Synthesis and Diels–Alder Reactions of Thioisobenzofurans

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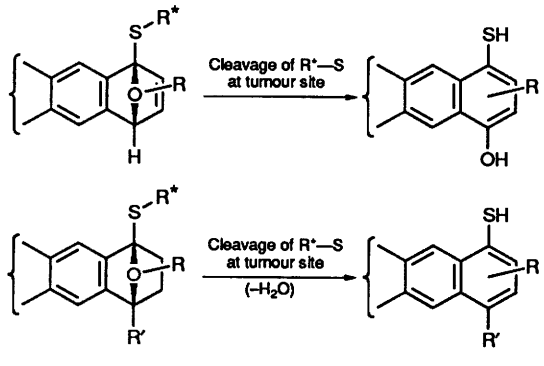
Anions prepared by deprotonation of benzofused thionolactones reacted with alkylating agents preferentially on sulfur. The resulting isobenzofurans underwent Diels–Alder reactions with dienophiles. This chemistry was developed as a one-pot procedure for the synthesis of bridged precursors of polycyclic aromatic compounds. The structure of one of the adducts, dimethyl 9-*exo*-10-*endo*-1-methylsulfanyl-8-phenyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6-triene-9,10-dicarboxylate **5a**, was determined by single-crystal X-ray diffraction. The versatility of this approach was extended by lithiation of the intermediate anion whereby alkylation introduced a further substituent on the aromatic nucleus. This methodology may be appropriate for the synthesis of anti-tumour prodrugs.

Isobenzofurans are highly reactive dienes for Diels–Alder reactions.[1] This reactivity has been exploited in the synthesis of biologically active polycyclic aromatic compounds. In these approaches the oxygen bridge in the initial Diels–Alder adducts is cleaved to reveal an aromatic ring. Appropriately functionalised polycyclic aromatic compounds have anti-tumour activity by virtue of their ability to intercalate between adjacent heterocyclic bases of DNA.[2] By contrast, non-planar precursors to such molecules are likely to exhibit low affinity for DNA. This allows us to think of isobenzofuran-derived Diels–Alder adducts as low cytotoxicity precursors, 'prodrugs', of intercalating agents. The activation of such adducts selectively at a tumour site might form the basis of anti-cancer chemotherapies with reduced side effects. Prodrug activation strategies have been pursued with increasing vigour in recent times.[3] Since thiol groups can be released from appropriately substituted precursors at tumours (*e.g.*, by bioreduction[4] or by antibody-directed enzyme catalysis[5]) we targeted isobenzofuran Diels–Alder adducts with bridgehead sulfide groups as potential anti-tumour prodrugs where cleavage of a sulfide linkage can lead to aromatisation of the oxanorbornyl ring system (Scheme 1). We here report a synthetic route to molecules of this type.



Scheme 1

Results and Discussion

Our approach to the synthesis of sulfide-substituted isobenzofurans paralleled the route to silyloxyisobenzofurans pioneered by Iwao *et al.*[6] This strategy involved alkylation on the sulfur atoms of anions prepared by deprotonation of thionophthalides. Trapping of the resulting isobenzofurans with dienophiles gave rise to the desired Diels–Alder adducts.

Lactones **1a** and **1b** were refluxed in toluene with Lawesson's reagent.[7] The yellow crystalline thionolactones **2a** and **2b** were formed in 80% yield or greater. These thionolactones were deprotonated with stoichiometric amounts of lithium diisopropylamide (LDA) or lithium hexamethyldisilazide (LHMDS), and were alkylated with either iodomethane or dimethyl sulfate in tetrahydrofuran (THF). No attempt was made to isolate the methylsulfanylisobenzofurans **3a** and **3b**, the presumed alkylation products; instead the reaction mixture was treated directly with a solution of excess of dienophile, such as dimethyl fumarate, dimethyl acetylenedicarboxylate or *N*-phenylmaleimide. In all cases the desired Diels–Alder adducts were isolated in reasonable yield (30–75%) from this one-pot procedure (Scheme 2).

