Synthesis of 10-methyl-Δ^4-octalins by Diels–Alder reactions of 2*H*-thiopyran surrogates for 1-ethenyl-2-methylcyclohexene

Dale E. Ward and Yuanzhu Gai

Abstract: Diels–Alder reactions of 1-ethenyl-2-methylcyclohexene derivatives could be a versatile route to a variety of natural product skeletons that possess a 10-methyldecalin substructure with additional substitution at C-8 and C-9. These dienes are unreactive due (in part) to the presence of the vinyl methyl group, which destabilizes the necessary s-*cis* conformation. The use of 2*H*-thiopyran diene surrogates for 1-ethenyl-2-methylcyclohexene is investigated. The desired Diels–Alder adducts were not obtained by reaction of 6,7,8,8a-tetrahydro-5,5-dimethyl-3-tris(1-methylethyl)silyloxy-1*H*-2-benzothiopyran (**7***c*) or 1,5,7,8-tetrahydrospiro[6*H*-2-benzothiopyran-6,2′-[1,3]dioxolane] (**17**) with *N*-phenylmaleimide. Reactions of 3-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-4-[(tris(1-methylethyl)silyl)oxy]-2*H*-thiopyran (**19**) with maleimide, *N*-methylmaleimide, and *N*-phenylmaleimide under thermal conditions and with *N*-methylmaleimide, *N*-phenylmaleimide, 3-(propenoyl)-2-oxazolidinone, and methyl acrylate under Lewis acid mediated conditions ($EtAlCl_2$, $TiCl_4$) gave Diels–Alder adducts in moderate to good yields. In each case, those adducts were readily converted into products that are synthetically equivalent to Diels–Alder adducts of **17** with the same dienophiles. Desulfurization of those products gives 10-methyl-Δ^4-octalins (2,3,4,4a,5,6,7,8-octahydro-4a-methylnapthalenes) that are synthetically equivalent to hypothetical Diels–Alder adducts of 1-ethenyl-2-methylcyclohexene-5-one.

Key words: Diels–Alder, 2*H*-thiopyran, *cis*-substituted 1,3-diene surrogate, 1-ethenyl-2-methylcyclohexene, octahydro-4a-methylnapthalene derivatives.

Résumé : Les réactions de Diels–Alder des dérivés du 1-éthényl-2-méthylcyclohexène pourraient être des voies versatiles pour atteindre les squelettes de produits naturels comportant une sous-structure 10-méthyldécaline et des substituants additionnels en C-8 et en C-9. Ces diènes ne sont pas réactifs à cause (en partie) de la présence du groupe vinyle qui déstabilise la conformation s-*cis* nécessaire. On a étudié la possibilité d'utiliser un diène du 2*H*-thiopyrane comme substitut du 1-éthényl-2-méthylcyclohexène. On n'a pas obtenu les adduits de Diels–Alder désirés lors de la réaction de la *N*-phénylmaléimide avec le 6,7,8,8a-tétrahydro-5,5-diméthyl-3-tris(1-méthylethyl)silyloxy-1*H*-2-benzothiopyrane (**7***c*) ou avec le 1,5,7,8-tétrahydrospiro[6*H*-2-benzothiopyrane-6,2′-[1,3]dioxolane] (**17**). Les réactions du 3-[2-(2-méthyl-1,3-dioxolan-2-yl)éthyl]-4-[(tris(1-méthyléthyl)silyl)oxy]-2*H*-thiopyrane (**19**) avec les maléimide, *N*-méthylmaléimide et *N*-phénylmaléimide dans des conditions thermiques et avec les *N*-méthylmaléimide et *N*-phénylmaléimide, la 3-(propénoyl)-2-oxazolidinone et l'acrylate de méthyle dans des conditions catalysées par un acide de Lewis ($EtAlCl_2$, $TiCl_4$) ont permis d'obtenir des adduits de Diels–Alder avec de bons rendements. Dans chacun des cas, il a été possible de transformer facilement ces adduits en produits synthétiquement équivalents aux adduits de Diels–Alder du produit **17** avec les mêmes diénophiles. La désulfurisation de ces produits fournit les 10-methyl-Δ^4-octalines (2,3,4,4a,5,6,7,8-octahydro-4a-méthylnapthalenes) qui sont synthétiquement équivalentes aux adduits hypothétiques de Diels–Alder de la 1-éthényl-2-méthylcyclohexèn-5-one.

Mots clés : Diels–Alder, 2*H*-thiopyrane, substitut d'un 1,3-diène *cis*-substitué, 1-éthényl-2-méthylcyclohexène, dérivés octahydro-4a-méthylnapthalènes.

[Traduit par la rédaction]

Received November 21, 1996.

This paper is dedicated to Professor William A. Ayer on the occasion of his 65th birthday.

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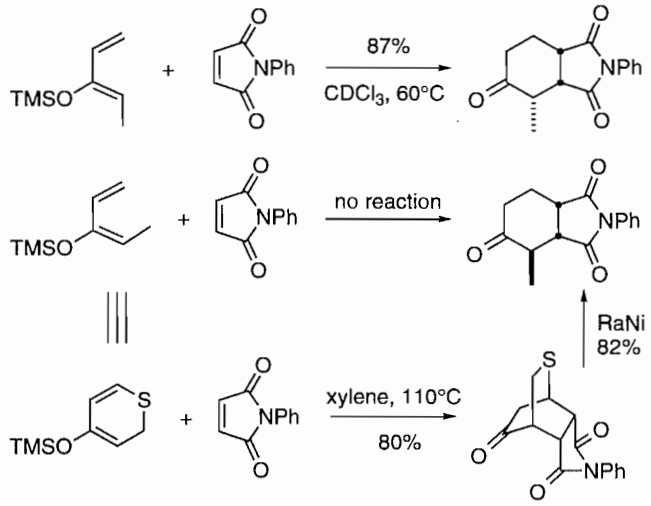
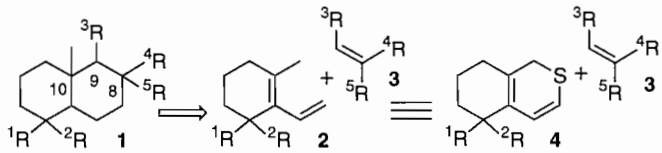
Scheme 1.



Scheme 2.

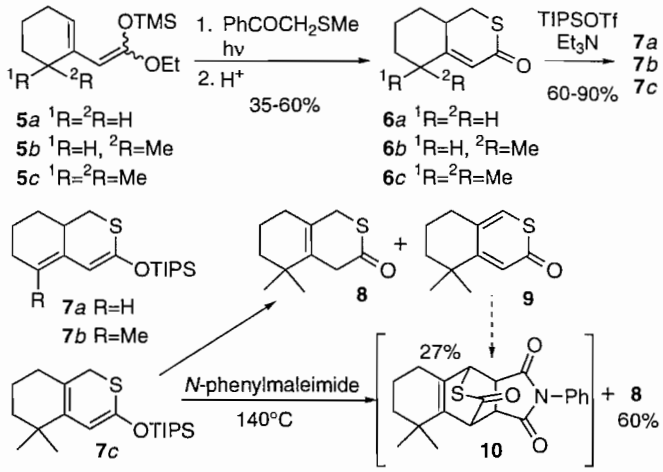


Introduction

The Diels–Alder reaction is perhaps the most powerful and versatile reaction in the synthetic chemist's arsenal (1). The increase in molecular complexity resulting from the simultaneous formation of two σ-bonds and up to four stereogenic centers coupled with the attributes of wide generality, atom economy, and predictable regio- and stereoselectivity contribute to the unrivaled synthetic utility of this reaction. The scope of this process is often limited by the poor reactivity associated with *cis*-substituted dienes (2) (Scheme 1). Recently, we have investigated the potential of 2*H*-thiopyrans to act as surrogates for *cis*-dienes in a strategy to overcome this limitation and thereby expand the scope of the Diels–Alder reaction (3). We have developed methods for the preparation of various substituted 2*H*-thiopyrans and have systematically investigated their Diels–Alder reactivity under a variety of conditions in both inter- (3*b*, 3*d*) and intra-molecular cases (3*g*). Adducts resulting from reactions of 2*H*-thiopyrans with dienophiles are, after desulfurization, synthetically equivalent to adducts from unreactive *cis*-dienes (3*a*, 3*g*).

