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Dihydrothiophenes as Precursors to Fused Quinolines, Quinolones and Coumarins via *o*-Quinodimethane Intermediates[1]

Lindsay A. White and Richard C. Storr *

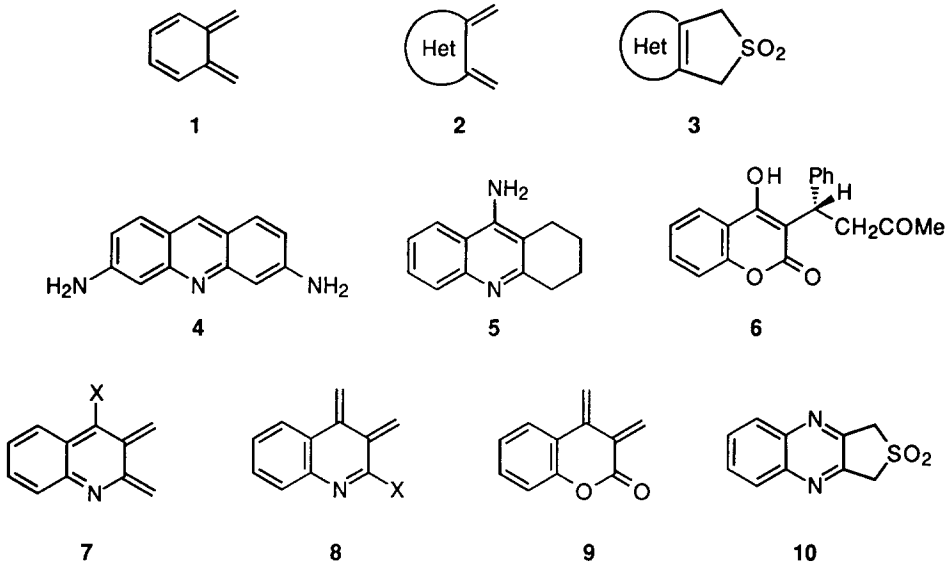
School of Chemistry, The University of Liverpool, P.O. Box 147, Liverpool L69 3BX, England

Abstract: *3-Methoxycarbonyl-4-keto-2,5-dihydrothiophene is a convenient starting point for synthesis of a range of 3,4- and 2,3-quinoline and quinolone and coumarin fused dihydrothiophene dioxides. With the exception of the 2,3-quinoline derivatives these all lose sulfur dioxide on thermolysis to give the corresponding o-quinodimethanes which can be intercepted in Diels-Alder reactions.*

INTRODUCTION

In the last three decades *o*-quinodimethane **1** and its derivatives have proved to be key intermediates in the synthesis of a wide range of organic compounds. Recently, interest has focussed on the development of routes to their heterocyclic analogues **2**.[2] A large number of these, especially those based on 5-membered heterocycles, are now known and their potential in synthesis is ripe for exploitation. Thermal extrusion of sulfur dioxide from heterocyclic-fused sulfolenes **3** is firmly established as an attractive and versatile method of generation of these heterocyclic quinodimethanes. The required sulfolenes are easily prepared, either by construction of the heterocycle onto a suitable, activated sulfolene or 2,5-dihydrothiophene, or by building the sulfolene ring onto the preformed heterocycle. The former method is preferable as it may allow the preparation of a wide range of heterocyclic systems from one common precursor. Further advantages of this cheletropic extrusion approach to quinodimethanes are that there are no limitations in scale, by-products are volatile, intermolecular trapping can be effected easily, and as a consequence of the acidity of the protons α to the sulfolene moiety, functionalisation of the exocyclic methylene groups can be readily achieved permitting *inter alia* intramolecular cycloaddition reactions.

In comparison with the 5-membered heterocyclic analogues of *o*-quinodimethane, the 6-membered systems have received less attention. In addition, most of the previous studies on the latter have been concerned with the methods of generation and few involve their synthetic applications. However, many biologically active compounds are polycyclic and based on 6-membered heterocycles. Particularly widespread are compounds incorporating the quinoline[3] and coumarin[4] nucleii, for example, the antibacterial agent Proflavine **4,** the acetylcholinesterase inhibitor Tacrine **5**, which is of interest in the treatment of Alzheimer's disease, and the anticoagulant Warfarin **6**. It, therefore, seemed timely to investigate the hitherto unknown coumarin **9** and quinoline 2,3- and 3,4-quinodimethanes **7** and **8** as precursors to such systems.



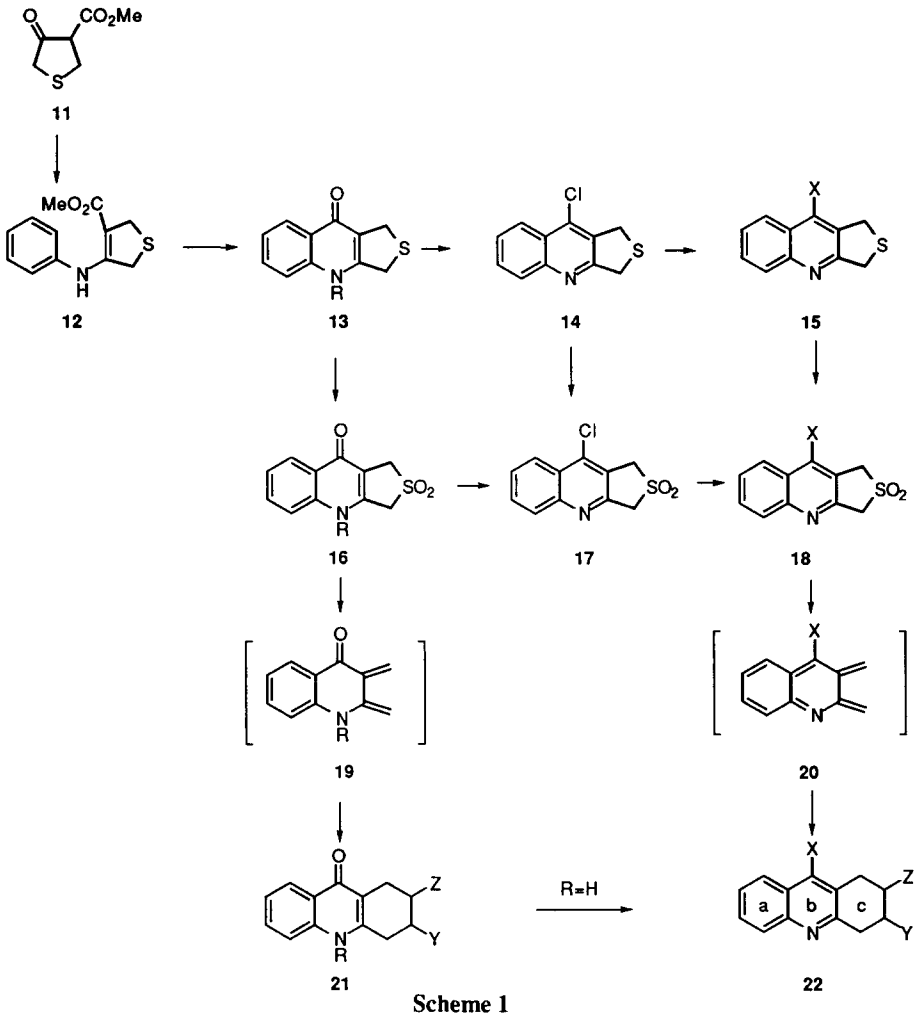
RESULTS AND DISCUSSION

Approach to 2,3-fused quinolines and quinolones

The basic strategy of our approach to the tetrahydroacridine nucleus **22** is outlined in Scheme 1. A key intermediate in this scheme is the known quinolone **13** (R=H) [8] which is obtained from the condensation of the keto ester **11** [6] and aniline. Use of other amines should allow the introduction of functionality into the 'a' ring of the final product. It was envisaged that conversion of **13** (R=H) to the chloro derivative **14** would open the way to a range of *o*-quinodimethane precursors **18** via nucleophilic displacement and oxidation. Functionalisation α to the sulfur of the sulfolene moiety via the derived carbanion and final Diels-Alder trapping of the thermally generated *o*-quinodimethane **20** provides for a variety of substituents in the 'c' ring. The success of this approach depends on the thermal extrusion of sulfur dioxide from the quinoline fused sulfolene **18**. In general, the ease of cheletropic extrusion of sulfur dioxide from 3-sulfolenes depends on the bond order of the sulfolene 3,4-bond; simple 3-sulfolenes (bond order 2) lose sulfur dioxide rapidly at 110°C whereas benzosulfolenes (bond order 1.5) require temperatures approaching 200°C. Bond fixation in the quinoline derivatives **18** further reduces the bond order and extrusion of sulfur dioxide might well be difficult. Indeed, extrusion of sulfur dioxide from the related quinoxolene-sulfolene **10** proved to be impractical.[7] With this in mind, the strategy was designed so as to offer an alternative route to the final targets **22** via the non aromatic quinolone sulfolenes **16** and quinodimethanes **19**.