When dimethyl fumarate was employed as the dienophile, mixtures of diastereoisomeric products arose in an approximately four-to-one ratio. In the phenyl series the stereochemistry of the major diastereoisomer **5a** was determined by X-ray crystallography. A similar stereoselectivity was observed in the reactions of dimethyl fumarate with unsubstituted isobenzofuran **3b**. The stereochemistry of the adducts **5b** and **6b** generated in the latter reaction was assigned on the basis of the coupling observed to the bridgehead hydrogen in the ^{1}H NMR spectra (coupling being observed between the bridgehead hydrogen and a neighbouring *exo*-hydrogen in compound **6b** but not for the diastereoisomer **5b**[8]).

The reactions of dimethyl acetylenedicarboxylate with isobenzofurans **3a** and **3b** led to the expected Diels–Alder adducts **4a** and **4b**. In addition a further product was isolated. This was the Michael adduct **8**, corresponding to addition of diisopropylamine to an excess of dienophile.

When *N*-phenylmaleimide reacted with the isobenzofuran **3a** a single product, *cis*-compound **7a**, was obtained. The *endo* stereochemistry of this product was confirmed by X-ray crystallography.[9]

The scope of the one-pot deprotonation–alkylation–cycloaddition procedure was extended by exploiting the known propensity[10] of isobenzofurans to undergo lithiation on treatment with LDA. Treatment of thionolactone **2b** with two mole equivalents of LDA followed by methylation and trapping with dienophile gave rise to *C*-methylated methylsulfanyl Diels–Alder adducts **4c** (from dimethyl acetylenedicarboxylate), and **5c** and **6c** (from dimethyl fumarate). These adducts correspond

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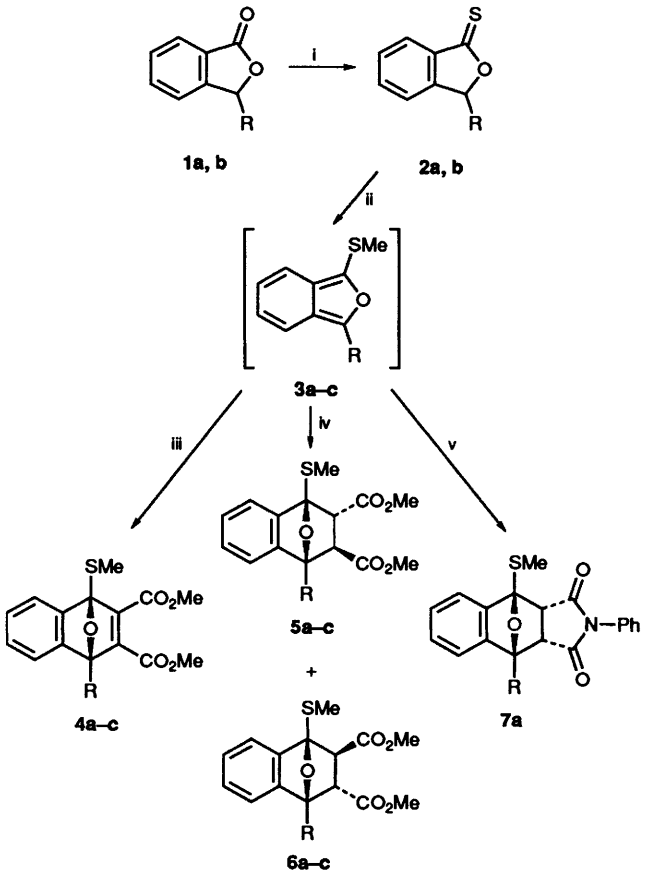
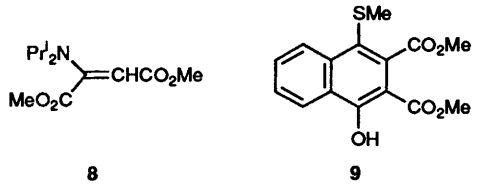


Scheme 2 *Reagents:* i, $(ArPS_2)_2$; ii, $LiNR'_2$, MeX; iii, $MeO_2CC{\equiv}C\text{-}CO_2Me$; iv, (*E*)-$MeO_2CCH{=}CHCO_2Me$; v, *N*-phenylmaleimide



to Diels–Alder trapping of the isobenzofuran **3c**. The stereoselectivity of the Diels–Alder reaction of the isobenzofuran **3c** with dimethyl fumarate was similar to that of compounds **3a** and **3b** and the stereochemistry of adducts **5c** and **6c** was assigned by analogy. Evidently, lithiation of the sulfur-substituted isobenzofuran nucleus occurs sufficiently readily that dianions can be generated under mild conditions.