Several structurally and biologically interesting natural products have substructures that incorporate a fused decalin ring system with a C-10 angular methyl group and alkyl substitution at C-8 and C-9 (**1**; e.g., drimanes, labdanes, triterpenes, steroids, etc.) (4). The most commonly employed synthetic approaches to this type of structure include Robinson annulation, polyene cyclization, or Diels–Alder reaction (5). These methods are not always compatible with the required substitution pattern of many of the target structures, often necessitating a linear multistep adjustment (5). For example, a Diels–Alder reaction of the generalized diene and dienophiles **2** and **3** could provide a versatile approach to these structures (Scheme 2). However, despite several attempts (6), this approach is successful only when $^1R = {}^2R$ =Me and only with certain dienophiles (e.g., dimethyl acetylenedicarboxylate, quinone). By contrast, to the best of our knowledge, there are no reports of successful Diels–Alder reaction of the diene **2** with $^1R = {}^2R$ = H. Dienes such as **2** can be regarded as *cis*-substituted and, as such, their low Diels–Alder reactivity can be attributed (in part) to the steric destabilization of the s-*cis* conformation. The modest success observed with **2** ($^1R = {}^2R$ = Me) is presumably due to the destabilization of the s-*trans* conformation by the geminal dimethyl group. We considered that the low reactivity of dienes such as **2** could be overcome by exploiting the chemistry of 2*H*-thiopyrans (e.g., **4**). Herein we report our preliminary results on the synthesis of 10-methyloctalins by Diels–Alder reactions of 2*H*-thiopyran surrogates of **2**.

Scheme 3.

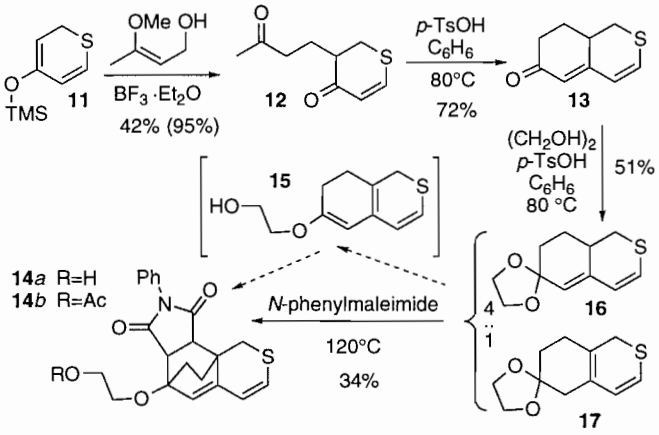


Results and discussion

Our initial attempts at the synthesis of a 5,6,7,8-tetrahydro-1*H*-2-benzothiopyran (**4**) derivative involved the Diels–Alder reaction of the trimethylsilyl dienolate of cyclohexylideneacetate (**5***a*) with thioformaldehyde generated in situ according to the method of Vedejs et al. (7) to give the benzothiopyranone **6***a* after work-up (Scheme 3). Enolsilylation of **6***a* according to the usual protocol (3*b*) gave only the exocyclic diene **7***a*. The 5-methylbenzothiopyranone **6***b* was similarly prepared as a 1:1 mixture of diastereomers but also gave the exocyclic diene **7***b* upon enolsilylation. Reactions of the dienes **7***a* and **7***b* with *N*-phenylmaleimide in the presence of dichloromaleimide (8)[2] failed to give Diels–Alder adducts. Finally, treatment of the 5,5-dimethylbenzothiopyranone derivative **6***c* with triisopropylsilyl trifluoromethansulfonate (TIPSOTf) and Et_3N gave the unstable endocyclic diene **7***c*. Attempted Diels–Alder reaction of **7***c* with *N*-phenylmaleimide did not produce the expected product but gave an adduct tentatively identified as **10** in low yield. Subsequently, we found that **7***c* is rapidly converted into a mixture of **8** and **9** on standing and therefore presume that **10** resulted from the reaction of **9** (formed from **7***c* in situ) with the dienophile.

[2] Dichloromaleimide promotes diene isomerization (8) (cf. ref. 3*b*).

Scheme 4.



In an effort to form a more stable benzothiopyran derivative, the diene **11** (3b) was treated with 3-methoxy-2-butenol (9) and $BF_3{\cdot}Et_2O$ to give **12** (10) (Scheme 4). Cyclization of **12** under acidic conditions gave the dienone **13**, which, after reaction with ethylene glycol and 4-methylbenzenesulfonic acid (*p*-TsOH), gave a 4:1 mixture of the exocyclic and endocyclic dienes **16** and **17**, respectively. Reaction of the **16/17** mixture with *N*-phenylmaleimide again did not produce the expected adduct but gave **14***a* in 34% yield.[3] Although the mechanism is uncertain, the structure of **14***a* is consistent with a Diels–Alder reaction of the dienophile and the putative diene (i.e., **15**) resulting from elimination of the ethylene ketal in **16** and (or) **17**.

The failure of our 5,6,7,8-tetrahydro-1*H*-2-benzothiopyran derivatives **7***c* and **17** to undergo the expected Diels–Alder reactions led us to consider an alternative scenario where the desired adduct would result from an initial Diels–Alder reaction of a suitably substituted thiopyran diene followed by closure of the second carbocyclic ring (Scheme 5). Towards this end, the dione **12** was converted into the monoketal **18**, which, upon treatment with TIPSOTf and Et_3N, gave the diene **19**. Reaction of **19** with maleimide or *N*-substituted derivatives in benzene solution at 130–140°C gave ca. 7–10:1 mixtures (^{1}H NMR) of *endo* and *exo* Diels–Alder adducts **20** and **21**, respectively, in 30–35% yield.[4] The stereochemistry of the adducts was readily assigned, as previously (3*b*,*d*,*g*), based on the characteristic magnitudes of the H–H coupling constants observed for 2-thiabicyclo[2.2.2]octanes (see Fig. 1). Treatment of **20***a* with aqueous HF in acetonitrile provided the dione **22***a*, which, gratifyingly, underwent acid-catalyzed cyclization to **23***a* on heating with *p*-TsOH. The enone **23***b* was prepared analogously. Diels–Alder reactions of **19** with *N*-phenyl- and *N*-methylmaleimide in the presence of $EtAlCl_2$ gave the diones **22***a* and **22***b*, respectively, in good yields after acidic work-up (3*d*). Lewis acid mediated reactions of **19** with 3-propenoyl-2-oxazolidinone and with

Scheme 5.