The quinolone **13** (R=H) was synthesised from the readily available keto ester **11** by reaction with aniline to give the enamine **12** which was cyclised by heating in biphenyl at 300°C.[5] It is extremely insoluble in organic solvents due to intramolecular hydrogen bonding, and thus could simply be filtered from the reaction mixture. The chloroquinoline **14**, obtained by treatment of **13** with phosphorus oxychloride, lacks such hydrogen bonding and is much more soluble. Attempted sulfoxidation of **14** to the quinoline-fused

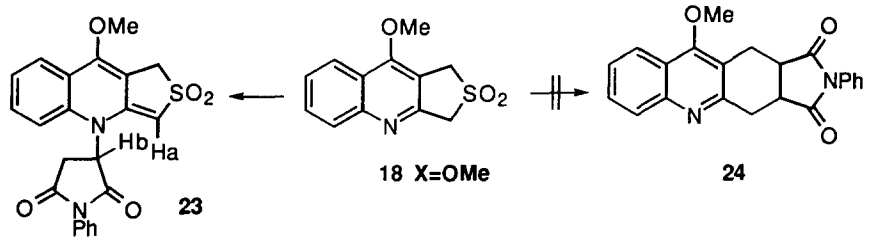
sulfolene **17** was unsuccessful but the latter was obtained by oxidation of **13** (R=H) to the corresponding sulfolene followed by reaction with phosphorus oxychloride. Nucleophilic displacement of the chloro substituent of **14** by treatment with sodium methoxide gave the 9-methoxy derivative **15** (X=OMe) which on oxidation with 2 mole equivalents of *m*CPBA yielded the quinoline-fused sulfolene **18** (X=OMe).



Scheme 1

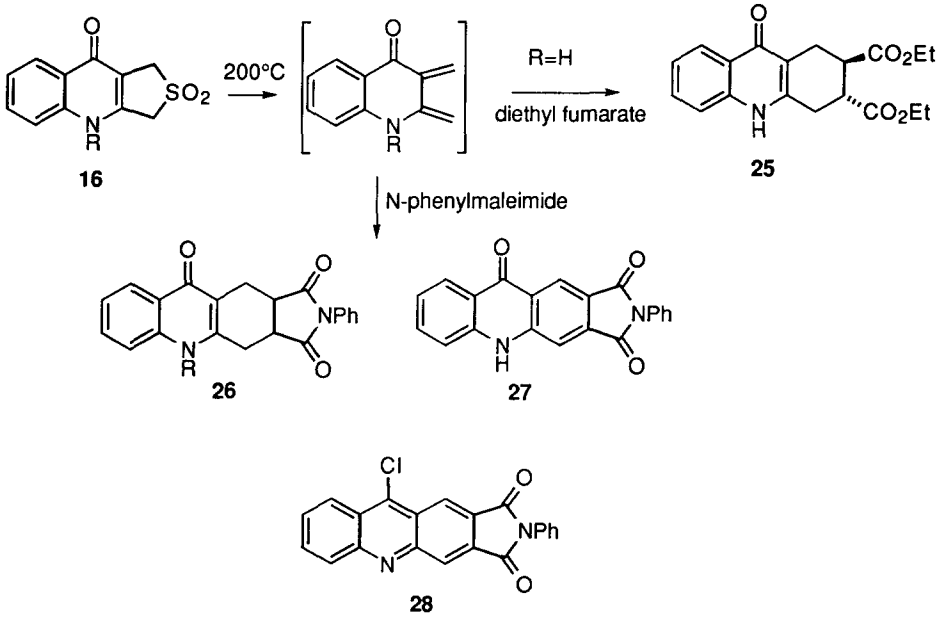
Attempts to extrude sulfur dioxide from these two quinoline fused sulfolenes **17** and **18** (X=OMe) confirmed our fears that the low C_3-C_4 bond order of the sulfolene rings would render such a process impractical. Thus heating of **17** in the presence of N-phenylmaleimide at temperatures up to 250°C led to decomposition and none of the expected *o*-quinodimethane adduct. The methoxyquinoline **18** (X=OMe), on heating at reflux in sulfolane in the presence of N-phenylmaleimide for 6 hours, gave a complex mixture from which a single product was isolated in low yield by chromatography. This was not the expected 1:1 Diels-

Alder adduct **24**, formed via an intermediate quinoline 2,3-quinodimethane, but a structure, assigned as **23**, in which sulfur dioxide was retained (Scheme 2).



Scheme 2

This adduct presumably arises from nucleophilic attack of the quinoline nitrogen on the electrophilic dienophile followed by loss of a proton. Spectral evidence strongly supports the structure **23**, in particular, the signals in the ^1H spectrum for the sulfolene CH_2 groups at δ 4.67 and δ 4.74 and the olefinic proton Ha at δ 5.25 ppm. Surprisingly, the olefinic proton Ha appeared as a doublet and the signal due to Hb on the maleimide ring was also more complex than expected, appearing as a doublet of doublets of doublets at δ 3.96 ppm. Examination of the coupling constants indicated that this unexpected splitting pattern was due to Ha/Hb coupling and this four-atom coupling was finally verified by a 400MHz COSY 2D spectrum.



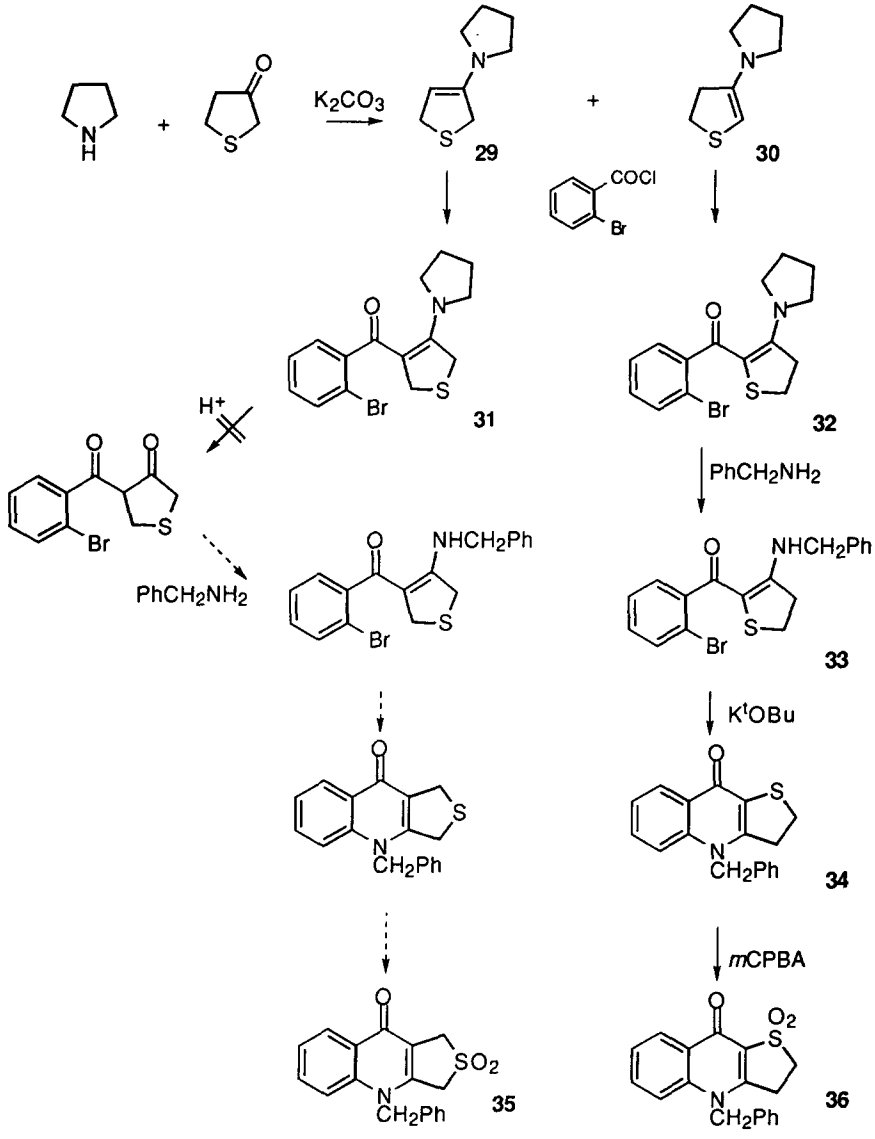
Scheme 3

This, not unexpected, failure to achieve extrusion of sulfur dioxide from the quinoline sulfolenes **17** and **18** (X=OMe) led us to consider quinolone sulfolenes as precursors to the quinolone quinodimethanes

which could serve as quinoline *o*-quinodimethane equivalents. Extrusion of sulfur dioxide from **16** (R=H) with its higher C_3-C_4 sulfolene bond order should occur at a much lower temperature than that required for **18**. Interception of the quinolone quinodimethane **19** (R=H) thus generated with dienophiles, and treatment of the resulting cycloadducts **21** (R=H) with phosphorus oxychloride, should give the desired quinoline nucleus **22** (Scheme 1).

