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The Synthesis of Bicyclic *ortho*-Quinodimethanes from Tricyclic Sulfones

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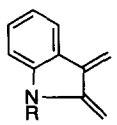
Abstract: The first synthesis of bicyclic *ortho*-quinodimethanes from tricyclic sulfone precursors has been achieved. The required sulfones, 3,4,5,6-tetrahydro-1H-cyclohex[cd]benzothiophene-2,2-dioxide and 1,3,4,5,6,7-hexahydrocyclohept[cd]benzothiophene-2,2-dioxide, were prepared from α-tetralone and benzosuberone utilizing a ring closure proceeding through a sulfonium salt intermediate. The same strategy failed when trying to prepare the tricyclic sulfone of the indane series. Other contrasting reactivity was also noticed when comparing the ability and ease of formation of tricyclic ether compounds. These results indicate that the later ring system is considerably strained.

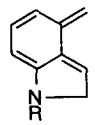
Postulated as an intermediate species over forty years ago,[1] *ortho*-quinodimethane **1** and its derivatives have been the subject of numerous studies and reviews.[2,3] Although there are many ways to generate these transient species, chelotropic extrusion of sulfur dioxide from cyclic sulfones continues to be a popular method. Recent reports in the literature have focused primarily on the synthesis of bicyclic sulfones derived from heterocyclic systems, led primarily by Storr[4-9] and others[10-12] affording *ortho*-quinodimethanes of type **2**. There have, however, been few reports of *ortho*-quinodimethanes derived from the indole nucleus. Pindur et al[13,14] have reported a number of methods to generate **3** and the results of cycloadditions with a variety of dienophiles. Magnus and coworkers[15] have used intermediates of type **3** in their synthesis of the aspidosperma type alkaloids. To the best of our knowledge, there are no reports dealing with compounds of type **4**. Recent work in our laboratory has caused us to consider these as potential intermediates.

1

2



3

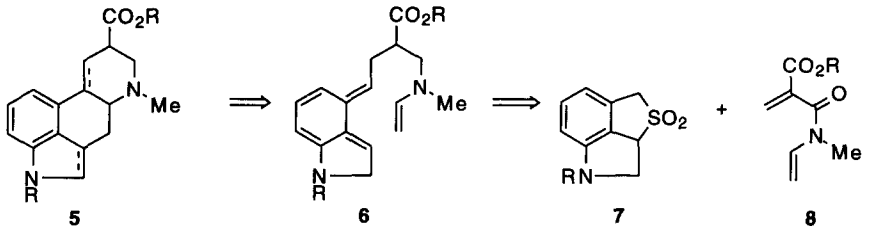


4

In a study directed towards the synthesis of ergot alkaloids (**5**), shown retrosynthetically in Scheme 1, we were intrigued with the possibility of using an *ortho*-quinodimethane (**6**) to construct the tetracyclic core of tetrahydrolysergine **5**. Central to this approach was the employment of sulfone **7** as the masked *ortho*-quinodimethane. It was anticipated that introduction of the required tether would be accomplished via conjugate addition of the anion derived from sulfone **7** to receptor **8**. Thermal elimination of sulfur dioxide would

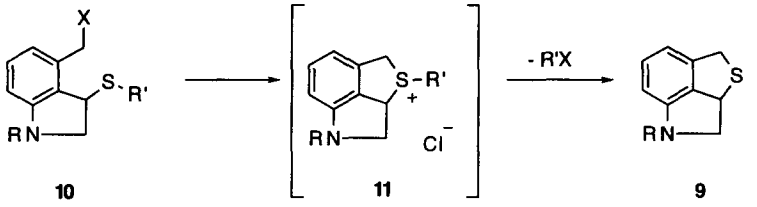
provide bicyclic *ortho*-quinodimethane **6**, which, after intramolecular cycloaddition, would afford the tetrahydroergoline skeleton **5**. Studies were therefore initiated towards the synthesis of **7**.

Scheme 1



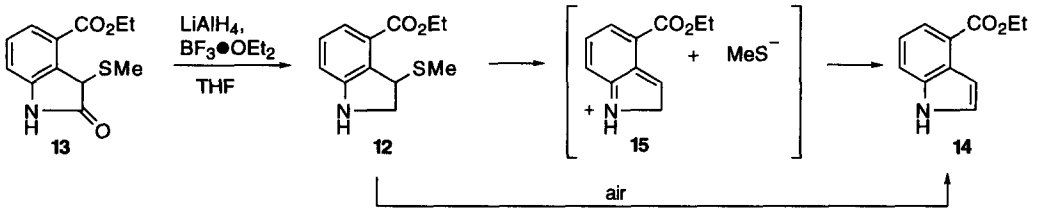
Initially, we believed that sulfone **7** could be derived from sulfide **9**. It was expected that activation of the 4-position of a 3-thioalkylindoline as shown in **10** would provide sulfonium salt **11**, dealkylation of which would afford sulfide **9**.

Scheme 2

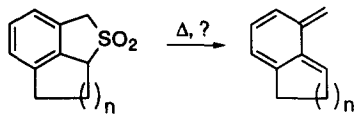


However, this sulfonium salt strategy was hampered by the instability of 3-alkylthioindolines. Although **12** could be prepared from oxindole **13**, the ester group of **12** could not be reduced prior to desulfenylation. Treatment of **12** with mild reducing agents led to the formation of indole **14** prior to reduction of the ester group. 3-Alkylthioindolines undergo a facile elimination of the thiolate group, presumably through intermediate **15**, resulting in the formation of indole **14**.[16] Evidence that this transformation was not base promoted came from the observation that **12** led to **14** even standing at room temperature.