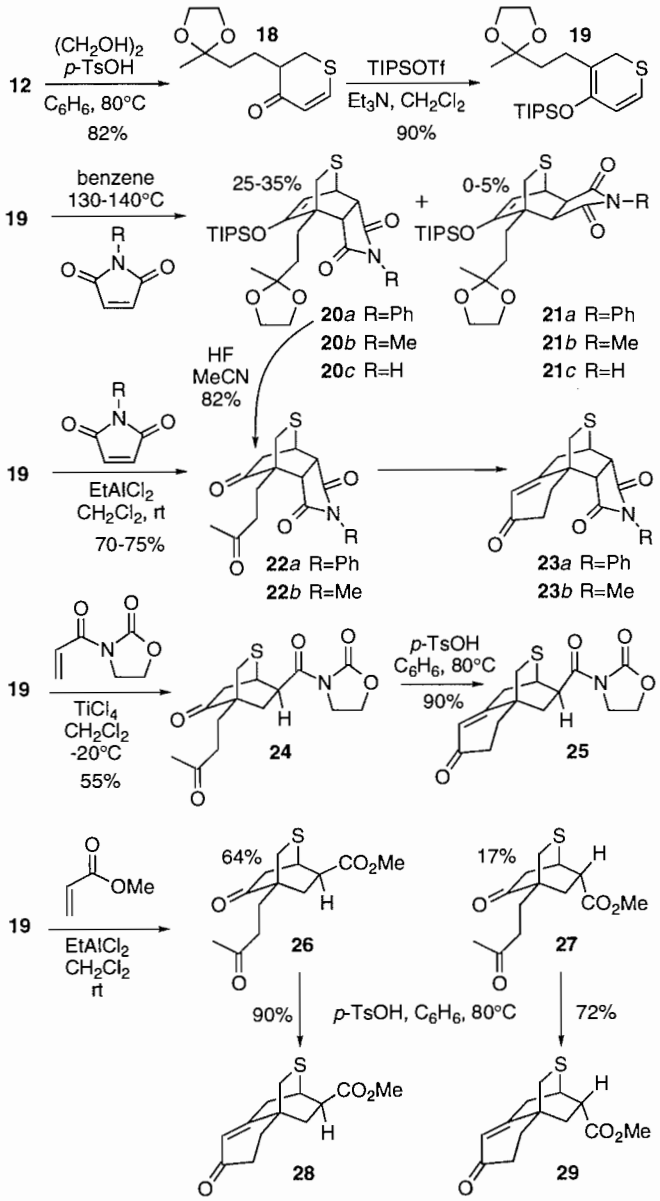
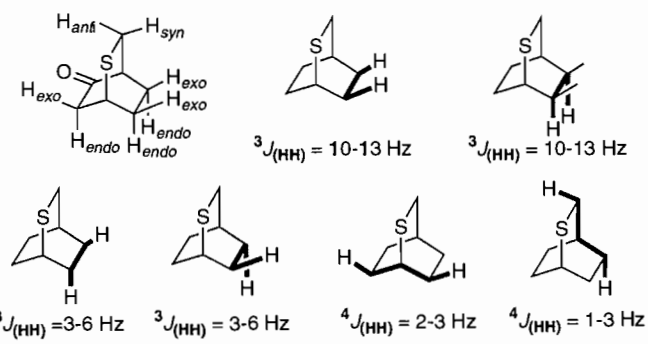


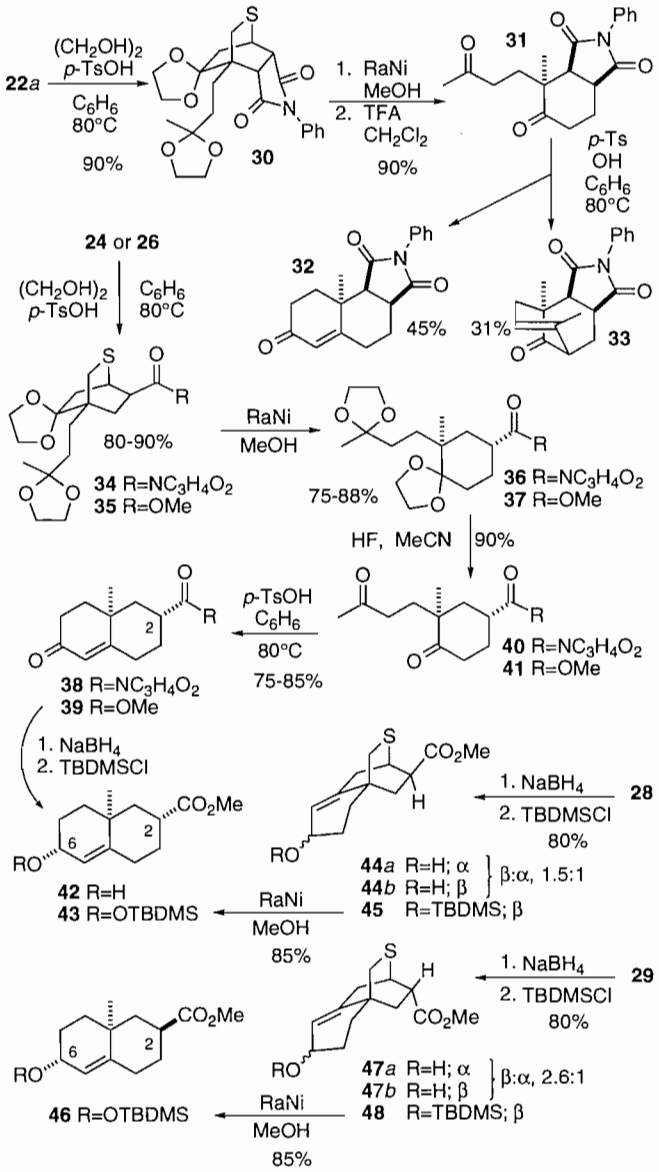
Fig. 1. Typical $^3J_{(HH)}$ and $^4J_{(HH)}$ coupling constants for 2-thiabicyclo[2.2.2]octan-5-ones.



[3] The corresponding acetate **14***b* was also characterized.

[4] The *endo* adducts **20***a*,*b*,*c* were isolated and characterized. In each case, the corresponding *exo* adducts could be detected in the ^{1}H NMR spectra of the reaction mixtures (*endo*:*exo* ca. 7–10:1) but only **21***a* was isolated and characterized.

Scheme 6.



methyl acrylate were highly *exo*-selective in analogy with similar reactions with a less substituted thiopyran diene (cf. **11**) (3*d*). The product diones **24**, **26**, and **27** readily cyclized to the corresponding enones **25**, **28**, and **29**. The enones **23**, **25**, **28**, and **29** can be regarded as synthetically equivalent to Diels–Alder adducts of the 5,6,7,8-tetrahydro-1*H*-2-benzothiopyran derivative **17**.

Despite considerable experimentation, we were unable to cleanly obtain 10-methyl-Δ^4-octalin-3-one derivatives by direct desulfurization of the enones **23**, **25**, **28**, and **29** with Raney nickel or with nickel boride (11). In each case, a mixture of products was obtained in which reduction or migration of the double bond and (or) reduction or deoxygenation of the ketone had occurred in addition to desulfurization. This problem could be avoided by effecting desulfurization prior to the aldol cyclization (Scheme 6). Thus, acid-catalyzed reaction of **22***a* (or **20***a*) with ethylene glycol gave the bisketal **30**, which was smoothly desulfurized on treatment with Raney Ni to give the diketone **31** after an acidic work-up. Aldol condensation of **31** gave the desired **32** along with a substantial amount of the regioisomeric product **33**. Similarly, the diones **24** and **26** were subjected to the same series of reactions to obtain the desired 10-methyl-Δ^4-octalin-3-one derivatives **38** and **39**.[5] The expected *cis* stereochemistry for **38** and **39** was confirmed by the small vicinal coupling constants for HC-2 (numbering according to formal nomenclature)[5] in the respective ^{1}H NMR spectra, which clearly indicated an equatorial proton.[5]