Due to its extreme insolubility in organic solvents oxidation of quinolone **13** (R=H) was carried out using two equivalents of *m*CPBA in a large volume of methanol (Scheme 1). As a consequence of the insolubility of both the starting material and the product the reaction was monitored by ^{1}H nmr in hot d^6 DMSO. Typically, the reaction was complete within 24 hours. The quinolone-fused sulfolene **16** (R=H) was removed by filtration and washed with copious amounts of cold methanol in order to ensure complete removal of the residual benzoic acid. Thermolysis of **16** (R=H) in refluxing 1,2,4-trichlorobenzene for 3 hours in the presence of N-phenylmaleimide gave a solid product which was removed by filtration and washed with petroleum ether (Scheme 3). ^{1}H nmr analysis of this solid proved impossible due to its extreme insolubility but mass spectroscopy provided some evidence for the presence of the desired Diels-Alder adduct **26** (R=H) M^+344, and possibly some aromatised adduct **27** M^+340. In an attempt to overcome the insolubility of the cycloaddition products, the crude reaction mixture was treated with phosphorus oxychloride. The resulting product was much more soluble in organic solvents as a consequence of the removal of the free N-H, and thus could be purified by column chromatography. Analysis of the pure product showed it to be the fully aromatic chloro-derivative **28**, rather than the desired quinoline structure. The isolation of **28** does, however, confirm the predicted ease of generation of a quinolone 2,3-quinodimethane intermediate compared to the analogous quinoline system. Thermolysis of quinolone **16** (R=H) in tetramethylene sulfone containing diethyl fumarate yielded a solid product which was slightly more soluble than that obtained from the reaction with N-phenylmaleimide. ^{1}H nmr analysis was performed in hot $CDCl_3$ and confirmed formation of the desired Diels-Alder adduct **25**.

The N-methyl derivative **13**, (R=Me) obtained by methylation of **13** (R=H) with with MeI/K_2CO_3, is much more soluble and easily handled.[8] The site of methylation was unambiguously established by the difference of this compound from the isomeric O-methyl derivative previously prepared by displacement of chlorine in **14** by methoxide ion. Sulfoxidation of **13** (R=Me) with *m*CPBA gave the quinolone **16** (R=Me), which on thermolysis in 1,2,4-trichlorobenzene at 200^{o}C in the presence of N-phenylmaleimide gave the Diels-Alder adduct **26** (R=Me) (Scheme 3). Once again these conditions illustrate the relative ease of extrusion of sulfur dioxide from the quinolone system. These reactions involving an N-substituted quinolone 2,3-quinodimethane were more satisfactory than those of the parent system **16** (R=H) as the products were much more soluble and thus easily purified. However, in order for the quinolone system to serve as a synthetic equivalent to the quinoline nucleus, a removable N-protecting group on quinolone-fused sulfolene **16** (R=H) is required. Such a group will remove the problems of insolubility, permit generation of the quinodimethane, and on removal from the cycloadducts, will liberate a free N-H, so that treatment with phosphorus oxychloride, will allow quinoline formation. Unfortunately, treatment of quinolones **13** (R=H) and **16** (R=H) with a base, either sodium methoxide or sodium hydride, and benzyl bromide, *p*-methoxybenzyl chloride or (trimethylsilyl)ethoxymethyl chloride, gave the desired N-protected quinolones in only very poor yields. An alternative strategy for the preparation of N-protected quinolones was, therefore, devised as outlined in Scheme 4.

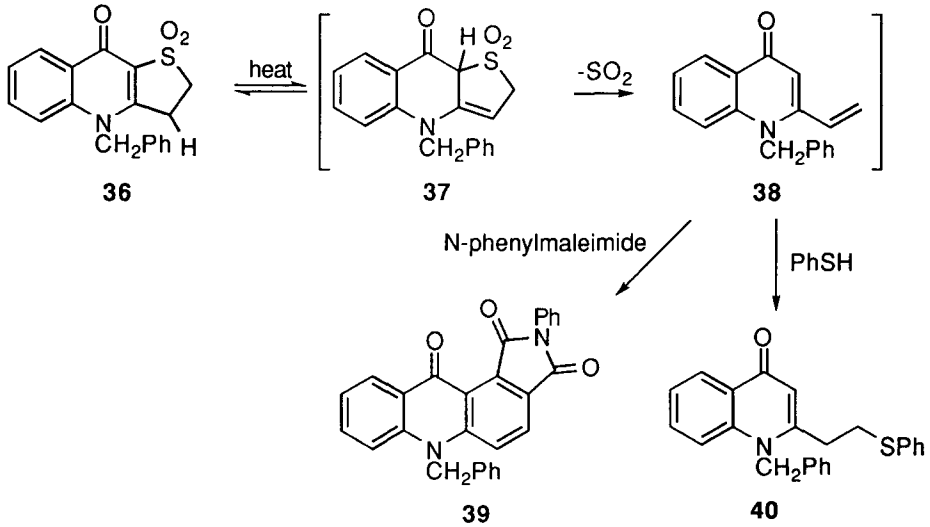


Scheme 4

Preparation of a 3:1 mixture of the known enamines **29** and **30** was achieved by reaction of distilled 3-ketotetrahydrothiophene with pyrrolidine in the presence of potassium carbonate.[9] The resulting mixture of enamines was unstable in air and so was treated directly with 2-bromobenzoyl chloride and triethylamine to give a mixture of acylated products **31** and **32** again in an approximate ratio of 3:1. This mixture of isomers was separated by careful column chromatography. The major isomer, assumed to be **31**, showed two clean triplets corresponding to the methylene groups in its ^{1}H nmr spectrum whilst in the minor isomer **32** these signals were coincident. The plan was to subject the major isomer to amine exchange with benzylamine

whereupon cyclisation via an aryne intermediate and oxidation would lead to the benzyl protected quinolone **35**. However, **31** was recovered unchanged after prolonged treatment with benzylamine in refluxing toluene containing a catalytic amount of *p*-toluenesulfonic acid in a Dean-Stark apparatus. The lack of reactivity of this enamide was further underlined by its failure to undergo hydrolysis even on refluxing with 70% sulfuric acid.

In contrast the minor isomer **32** underwent facile transamination with benzylamine to yield **33**. An explanation for this is that, in the addition-elimination reaction of this isomer, the negative charge produced is located α to the sulfur atom where it is known to be stabilised. In the case of **31** the negative charge is β to the sulfur atom which therefore cannot exert its full stabilisation effect. Treatment of **33** with potassium *tert*-butoxide in *tert*-butanol gave the desired quinolone **34** via a benzyne cyclisation reaction in good yield. Sulfoxidation of **34** to the sulfolene **36** was performed with 2 equivalents of *m*CPBA. This 2-sulfolene **36** was not expected to undergo thermal extrusion of sulfur dioxide as it lacks the necessary C_3-C_4 double bond. However, thermolysis of **36** at 214°C in the presence of N-phenylmaleimide did result in loss of sulfur dioxide and formation of a cycloadduct whose ^1H nmr spectrum consisted only of a benzylic CH_2 group and aromatic protons (Scheme 5). The structure of this cycloadduct was thus assigned as **39** and its formation may be explained by a 1,3-[H] tautomerisation in **36** under the reaction conditions to yield **37**. This can now lose sulfur dioxide by a cheletropic process to give the vinyl quinolone **38** which is intercepted in a Diels-Alder reaction to give an adduct which undergoes dehydrogenation. Further evidence that this is the case was gained on thermolysis of **36** in the presence of the nucleophilic trap, thiophenol. The ^1H nmr spectrum of the product formed showed a clean pair of triplets, each integrating for two protons, which can be assigned to two adjacent CH_2 groups, and a singlet integrating for one proton at δ 6.38 which can be assigned to a vinyl proton. From this evidence we conclude that nucleophilic addition to intermediate **38** had occurred resulting in the formation of **40**.