Scheme 3



Although other routes to **7** can be envisaged, similar problems led us to investigate a more fundamental question: can tricyclic sulfones of the type **16-18** be easily prepared, and does sulfur dioxide extrusion to afford *ortho*-quinodimethanes **19** occur at readily accessible temperatures?

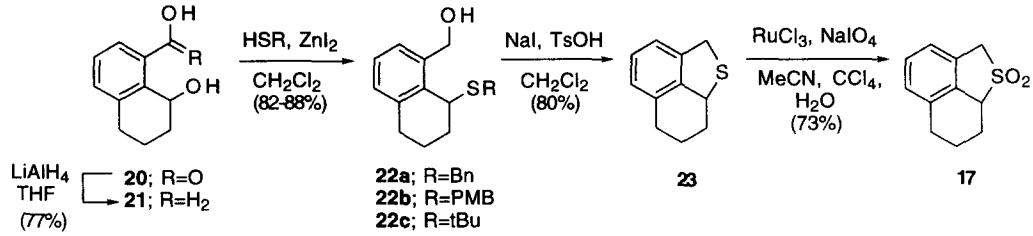


16; n=1
17; n=2
18; n=3

19; n=1-3

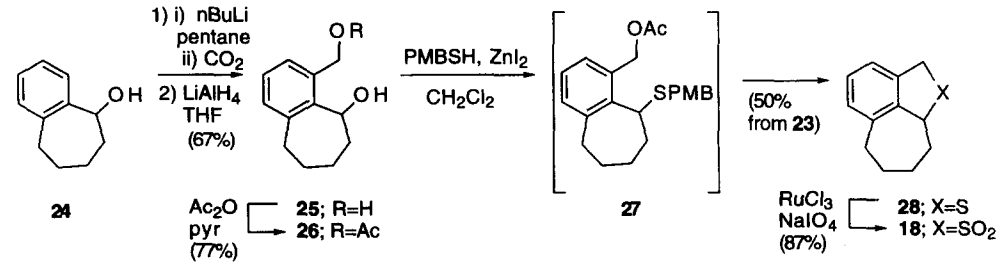
The synthesis of sulfone **17** was accomplished as shown below (Scheme 4). Reduction of hydroxy acid **20**[17] with lithium aluminum hydride in tetrahydrofuran afforded diol **21** in 77% yield. Addition of zinc(II) iodide to a methylene chloride solution of diol **21** containing a slight excess of the appropriate thiol led to hydroxy-sulfides **22a-c** in yields ranging from 82-88%. Formation of sulfide **23** was best accomplished by reaction of the hydroxy-sulfide with 1.5 equivalents of sodium iodide and *para*-toluenesulfonic acid. Although sulfides **22a-c** all afforded the desired tricyclic sulfide, sulfide **22b** (PMB = *para*-methoxybenzyl) afforded sulfide **23** most efficiently. Sulfide **23**, an odoriferous dark green oil, was immediately oxidized to sulfone **17** in 73% yield using the method reported by Sharpless.[18]

Scheme 4



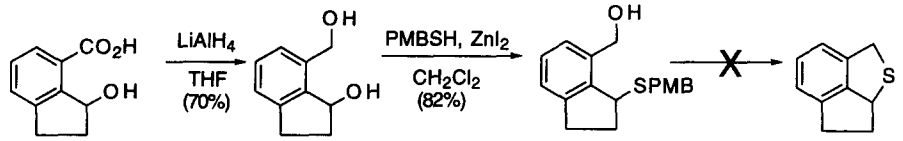
The sulfone **18** was prepared by an analogous sequence as shown in Scheme 5. *Ortho*-metallation of benzosuberanol **24**, carboxylation and subsequent reduction with lithium aluminum hydride afforded diol **25**. Direct conversion of diol **25** to hydroxy-sulfide **27** was curtailed by formation of the tricyclic ether, even when conducted in the presence of a large excess of thiol. Acetylation of the primary hydroxyl group of **25** at low temperature (0 °C) followed by ionization of the secondary benzylic alcohol of **26** in the presence of *para*-methoxybenzyl mercaptan (PMBSH) provided sulfide **28** directly in a yield of 50% from alcohol **26**. Oxidation, as discussed for **17**, afforded sulfone **18** in 87% yield.

Scheme 5



Some problems were encountered when this sequence was applied to diol **29** (Scheme 6). Although formation of the hydroxy-sulfide **31** was straightforward from diol **29**, attempted ring closure resulted in complex reaction mixtures, with no evidence in support of the formation of **32**. In contrast to the facile ring closure of **22** and **27** which occurred cleanly, reaction of **31** resulted in complex reaction mixtures. This anomalous result seems to indicate that **32** is considerably strained, or geometry limitations do not allow for the nucleophile, electrophilic carbon and leaving group to align with the trajectory necessary for an S_N2 displacement.