Alternatively, the enones **28** and **29** were reduced with $NaBH_4$ in methanol to give, in each case, a diastereoisomeric mixture of alcohols **44***a*,*b* and **47***a*,*b*, respectively. The major alcohol isomers **44***b* and **47***b* were each converted into the corresponding *tert*-butyldimethylsilyl (TBDMS) ethers (**45** and **48**) and then desulfurized by treatment with Raney nickel to give the desired 10-methyl-Δ^4-octalin-3-one derivatives **43** and **46**,[5] respectively (Scheme 6).[6] The expected relative stereochemistry between the methyl and methoxycarbonyl groups was confirmed as *cis* for **43** and *trans* for **46** by the vicinal coupling constants observed for HC-2 in the ^{1}H NMR spectra; this proton was clearly equatorial in **43** and axial in **46**. The relative stereochemistry at C-6 in **43** (and thus in **45** and **44***a*,*b*) was determined by $NaBH_4$ reduction of **39** followed by formation of the TBDMS ether which gave a product (**43**) identical to that obtained from desulfurization of **45**. Ample literature precedent suggests that hydride reduction of Δ^4-octalin-3-one derivatives like **39** should selectively produce the alcohol with the hydroxyl group *cis* to the substituent at the ring junction (i.e., Me) (12). The stereochemistry at C-6 in **46** was assigned based on the close similarity of the HC-6 protons in the NMR spectra of **43** and **46** and on the assumption that the reductions of **28** and **29** occur with the same diastereofacial selectivity.

In summary, the 5,6,7,8-tetrahydro-1*H*-2-benzothiopyran derivatives **7***c* and **17**, prepared as surrogates for the unreactive 1-ethenyl-2-methylcyclohexene, failed to produce the desired Diels–Alder adducts. By contrast, the protected 2-oxobutyl-2*H*-thiopyran diene **19** reacted with maleimide and acrylate dienophiles to give adducts (**20**, **22**, **24**, **26**) in modest to good yields. The observed stereoselectivities, *endo* with maleimides and *exo* with acrylate dienophiles, are in accord with previous results obtained with less substituted 2*H*-thiopyran dienes like **11**. The Diels–Alder adducts are easily and efficiently converted into products that are synthetically equivalent to Diels–Alder adducts of **17**. Desulfurization of those products gives 10-methyl-Δ^4-octalin derivatives that are synthetically equivalent to hypothetical Diels–Alder adducts of 3-ethenyl-4-methyl-3-cyclohexenone. Depending on the scope and stereoselectivity of the Diels–Alder reactions of **19** and analogues, this approach should be applicable to the synthesis of a variety of natural product skeletons. We are actively investigating this strategy.

[5] Formally these are 1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-oxonaphthalene-2-carboxylic acid derivatives.

[6] Similar reaction of the minor alcohol isomers proceeded analogously; however, the products were not fully characterized in these cases.

Experimental

General methods

All solvents were distilled prior to use. Pyridine and Et_3N were distilled from CaH_2 and stored over KOH pellets. i-Pr_2NH was freshly distilled from CaH_2. Anhydrous solvents were distilled under argon as follows: ether and tetrahydrofuran (THF) from benzophenone potassium ketyl; benzene, toluene, and CH_2Cl_2 from P_2O_5 and stored over 3Å molecular sieves; MeOH from $Mg(OMe)_2$. Benzene solutions for Diels–Alder reactions were degassed by bubbling argon through the solvent (solution) followed by three freeze–thaw cycles under high vacuum (0.01 Torr; 1 Torr = 133.3 Pa). Unless otherwise noted, reactions were carried out under an atmosphere of argon and reaction temperatures refer to the bath. Concentration refers to removal of volatiles at water aspirator pressure on a rotary evaporator.

Preparative TLC was carried out on glass plates (20 × 20 cm) precoated (0.25 mm) with silica gel 60 F_{254}. Materials were detected by visualization under an ultraviolet lamp (254 nm) and (or) by treating a 1 cm vertical strip removed from the plate with a solution of phosphomolybdic acid (5%) containing a trace of ceric sulfate in aqueous sulfuric acid (5% v/v), followed by charring on a hot plate. Flash column chromatography (FCC) was performed according to the method of Still et al. (13) with Merck Silica Gel 60 (40–63 μm). Medium-pressure chromatography (MPC) was performed with minor modifications of the procedure reported by Taber (14). All mixed solvent eluents are reported as v/v solutions.

Spectral data

Low-resolution mass spectra (LRMS) were recorded on a magnetic scanning MS-12 instrument. EI ionization was accomplished at 70 eV and CI at 50 eV with ammonia as the reagent gas; only partial data are reported. IR spectra were recorded on a Fourier transform interferometer using a diffuse reflectance cell; only diagnostic peaks are reported. Unless otherwise noted, NMR spectra were measured in $CDCl_3$ solution at 300 MHz for ^1H and 75 MHz for ^{13}C. For ^1H NMR, residual $CHCl_3$ in $CDCl_3$ was employed as the internal standard (7.26 δ); for ^{13}C NMR, $CDCl_3$ was employed (77.0 δ). The ^1H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad), ap (apparent); the list of coupling constants (J) corresponds to the order of the multiplicity assignment. ^1H NMR spectra were normally obtained with a digital resolution of 0.244 Hz/pt (sweep width = 4000 Hz, FID = 32 K data points) and coupling constants are reported to the nearest 0.5 Hz. The ^1H NMR assignments were made on the basis of chemical shift and multiplicity and were confirmed, where necessary, by homonuclear decoupling and (or) NOE experiments. The multiplicity of ^{13}C NMR signals refers to the number of attached H's (i.e., s = C, d = CH, t = CH_2, q = CH_3) and was determined by J-modulation (15). The ^{13}C assignments were made on the basis of chemical shift, multiplicity, and consistency within a series of similar structures. Assignments for ^{13}C signals of the same multiplicity and similar chemical shift (i.e., $\Delta\delta < 1$ ppm) are tentative. Elemental analyses were performed using a Perkin–Elmer 2400 CHN elemental analyzer.

Materials

2,2-Dimethylcyclohexanone (16), methyl phenacyl sulfide (17), 3-methoxy-2-butenol (9), **11** (3b), 3-propenoyl-2-oxazolidinone (18) were prepared as reported. Methyl acrylate was freshly distilled. All other reagents were commercially available and, unless otherwise noted, were used as received.

General procedure for preparation of ***5***

Ethyl cyclohexylidenethanoate and the 2′-methyl and 2′,2′-dimethyl derivatives were prepared in 60–70% yields by reactions of triethyl phosphonoacetate with the corresponding cyclohexanones according to the procedure of Wood and coworkers (19). Vinyl ketene acetals were prepared according to the procedure of Savard and Brassard (20): The esters (1–1.5 g) were added dropwise to a stirred solution of LDA (prepared from i-Pr_2NH (1.1 equiv.) and n-BuLi (1 equiv.)) in dry THF (1 mL/mmol of ester) at −78°C. After 1 h, TMSCl (1.5 equiv.) was added to the mixture at −78°C. The reaction mixture was allowed to slowly warm to room temperature (rt) and then was concentrated and the residue distilled to give the products.

*1-[2-Ethoxy-2-(trimethylsilyloxy)ethenyl]cyclohexene (****5****a)* (1 g, 80% yield): bp 95–100°C (3 Torr). ^1H NMR δ: 5.56 (1H, dd, J = 3, 3 Hz, HC-2), 4.08 (1H, s, HC-1′), 3.75 (2H, q, J = 7 Hz, H_2CO), 2.28–220 (2H, m), 2.12–2.00 (2H, m), 1.70–1.48 (4H, m), 1.28 (3H, t, J = 7 Hz, H_3CC), 0.22 (9H, s, H_3CSi).