Whilst the Diels–Alder adducts were stable and could be isolated and handled in a conventional fashion, in some cases decomposition, involving cleavage of the bridgehead, was observed on extended storage. This is an acid-catalysed process and could be accelerated by treatment with organic acids or silica. The Diels–Alder adducts could be readily distinguished from isomeric decomposition products by mass spectrometry since only the former exhibited strong ions corresponding to retro-Diels–Alder fragmentation. As an example, decomposition of adduct **4b** led to naphthalene derivative **9** in a process which mimics the proposed prodrug activation process. Although this modest chemical instability might provide a challenge to the development of pharmaceutically relevant prodrugs it provides support for the validity of this approach to bridged Diels–Alder adducts as prodrug precursors to polycyclic intercalating compounds, and appropriately substituted isobenzofurans are under study for this purpose.

Experimental

Mps were measured on a Reichert Hotstage microscope, or on a Stuart Scientific SMP1 block, and are uncorrected. ^1H NMR spectra were recorded on a Varian Unity instrument at 300 MHz, for solutions in [^2H]chloroform referenced to residual chloroform; or on a Brüker AM500 at 500 MHz for solutions in [$^2H_6$]benzene where stated. *J*-Values are given in Hz. ^{13}C NMR spectra were recorded on a Gemini 200 or Brüker AC200 instrument at 50.3 MHz for solutions in [^2H]chloroform. Unless stated, mass spectra were generated by electron impact on a Kratos MS80RFA spectrometer operating at 4 kV accelerating voltage; where specified, chemical ionisation with ammonia (CI) was employed using a V.G. Masslab 20–250. IR spectra were determined on a Perkin-Elmer 1600 FTIR spectrophotometer. Solvents were purified by routine means; THF was dried by distillation from sodium prior to use. Moisture-sensitive reactions were performed under dry nitrogen. Radial chromatography was performed on a chromatotron using a 4 mm silica plate and an elution gradient of 100% light petroleum (distillation range 50–70 °C) to 100% diethyl ether followed by washing of the plate with methanol; the eluent for flash chromatography was a 4:1 mixture of light petroleum (distillation range 30–40 °C) and ethyl acetate.

General Method for the Preparation of Thionolactones.—A solution of lactone in toluene was refluxed with Lawesson's reagent (0.5 mol/mol lactone) for *ca.* 17 h during which time the reaction solution deepened in colour. Toluene was removed under reduced pressure and the residue was taken up in a volume of diethyl ether comparable to the original volume of toluene. Small amounts of unchanged Lawesson's reagent precipitated first and then the desired thionolactone crystallised from the ethereal solution. Further thionolactone was obtained by chromatography of the supernatant.

3-Phenyl-1,3-dihydroisobenzofuran-1-thione **2a**, obtained in 65% yield [from lactone (4.8 mmol) in toluene (100 cm^3)], crystallised as fine yellow plate crystals, mp 97–99 °C (Found: C, 74.2; H, 4.35. $C_{14}H_{10}OS$ requires C, 74.3; H, 4.45%); δ_H 6.65 (1 H, s, OCH), 7.25–7.29 (2 H, m, ArH), 7.34 (1 H, dd, *J* 1 and 7.5, ArH), 7.38 (1 H, d, ArH), 7.40 (1 H, t, ArH), 7.55 (1 H, t, *J* 7.5, ArH), 7.67 (1 H, dt, *J* 1 and 7.5, ArH) and 8.11 (1 H, d, *J* 7.5, HC=CCO); δ_C 91.43, 122.59, 126.96, 127.68, 129.29, 129.81, 129.91, 134.32, 135.48 and 147.78; ν_{max}(KBr)/cm^{-1} 3030w (C–H), 1316, 1264, 1164 and 1099; *m/z* 226 (M^+, 100%. Found: M^+, 226.0445. $C_{14}H_{10}O^{32}S$ requires M, 226.0452), 197 (M – HCO^+, 35%. Found: *m/z* 197.0425. $C_{13}H_9S$ requires *m/z* 197.0425), 193 (M – SH^+, 23%. Found: *m/z* 193.0640. $C_{14}H_9O$ requires *m/z* 193.0654).