Scheme 6

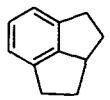


30 **29** **31** **32**

To probe the question of ring strain in tricycle **32**, molecular mechanics calculations were carried out using the Sybyl force field.[19] Comparing the results (Table 1) of the series of sulfides shows that the ring system in **32** is subject to considerably more strain than either **23** or **28**. Although the slight increase in strain as the ring size of the fused ring changes from six to seven is expected (**23** to **28**), the dramatic increase in strain energy for sulfides **32** as compared to **23** may explain the failure of forming **32** using the methodology outlined above (Scheme 6).

Table 1 - Calculated Strain Energy for Sulfides **23, 28** and **32** and Tricycle **I**

	Sulfide **32**	Sulfide **23**	Sulfide **28**	Tricycle **I**
Strain Energy	17.91kcal/mol	6.25 kcal/mol	10.26 kcal/mol	26.95 kcal/mol



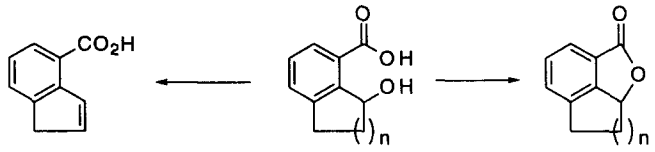
I

It is interesting to note, however, that Rapoport has prepared **I** over 40 years ago.[20] The successful synthesis of **I**, a ring system that is much more strained than sulfide **32** on the basis of molecular mechanic calculations, suggests that **32** can be prepared. Instead, we favor the argument that the S_N2 reaction, as outlined in Scheme 6, is not a viable route to **32** due to a geometry limitation imposed by the tethered five-membered ring. In order for an S_N2 reaction to be successful, the nucleophile, electrophilic center and leaving group must align in a 180° path. This geometry is not be accessible in systems like **31** due to the rigidity of the system caused by the presence of the fused five-membered ring.

The trend of forming 6-6-5 and 6-7-5 tri-fused ring systems but failing to form a 6-5-5 system was not limited to these sulfides. A similar trend was noticed for tricyclic lactone formation (Scheme 7). *Ortho*-metallation of benzosuberanol followed by quenching with carbon dioxide provided a lactone (**37**) that could not

be converted to hydroxy acid **36** in our hands. The same sequence with α-tetralol as starting material afforded the hydroxy acid (**20**) that we and others[17] have successfully lactonized to **34**. However, hydroxy-acid **30** formed indenecarboxylic acid **33** rather than lactone **35** when treated with *para*-toluenesulfonic acid in tetrahydrofuran.[21]

Scheme 7



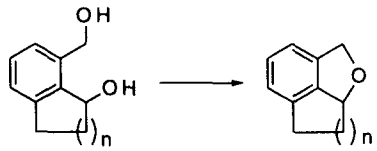
33

20; n=2
30; n=1
36; n=3

34; n=2
35; n=1
37; n=3

This trend also applied to the ease of tricyclic ether formation (Scheme 8). In the case of diol **25**, ether formation was so favorable that the intermediate benzylic cation generated via ionization of the secondary benzylic alcohol with Lewis acids could not be trapped by external nucleophiles. This occurred when trying to prepare hydroxy-sulfides, as discussed above, and also when attempting an ionic hydrogenation with triethylsilane.[22] Even when using triethylsilane as the solvent, and adding either trifluoroacetic acid, borontrifluoride etherate or zinc (II) iodide at low temperatures, only ether **39** was formed. However, ionization of diol **29** in the *absence* of nucleophiles did not lead to formation of tricyclic ether **40**. Once again, complex reaction mixtures were the result. The failure to form **35** is quite surprising since the reaction takes place via a S_N1 mechanism and the rational based on geometry limitations breaks down. In this case, the p orbital of the benzylic cation cannot align with the hydroxyl group in a manner favorable for bonding.

Scheme 8



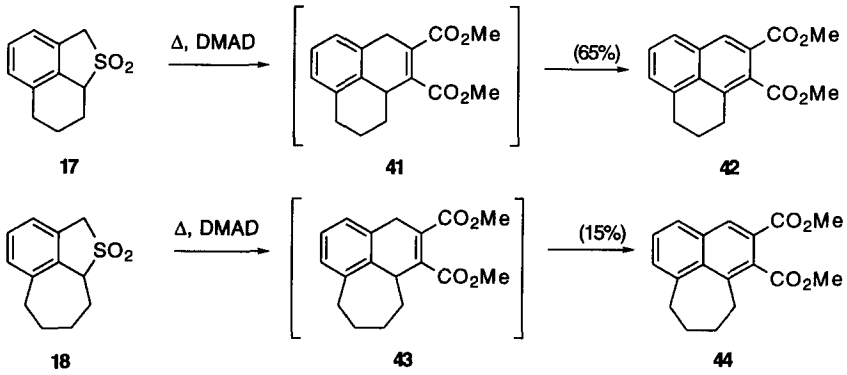
21; n=2
25; n=3
29; n=1

38; n=2
39; n=3
40; n=1

Having successfully prepared two new tricyclic sulfones **17** and **18**, their reactivity with a typical dienophile, dimethylacetylene dicarboxylate (DMAD), was studied (Scheme 9). Although no reaction was noted when **17** and DMAD were heated at reflux in xylene, or in toluene in a sealed tube at 250 °C for up to 12 hours, it was found that when either **17** or **18** was heated with excess DMAD in the absence of solvent at 250-320 °C for 15-20 minutes under air, cycloaddition did occur. The intermediate dihydronaphthalenes **41** and **43** were oxidized under the reaction conditions to provide the naphthalenes **42** and **44**. Both compounds, isolated in yields of 65 and 15% respectively on purification by column chromatography, were identical to compounds prepared via an alternative route.[23] The lower yield of **44** compared to **42** is probably a reflection of the fact

that the intermediate *ortho*-quinodimethane is distorted. We have previously shown that a bicyclic *ortho*-quinodimethane in which one arm of the diene is tied back in a seven membered ring is not flat.[23] This deviation from planarity presumably makes the extrusion of SO_2 a higher energy pathway. Even under the harsh conditions employed for the reaction of **18** and DMAD (320 °C, 20 minutes), some starting sulfone **18** was still recovered.