*1-[2-Ethoxy-2-(trimethylsilyloxy)ethenyl]-6-methylcyclohexene, (****5****b)* (1.4 g, 75% yield): bp 95–100°C (2 Torr). ^1H NMR δ: 5.12 (1H, dd, J = 4, 4 Hz, HC-2), 3.98 (1H, s, HC-1′), 3.77 (2H, q, J = 7 Hz, H_2CO), 2.50–2.40 (1H, m), 2.07–1.98 (2H, m), 1.80–1.40 (4H, m), 1.26 (3H, t, J = 7 Hz, H_3CCH_2), 1.15 (3H, d, J = 7 Hz, H_3CC-6), 0.23 (9H, s, H_3CSi).

*1-[2-Ethoxy-2-(trimethylsilyloxy)ethenyl]-6,6-dimethylcyclohexene (****5****c)* (0.72 g, 62% yield): bp 92–95°C (3 Torr). ^1H NMR δ: 5.87 (1H, t, J = 4 Hz, HC-2), 4.00 (1H, s, HC-2′), 3.77 (2H, q, J = 7 Hz, H_2CO), 2.10–2.00 (2H, m, H_2C-3), 1.70–1.40 (6H, m), 1.29 (3H, t, H_3CCH_2), 1.02 (6H, s, H_3CC-6), 0.22 (9H, s, H_3CSi).

General procedure for the preparation of ***6***

A degassed solution of methyl phenacyl sulphide (19) (1 equiv.) and the ketene acetal **5** (2 equiv.) in dry benzene (5 mL/mmol of **5**) was irradiated at rt for 2 h through a 6% aqueous $CuSO_4$ filter using a 100 W sun lamp. Trifluoroacetic acid (TFA; several drops) was added to the mixture and, after stirring for 1.5 h at rt, the reaction mixture was concentrated and fractionated by FCC (15–30% ether in hexane) to give the products.

*1,5,6,7,8,8a-Hexahydro-3*H*-2-benzothiopyran-3-one, (****6****a)* (100 mg, 60% yield): IR ν_{max}: 2931, 1639, 1207, 1156 cm^{-1}; ^1H NMR δ: 5.93 (1H, dd, J = 2, 2 Hz, HC-4), 3.08–3.02 (2H, m, HC-1), 2.60–2.40 (2H, m, HC-5), 2.32–2.18 (1H, m, HC-8a), 2.08–1.83 (3H, m), 1.61–1.25 (3H, m); ^{13}C NMR δ: 189.9 (s, C-3), 163.9 (s, C-4a), 123.7 (d, C-4), 36.7 (d, C-8a), 36.1 (t, C-5), 33.1 (t), 33.0 (t), 26.4 (t), 25.2 (t); LRMS (EI), m/z (relative intensity): 168 ($[M]^+$, 15), 140 (100), 111 (28), 97 (24), 79 (26). Elemental anal. calcd. for $C_9H_{12}OS$: C 64.25, H 7.19; found: C 64.10, H 7.07.

*1,5,6,7,8,8a-Hexahydro-5-methyl-3*H*-2-benzothiopyran-3-one (**6**b)* (342 mg, 34%): IR ν_{max}: 2930, 1639, 1177 cm^{-1}; ^1H NMR δ: 5.97 (0.5H, d, J = 1.5 Hz), 5.94 (0.5H, s), 3.35 (0.5H, dd, J = 5, 13.5 Hz), 2.99 (1.5H, m), 2.80–2.60 (1H, m), 2.51–2.41 (0.5H, m), 2.32–2.22 (0.5H, m), 2.02–1.75 (2H, m), 1.75–1.50 (1H, m), 1.64 (2.5H, m), 1.38–1.25 (0.5H, m), 1.18 (1.5H, d, J = 7 Hz), 1.10 (1.5H, d, J = 7 Hz); LRMS (EI), *m/z* (relative intensity): 182 ($[M]^+$, 37), 154 (100), 139 (46), 111 (35).

*1,5,6,7,8,8a-Hexahydro-5,5-dimethyl-3*H*-2-benzothiopyran-3-one (**6**c)* (187 mg, 37%): IR ν_{max}: 2930, 1636, 1160 cm^{-1}; ^1H NMR δ: 6.08 (1H, d, J = 1.5 Hz, HC-4), 3.05–2.95 (2H, m, H_2C-1), 2.78–2.66 (1H, m, HC-8a), 2.00–1.90 (1H, m), 1.80–1.55 (3H, m), 1.50–1.25 (2H, m), 1.16 (3H, s, H_3C), 1.12 (3H, s, H_3C); LRMS (EI), *m/z* (relative intensity): 196 ($[M]^+$, 17), 168 (91), 153 (100).

General procedure for enolsilylation of thiopyranones
A solution of thiopyranone (1 equiv.), Et_3N (2.5 equiv.), and TIPSOTf (1.25 equiv.) in CH_2Cl_2 (ca. 10 mL/mmol of thiopyranone) was stirred under argon at rt for 0.5–3 h. The mixture was poured onto 5% Na_2CO_3 and extracted with ether (×3). The combined organic layers were dried over Na_2SO_4, concentrated, and fractionated by FCC (hexane; SiO_2 pretreated with Et_3N in hexane) to give the product. The dienol silyl ethers were freshly prepared and used immediately and the proposed structures were characterized only by ^1H NMR.

*6,7,8,8a-Tetrahydro-3-tris(1-methylethyl)silyloxy-1*H*-2-benzothiopyran (7*a*)* (3 h; 64 mg, 98%): ^1H NMR δ: 5.61 (1H, s, HC-4), 5.28 (1H, br s, HC-5), 2.73 (1H, dd, J = 11, 12 Hz, HC-1), 2.66 (1H, dd, J = 3.5, 12 Hz, HC-1), 2.48–2.33 (1H, m, HC-8a), 2.12–2.05 (2H, m, HC-6), 1.95–1.78 (2H, m), 1.68–1.51 (1H, m), 1.25–1.05 (21H, m).

*6,7,8,8a-Tetrahydro-5-methyl-3-tris(1-methylethyl)silyloxy-1*H*-2-benzothiopyran (7*b*)* (2 h; 15 mg, 72%): ^1H NMR δ: 5.90 (1H, s, HC-4), 2.72 (1H, dd, J = 12, 12 Hz, HC-1), 2.62 (1H, dd, J = 3.5, 12 Hz, HC-1), 2.42–2.38 (1H, m, HC-8a), 2.15–1.50 (6H, m), 1.66 (3H, br s, H_3CC-5).

*6,7,8,8a-Tetrahydro-5,5-dimethyl-3-tris(1-methylethyl)silyloxy-1H-2-benzothiopyran (7*c*)*
This diene was particularly unstable. Work-up of a reaction of **6***c* (5 mg, 0.025 mmol), Et_3N (0.02 mL, 0.15 mmol), and TIPSOTf (0.015 mL, 0.05 mmol) after 20 min gave a crude product that was a 1.8:1 mixture of **7***c* and **6***c*, respectively; ^1H NMR δ for **7***c*: 5.58 (1H, s, HC-4), 3.24 (1H, s, HC-1), 2.07 (2H, br t, J = 6 Hz, HC-8), 1.75–1.55 (2H, m), 1.48–1.40 (2H, m), 1.30–1.00 (21H, m, H_3CCHSi), 0.96 (6H, s, H_3CC-5). Fractionation by PTLC (66% ether in hexane) of the residue after concentration gave 5,6,7,8-tetrahydro-5,5-dimethyl-1*H*-2-benzothiopyran-3(4*H*)-one (**8**; 1.2 mg, 24%): ^1H NMR δ: 3.45 (2H, s, HC-1), 3.12 (2H, s, HC-4), 2.15 (2H, br t, J = 6 Hz, HC-8), 1.71–1.60 (2H, m), 1.52–1.45 (2H, m), 1.00 (6H, s, H_3C); and 5,6,7,8-tetrahydro-5,5-dimethyl-3*H*-2-benzothiopyran-3-one (**9**; 1.4 mg, 29%): ^1H NMR δ: 7.00 (1H, s, HC-1), 6.65 (1H, s, HC-4), 2.68 (2H, br t, J = 6 Hz, HC-8), 1.80–1.70 (2H, m), 1.67–1.57 (2H, m), 1.26 (6H, s, H_3C).