1,3-Dihydroisobenzofuran-1-thione **2b** was obtained in 89% yield [from lactone (5 mmol) in toluene (100 cm^3)] and recrystallised from diethyl ether as large yellow needles, mp 106–109 °C; δ_H 5.59 (2 H, s, OCH_2), 7.50–7.52 (2 H, m, ArH), 7.70 (1 H, t, *J* 8, ArH) and 8.07 (1 H, d, *J* 8, ArH); δ_C 121.61, 126.71, 126.87, 129.35, 134.03, 136.81 and 144.91; ν_{max}(KBr)/cm^{-1} 2958w (C–H), 1315, 1275, 1165, 1095 and 769; *m/z* 150 (M^+, 100%. Found: M^+, 150.0139. $C_8H_6O^{32}S$ requires M, 150.0139), 121 (M – CHO^+, 85%. Found: *m/z*, 121.0138. $C_7H_5{}^{32}S$ requires *m/z* 121.0112), 89 (M – $CHOS^+$, 18%. Found: *m/z* 89.0408. C_7H_5 requires *m/z* 89.0391).

General Method for the Preparation of 2-(Methylsulfanyl)-isobenzofurans and Trapping with Dienophiles.—A solution of thionolactone **2** in THF was added to an equal volume of a

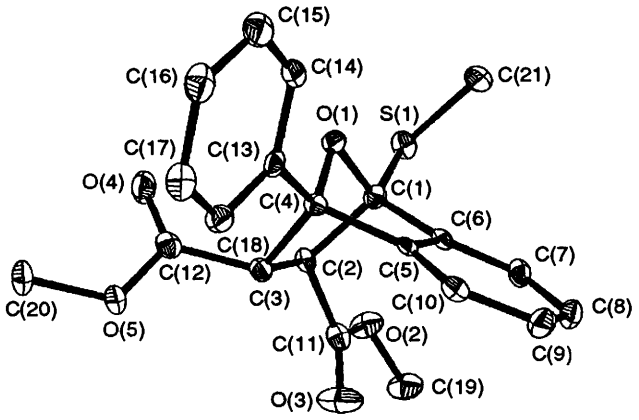


Fig. 1 The atom labels on the crystal structure differ from the numbering scheme used in the naming of compound **5a**. The relationship between the numbering schemes is as follows:

X-ray	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10 O-1
Name	C-1	C-10	C-9	C-8	C-7	C-2	C-3	C-4	C-5	C-6 O-11

cooled (−78 °C), stirred solution (~0.1 mol dm^{-3}) of LDA (or LHMDS where stated) (~1.2–1.5 mol equiv. unless stated) in THF, thereby producing a deep red solution. Approximately 1 h later a slight excess of methylating agent (iodomethane unless stated) was added dropwise. The solution was allowed to warm to room temperature during 2 h and then a solution (~1 mol dm^{-3}) of dienophile (2 mol equiv.) in THF was added. Two hours later the solvent was removed under reduced pressure and the residue was partitioned between water and ethyl acetate. The product was isolated by radial chromatography or, in some instances, by flash chromatography.

Reaction of thione **2a** (0.35 mmol) with dimethyl acetylenedicarboxylate as dienophile gave dimethyl 1-methylsulfanyl-8-phenyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraene-9,10-dicarboxylate **4a** as a yellow oil in 43% yield; δ_H 2.32 (3 H, s, SMe), 3.65 (3 H, s, CO_2Me), 3.78 (3 H, s, CO_2Me), 7.10–7.18 (2 H, m, ArH), 7.42–7.52 (5 H, m, ArH), 7.65 (1 H, d, ArH) and 7.72 (1 H, d, ArH); *m/z* 382 (M^+, 9%. Found: M^+, 382.0884. $C_{21}H_{18}O_5{}^{32}S$ requires M, 382.0875), 320 (35) 233 (51), 189 (50) and 105 (100).

Dimethyl 2-(diisopropylamino)butenedioate **8** was isolated as a yellow semi-crystalline side-product from the Diels–Alder reaction; mp 75–87 °C; δ_H 1.29 (12 H, d, *J* 6.9, $CHMe_2$) 3.60–3.69 (2 H, m, $CHMe_2$), 3.62 (3 H, s, CO_2Me), 3.92 (3 H, s, CO_2Me) and 4.77 (1 H, s, HC=); ν_{max}(KBr)/cm^{-1} 2981 (CH), 1693 (C=O), 1560 and 1131; *m/z* 243 (M^+, 54%. Found: M^+, 243.1468. $C_{12}H_{21}NO_4$ requires M, 243.1471), 228 (M − $CH_3{}^+$, 72%. Found: *m/z* 228.1249. $C_{11}H_{18}NO_4$ requires *m/z* 228.1236), 154 (83%. Found: *m/z* 154.0512. $C_7H_8NO_3$ requires *m/z* 154.0504) and 100 (100%. Found: *m/z* 100.0413. $C_4H_6NO_2$ requires *m/z* 100.0399).