Scheme 9



In conclusion, we have prepared two new tricyclic sulfones which have unprecedented ring systems and have generated for the first time, bicyclic *ortho*-quinodimethanes from tricyclic sulfones. The failure of diol **29** to form either the tricyclic ether **35** or the tricyclic sulfide **32**, and the inability to convert **30** to lactone **38** indicate that this tricyclic ring system is considerably strained and simple S_N1 and S_N2 reactions cannot overcome this barrier. However, 6,6,5- and 6,7,5-tricyclic fused ring systems, represented by **17** and **18** respectively, are readily accessible using this method.

Experimental

General

All reactions were conducted under an inert atmosphere in flame-dried glassware that had been cooled under a stream of dry nitrogen. Melting points were determined on a Fisher-Johns Unimelt melting point apparatus and are uncorrected. Infrared spectra were recorded with a Bomem MB 101 FT-IR spectrometer with solution cells using the highest grade of methylene chloride available. Proton and carbon nuclear magnetic resonance were recorded on either a Bruker AMX-500, Varian XL-300 or Varian Gemini 200 operating at frequencies of 500, 300 and 200 MHz for proton and 125, 75 and 50 MHz for carbon, using the specified solvent and are reported relative to TMS = 0.00 ppm. Low and high resolution mass spectra were recorded on a VG 7070 mass spectrometer or a Concept II instrument. Peak intensities are reported as a percentage of the base peak.

The phrase "usual work up" refers to drying the solvent over anhydrous magnesium sulfate, filtering and removing the solvent under reduced pressure using a Buchi Rotovapor. The term chromatography refers to flash chromatography performed using 230-400 mesh silica gel supplied by Terochem Laboratories in the solvent specified. All solvents were routinely distilled prior to use. All starting materials were used as received

from commercial sources except for the following: triethylamine (BDH) was distilled from CaH_2 and THF (BDH) was dried and distilled from sodium with benzophenone as an indicator.

3-Methylthio-4-carboethoxyindoline (12).

A cooled (0 °C) solution of oxindole **13** (500 mg, 1.99 mmol) and borontrifluoride etherate (0.50 mL, 3.95 mmol) in THF (10 mL) was added dropwise to a suspension of lithium aluminum hydride (75 mg, 1.98 mmol) in THF (10 mL). The resulting solution was stirred at 0 °C for 1h, heated at reflux for 3.5 h, then cooled to RT and quenched by the careful addition of an aqueous solution of potassium sodium tartrate (10%, 50 mL) and ethyl acetate (50 mL). After stirring for 1h, the organic phase was separated and worked up as usual affording two compounds. The first to elute (R_f=0.25, 4:1 hexanes/ethyl acetate) was the title compound, the second (R_f=0.10, 4:1 hexanes/ethyl acetate) was determined to be 3-methylthio-4-carboethoxyindole (145 mg, 40%). Spectroscopic data for **12**: cloudy yellow oil (200 mg, 42%). **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.35 (t, 3H, *J* = 8.0 Hz), 2.00 (s, 3H), 3.65 (d, 1H, *J* = 7.0 Hz), 3.70 (br, 1H), 3.89 (dd, 1H, *J* = 7.0, 1.0 Hz), 4.35 (m, 2H), 4.92 (d, 1H, *J* = 7.0 Hz), 6.80 (d, 1H, *J* = 7.5 Hz), 7.11 (t, 1H, *J* = 7.5 Hz) , 7.38 (d, 1H, *J* = 7.5 Hz) ppm; **EI-MS** m/z (%): 237 ($M^{\bullet+}$, 2.5), 189 (39.7), 144 (100), 116 (49.6); **HRMS** for $C_{12}H_{15}NO_2S$ Calcd: 237.08235; Found: 237.08185.

Ethyl indole-4-carboxylate (14).

^{1}H-NMR (200 MHz, $CDCl_3$) δ: 1.50 (t, 3H, *J* = 8.0 Hz), 4.40 (d, 2H, *J* = 8.0 Hz), 7.15 - 7.50 (m, 5H), 8.80 (br, 1H); **mp**: 72-73 °C (lit.[24] 73-74 °C).

Hydroxy-acids **20**, **30** and lactone **37** were prepared according to the general procedure of Seebach.[17] The preparation of lactone **37** is representative:

1-Hydroxy-benzosuberane-8-carboxylic acid lactone (37).