*Attempted Diels–Alder reaction of 7*c
Enolsilylation of **6***b* (8.8 mg, 0.045 mmol) for 30 min at rt gave an oil (14 mg) after work-up and fractionation. A solution of the oil and *N*-phenylmaleimide (8 mg, 0.045 mmol) in $C_6D_5CD_3$ (0.4 mL) was sealed in a NMR tube and heated at 140°C for 72 h. The mixture was concentrated and fractionated by PTLC (66% ether in hexane) to give **8** (4.7 mg, 60%) and a product tentatively indentified as 3a,4,5,6,7,8,9,9a-octahydro-5,5-dimethyl-2-phenyl-9,4-epithiomethano-1*H*-benz[*e*]isoindole-1,3(2*H*),11-trione (**10**; 4 mg, 27%): ^1H NMR δ: 7.16–7.50 (5H, m, Ar-H), 4.36 (1H, d, J = 4 Hz, HC-9), 4.20 (1H, d, J = 3 Hz, HC-4), 3.75 (1H, dd, J = 4, 9 Hz, HC-9a), 3.50 (1H, dd, J = 3, 9 Hz, HC-3a), 2.35–2.12 (2H, m, H_2C-8), 1.80–1.55 (2H, m), 1.50–1.40 (2H, m), 1.02 (3H, s, H_3C), 0.86 (3H, s, H_3C).

*3,4-Dihydro-3-(3-oxobutyl)-4*H*-thiopyran-4-one (**12**)*
A solution of $BF_3{\cdot}Et_2O$ (0.35 mL, 2.7 mmol) in dry ether (0.4 mL) was added dropwise to a stirred solution of **11** (2.8 g, 15 mmol) and 3-methoxy-2-butenol (9) (1.02 g, 10 mmol) in CH_3NO_2 (28 mL) at −20°C under argon. After 1 h, the reaction mixture was quenched by addition of saturated $NaHCO_3$ and was extracted with CH_2Cl_2 (×3). The combined organic layers were dried over Na_2SO_4, concentrated, and fractionated by FCC (75% ether in hexane) to give recovered starting material as 2,3-dihydro-4*H*-thiopyran-4-one (1 g, 58%) and **12** (10) (0.78 g, 42%): IR ν_{max}: 3033, 1712, 1657, 1583, 1551 cm^{-1}; ^1H NMR δ: 7.37 (1H, dd, J = 10 Hz, HC-6), 6.10 (1H, d, J = 10 Hz, HC-5), 3.33 (1H, dd, J = 4, 13.5 Hz, HC-2), 3.07 (1H, dd, J = 9, 13.5 Hz, HC-2), 2.58 (2H, t, J = 7.5 Hz, H_2C-2′), 2.59–2.50 (1H, m, HC-3), 2.16 (3H, s, H_3C-4′), 2.16–2.07 (1H, m, HC-1′), 1.88–1.79 (1H, m, HC-1′); ^{13}C NMR δ: 208.1 (s, C-3′), 195.5 (s, C-4), 145.4 (d, C-6), 122.9 (d, C-5), 44.3 (d, C-3), 40.8 (t, C-2′), 32.4 (t, C-2), 30.0 (q, C-4′), 22.8 (t, C-1′); LRMS (CI, NH_3), *m/z* (relative intensity): 185 ($[M+1]^+$, 100), 167 (34), 113 (18).

*1,7,8,8a-Tetrahydro-6*H*-2-benzothiopyran-6-one (**13**)*
A solution of **12** (0.184 g, 1 mmol) and *p*-TsOH (10 mg, 0.05 mmol) in benzene (10 mL) was heated under reflux for 4.5 h. The cooled (rt) reaction mixture was washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (75% ether in hexane) to give recovered **12** (26 mg, 14%) and **13** (0.12 g, 72%): IR ν_{max}: 3038, 1641, 1583, 1548 cm^{-1}; ^1H NMR δ: 6.73 (1H, d, J = 10 Hz, HC-3), 6.34 (1H, d, J = 10 Hz, HC-4), 5.78 (1H, s, HC-5), 2.85–2.75 (3H, m, H_2C-1, HC-8a), 2.56 (1H, ddd, J = 2.5, 4.5, 17 Hz, HC-7), 2.43 (1H, ddd, J = 5, 14, 17 Hz, HC-7), 2.22–2.12 (1H, m, HC-8), 1.82–1.68 (1H, m, HC-8); ^{13}C NMR δ: 198.7 (s, C-6), 153.6 (s, C-4a), 132.9 (d, C-3), 124.6 (d, C-4), 123.2 (d, C-5), 37.9 (t, C-7), 35.9 (d, C-8a), 31.3 (t, C-1 or C-8), 30.6 (t, C-8 or C-1); LRMS (EI), *m/z* (relative intensity): 166 ($[M]^+$, 100), 138 (36), 110 (98).

*3a,9b-Dihydro-4-[(2-hydroxyethyl)oxy]-9*H*-4,9a-ethanothiopyrano[3,4-e]isoindole-1,3(2*H*,4*H*)-trione (**14***a*)*
A solution of the 4:1 mixture of **16** and **17** (18 mg, 0.085 mmol) and *N*-phenylmaleimide (15 mg, 0.085 mmol) in C_6D_6 (0.5 mL) was sealed in a NMR tube and heated at 120°C. After 87 h, ^1H NMR revealed the absence of **16** and **17**. The solution was concentrated and fractionated by FCC (ethyl acetate) to

give **13** (4 mg, 28%) and **14***a* (11 mg, 34%): IR ν_{max}: 3411, 1703, 1497 cm^{-1}; ^1H NMR δ: 7.38–7.29 (3H, m, Ar-H), 7.05–7.00 (2H, m, Ar-H), 6.30 (1H, d, J = 9.5 Hz, HC-7), 6.23 (1H, d, J = 9.5 Hz, HC-6), 5.87 (1H, s, HC-5), 4.16 (1H, d, J = 13 Hz, HC-3b), 3.90–3.68 (4H, m, H_2CO), 3.34 (1H, d, J = 8.5 Hz, HC-9), 2.99 (1H, d, J = 8.5 Hz, HC-9), 2.49 (1H, d, J = 13 Hz, HC-9b), 2.33–2.20 (1H, m, HC-10 or HC-11), 2.10–1.95 (1H, m, HC-10 or HC-11), 1.65–1.48 (2H, m, HC-10, HC-11); ^{13}C NMR δ: 175.4 (s, C=O), 174.0 (s, C=O), 135.4 (s, C-5a), 131.9 (s, C_6H_5), 128.5 (d ×2, C_6H_5), 128.0 (d, C_6H_5), 126.6 (d ×2, C_6H_5), 126.6 (d, C-7), 123.5 (d, C-5 or C-6), 123.4 (d, C-5 or C-6), 78.3 (s, C-4), 64.1 (t, CH_2O), 60.5 (t, CH_2O), 48.2 (d, C-3a), 44.6 (d, C-9b), 40.6 (s, C-9a), 30.4 (t, C-9), 27.9 (d, C-10 or C-11), 27.5 (t, C-10 or C-11); LRMS (CI, NH_3), *m/z* (relative intensity): 384 ($[M+1]^+$, 100), 210 (38).