Reaction of compound **2a** (2.65 mmol) with dimethyl fumarate as dienophile gave a ~4:1 ratio of dimethyl 9-*exo*-10-*endo*-1-methylsulfanyl-8-phenyl-11-oxatricyclo[6.2.1.$0^{2,7}$]-undeca-2,4,6-triene-9,10-dicarboxylate **5a** and dimethyl 9-*endo*-10-*exo*-1-methylsulfanyl-8-phenyl-11-oxatricyclo[6.2.1.$0^{2,7}$]-undeca-2,4,6-9,10-dicarboxylate **6a** as an oil in 70% combined yield. Recrystallisation of samples of the major stereoisomer, obtained by chromatography, from methanol, gave very clear chunky crystals of compound **5a**, mp 125–128 °C (Found: C, 65.8; H, 5.2. $C_{21}H_{20}O_5S$ requires C, 65.6; H, 5.24%); δ_H 500 MHz; C_6D_6) 2.18 (3 H, s, SMe), 3.04 (3 H, s, CO_2Me), 3.23 (3 H, s, CO_2Me), 3.93 (1 H, d, *J* 4.4, $CHCO_2Me$), 4.40 (1 H, d, *J* 4.4, $CHCO_2Me$), 6.97 (1 H, dt, *J* 0.8 and 7.5, ArH), 7.06 (1 H, dt, *J* 0.8 and 7.5, ArH), 7.10 (1 H, d, *J* 7.4, ArH), 7.16 (1 H, m, ArH), 7.2–7.25 (2 H, m, ArH), 7.37 (1 H, d, *J* 7.4) and 7.70 (2 H, m, ArH); δ_C 12.39, 51.88, 52.31, 55.53, 55.85, 90.53, 94.76, 119.29, 121.12, 125.97, 127.83, 128.24, 128.36, 128.49, 134.68, 141.56, 146.90, 169.65 and 171.74; ν_{max}(KBr)/cm^{-1} 2952 (CH), 1741 (C=O), 1435, 1307, 1225 and 761; *m/z* 353 (M − CH_3O^+, 15%), 240 (100) and 225 (95).

Crystal Data of Compound **5a**.—Mp 125–128 °C, $C_{21}H_{20}O_5S$, *M* = 384.4. Monoclinic, *a* = 12.417(2), *b* = 9.203(2), *c* = 16.714(3) Å, *β* = 102.46(3)°, *V* = 1865.0(6) $Å^3$ (by least-squares refinement on diffractometer angles for 20 automatically centred reflections, *λ* = 0.710 73 Å), space group $P2_1/c$, (No. 14), *Z* = 4, D_x = 1.369 g cm^{-3}. Tablets. Crystal dimensions: 0.78 × 0.40 × 0.21 mm^3, *μ*(Mo-K*α*) = 0.203 mm^{-1}.

Data collection and processing. Siemens P4 diffractometer operated at −143 °C, *ω* scans width 1°; speed variable, graphite-monochromated Mo-K*α* radiation; 2887 reflections measured 2.5 ⩽ *θ* ⩽ 25.0, +*h*, +*k*, ±*l*), 2726 unique [merging *R* = 0.022 after absorption correction (max., min. transmission factors = 0.98, 0.88)] giving 2280 with $I > 2\sigma(I)$.

Structure analysis and refinement. Direct methods followed by full-matrix least-squares refinement based on F^2 with all non-hydrogen atoms anisotropic and hydrogen atoms in calculated positions with *U* isotropic temperature factors set at 1.2 times attached carbon atoms. The final wR_2-value (based on F^2 for all 2726 data) was 0.093 with a corresponding conventional *R*-value (based on *F*) of 0.040. Structure solution was effected using SHELXS-86.[11] Refinement and calculation of all tabulated data was by way of SHELXL-93.[12] The molecular structure is presented in Fig. 1.†

The minor diastereoisomer **6a**, admixed with some of the major isomer, showed δ_H 2.14 (3 H, s, Me), 3.31 (1 H, d, *J* 4.0, $CHCO_2Me$), 3.46 (3 H, s, CO_2Me), 3.84 (3 H, s, CO_2Me), 4.47 (1 H, d, *J* 4.0, $CHCO_2Me$), 7.15 (1 H, dd, *J* 1 and 7.5, ArH), 7.25 (2 H, m, ArH), 7.4–7.5 (4 H, m, ArH), 7.78 (1 H, m, ArH) and 7.79 (1 H, m, ArH).