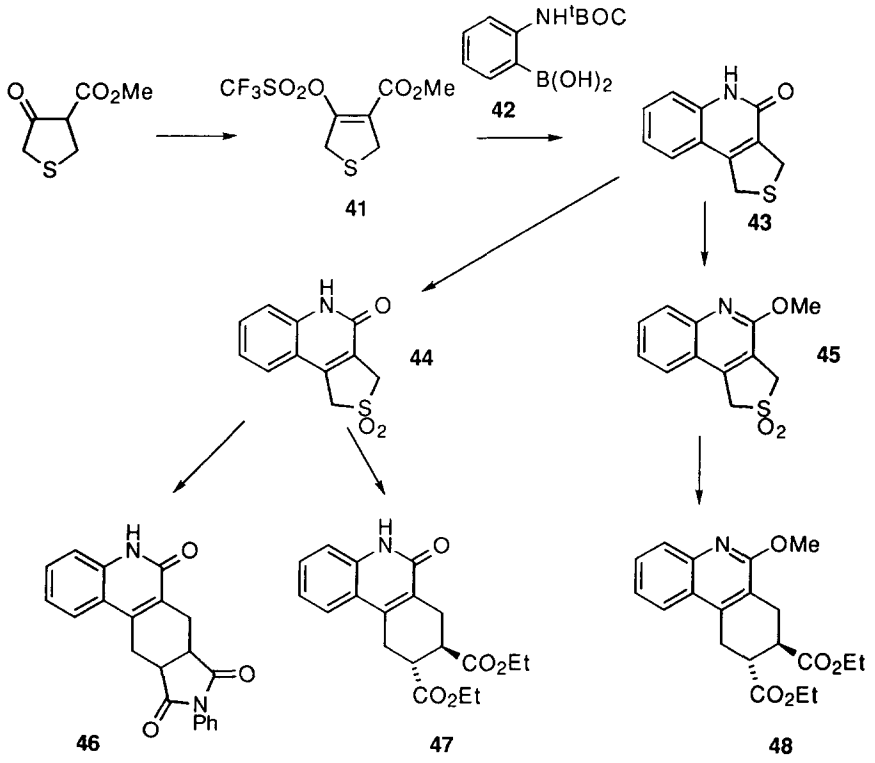


Scheme 5

This unexpected extrusion of sulfur dioxide from a heterocyclic-fused 2-sulfolene opens up a new route for the preparation of heterocyclic vinyl compounds and is worthy of further investigation. These experiments also establish that quinoline 2,3-quinodimethanes cannot be produced directly by extrusion of sulfur dioxide from the quinoline fused sulfolenes. However, quinolone analogues are easily generated providing ready access to fused quinolones and, in principle, with suitable manipulation might serve as synthetic equivalents for quinoline 2,3-quinodimethanes.

Approach to 3,4-fused quinolines and quinolones

Extrusion of sulfur dioxide from the quinoline 3,4-sulfolenes **8** should not present the same problems encountered with the 2,3-isomers in view of the higher C_3-C_4 bond order. Once again, the keto ester **11** is a convenient starting point for a route to quinoline and quinolone 3,4-quinodimethanes,[10] which allows for the introduction of a wide range of substituents (Scheme 6). The key synthetic step involves a Suzuki coupling reaction.



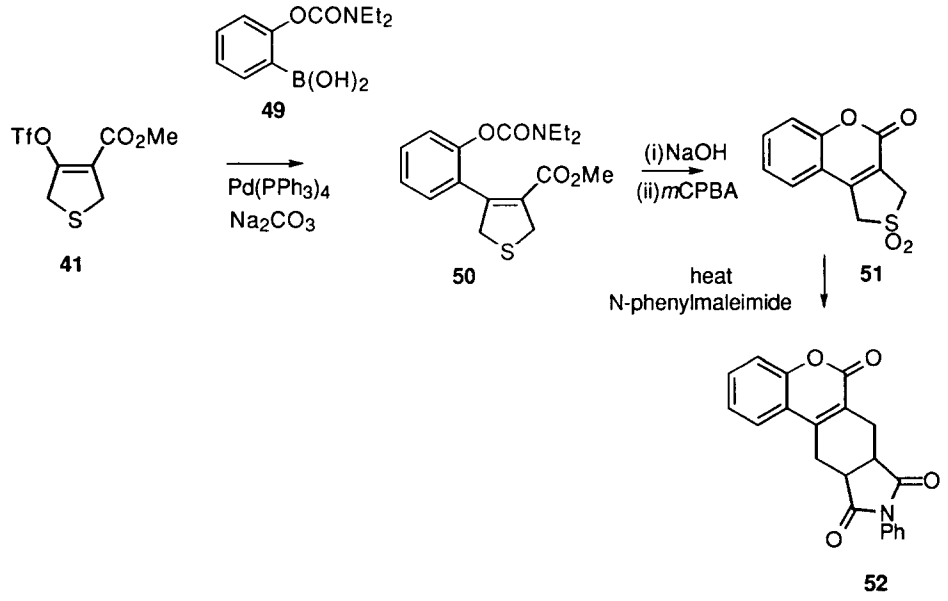
Scheme 6

Keto-ester **11** was converted to the relatively stable enol triflate **41** with triflic anhydride and Hunig's base.[11] Suzuki coupling of **41** with boronic acid **42** [12] gave the quinolone **43** in one pot since thermal deprotection of the *tert*-butoxycarbonyl group occurs *in situ*. Quinolone **43** was slightly more soluble than the analogous 2,3-system **13** (R=H) and on treatment with *m*CPBA yielded the quinolone-fused sulfolene **44**. As

expected, cheletropic extrusion of sulfur dioxide from **44** was readily achieved, and in the presence of the dienophiles N-phenylmaleimide and diethyl fumarate the Diels-Alder adducts **46** (70%) and **47** (79%) were produced respectively. Formation of the aromatic quinoline-fused sulfolene **45** was effected by sequential treatment of **43** with phosphorous oxychloride, sodium methoxide and *m*CPBA. As previously observed the quinolines were much more soluble in organic solvents than the quinolones. Thermolysis of **45** in refluxing 1,2,4-trichlorobenzene for 3 hours in the presence of diethyl fumarate gave the methoxyquinoline quinodimethane adduct **48** (64%). Thus, although direct generation of quinoline 2,3-quinodimethane was unsuccessful, the analogous 3,4-system could be generated with ease and intercepted in Diels-Alder reactions because of the higher degree of double bond character in the sulfolene precursor.

Approach to fused Coumarin derivatives

The Suzuki cross-coupling reaction strategy can be applied to the generation of the hitherto unknown coumarin 3,4-quinodimethane **9**. Thus the boronic acid **49** [14] was prepared by treatment of phenol, protected as the carbamate[13], with butyllithium and trimethylborate. This and the enol triflate **41** were then subjected to the palladium cross-coupling reaction conditions of Suzuki to yield **50** (Scheme 7). In contrast to the *tert*-butoxycarbonyl group, used in the preparation of the quinolone and quinoline 3,4-sulfolenes, the carbamate group is not heat sensitive. However, treatment of **50** with 2M sodium hydroxide in THF yielded a coumarin derivative *via* a deprotection-cyclisation sequence. Sulfoxidation of this cyclised compound with *m*CPBA gave **51** which on thermolysis in 1,2,4-trichlorobenzene for 1 hour gave the coumarin 3,4-quinodimethane derived adduct **52** (78%). Thus, keto-ester **11** and the Suzuki coupling reaction facilitate the preparation of a wide range of heterocyclic systems.



Scheme 7

In conclusion, routes to the quinoline, quinolone and coumarin 3,4-quinodimethanes and to the quinolone 2,3-quinodimethane systems from the corresponding sulfones have been established. Although the quinoline 2,3-quinodimethanes cannot be produced directly the 2,3-quinolone analogues serve as synthetic equivalents. The possibilities for functionalisation of the common dihydrothiophene precursor **11** or the sulfones **16, 44, 45** and **51**, the use of substituted anilines or boronic acids and the range of dienophiles offer considerable versatility for the synthesis of target heterocycles.

EXPERIMENTAL

General. ^{1}H and ^{13}C nmr spectra were recorded on a Bruker AC 200 spectrometer operating at 200 and 50.29 MHz respectively. Infra-red spectra were recorded in the range 4000 to 600 cm^{-1} using a Perkin-Elmer 298 instrument. Solid samples were run as Nujol mulls and liquids as thin films. Mass spectra were recorded on a VG Analytical 7070E or a Trio 1000 Quadrapole GC mass spectrometer. Microanalyses were performed in the University of Liverpool Department of Chemistry microanalytical laboratory. Melting points (m.p.) were determined on a Reichert hot stage apparatus and are uncorrected. Commercial *m*-chloroperbenzoic acid was purified (90%) by washing with a KH_2PO_4/Na_2HPO_4 buffer. Flash column chromatography was performed using Merck 9385 silica as the stationary phase.

1,3-Dihydro-4H-thieno[3,4-*b*]quinolin-9-one 2,2-dioxide (16, R=H)

To a suspension of **13** (R=H) [8] (1.0 g, 4.9 mmol) in methanol (100 ml) was added a solution of mCPBA (2.3 g, 11 mmol) in methanol (100 ml) dropwise at room temperature. After stirring the resulting mixture for 24 hours the solid was removed by filtration and washed with methanol to yield **16** (R=H) (0.98 g, 85%), as a yellow solid, m.p. 136-138°C. ν_{max}(nujol) 3092(NH), 1629(C=O), 1377 and 1133(S=O) cm^{-1}; δ_H(d^6 DMSO 55°C) 4.20 (s, 2H), 4.66 (s, 2H), 7.48 (tr, 1H, J 6.6 Hz), 7.69 (d, 1H, J 6.6 Hz), 7.82 (tr, 1H, J 6.6 Hz) and 8.06 (d, 1H, J 6.6 Hz); m/z M^+235(7%), 201(51), 171(100), 143(28), 115(17) and 77(13). Accurate mass: 235.03042, $C_{11}H_9NO_3S$ requires 235.03032.