A solution of *n*-BuLi (27.2 mL, 2.5 M in hexanes, 68.0 mmol) was added dropwise to a solution of benzosuberanol **24** (5.00 g, 30.9 mmol) and *N,N,N'N'*-tetramethylethylenediamine (7.90 g, 67.9 mmol) in pentane (500 mL). The resulting cloudy yellow reaction mixture was heated at reflux for 12 h, cooled to -78 °C, and treated with an excess of solid carbon dioxide. The reaction mixture was slowly allowed to warm to RT, acidified with concentrated hydrochloric acid, and the aqueous phase extracted with diethyl ether (5 x 100 mL). The combined organic extracts were concentrated, and the title compound was isolated as an off-white solid. Recrystallization from diethyl ether/hexanes provided the title compound as white plates (4.35 g, 75%); **mp**: 75.0 °C; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.20 - 1.50 (m, 2H), 1.60 - 1.90 (m, 1H), 2.00 - 2.30 (m, 2H), 2.40 - 2.60 (m, 1H), 2.70 - 3.00 (m, 2H), 5.20 (dd, 1H, *J* = 12.0, 3.6 Hz), 7.30 - 7.40 (m, 2H), 7.80 (d, 1H, *J* = 7.5 Hz) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 27.5, 27.7, 32.9, 35.16, 82.6, 122.9, 125.6, 129.0, 133.4, 138.2, 150.7, 170.8 ppm; **IR** (CH_2Cl_2): 1762 cm^{-1}; **EI-MS** m/z (%): 188 ($M^{\bullet+}$, 100), 159 (99.3), 131 (82.2); **HRMS** for $C_{12}H_{12}O_2$: 188.08373; Found: 188.08726; **CA** for $C_{10}H_{10}O_2$ Calcd: C (76.57), H (6.43); Found: C (76.67), H (6.45).

1-Indanol-7-carboxylic acid (30).

The crude material (thick red oil) could be crystallized as a white solid (3.93 g, 65%) by the addition of diethyl ether and hexanes; **mp**: 128 °C (lit.[21] 128.0-128.5 °C) **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 2.10 - 2.30 (m, 1H), 2.40 - 2.60 (m, 1H), 2.80 - 3.00 (m, 1H), 3.10 - 3.30 (m, 1H), 5.64 (dd, 1H, *J* = 8.0, 4.0 Hz), 7.37 (t, 1H, *J* = 7.5 Hz), 7.51 (d, 1H, *J* = 7.5 Hz), 7.96 (d, 1H, *J* = 7.5 Hz) ppm.

1-Hydroxy-1,2,3,4-tetrahydronaphthalene-8-carboxylic acid (20):

The title compound was isolated as a white crystalline solid after recrystallization from diethyl ether and hexanes; **mp**: 125 °C (lit.[17]:115-118 °C, lit.[21] 133-134 °C); **^{1}H-NMR** ($CDCl_3$, 200 MHz) δ: 1.60 - 1.80 (m, 2H), 1.90 - 2.20 (m, 2H), 2.60 - 3.00 (m, 2H), 5.05 (t, 1H, *J* = 5.0 Hz), 7.10 - 7.30 (m, 2H), 7.75 (d, 1H, *J* = 8.0 Hz) ppm; **^{13}C-NMR** ($CDCl_3$, 75 MHz) δ: 16.6, 29.7, 30.0, 63.3, 126.9, 129.1, 129.2, 134.6, 138.1, 139.3, 172.2 ppm; **EI-MS** m/z (%): 192 (8.4, $M^{\bullet+}$), 174 (67.1), 146 (54.3), 118 (100); **HRMS** for $C_{11}H_{12}O_3$; Calc: 192.07864; Found: 192.07682.

Diols **21**, **25** and **29** were prepared following the same general procedure. The procedure given for diol **25** is representative.

1-Hydroxy-9-hydroxymethylbenzosuberane (25).

A solution of lactone **39** (4.00 g, 21.3 mmol) in THF (50 mL) was added dropwise to a suspension of lithium aluminum hydride (0.80 g, 21.1 mmol) in THF (100 mL). The resulting mixture was stirred at RT for 1 h, at reflux for 2 h, cooled to RT, and then was poured *carefully* into an aqueous solution of potassium sodium tartrate (10%, 100 mL). Ethyl acetate (150 mL) was then added and the mixture was stirred for 10 h. Separation of the organic phase and usual work up afforded the title compound as a thick, clear oil that slowly solidified on standing. Recrystallization from diethyl ether/hexanes afforded diol **25** as a white crystalline solid (3.62 g, 89%). **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.40 - 1.50 (m, 1H), 1.55 - 1.90 (m, 3H), 2.00 - 2.10 (m, 2H), 2.60 - 2.80 (m, 1H), 3.10 - 3.30 (m, 1H), 4.40 (d, 1H, *J* = 12.5 Hz), 4.70 (d, 1H, *J* = 12.5 Hz), 5.25 (dd, 1H, *J* = 12.0, 1.0 Hz), 7.00 - 7.15 (m, 3H) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 24.5, 27.6, 33.4, 35.4, 65.0, 69.8, 127.5, 127.9, 131.0, 138.1, 141.7, 143.6 ppm; **IR** (CH_2Cl_2): 3596, 3392 cm^{-1}; **CA**: For $C_{12}H_{16}O_2$: Calc. C (74.97), H (8.39); Found: C (74.72), H (8.61).

1-Hydroxy-8-hydroxymethyl-1,2,3,4-tetrahydronaphthalene (21).