Reaction of compound **2b** (0.37 mmol) with 0.95 mol equiv. of LDA as base, dimethyl sulfate as alkylating agent and dimethyl acetylenedicarboxylate as dienophile gave dimethyl methylsulfanyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraene-9,10-dicarboxylate **4b** as a yellow oil in 32% yield; δ_H 2.31 (3 H, s, SMe), 3.84 (3 H, s, CO_2Me), 3.77 (3 H, s, CO_2Me, 5.98 (1 H, s, OCH), 7.10–7.16 (2 H, m, ArH) and 7.36–7.41 (2 H, m, ArH); *m/z* 306 (M^+, 100%. Found: M^+, 306.0571. $C_{15}H_{14}O_5S$ requires M, 306.0562) and 164 (96%. Found: *m/z* 164.0311. C_9H_8OS requires *m/z* 164.0296).

Reaction of compound **2b** (0.37 mmol) with 0.95 mol equiv. of LDA as base, dimethyl sulfate as alkylating agent and dimethyl fumarate as dienophile gave a mixture of dimethyl 9-*exo*-10-*endo*-1-methylsulfanyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6-triene-9,10-dicarboxylate **5b** and dimethyl 9-*endo*-10-*exo*-1-methylsulfanyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6-triene-9,10-dicarboxylate **6b** in 75% yield. A sample of the major diastereoisomer, **5b**, was obtained pure as a yellow oil; δ_H 2.22 (3 H, s, Me), 3.20 (1 H, d, *J* 4, CH), 3.55 (3 H, s, CO_2Me), 3.81 (3 H, s, CO_2Me), 3.81 (1 H, d, *J* 4, CH), 5.68 (1 H, s, OCH) and 7.2–7.4 (4 H, m, ArH); *m/z* 308 (M^+, 2%. Found: M^+, 308.0727. $C_{15}H_{16}O_5{}^{32}S$ requires M, 308.0718) and 164 (100).

The remaining product was a mixture of both isomers. The minor isomer **6b** showed δ_H 2.09 (3 H, s, SMe), 3.11 (1 H, d, *J* 4.5, CH), 3.53 (3 H, s, CO_2Me), 3.83 (3 H, s, CO_2Me), 4.16 (1 H, t, *J* 4.5, CH), 5.61 (1 H, d, *J* 4.5, OCH) and 7.2–7.4 (4 H, m, ArH).

Reaction of compound **2a** (1.0 mmol) with LHMDS as base and *N*-phenylmaleimide as dienophile gave 9-*endo*,10-

† *Supplementary publication:* tables of atomic coordinates and bond lengths and angles have been deposited with the Cambridge Crystallographic Data Centre. For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1995, Issue 1.

endo-1-methylsulfanyl-8,11-diphenyl-11-aza-14-oxatetracyclo-[6.5.1.$0^{2,7}0^{9,13}$]tetradeca-2,4,6-triene-10,12-dione **7a** in 73% yield. Recrystallisation from chloroform–light petroleum gave crystals, mp 202–205 °C (Found: C, 72.2; H, 4.9; N, 3.55. $C_{25}H_{19}NO_3S$ requires C, 72.6; H, 4.6; N, 3.4%); δ_H 2.36 (3 H, s, SMe), 3.95 [1 H, d (of ABq), *J* 8.4, CHCO], 4.16 [1 H, d (of ABq), *J* 8.4, CHCO], 6.47 (2 H, m, ArH), 7.05 (1 H, d, *J* 7.3, ArH), 7.2–7.5 (9 H, m, ArH) and 7.97 (2 H, dd, *J* 7.3 and 8.0, ArH); δ_C 12.49, 54.15, 54.58, 90.51, 94.61, 121.25, 121.47, 126.27, 127.01, 128.50, 128.61, 128.70, 128.78, 128.89, 130.94, 135.84, 139.96, 144.68, 171.52 and 172.96; $\nu_{max}(CHCl_3)/cm^{-1}$ 1755, 1700, 1562, 1500 and 1381; *m/z* (CI) 414 (MH^+, 100%) and 241 (90).