9-Chloro-1,3-dihydrothieno[3,4-*b*]quinoline 2,2-dioxide (17)

A mixture of the sulfolene **16** (R=H) (0.5 g, 2.13 mmol) and freshly distilled phosphoryl chloride (4 ml) were heated at reflux for 10 minutes. The reaction mixture was allowed to cool, poured onto ice and neutralised with 2M ammonium hydroxide solution. The resulting precipitate was removed by filtration and purified by flash column chromatography (alumina, 1% methanol in dichloromethane as eluant) to yield pure **17** (0.23 g, 43%) as a red solid. ν_{max}(nujol) 1377(S=O) and 1136 (S=O) cm^{-1}; δ_H($CDCl_3$) 4.60(s, 2H), 4.69(s, 2H), 7.71(dtr, 1H, J 1.65 and 7.15 Hz), 7.84(dtr, 1H, J 1.65 and 7.15 Hz), 8.08(d, 1H, 7.15 Hz), 8.22(dd, 1H, J 1.65 and 7.15 Hz); m/z M^+253/255(18/7%), 189/191(100/32), 154(63), 127(17) and 77(13).Accurate mass: 252.99712, $C_{11}H_8{}^{35}ClNO_2S$ requires 252.99643.

9-Methoxy-1,3-dihydrothieno[3,4-*b*]quinoline (15, R=OMe)

9-Chloro-1,3-dihydrothieno[3,4-*b*]quinoline **14** (0.45 g, 2.5 mmol) was heated under reflux in methanol

(25 ml) containing an excess of sodium methoxide (0.66 g, 12 mmol). After 8 hours the solvent was removed under reduced pressure and the residue purified by flash column chromatography (alumina, dichloromethane as eluant) to yield pure **15** (R=OMe) as a colourless solid (0.47 g, 98%), m.p. 78-80°C. (Found: C, 65.96; H, 5.08; N, 6.43. $C_{12}H_{11}NOS$ requires C, 66.33; H, 5.10 and N, 6.45%); $\delta_H(CDCl_3)$ 4.14 (s, 3H, OMe), 4.39 (s, 2H), 4.47 (s, 2H), 7.64 (tr, 1H, J 8.3 Hz), 7.68 (tr, 1H, J 8.3 Hz), 7.98 (d, 1H, J 8.3 Hz) and 8.14 (d, 1H J 8.3 Hz); m/z M^+217(98%), 201(41), 186(100), 173(13), 140(12), 102(13), 76(11) and 63(11). Accurate mass: 217.05607, $C_{12}H_{11}NOS$ requires 217.05614.

9-Methoxy-1,3-dihydro[3,4-*b*]quinoline 2,2-dioxide (18, R=OMe)

To a suspension of potassium carbonate (1.33 g, 9.7 mmol) in dichloromethane (30 ml) was added **15** (R=OMe) (0.7 g, 3.2mmol). The reaction vessel was cooled to 0°C and a solution of *m*CPBA (1.24 g, 6.4 mmol) in dichloromethane (15 ml) was added dropwise over 15 minutes. The resulting mixture was allowed to warm to room temperature and stirred for a further 24 hours. The solution was filtered and the precipitated salts washed with copious quantities of dichloromethane. The solvent was removed under reduced pressure to give the crude sulfolene which was purified by flash column chromatography (alumina, dichloromethane/ethyl acetate 6:1 as eluant) to yield **18** (R=OMe) (0.4 g, 50%) as a colourless solid, m.p. 202-204°C. (Found: C, 57.60; H, 4.45; N, 5.38. $C_{12}H_{11}NO_3S$ requires C, 57.82; H, 4.45 and N, 5.38%); ν_{max}(nujol) 1342(S=O) and 1150(S=O) cm^{-1}; $\delta_H(CDCl_3)$ 4.15 (s, 3H, OMe), 4.60 (s, 2H), 4.69 (s, 2H), 7.58 (tr, 1H, J 8.3 Hz), 7.77 (tr, 1H, J 8.3 Hz), 8.02 (d, 1H, J 8.3 Hz) and 8.16 (d, 1H, J 8.3 Hz); m/z M^+249(25%), 185(100), 170(10), 154(17), 130(19), 115(13) and 102(9). Accurate mass: 249.04618, $C_{12}H_{11}NO_3S$ requires 249.04596.

4-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-9-methoxy-1,4-dihydrothieno[3,4-*b*]quinoline 2,2-dioxide (23)

Sulfolene **18** (R=OMe) (0.5 g, 2.0 mmol) and N-phenylmaleimide (0.41 g, 2.4 mmol) were heated together at 214°C in 1,2,4-trichlorobenzene (4 ml) for 6 hours. Concentration of the reaction mixture via bulb-to-bulb distillation at reduced pressure, followed by purification of the crude residue by flash column chromatography (silica gel, dichloromethane as eluant) gave the conjugate addition product **23** as a yellow solid (0.21 g, 25%), m.p. 160-162°C. $\nu_{max}(CH_2Cl_2)$ 1702(C=O), 1366(S=O) and 1170(S=O) cm^{-1}; $\delta_H(CDCl_3)$ 2.74 (dd, 1H, J 5.5 and 18.7 Hz), 3.14 (dd, 1H, J 9.4 and 18.7 Hz), 3.96 (ddd, 1H, J 2.5, 5.5 and 9.4 Hz), 4.20 (s, 3H, OMe), 4.67(d, 1H, J 16.0 Hz), 4.74(d, 1H, J 16.0 Hz), 5.25 (d, 1H, J 2.5 Hz), 7.45-7.55 (m, 6H), 7.60 (tr, 1H, J 8.3 Hz), 7.83 (d, 1H J 8.3 Hz) and 8.12 (d, 1H, J 8.3 Hz); m/z M^+422(24%), 249(100), 210(32), 196(69), 167(56), 119(15), 106(26), 91(21) and 77(25). Accurate mass: 422.09395, $C_{22}H_{18}N_2O_5S$ requires 422.09364.

10-Chloro-2-phenyl-1,3-dihydropyrrolo[3,4-*b*]acridine-1,3-dione (28)

A mixture of sulfolene **16** (R=H) (0.3 g, 1.3 mmol) and N-phenylmaleimide (0.22 g, 1.3 mmol) in 1,2,4-trichlorobenzene (3 ml) were heated, under an atmosphere of nitrogen, at 220°C for 3 hours. The reaction mixture was allowed to cool and a precipitate resulted. The solid was removed by filtration and washed with petroleum. The remaining brown solid proved too insoluble to analyse by nmr spectroscopy but a crude mass spectrum provided some evidence for the formation of the desired Diels-Alder adduct **26 (R=H)** and possibly some aromatised adduct **27**. m/z M^+344(31%), 340(38), 295(15), 196(100), 167(16) and 77(19). In an

attempt to overcome the problem of insolubility, the product was treated with phosphorus oxychloride (2 ml) and the resulting mixture heated under reflux for 10 minutes. On cooling the reaction mixture was poured onto ice and neutralised with 2M ammonium hydroxide solution yielding a brown solid which was removed by filtration washed with water and dissolved in dichloromethane. Purification of the crude product by flash column chromatography (silica gel, dichloromethane as eluant) gave pure **28** (0.21 g, 47%) as a yellow solid, m.p. >250°C. ν_{max}(nujol) 1722 (C=O) cm^{-1}; δ_H($CDCl_3$) 7.46-7.57(m, 5H), 7.78(tr, 1H, J 8.25 Hz), 7.95(tr, 1H, J 8.25 Hz), 8.30(d, 1H, J 8.25 Hz), 8.49(d, 1H, J 8.25 Hz), 8.75(s, 1H) and 9.08(s, 1H); m/z M^+360/358(35/100%), 314(54), 279(32), 238(20), 211(23), 176(62), 149(22) and 77(30). Accurate mass: 358.05121, $C_{21}H_{11}ClN_2O_2$ requires 358.05090.

***trans*-3,4-Biscarboethoxy-1,2,3,4-tetrahydroacridin-9-one (25)**

A mixture of quinolone **16** (R=H) (0.3 g, 1.3 mmol) and diethyl fumarate (0.21 ml, 1.3 mmol) were heated in tetramethylene sulfolene (2 ml) at reflux under an atmosphere of nitrogen for 3 hours. The reaction mixture was allowed to cool, poured onto ice water and the resulting brown precipitate removed by filtration and washed with petroleum to yield the Diels-Alder adduct **25** (0.21 g, 48%) as a brown solid, m.p. 204-206°C. ν_{max}(nujol) 1730(C=O) and 1634(C=C) cm^{-1}; δ_H($CDCl_3$, 40°C) 1.21(2xtr, 6H, J 7.15 Hz), 2.14-3.11(m, 6H), 4.14(2xq, 4H, J 7.15 Hz), 7.27-7.51(m, 3H), 8.29(d, 1H, J 8.3 Hz) and 10.32(s, br, 1H, NH); m/z M^+343(13%), 270(100), 196(92), 167(17) and 77(7). Accurate mass: 343.14204, $C_{19}H_{21}NO_5$ requires 343.14197.