*2-[(1,2,3,3a,4,9b-Hexahydro-1,3-dioxo-9*H*-4,9a-ethanothiopyrano[3,4-*e*]isoindol-4-yl)oxy]ethyl ethanoate (**14***b*)*

A solution of **14***a* (9 mg, 0.023 mmol), pyridine (1 drop), and acetic anhydride (2 drops) in CH_2Cl_2 (ca. 1 mL) was stirred at rt for 38 h. The mixture was diluted with CH_2Cl_2, washed with 1 N HCl and water, dried over Na_2SO_4, and concentrated from toluene (×2) to give **14***b* (9 mg, 92%); IR ν_{max}: 3062, 1773, 1735, 1701, 1596, 1497 cm^{-1}; ^1H NMR δ: 7.46–7.30 (3H, m, Ar-H), 7.18–7.11 (2H, m, Ar-H), 6.38 (1H, d, J = 10 Hz, HC-7), 6.30 (1H, d, J = 10 Hz, HC-6), 5.97 (1H, s, HC-5), 4.36 (1H, d, J = 13 Hz, HC-3a), 4.34–4.28 (2H, m, H_2COCO), 4.07–4.00 (1H, m, HCO), 3.85–3.77 (1H, m, HCO), 3.35 (1H, d, J = 8.5 Hz, HC-9), 3.02 (1H, d, J = 8.5 Hz, HC-9), 2.54 (1H, d, J = 13 Hz, HC-9b), 2.33–2.24 (1H, m, HC-10 or HC-11), 2.08 (3H, s, H_3CCO), 2.06–1.95 (1H, m, HC-10 or HC-11), 1.62–1.45 (2H, m, HC-10, HC-11); ^{13}C NMR δ: 175.3 (s, C=O), 173.3 (s, C=O), 171.3 (s, O=CCH_3), 136.2 (s, C-4a), 131.7 (s, C_6H_5), 129.1 (d ×2, C_6H_5), 128.6 (d, C_6H_5), 126.5 (d ×2, C_6H_5), 126.3 (d, C-7), 124.9 (d, C-5 or C-6), 123.5 (d, C-5 or C-6), 79.1 (t, CH_2O), 63.7 (t, CH_2O), 61.3 (s, C-4), 49.0 (d, C-3a), 45.4 (d, C-9b), 41.5 (s, C-9a), 32.0 (t, C-9), 28.9 (t, C-10 or C-11), 28.4 (t, C-10 or C-11), 21.0 (q, CH_3CO); LRMS (CI, NH_3), *m/z* (relative intensity): 426 ($[M+1]^+$, 24), 87 (100).

*1,7,8,8a-Tetrahydrospiro[6*H*-2-benzothiopyran-6,2′-[1,3]dioxolane] (**16**) and 1,5,7,8-tetrahydrospiro[6*H*-2-benzothiopyran-6,2′-[1,3]dioxolane] (**17**)*

A solution of **13** (50 mg, 0.3 mmol), ethylene glycol (ca. 0.1 mL), and pyridinium *p*-toluenesulfonate (PPTS, 3 mg) in benzene (1 mL) was heated under reflux for 2 h. The cooled (rt) reaction mixture was diluted with benzene, washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (75% ether in hexane) to give recovered **13** (12 mg, 24%) and product as a 4:1 mixture of **16** and **17** (32 mg, 51%): IR ν_{max}: 3019, 1629, 1373, 1124 cm^{-1}; ^1H NMR δ for **16**: 6.24 (1H, dd, J = 1.5, 10 Hz, HC-3), 6.14 (1H, d, J = 10 Hz, HC-4), 5.36 (1H, br s, HC-5), 4.05–3.85 (4H, m, H_2CO), 2.77 (1H, d, J = 12.5 Hz, HC-1), 2.66 (1H, ddd, J = 1.5, 3.5, 12.5 Hz, HC-1), 2.58–2.46 (1H, m, HC-8a), 2.03–1.78 (3H, m, H_2C-7, HC-8), 1.57 (1H, m, HC-8); δ for **17**: 6.15 (1H, d, J = 10 Hz, HC-3), 5.89 (1H, d, J = 10 Hz, HC-4), 3.18 (2H, br s, H_2C-1), 2.71 (2H, s, H_2C-5); ^{13}C NMR δ for **16**: 138.4 (s, C-4a), 124.0 (d, C-3), 123.8 (d, C4 or C-5), 123.6 (d, C5 or C-4), 106.3 (s, C-6), 64.9 (t, CH_2O), 64.4 (t, CH_2O), 36.3 (d, C-8a), 34.0 (t, C-1), 31.6 (t, C-7), 28.8 (t, C-8); LRMS (CI, NH_3), *m/z* (relative intensity): 211 ($[M+1]^+$, 100), 182 (20), 163 (8), 138 (22), 110 (15).

*3,4-Dihydro-3-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-4*H*-thiopyran-4-one (**18**)*

A solution of **12** (230 mg, 1.25 mmol), ethylene glycol (0.5 mL, excess), and PPTS (20 mg) in benzene (15 mL) was heated under reflux for 2 h. The cooled (rt) reaction mixture was washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, and concentrated to give an oil (this was a mixture of mono- and bis-ketals). The oil was dissolved in acetone that contained several drops of water and stirred with PPTS (20 mg) for 2 h. The mixture was concentrated, diluted with ether, washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (75% ether in hexane) to give **18** (234 mg, 82%): IR ν_{max}: 1658, 1551, 1060 cm^{-1}; ^1H NMR δ: 7.45 (1H, d, J = 10 Hz, HC-6), 6.12 (1H, d, J = 10 Hz, HC-5), 3.99–3.87 (4H, m, H_2CO), 3.31 (1H, dd, J = 3.5, 13.5 Hz, HC-2), 3.05 (1H, dd, J = 9, 13.5 Hz, HC-2), 2.58–2.48 (1H, m, HC-3), 2.02–1.92 (1H, m, HC-1′), 1.80–1.55 (3H, m, HC-1′,H_2C-2′), 1.24 (3H, s, H_3C); ^{13}C NMR δ: 195.9 (s, C-4), 145.1 (d, C-6), 123.0 (d, C-5), 109.6 (s, C-2″), 64.7 (t, CH_2O), 64.6 (t, CH_2O), 45.1 (d, C-3), 36.2 (t, C-2), 31.8 (t, C-2′), 23.9 (q, CH_3), 22.7 (t, C-1′); LRMS (CI, NH_3), *m/z* (relative intensity): 229 ($[M+1]^+$, 100), 87 (66). Elemental anal. calcd. for $C_{11}H_{16}O_3S$: C 57.87, H 7.06, found: C 58.06, H 7.05.

*3-[2-(2-Methyl-1,3-dioxolan-2-yl)ethyl]-4-[(tris(1-methylethyl)silyl)oxy]-2*H*-thiopyran (**19**)*

TIPSOTf (0.24 mL, 0.90 mmol) was added to a stirred solution of **18** (171 mg, 0.75 mmol) and Et_3N (0.32 mL, 2.2 mmol) in CH_2Cl_2 (8 mL) at rt. After 20 min, the reaction mixture was concentrated and fractionated by FCC (pentane; silica gel pretreated with 10% v/v Et_3N in pentane) to give **19** (260 mg, 90%): IR ν_{max}: 1657, 1611, 1463, 1223 cm^{-1}; ^1H NMR δ: 6.18 (1H, d, J = 9.75 Hz, HC-6), 5.94 (1H, d, J = 9.75 Hz, HC-5), 3.99–3.90 (4H, m, H_2CO), 3.30 (2H, s, H_2C-2), 2.39–2.30 (2H, m, H_2C-1′), 1.80–1.70 (2H, m, H_2C-2′), 1.16 (3H, s, H_3CC-2″), 1.20–1.00 (21H, m, $(H_3C)_2CHSi$); ^{13}C NMR δ: 144.0 (s, C-4), 122.9 (d, C-6), 122.3 (d, C-5), 109.8 (s, C-3′), 107.0 (s, C-3), 64.7 (t ×2, CH_2O), 37.0 (t, C-2), 29.4 (t, C-1′), 24.6 (t, C-2′), 23.9 (q, CH_3C-2″), 18.0 (q, CH_3CHSi), 13.2 (d, CHSi); LRMS (CI, NH_3), *m/z* (relative intensity): 385 ($[M+1]^+$, 100), 227 (76).

