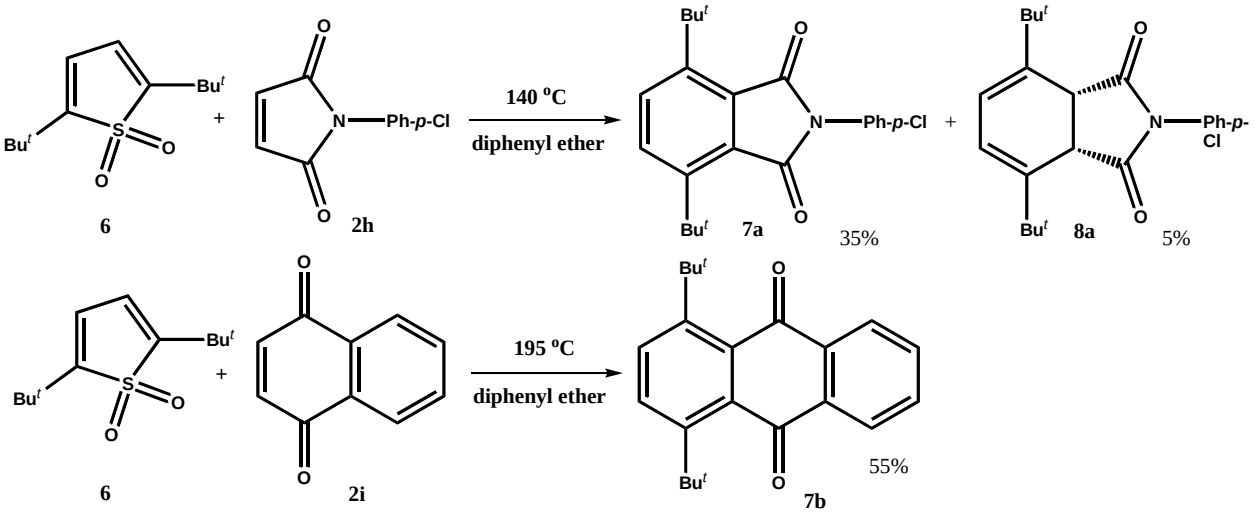
1a: R = CH_3 **4b**: R = CH_3

3a (R = CH_3), **3i** (R = H) form exclusively (the reaction completes at 45 ºC in 90 min.)