3-(2-Bromobenzoyl)-4-pyrrolidin-1-yl-2,5-dihydrothiophene (31) and 2-(2-bromobenzoyl)-3-pyrrolidin-1-yl-4,5-dihydrothiophene (32)

A solution of 2-bromobenzoyl chloride (3.6 g, 16 mmol) in dichloromethane (15 ml) was added dropwise, over a 20 minute period, to an ice-cooled solution of enamines **29** and **30** (2.5 g, 16 mmol) and triethylamine (1.8 ml, 16 mmol) in dichloromethane (15 ml). The resulting orange mixture was allowed to stir at room temperature overnight. The reaction mixture was diluted with DCM (20 ml) and washed with water (1x20 ml), 1M sodium hydrogen carbonate solution (1x20 ml) and water (1x20 ml). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give an orange oil. Purification of the crude reaction mixture by gravity column chromatography (silica gel, ether as eluant) allowed separation of the two isomeric products.

First eluted: **31** (2.9 g, 52%) as a yellow oil. (Found: C, 53.24; H, 4.77; N, 4.11. $C_{15}H_{16}BrNOS$ requires C, 53.26; H, 4.77 and N, 4.14%); ν_{max}(nujol) 1717(C=O) and 1633(C=C) cm^{-1}; δ_H($CDCl_3$) 1.84-2.01(m, 8H), 3.19(tr, 2H, J 6.6 Hz), 3.66(tr, 2H, J 6.6 Hz), 7.19-7.40(m, 3H) and 7.58(d, 1H, J 7.15 Hz); m/z M^+339/337(3/5%), 258(100), 185(40), 183(44), 155(32), 153(52) and 70(50). Accurate mass: 339.01109, $C_{15}H_{16}BrNOS$ requires 339.01155.

Second eluted: **32** (1.4 g, 26%) as a yellow solid, m.p. 126-128°C. (Found: C, 53.22; H, 4.81; N, 4.08. $C_{15}H_{16}BrNOS$ requires C, 53.26; H, 4.77 and N, 4.14%); ν_{max}(nujol) 1716(C=O) and 1589(C=C) cm^{-1}; δ_H($CDCl_3$) 1.95-2.02(m, 4H), 2.96-3.14(m, 4H), 3.57(tr, 4H, J 6.6 Hz), 7.15-7.40(m, 3H) and 7.56(d, 1H, J 7.7 Hz); m/z M^+339/337(14/15%), 258(27), 256(33), 226(47), 185(47), 183(53), 155(43), 153(37) and70(100). Accurate mass: 337.01363, $C_{15}H_{16}BrNOS$ requires 337.01358.

2-(2-Bromobenzoyl)-3-N-benzylamino-4,5-dihydrothiophene (33)

A mixture of enamine **32** (1.7 g, 5.0 mmol), benzylamine (0.6 g, 5.5 mmol) and a catalytic amount of *p*-toluenesulfonic acid in toluene (25 ml) were heated at reflux for 1 hour in a Dean-Stark apparatus under nitrogen. The reaction mixture was allowed to cool, diluted with toluene (30 ml), washed with water (1x25 ml), 1M sodium hydrogen carbonate solution (1x25 ml) and water (1x25 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude oily residue by flash column chromatography (silica gel, 30% ethyl acetate in petroleum as eluant) gave pure **33** (1.2 g, 63%) as a yellow oil. ν_{max}(film) 3061(NH), 1610(C=O) and 1540(C=C) cm^{-1}; δ_H($CDCl_3$) 3.56(s, 2H), 3.86(s, 2H), 4.44(d, 2H, J 6.6 Hz), 7.07-7.32(m, 8H), 7.46(d, 1H J 7.7 Hz) and 10.56(s, br, 1H, NH); m/z M^+373/375(14/13%), 203(9), 175(13) and 91(100). Accurate mass: 373.01346, $C_{18}H_{16}BrNOS$ requires 373.01358.

4-Benzyl-2,3-dihydrothieno[3,2-*b*]quinolin-9-one (34)

Potassium *tert*-butoxide (0.4 g, 3.1 mmol) was added to a stirred suspension of enaminone **33** (1.0 g, 2.8 mmol) in *tert*-butanol (20 ml) and the resulting mixture heated at reflux, under an inert atmosphere, overnight. The reaction mixture was allowed to cool, concentrated *in vacuo* and purified by flash column chromatography (silica gel, 50% ethyl acetate in petroleum as eluant) to give pure **34** (0.6 g, 72%) as a yellow solid, m.p. 198-200°C. (Found: C, 73.35; H, 5.01; N, 4.57. $C_{18}H_{15}NOS$ requires C, 73.69; H, 5.15 and N, 4.77%); ν_{max}(nujol) 1721(C=O) and 1612(C=C) cm^{-1}; δ_H($CDCl_3$) 3.14-3.23(m, 2H), 3.35-3.42(m, 2H), 5.27(s, 2H), 6.94(d, 2H, J 7.7 Hz), 7.12-7.33(m, 6H) and 8.30(d, 1H, J 7.7 Hz); m/z M^+293(62%), 202(15), 174(15), 130(15), 91(100) and 65(31). Accurate mass: 293.08788, $C_{18}H_{15}NOS$ requires 293.08743.

4-Benzyl-2,3-dihydrothieno[3,2-*b*]quinolin-9-one 1,1-dioxide (36)

To a solution of sulfide **34** (0.6 g, 2.0 mmol) in dichloromethane (50 ml) at 0°C was added potassium carbonate (0.9 g, 6.2 mmol). A solution of *m*CPBA (0.8 g, 4.1 mmol) in dichloromethane (50 ml) was added dropwise and the resulting mixture allowed to stir at room temperature overnight. Removal of the inorganic salts by filtration and concentration of the organic phase at reduced pressure yielded a yellow solid. Recrystallisation of this solid from acetone gave pure **36** (0.36 g, 54%) as a colourless solid, m.p. 240-242°C. (Found: C, 66.29; H, 4.61; N, 4.20. $C_{18}H_{15}NO_3S$ requires C, 66.44; H, 4.65 and N, 4.30%); ν_{max}(nujol) 1730(C=O), 1377(S=O) and 1122(S=O) cm^{-1}; δ_H($CDCl_3$) 3.37-3.41(m, 2H), 3.48-3.51(m, 2H), 5.46(s, 2H), 7.05(d, 2H, J 7.7 Hz), 7.18(tr, 1H, J 7.7 Hz), 7.31-7.48(m, 5H) and 8.20(d, 1H, J 7.7 Hz); m/z M^+325(10%), 261(12), 92(25), 91(100) and 65(23). Accurate mass: 325.07746, $C_{18}H_{15}NO_3S$ requires 325.07727.

6-Benzyl-1,3-dihydropyrrolo[3,4-*a*]acridin-1,3,11-trione (39)

A mixture of sulfolene **36** (40 mg, 0.12 mmol) and N-phenylmaleimide (30 mg, 0.18 mmol) in 1,2,4-trichlorobenzene (1 ml) were heated at 220°C, under a nitrogen atmosphere, overnight. The reaction mixture was allowed to cool and the solvent removed by bulb-to-bulb distillation at reduced pressure. Purification of the crude residue by flash column chromatography (silica gel, 50% ethyl acetate in petroleum as eluant) gave the aromatised Diels-Alder adduct **39** as an orange oil. Recrystallisation of this oil from cyclohexane/dichloromethane gave pure (258) (20 mg, 42%) as an orange solid, m.p. 258-260°C.

$\nu_{max}(CH_2Cl_2)$ 1718(C=O) and 1647(C=O) cm^{-1}; $\delta_H(CDCl_3)$ 5.53(s, 2H), 7.36-7.39(m, 14H), 8.06(d, 1H, J 9.1 Hz) and 8.55(d, 1H, J 7.5 Hz); $\delta_C(CDCl_3)$ 115.52, 120.21, 121.43, 123.42, 125.48, 126.02, 126.77, 127.06, 127.81, 128.27, 128.93, 129.58, 134.32, 134.47, 145.23, 147.49 and 182.65; m/z M^+430(6%) and 91(100). Accurate mass: 430.13162, $C_{28}H_{18}N_2O_3$ requires 430.13174.