Reaction of compound **2b** (0.55 mmol) with 2 mol equiv. of LDA as base and dimethyl acetylenedicarboxylate as dienophile gave a mixture of dimethyl 1-methyl-8-methylsulfanyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraene-9,10-dicarboxylate **4c** and dimethyl 1-methylsulfanyl-11-oxatricyclo-[6.2.1.$0^{2,7}$]undeca-2,4,6,9-tetraene-9,10-dicarboxylate **4b** in 31% yield. The former crystallised as microcrystals, mp 95–97 °C; δ_H 2.03 (3 H, s, CMe), 2.31 (3 H, s, SMe), 3.75 (3 H, s, CO_2Me), 3.80 (3 H, s, CO_2Me), 7.10–7.12 (2 H, m, ArH) and 7.29–7.36 (2 H, m, ArH); ν_{max}(KBr)/cm^{-1} 2953 (C–H), 1720 (C=O), 1384 and 1265; *m/z* 320 (M^+, 33%. Found: M^+, 320.0721. $C_{16}H_{16}O_5{}^{32}S$ requires M, 320.0718), 178.0434 (100%. Found: *m/z* 178.0434. $C_{10}H_{10}O^{32}S$ requires *m/z* 178.0452).

Reaction of compound **2b** (0.57 mmol) with 2 mol equiv. of LDA as base and dimethyl fumarate as dienophile gave a mixture of dimethyl 9-*endo*-10-*exo*-1-methyl-8-methylsulfanyl-11-oxatricyclo[6.2.1.$0^{2,7}$]undeca-2,4-triene-6-9,10-dicarboxylate **5c** and dimethyl 9-*exo*-10-*endo*-1-methyl-8-methylsulfanyl-11-oxatricyclo (6.2.1.$0^{2,7}$]undeca-2,4,6-triene-9,10-dicarboxylate **6c**, isolated as a yellow oil in 68% yield. After repeated chromatography a pure sample of the major isomer **5c**, also an oil, was obtained; δ_H 2.05 (3 H, s, CMe), 2.09 (3 H, s, SMe), 3.22 (1 H, d, *J* 4.5, CH), 3.49 (3 H, s, CO_2Me), 3.78 (1 H, d, *J* 4.5, CH), 3.82 (3 H, s, CO_2Me) and 7.16–7.38 (4 H, m, ArH); *m/z* 291 ($M - CH_3O^+$, 5%. Found: *m/z* 291.0694. $C_{15}H_{15}O_4{}^{32}S$ requires *m/z* 291.0691) and 178 ($M - C_6H_8O_4{}^+$, 100%. Found: *m/z* 178.0450. $C_{10}H_{10}O^{32}S$ requires *m/z* 178.0453).

Adduct **6c**, admixed with its diastereoisomer **5c**, showed δ_H 1.79 (3 H, s, CMe), 2.28 (3 H, s, SMe), 3.09 (1 H, d, *J* 4.5, CH), 3.54 (3 H, s, CO_2Me), 3.80 (3 H, s, CO_2Me), 3.92 (1 H, d, *J* 4.5, CH) and 7.2–7.4 (4 H, m, ArH).

Adducts **5b** and **6b** were also isolated from the reaction with compound **2b** in 6% yield; their spectral data were identical with those of previously prepared samples.

Diels–Alder adduct **4b** underwent acid-catalysed decomposition to dimethyl 1-hydroxy-4-(methylsulfanyl)naphthalene-2,3-dicarboxylate **9**, a yellow oil; δ_H 2.31 (3 H, s, SMe), 3.76 (3 H, s, CO_2Me), 3.84 (3 H, s, CO_2Me), 7.63 (1 H, dt, *J* 1.5 and 7, ArH), 7.80 (1 H, t, *J* 7.5, ArH), 8.50 (1 H, d, *J* 8.5, ArH) and 8.59 (1 H, d, *J* 8.5, ArH); *m/z* 306 (M^+, 100%. Found: M^+, 306.0554. $C_{15}H_{14}O_5{}^{32}S$ requires M, 306.0562), 259 (28) and 115 (13).

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