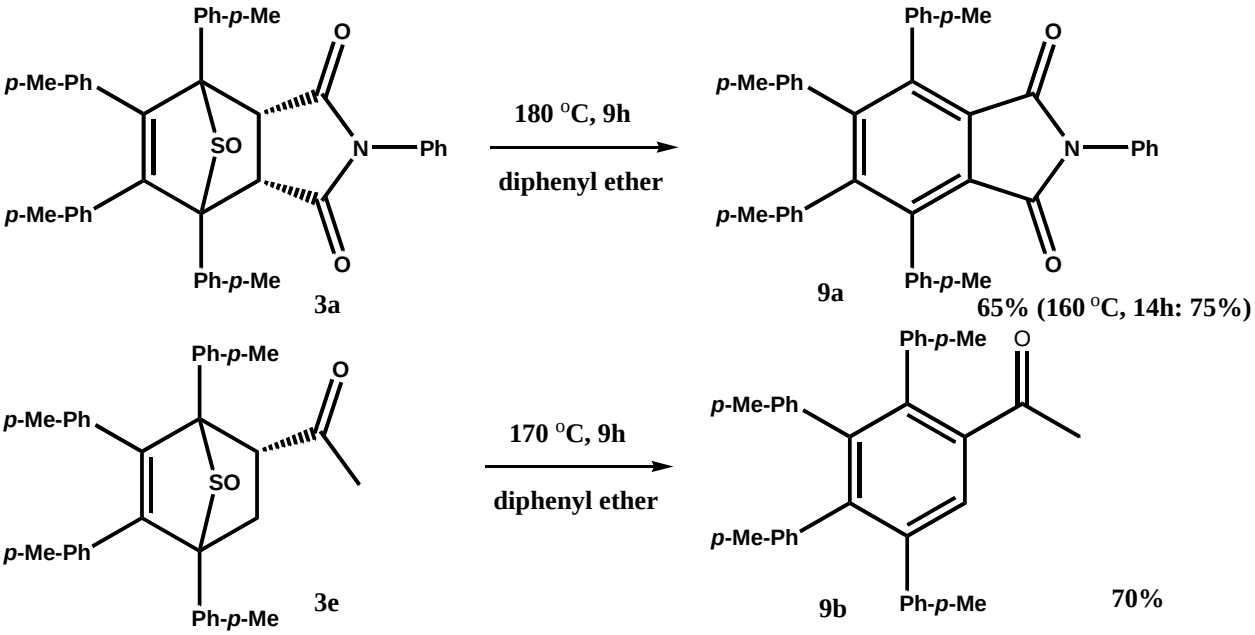
Scheme 2



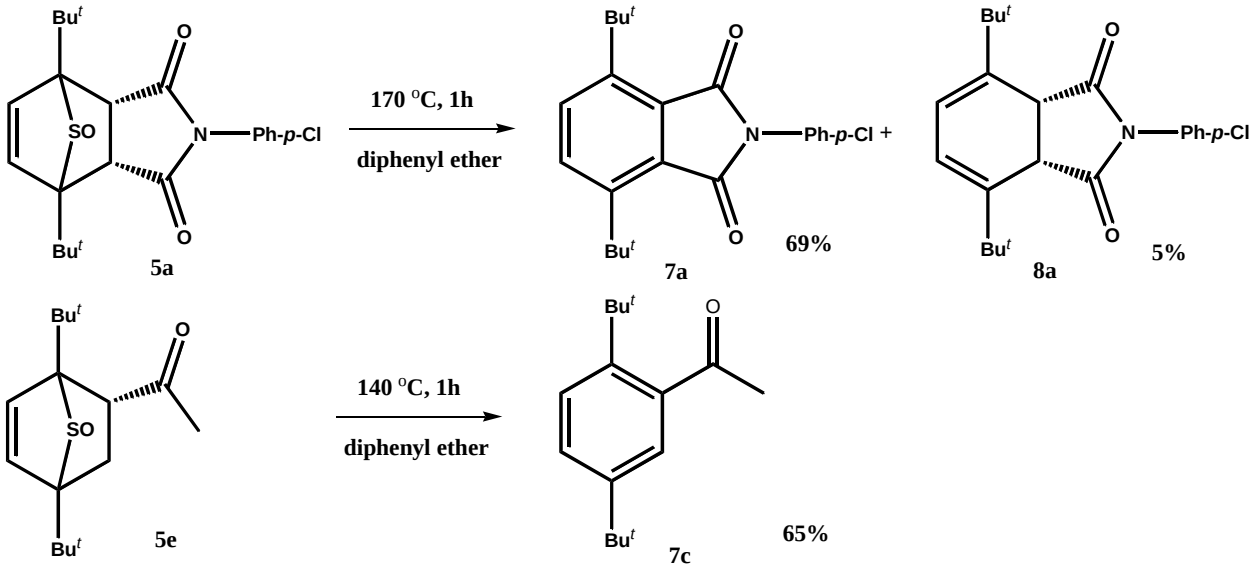
Scheme 3



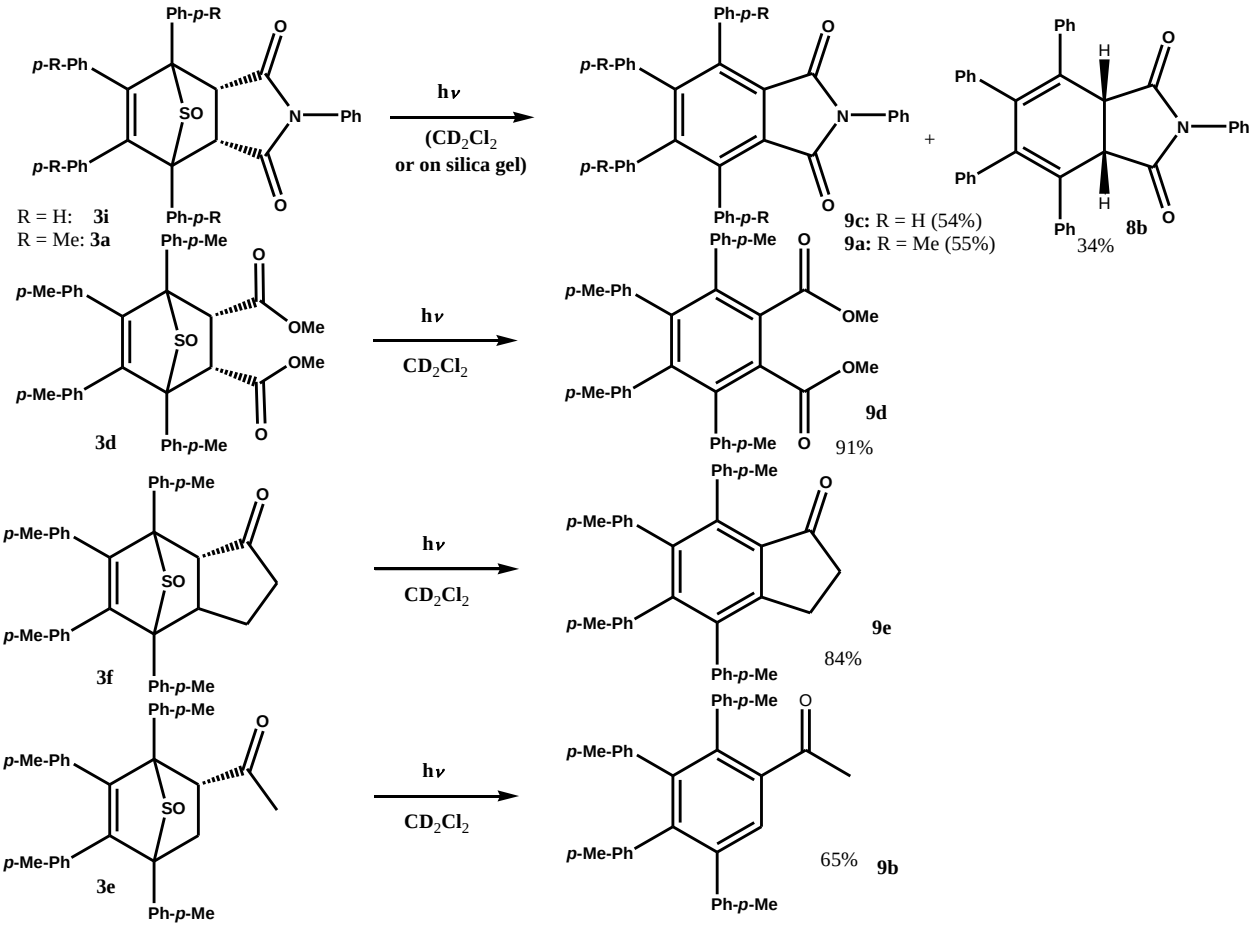
Scheme 4



Scheme 5



Scheme 6



Scheme 7