1-Benzyl-2-(2-phenylthioethyl)quinololin-4-one (40)

A mixture of sulfolene **36** (0.2 g, 0.6 mmol) and thiophenol (97%, 0.1 g, 0.9 mmol) in 1,2,4-trichlorobenzene (2 ml) were heated at reflux, under an atmosphere of nitrogen, for 5 hours. The reaction mixture was allowed to cool and the solvent removed by bulb-to-bulb distillation at reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, ethyl acetate as eluant) to yield pure **40** (0.1 g, 48%) as a yellow oil. ν_{max}(film) 1624(C=O) and 1599(C=C) cm^{-1}; $\delta_H(CDCl_3)$ 2.95(tr, 2H, J 8.8 Hz), 3.18(tr, 2H, J 8.8 Hz), 5.34(s, 2H), 6.38(s, 1H), 6.90-6.94(m, 2H), 7.19-7.34(m, 10H), 7.51(tr, 1H, J 8.25 Hz) and 8.44(d, 1H, J 8.25 Hz); m/z M^+371(18%), 338(52), 261(89), 110(83), 91(100) and 77(27). Accurate mass: 371.13453, $C_{24}H_{21}NOS$ requires 371.13440.

4-Carbomethoxy-2,5-dihydrothieno-3-yl triflate (41)

A solution of β-keto-ester **11** (1.0 g, 6.2 mmol) in DCM (60 ml) was cooled under an atmosphere of nitrogen to -78°C. Diisopropylethylamine (1.3 ml, 7.2 mmol) was added to this solution and, after stirring for 10 minutes, trifluoromethanesulfonic anhydride (1.2 ml, 7.2 mmol) was added dropwise to the resulting mixture. The reaction mixture was allowed to warm to room temperature and the solvent removed under reduced pressure. Purification of the crude product was achieved by flash column chromatography (neutral alumina, 20% ethyl acetate in petroleum as eluant) to give pure **41** (1.42 g, 78%) as a colourless oil. ν_{max}(nujol) 1729(C=O), 1670(C=C) and 1431(S=O) and 1156(S=O) cm^{-1}; $\delta_H(CDCl_3)$ 3.84(s, 3H, OMe) and 3.97(s, 4H); m/z M^+292(4%), 261(9), 159(31), 127(100), 69(28), 59(51) and 45(42). Accurate mass: 291.96882, $C_7H_7F_3O_5S_2$ requires 291.96872.

1,3-Dihydrothieno[3,4-*c*]quinolin-4-one (43)

A heterogeneous mixture of triflate **41** (0.78 g, 2.7 mmol), tetrakis(triphenylphosphine)palladium(0) (0.15 g, 0.13 mmol), 2M aqueous sodium carbonate (2.6 ml, 5.1 mmol) and crude boronic acid (**42**) [12] (1.4 g, 6.2 mmol) in DME (80 ml) was heated under reflux under a nitrogen atmosphere for 6 hours. The reaction mixture was allowed to cool and the resulting yellow solid removed by filtration. Recrystallisation of this solid from ethanol gave pure **43** (0.39 g, 72%); m.p. 258-260°C. ν_{max}(nujol) 1729(C=O) and 1647(C=C) cm^{-1}; $\delta_H(d^6$ DMSO) 4.06(tr, 2H, J 3.9 Hz), 4.49(tr, 2H, J 3.9 Hz), 7.15(dtr, 1H, J 1.1 and 7.7 Hz), 7.30(d, 1H, J 7.7 Hz) and 7.41-7.50(m, 2H); m/z M^+203(88%), 184(59), 115(22) and 77(8). Accurate mass: 203.03968, $C_{11}H_9NOS$ requires 203.04048.

1,3-Dihydrothieno[3,4-*c*]quinolin-4-one 2,2-dioxide (44)

To a mixture of the sulfide **43** (1.0 g, 4.9 mmol) in methanol (30 ml) was added dropwise a solution of *m*CPBA (1.8 g, 10 mmol) in methanol (20 ml) and the resulting mixture stirred at room temperature overnight. The precipitate was removed by filtration and washed with ice-cold methanol (15 ml). The remaining colourless solid was pure **44** (0.7 g, 60%), m.p. 264-265°C. ν_{max}(nujol) 1729(C=O), 1646(C=C),

1307(S=O) and 1140(S=O) cm^{-1}; δ_H(d^6 DMSO) 4.34(s, 2H), 4.90(s, 2H), 7.27(dtr, 1H, J 1.1 and 7.7 Hz), 7.39(dd, 1H, J 1.1 and 7.7 Hz), 7.51-7.59(m, 2H) and 9.23(s, br, 1H, NH); m/z M^+235(39%), 171(100), 143(73), 115(64), 72(15) and 59(32). Accurate mass: 235.03065, $C_{11}H_9NO_3S$ requires 235.03030.

4-Chloro-1,3-dihydrothieno[3,4-*c*]quinoline

A mixture of sulfide **43** (1.3 g, 6.4 mmol) and freshly distilled phosphoryl chloride (10 ml) were heated at reflux for 1.5 hours. The reaction mixture was allowed to cool, poured onto ice and neutralised with 2M ammonium hydroxide solution. The resulting precipitate was removed by filtration and purified by flash column chromatography (alumina, 40% hexane in dichloromethane as eluant) to yield pure compound (0.7 g, 64%) as a colourless solid, m.p. 154-155°C. ν_{max}(nujol) 1647(C=N) cm^{-1}; δ_H($CDCl_3$) 4.48(tr, 2H, J 3.3 Hz), 4.72(tr, 2H, J 3.3 Hz), 7.61(dtr, 1H, J 1.65 and 6.6 Hz), 7.71-7.78(m, 2H) and 8.08(dd, 1H, J 1.65 and 6.6 Hz); m/z M^+223/221(31/100%), 184(57), 140(57), 115(20) and 79(23).

4-Methoxy-1,3-dihydrothieno[3,4-*c*]quinoline

A mixture of sulfide (0.5 g, 2.3 mmol) and freshly prepared sodium methoxide (0.6 g, 11 mmol) in methanol (15 ml) were heated at reflux under an atmosphere of nitrogen for 1.5 hours. The reaction mixture was allowed to cool and the solvent removed at reduced pressure. The resulting residue was dissolved in DCM, washed with water (2x10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. Recrystallisation of the crude product from methanol gave pure compound (0.34 g, 69%) as a colourless solid, m.p. 85-87°C. (Found: C, 66.27; H, 5.09; N, 6.45. $C_{12}H_{11}NOS$ requires C, 66.33; H, 5.10 and N, 6.45%); ν_{max}(nujol) 1621(C=N) cm^{-1}; δ_H($CDCl_3$) 4.10(s, 3H, OMe), 4.32(tr, 2H, J 3.3 Hz), 4.60(tr, 2H, J 3.3 Hz), 7.41(tr, 1H, J 7.7 Hz), 7.59-7.65(m, 2H) and 7.90(dd, 1H, J 1.65 and 7.7 Hz); m/z M^+217(100%), 202(69), 184(34), 172(12), 140(13) and115(18). Accurate mass: 217.05590, $C_{12}H_{11}NOS$ requires 217.05614.

4-Methoxy-1,3-dihydrothieno[3,4-*c*]quinoline 2,2-dioxide (45)

To a solution of sulfide (0.3 g, 1.4 mmol) in DCM (20 ml) containing potassium carbonate (0.57 g, 4.1 mmol) was added dropwise a solution of *m*CPBA (0.56 g, 2.9 mmol) in DCM (15 ml) and the resulting solution stirred at room temperature for 3 hours. Removal of the inorganic salts by filtration and removal of the solvent under reduced pressure gave the crude product which could be purified by recrystallisation from methanol to give pure **45** (0.25 g, 73%) as a colourless solid, m.p. 198-200°C. (Found: C, 57.33; H, 4.46; N, 5.48. $C_{12}H_{11}NO_3S$ requires C, 57.82; H, 4.45 and N, 5.62%); ν_{max}(nujol) 1619(C=N), 1316(S=O) and 1133(S=O) cm^{-1}; δ_H($CDCl_3$) 4.12(s, 3H, OMe), 4.46(s, 2H), 4.67(s, 2H), 7.48-7.56(m, 2H), 7.70(dtr, 1H, J 1.65 and 8.3 Hz) and 7.92(d, 1H, J 8.3 Hz); m/z M^+249(34%), 185(100), 154(19), 140(12), 127(12), 115(24) and 77(12). Accurate mass: 249.04618, $C_{12}H_{11}NO_3S$ requires 249.04596.

***trans*-8,9-Biscarboethoxy-6H-7,8,9,10-tetrahydrophenanthridin-6-one (47)**

Sulfolene **44** (0.2 g, 0.85 mmol) and diethyl fumarate (0.18 g, 1.0 mmol) were heated together overnight at 180°C in 1,2,4-trichlorobenzene (2 ml). The reaction mixture was allowed to cool and hexane (10 ml) added. The precipitate was removed by filtration and washed with hexane to yield pure **47** (0.23 g, 79%) as a pale yellow solid, m.p. 196-198°C. ν_{max}(nujol) 1739(C=O) and 1646(C=O) cm^{-1}; δ_H(d^6 DMSO) 1.16(tr, 3H, J 7.15 Hz), 1.18(tr, 3H, J 7.15 Hz), 2.85-3.19(m, 6H), 4.01-4.15(m, 4H), 7.14(tr, 1H, J 7.7 Hz), 7.25(dd, 1H, J

7.7 Hz), 7.42(tr, 1H, J 1.1 and 7.7 Hz), 7.64(d, 1H, J 7.7 Hz) and 9.56(s, br, 1H, NH); m/z M^+343(22%), 298(19), 270(81), 196(100), 178(44), 167(14), 152(11) and 115(7). Accurate mass: 343.14204, $C_{19}H_{21}NO_5$ requires 343.14197.