Hydroxy-acid **21** was reduced to diol **25** following the general procedure affording the title compound as a white solid (77%); **mp**: 74 °C; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.70 - 2.20 (m, 4H), 2.70 - 3.00 (m, 1H), 3.58 (br, 2H), 4.42 (d, 1H, *J* = 12.2 Hz), 4.90 (d, 1H, *J* = 12.2 Hz), 5.00 (t, 1H, *J* = 4.0 Hz), 7.05 - 7.25 (m, 3H) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 17.2, 30.0, 31.6, 36.7, 64.2, 64.2, 127.8, 127.9, 129.8, 136.9, 138.0, 139.9 ppm; **IR** (CH_2Cl_2): 3597, 3402 cm^{-1}.

1-Hydroxy-7-hydroxymethylindane (29).

Hydroxy acid **30** was reduced to diol **29** following the general procedure affording the title compound as a clear oil following column chromatography (2:1 hexanes/ethyl acetate) (70%). **^{1}H-NMR** (200 MHz,

$CDCl_3$) δ: 1.90 - 2.10 (m, 1H), 2.30 - 2.50 (m, 1H), 2.70 - 2.90 (m, 1H), 3.05 - 3.25 (m, 1H), 4.00 (br, 2H), 4.46 (d, 1H, *J* = 12.2 Hz), 4.79 (d, 1H, *J* = 12.2 Hz), 5.31 (dd, 1H, *J* = 7.0, 3.5 Hz), 7.00 - 7.10 (m, 1H), 7.12 - 7.30 (m, 2H) ppm; **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 30.4, 34.0, 64.0, 75.1, 124.7, 126.4, 128.7, 137.4, 143.4, 144.5 ppm; **IR** (CH_2Cl_2): 3590, 3382 cm^{-1}.

General Procedure for the preparation of 1-Alkylthio-8-hydroxymethyl-1,2,3,4-tetrahydronaphthalene (22).

Zinc(II) iodide (180 mg, 0.56 mmol) was added in one portion to a solution of diol **9** (100 mg, 0.56 mmol) and one equivalent of the appropriate thiol in methylene chloride (20 mL). The resulting mixture was stirred at RT for 2 h, after which time it was poured into water (50 mL) and extracted with methylene chloride (20 mL). The combined organic extract were subjected to standard work up. The resulting cloudy oil was chromatographed (3:1 hexanes/ethyl acetate) affording the final product.

1-Benzylthio-8-hydroxymethyl-1,2,3,4-tetrahydronaphthalene (22a) (pale yellow oil): **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.70 - 1.90 (m, 2H), 2.10 - 2.45 (m, 2H), 2.65 - 2.92 (m, 2H), 3.75 (d, 1H, *J* = 13.3 Hz), 3.85 (d, 1H, *J* = 13.3 Hz), 4.20 - 4.45 (m, 3H), 4.49 (d, 1H, *J* = 12.4 Hz), 6.95 - 7.45 (m, 8H) ppm; **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 17.5, 27.2, 29.3, 36.7, 39.7, 62.3, 127.2, 127.3, 127.5, 128.7, 128.9, 129.1, 133.4, 137.6, 137.6, 139.7 ppm; **IR** (CH_2Cl_2): 3599 cm^{-1}; **CI-MS** m/z (%): 285 [($M^{\bullet+}$+1), 2.8].

1-*p*-Methoxybenzylthio-8-hydroxymethyl-1,2,3,4-tetrahydronaphthalene (22b) (white solid); **mp**: 75 °C; **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.70 - 1.95 (m, 2H), 2.05 - 2.45 (m, 2H), 2.70 - 3.00 (m, 3H), 3.70 (d, 1H, *J* = 13.2 Hz), 3.78 (s, 3H), 3.80 (d, 1H, *J* = 13.2 Hz), 4.15 - 4.45 (m, 2H), 4.53 (d, 1H, *J* = 12.0 Hz), 6.85 (d, 1H, *J* = 7.0 Hz), 6.95 - 7.20 (m, 3H), 7.28 (d, 2H, *J* = 7.0 Hz) ppm; **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 17.4, 27.2, 29.3, 36.0, 39.7, 55.2, 62.2, 113.9, 127.2, 127.4, 129.0, 129.4, 130.0, 133.6, 137.5, 139.7, 158.6 ppm; **IR** (CH_2Cl_2): 3328 cm^{-1}; **CA**: For $C_{19}H_{22}SO_2$; Calc: C (72.58), H (7.05); Found: C (72.62), Found (7.17).

1-*t*-Butylthio-8-hydroxymethyl-1,2,3,4-tetrahydronaphthalene (22c) (white solid); **mp**: 140 °C; **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.55 (s, 9H), 1.80 - 2.00 (m, 1H), 2.00 - 2.10 (m, 1H), 2.25 - 2.40 (m, 1H), 2.45 - 2.60 (m, 1H), 2.80 - 3.00 (m, 2H), 3.40 (d, 1H, *J* = 8.6 Hz), 4.55 - 4.80 (m, 2H), 5.00 (d, 1H, *J* = 12.0 Hz), 7.00 - 7.35 (m, 3H) ppm; **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 16.9, 29.1, 29.7, 31.9, 39.2, 45.4, 62.9, 127.3, 127.9, 129.5, 134.7, 137.8, 139.2 ppm; **IR** (CH_2Cl_2): 3341 cm^{-1}; **CI-MS** m/z (%): 251 [($M^{\bullet+}$+1), (1.8)].

Tricyclic Sulfide 23.