2-Phenyl-6H-1,3,3a,4,11,11a-hexahydropyrrolo[3,4-*i*]phenanthridin-1,3,5-trione (46)

A mixture of sulfolene **44** (0.2 g, 0.85 mmol) and N-phenylmaleimide (0.18 g, 1.0 mmol) were heated at 180°C overnight in 1,2,4-trichlorobenzene (2 ml). The reaction mixture was allowed to cool and DCM (5 ml) added. The yellow solid product was removed by filtration and washed with hexane to leave pure **46** (0.2 g, 70%) as a pale yellow solid m.p. >250°C. ν_{max}(nujol) 1705(C=O) and 1645(C=O) cm^{-1}; δ_H(d^6 DMSO) 2.72(dd, 1H, J 8.3 and 15.1 Hz), 2.97(dd, 1H, J 6.6 and 15.1 Hz), 3.48-3.65(m, 4H), 6.96(dd, 1H, J 1.1 and 8.3 Hz), 7.21(tr, 1H, J 8.3 Hz), 7.30-7.48(m, 6H), 7.86(d, 1H, J 8.3 Hz) and 9.58(s, br, 1H, NH); δ_C(d^6 DMSO) 17.52, 20.79, 21.87, 23.35, 115.49, 118.21, 123.49, 126.59, 128.29, 128.86, 129.83, 137.59, 143.82, 160.07 and 178.46; m/z M^+344(100%), 196(98), 178(76), 167(28), 151(18), 115(12) and 77(16). Accurate mass: 344.11654, $C_{21}H_{16}N_2O_3$ requires 344.11609.

***trans*-8,9-Biscarboethoxy-6-methoxy-7,8,9,10-tetrahydrophenanthrene (48)**

A mixture of sulfolene **45** (0.13 g, 0.52 mmol) and diethyl fumarate (0.11 g, 0.63 mmol) were heated at reflux in 1,2,4-trichlorobenzene (2 ml) for 3 hours. After cooling the solvent was removed via bulb-to-bulb distillation at reduced pressure and the crude residue purified by flash column chromatography (silica gel, 20% ethyl acetate in petroleum as eluant). Pure **48** (0.12 g, 64%) was obtained as a colourless solid, m.p. 201-203°C. ν_{max}(nujol) 1734(C=O) and 1612(C=N) cm^{-1}; δ_H($CDCl_3$) 1.22(tr, 3H, J 7.15 Hz), 1.23(tr, 3H, J 7.15 Hz), 2.60(dd, 1H, J 4.4 and 16.5 Hz), 2.82-2.98(m, 3H), 3.12(dd, 1H, J 8.8 and 16.5 Hz), 3.37(dd, 1H, J 4.2 and 16.5 Hz), 3.97(s, 3H, OMe), 4.13(q, 2H, J 7.15 Hz), 4.15(q, 2H, J 7.15 Hz), 7.26(dtr, 1H, J 1.1 and 8.25 Hz), 7.45(dtr, 1H, J 1.1 and 8.25Hz), 7.61(d, 1H, J 8.3 Hz) and 7.71(d, 1H, J 8.3 Hz); m/z M^+357(56%), 312(28), 283(84), 210(100), 195(62), 178(63), 167(32), 152(22) and 77(6). Accurate mass: 357.15773, $C_{20}H_{23}NO_5$ requires 357.15762.

3-Carbomethoxy-4-(2-N,N-diethylcarbamoyloxyphenyl)-2,5-dihydrothiophene (50)

$Pd(PPh_3)_4$ (3 mole%) was added to triflate **41** (1.0 g, 3.4 mmol) in toluene (80 ml). Boronic acid **49** [14] (0.89 g, 3.8 mmol) was dissolved in the minimum volume of ethanol and added to this solution along with 2M aqueous sodium carbonate (4 ml). The resulting mixture was boiled under reflux under an atmosphere of nitrogen for 2 hours. Removal of the solvent *in vacuo* and purification by flash column chromatography (silica gel, 30% ethyl acetate in petroleum as eluant) yielded pure **50** (0.76 g, 66%) as a yellow oil. ν_{max}(nujol) 1725(C=O) cm^{-1}; δ_H($CDCl_3$) 1.19(tr, 6H, J 7.15 Hz), 3.34(q, 4H, J 7.15 Hz), 3.55(s, 3H, OMe), 4.12(s, 4H), 7.14-7.25(m, 3H) and 7.29-7.83(m, 1H); m/z M^+335(3%), 303(15), 203(24), 115(46), 100(100), 72(77) and 44(13). Accurate mass: 335.11911, $C_{17}H_{21}NO_4S$ requires 335.11911.

1,3-Dihydrothieno[3,4-*c*]chromen-4-one

To the cross coupling product **50** (1.0 g, 3.0 mmol) dissolved in THF (15 ml) was added 2M sodium hydroxide solution (10 ml) and the mixture heated under reflux overnight. On cooling the reaction mixture was neutralised with dilute HCl and the solids removed by filtration and washed with copious quantities of

ethyl acetate. The organic phase was dried ($MgSO_4$) and evaporated to give the pure coumarin sulfide (0.35 g, 57%) as a yellow solid, m.p. 176-178°C. (Found: C, 64.48; H, 3.91. $C_{11}H_8O_2S$ requires C, 64.69 and H, 3.95%); ν_{max}(nujol) 1714(C=O) cm^{-1}; δ_H($CDCl_3$) 4.22(tr, 2H, J 3.3 Hz), 4.46(tr, 2H, J 3.3 Hz), 7.30(dd, 1H, J 1.1 and 7.7 Hz), 7.40(tr, 1H, J 7.7 Hz), 7.42(d, 1H, J 7.7 Hz) and 7.56(dtr, 1H, J 1.1 and 7.7 Hz); m/z M^+204(100%), 176(25), 159(20), 147(36), 131(49), 115(10) and 102(13). Accurate mass: 204.02411, $C_{11}H_8O_2S$ requires 204.02451.

1,3-Dihydrothieno[3,4-*c*]chromen-4-one 2,2-dioxide (51)

To a mixture of the coumarin sulfide (0.3 g, 1.5 mmol) in methanol (20 ml) was added dropwise a solution of *m*CPBA (0.66 g, 3.1 mmol) in methanol (15 ml) and the resulting mixture stirred at room temperature overnight. Removal of the solid product by filtration and washing with methanol yielded pure **51** (0.26 g, 75%) as a colourless solid, m.p. 197-199°C. (Found: C, 56.01; H, 3.41. $C_{11}H_8NO_4S$ requires C, 55.92 and H, 3.41%); ν_{max}(nujol) 1729(C=O), 1305(S=O) and 1135(S=O) cm-^{1}; δ_H(d^6 DMSO) 4.35(s, 2H), 4.89(s, 2H), 7.35(dd, 1H, J 1.1 and 7.15 Hz), 7.41(tr, 1H, J 7.15 Hz), 7.60(tr, 1H, J 7.15 Hz) and 7.66(dd, 1H, J 1.1 and 7.15 Hz); m/z M^+236(6%), 172(100), 144(39), 115(47), 89(12) and 64(17). Accurate mass: 236.01396, $C_{11}H_8O_4S$ requires 236.01434.

2-Phenyl-1,3,3a,4,11,11a-hexahydrochromeno[3,4-*f*]isoindol-1,3,10-trione (52)

A mixture of sulfolene **51** (0.14 g, 0.6 mmol) and N-phenylmaleimide (0.12 g, 0.7 mmol) were heated under nitrogen at 180°C in 1,2,4-trichlorobenzene (2 ml) for 1 hour. The reaction mixture was allowed to cool and the solvent removed via bulb-to-bulb distillation at reduced pressure. The crude product was purified by flash column chromatography (silica gel, 2% methanol in dichloromethane as eluant) to yield pure **52** (0.16 g, 78%) as a yellow solid, m.p. 226-227°C. ν_{max}(nujol) 1705(C=O)cm^{-1}; δ_H(d^6 DMSO) 2.00(dd, 1H, J 7.7 and 15.9 Hz), 2.20(dd, 1H, J 7.7 and 15.9 Hz), 2.41(dd, 1H, J 3.8 and 15.9 Hz), 2.61-2.87(m, 3H), 6.21-6.27(m, 2H), 6.45-6.60(m, 5H), 6.73(dtr, 1H, J 1.65 and 8.3 Hz) and 7.00(dd, 1H, J 1.65 and 8.3 Hz); m/z M^+345(100%), 197(70), 169(9), 153(13), 115(28) and 91(12). Accurate mass: 345.09986, $C_{21}H_{15}NO_4$ requires 345.10010.

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