To a solution of hydroxy-sulfide **22b** (100 mg, 0.32 mmol) in methylene chloride (20 mL) was added *p*-toluenesulfonic acid (90.8 mg, 0.48 mol) and sodium iodide (72 mg, 0.48 mmol). The resulting solution was stirred at RT for 10 h, poured into water (50 mL) and extracted with methylene chloride (4 x 20 mL). The combined organic extracts were worked up in the usual manner, and the dark oily residue chromatographed (20:1 hexanes/ethyl acetate). The title compound was isolated as a slightly green oil (45 mg, 80%): **^{1}H-NMR**

(200 MHz, $CDCl_3$) δ: 1.48 - 1.70 (m, 1H), 1.70 - 1.95 (m, 1H), 2.05 - 2.22 (m 1H), 2.25 - 2.40 (m, 1H), 2.65 - 2.95 (m, 2H), 3.85 (d, 1H, *J* = 16.0 Hz), 4.32 (dd, 1H, *J* = 16.0, 1.0 Hz), 4.50 (d, 1H, *J* = 12.0 Hz), 6.90 - 7.20 (m, 3H) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 23.4, 26.2, 29.9, 26.4, 48.8, 121.4, 126.1, 127.0, 134.6, 140.7, 141.6 ppm; **EI-MS** m/z (%): 176 ($M^{\bullet+}$, 61.8), 148 (100); **HRMS** for $C_{11}H_{12}S$ Calc: 176.06597; Found: 176.06317.

Tricyclic Sulfone 17

A mixture of sulfide **23** (140 mg, 0.80 mmol) and sodium periodate (375 mg, 1.75 mmol) in acetonitrile (1 mL), carbon tetrachloride (1 mL) and water (1.5 mL) was stirred until it became homogenous. A catalytic amount of ruthenium(III) chloride hydrate was added and the resulting black reaction mixture stirred at RT for 3 h, after which time it was poured into diethyl ether (50 mL). The organic phase was separated and subjected to usual work up, affording sulfone **17** as a pale yellow solid (121 mg, 73%); **mp**: 130 °C; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.70 - 1.92 (m, 2H), 2.05 - 2.23 (m, 1H), 2.25 - 2.45 (m, 1H), 2.60 - 2.80 (m, 1H), 2.82 - 2.96 (m, 1H), 4.09 (d, 1H, *J* = 15.4 Hz), 4.15 (dd, 1H, *J* = 10.2, 1.0 Hz), 4.27 (d, 1H, *J* = 15.4 Hz), 7.00 - 7.20 (m, 2H), 7.30 - 7.50 (m, 1H) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 19.4, 21.2, 26.1, 55.6, 61.5, 123.0, 128.2, 128.4, 130.2, 131.4, 136.0 ppm; **IR** (CH_2Cl_2): 1317, 1133 cm^{-1}; **CI-MS** m/z (%): 209 (($M^{\bullet+}$+1), 100); **HRMS** for $C_{11}H_{12}$ ($M^{\bullet+}$-SO_2) Calc: 144.09390; Found: 144.09357.

1-Hydroxy-9-acetoxymethyl-benzosuberane (26).

A solution of acetic anhydride (265 mg, 2.60 mmol) in methylene chloride (5 mL) was added dropwise to a cooled (0°C) solution of diol **25** (500 mg, 2.60 mmol), triethylamine (312 mg, 3.09 mmol) and 4-*N,N*-dimethylaminopyridine (50 mg) in methylene chloride (30 mL). The resulting solution was stirred at 0 °C for 30 min, then poured into water (50 mL). Separation of the organic phase and usual workup afforded a clear oil. Chromatography (10:1 hexanes/ethyl acetate) afforded the title compound **26** as a clear oil (470 mg, 77%); **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.30 - 1.50 (m, 1H), 1.53 - 1.75 (m, 2H), 1.80 - 2.00 (m, 2H), 2.05 (s, 3H), 2.10 - 2.30 (m, 2H), 2.65 (dd, 1H, *J* = 16.0, 8.0 Hz), 3.35 (dt, 1H, *J* = 8.0, 1.0 Hz), 5.13 (d, 1H, *J* = 14.0 Hz), 5.19 (dd, 1H, *J* = 14.0 Hz), 5.15 (dd, *J* = 8.0, 2.5 Hz), 7.00 - 7.20 (m, 3H) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 21.0, 24.6, 28.2, 32.8, 35.8, 65.5, 69.1, 127.6, 128.6, 131.6, 133.0, 142.1, 144.3, 170.6 ppm; **IR** (CH_2Cl_2): 3200, 1710 cm^{-1}.

Tricyclic Sulfide 28

To a solution of mono-acetate **26** (200 mg, 0.85 mmol) in methylene chloride (20 mL) was added sequentially 4-methoxy-α-toluenethiol (158 mg, 1.02 mmol) and zinc(II) iodide (327 mg, 1.02 mmol). The resulting cloudy solution was stirred at RT for 10 h, after which time it was subjected to normal workup. Chromatography with hexanes afforded sulfide **28** as a yellow oil (80 mg, 50%); **^{1}H-NMR** (500 MHz,$CDCl_3$) δ: 1.10 - 1.30 (m, 1H), 1.60 - 1.80 (m, 2H), 2.00 - 2.20 (m, 3H), 2.70 - 2.90 (m, 2H), 4.21 (d, 1H, *J* = 12.5 Hz), 4.38 (dd, 1H, *J* = 12.5, 3.0 Hz), 4.74 (dd, 1H, *J* = 11.0, 3.0 Hz), 6.90 (d, 1H, *J* = 7.5 Hz), 7.00 (d, 1H, *J* = 7.5 Hz), 7.20 (t, 1H, *J* = 7.5 Hz) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 27.6, 31.3, 36.7, 37.6, 39.2, 55.0, 122.6, 126.9, 127.2, 139.8, 140.5, 144.3 ppm; **EI-MS** m/z (%): 190 ($M^{\bullet+}$, 100); **HRMS** for $C_{12}H_{14}S$ Calcd: 190.08162; Found: 190.08107.

Tricyclic Sulfone 18

Sulfone **18** was prepared from sulfide **28** (75 mg, 0.39 mmol) in a manner identical to that described for sulfone **17**. The title compound was isolated as a white solid (76 mg, 87%); **mp**: 135 °C; **^{1}H-NMR** (500 MHz, $CDCl_3$) δ: 1.35 - 1.45 (m, 1H), 1.50 - 1.61 (m, 1H), 1.68 - 1.80 (m, 1H), 1.95 - 2.05 (m, 1H), 2.15 - 2.25 (m, 1H), 2.38 - 2.48 (m, 1H), 2.70 - 2.85 (m, 1H), 4.27 (dd, 1H, *J* = 12.0, 2.0 Hz), 4.32 (d, 1H, *J* = 15.9 Hz), 4.36 (d, 1H, *J* = 15.9 Hz), 7.06 (d, 1H, *J* = 7.5 Hz), 7.09 (d, 1H, *J* = 7.5 Hz), 7.18 (t, 1H, *J* = 7.5 Hz) ppm; **^{13}C-NMR** (125 MHz, $CDCl_3$) δ: 27.4, 27.8, 29.6, 35.9, 56.3, 67.0, 123.3, 128.5, 129.0, 129.2, 136.7, 141.6 ppm; **IR** (CH_2Cl_2): 1312, 1118 cm^{-1}; **CI-MS** m/z (%): 223 (($M^{\bullet+}$+1) 100); **HRMS** for $C_{12}H_{14}$ ($M^{\bullet+}$-SO_2) Calcd: 158.10955; Found: 158.11004.

General procedure for the thermolysis of sulfones and trapping with DMAD.

One equivalent of sulfone **17** or **18** and five equivalents of DMAD were combined in a small round bottom flask, left open to the air, and heated with a sand bath to 250 - 280 °C for 15 minutes (sulfone **17**) or at 300 - 320 °C for 20 minutes (sulfone **18**). The reaction mixtures were then cooled to room temperature, and applied to a column of silica gel. Elution with 5:1 hexanes/ethyl acetate afforded compounds **42** and **44** that were identical to those prepared via another route.[23]

1-(*p*-Methoxybenzylthio)-4-hydroxymethyl-indane (31).

The title compound was prepared in a manner identical to that described for the preparation of **22b**. In this way, diol **29** (250 mg, 1.52 mmol) was converted into hydroxy sulfide **31** (375 mg, 82%), which was isolated as a white solid after purification via column chromatography (5:1 hexanes/ethyl acetate); **mp**: 130 °C; **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 2.20 - 2.40 (m, 2H), 2.70 - 2.90 (m, 2H), 3.05 - 3.25 (m, 1H), 3.70 (d, 1H, *J* = 12.5 Hz), 3.72 (d, 1H, *J* = 12.5 Hz), 3.78 (s, 3H), 4.30 (d, 1H, *J* = 12.0 Hz), 4.50 (d, 1H, *J* = 12.0 Hz), 4.63 (dd, 1H, *J* = 12.0, 2.0 Hz), 6.83 (d, 2H, *J* = 7.5 Hz), 7.10 - 7.30 (m, 5H) ppm.; **CA** Calc. for $C_{18}H_{20}SO_2$: C (71.97), H (6.72); Found: C (71.80), H (6.82).

Lactone 34

Isolated as a white solid, **mp**: 130 °C (lit.[17] 131.4 °C); **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.20 -1.50 (m, 1H), 1.80 - 2.00 (m, 1H), 2.10 - 2.30 (m, 1H), 2.40 - 2.60 (m, 1H), 2.70 - 2.80 (m, 1H), 3.00 - 3.15 (m, 1H), 5.20 (dd, *J* = 12.5, 5.5 Hz, 1H), 7.30 - 7.50 (m, 2H), 7.65 (d, *J* = 8.0 Hz, 1H) ppm.

Tricyclic Ether 39

Obtained as a clear oil; **^{1}H-NMR** (200 MHz, $CDCl_3$) δ: 1.30 -1.80 (m, 4H), 2.00 - 2.20 (m, 2H), 2.70 - 2.90 (m, 2H), 5.05 - 5.20 (m, 3H), 7.10 - 7.30 (m, 3H) ppm; **^{13}C-NMR** (50 MHz, $CDCl_3$) δ: 27.3, 28.2, 35.6, 36.2, 73.1, 86.0, 118.4, 127.2, 127.4, 137.3, 138.6, 142.2 ppm; **EI-MS** m/z (%): 174 ($M^{\bullet+}$, 100), 173 (76), 145 (85), 131 (49), 104 (36); **HRMS** for $C_{12}H_{14}O$ Calcd: 174.10447; Found: 174.10325.

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