*General procedure for thermal Diels–Alder reactions of **19** with maleimides*

A solution of **19** (0.07–0.15 g), BHT (0.1 equiv.), and the maleimide derivative (1.2 equiv.) in C_6D_6 or C_6H_6 (0.5–1 mL) was sealed in an NMR tube and heated at 130–140°C for 48–72 h. ^1H NMR of the reaction mixture indicated the presence of a 7–10:1 mixture of *endo*:*exo* adducts. The cooled (rt) solution was concentrated and fractionated by FCC (50% ethyl acetate in hexane) to give the adduct(s).

*General procedure for $EtAlCl_2$ mediated Diels–Alder reactions of **19** with maleimides*

$EtAlCl_2$ (1 M solution in hexane; 1 equiv.) was added to a stirred solution of the dienophile (1.2 equiv.) in dry CH_2Cl_2 (20 mL/mmol of **19**) at rt. A solution of **19** (20–50 mg; 1 equiv.) in CH_2Cl_2 (10 mL/mmol of **19**) was added via a

syringe to the mixture and, after 1 h, the reaction was quenched by addition of saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 and the combined organic layers were dried over Na_2SO_4 and concentrated. The enol ethers **20** could be obtained by fractionation of the residue by FCC (75% ether in hexane); however, because some hydrolysis could usually be detected at this point, it was convenient to complete the hydrolysis by dissolving the residue in CH_2Cl_2 (2 mL) containing TFA (2 drops). After stirring overnight, the mixture was concentrated and fractionated by FCC (ether) to provide **22**.

*(3a*S*, 4*R*, 7*R*, 7a*S*)-3a,4,7,7a-Tetrahydro-7-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-8-[(tris(1-methylethyl)silyl)oxy]-1,3-dioxo-2-phenyl-4,7-ethenothiopyrano[3,4-c]pyrrole-1,3(2H,-6H)-dione (**20**a)* (28% from thermal reaction of **19** with *N*-phenylmaleimide): IR ν_{max}: 3066, 1774, 1711, 1626, 1598 cm^{-1}; ^1H NMR δ: 7.18–7.47 (5H, m, Ar-H), 5.35 (1H, d, J = 7.5 Hz, HC-9), 4.08 (1H, dd, J = 3, 7.5 Hz, HC-4), 3.96 (4H, br s, H_2CO), 3.53 (1H, dd, J = 3, 8.5 Hz, HC-3a), 3.19 (1H, d, J = 11 Hz, HC-6_{syn}), 3.08 (1H, d, J = 8.5 Hz, HC-7a), 2.62 (1H, dt, J = 4.5, 13.5 Hz, HC-1′), 2.52 (1H, d, J = 11 Hz, HC-6_{anti}), 2.17 (1H, dd, J = 4.5, 13 Hz, HC-2′), 1.92 (1H, dt, J = 3, 13.5 Hz, HC-1′), 1.76 (1H, dt, J = 3, 13 Hz, HC-2′), 1.41 (3H, s, H_3CC-2″), 1.20–1.00 (21H, m, $(CH_3)_2CHSi$); ^{13}C NMR δ: 175.4 (s, C═O), 175.0 (s, C═O), 154.8 (s, C-8), 131.6 (s, C_6H_5), 129.2 (d ×2, C_6H_5), 128.5 (s, C_6H_5), 126.3 (d ×2, C_6H_5), 110.1 (s, C-2″), 102.2 (d, C-9), 64.8 (t, CH_2O), 64.7 (t, CH_2O), 49.8 (d, C-3a), 44.1 (s, C-7), 44.1 (d, C-7a), 35.9 (t, C-6), 35.7 (d, C-4), 33.3 (t, C-2′), 26.5 (t, C-1′), 23.9 (q, CH_3C-2″), 18.1 (q, CH_3CHSi), 12.6 (d, CHSi); LRMS (EI), *m/z* (relative intensity): 557 ($[M]^+$, 22), 470 (8), 424 (9), 340 (16), 87 (100), 73 (28), 59 (57).

*(3a*S*, 4*R*, 7*R*, 7a*S*)-3a,4,7,7a-Tetrahydro-2-methyl-1,3-dioxo-7-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-8-[(tris(1-methylethyl)silyl)oxy]-4,7-ethenothiopyrano[3,4-c]pyrrole-1,3-(2H,6H)-dione (**20**b)* (35% from thermal reaction of **19** with *N*-methylmaleimide): IR ν_{max}: 1775, 1703, 1626, 1463, 1434 cm^{-1}; ^1H NMR δ: 5.21 (1H, d, J = 7.5 Hz, HC-9), 3.96 (5H, m, HC-4, H_2CO), 3.35 (1H, dd, J = 3, 8.5 Hz, HC-3a), 3.10 (1H, d, J = 10.5 Hz, HC-6_{syn}), 2.90 (1H, d, J = 8.5 Hz, HC-7a), 2.83 (3H, s, H_3CN), 2.52 (1H, dt, J = 4.5, 13.5 Hz, HC-1′), 2.48 (1H, d, J = 10.5 Hz, HC-6_{anti}), 2.13 (1H, dt, J = 4.5, 13 Hz, HC-2′), 1.89 (1H, dt, J = 3.5, 13.5 Hz, HC-1′), 1.73 (1H, dt, J = 3.5, 13 Hz, HC-2′), 1.41 (3H, s, H_3CC), 1.20–1.00 (21H, m, $(H_3C)_2CHSi$); ^{13}C NMR δ: 176.5 (s, C═O), 176.2 (s, C═O), 154.6 (s, C-8), 110.1 (s, C-2″), 101.6 (d, C-9), 64.8 (t, CH_2O), 64.7 (t , CH_2O), 49.9 (d, C-3a), 44.1 (d, C-7a), 43.7 (s, C-7), 35.7 (t, C-6), 35.3 (d, C-4), 33.4 (t, C-2′), 26.5 (t, C-1′), 24.6 (q, CH_3N), 24.0 (q, CH_3), 17.9 (q, CH_3CSi), 12.5 (d, CHSi); LRMS (EI), *m/z* (relative intensity): 495 ($[M]^+$, 10), 383 (17), 278 (9), 115 (19), 88 (100), 73 (30), 59 (63).

*(3a*S*, 4*R*, 7*R*, 7a*S*)-3a,4,7,7a-Tetrahydro-7-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-8-[(tris(1-methylethyl)silyl)oxy]-1,3-dioxo-4,7-ethenothiopyrano[3,4-c]pyrrole-1,3(2H,6H)-dione (**20**c)* (36% from thermal reaction of **19** with maleimide): IR ν_{max}: 3213, 3080, 2944, 1778, 1720, 1712, 1627 cm^{-1}; ^1H NMR δ: 7.93 (1H, s br, HN), 5.29 (1H, d, J = 7.5 Hz, HC-9), 3.96 (5H, m, HC-3a, CH_2O), 3.41 (1H, dd, J = 3, 8.5 Hz, HC-4), 3.09 (1H, d, J = 11 Hz, HC-6_{syn}), 2.94 (1H, d, J = 8.5 Hz, HC-7a), 2.49 (1H, d, J = 11 Hz, HC-6_{anti}), 2.49 (1H, dt, J = 4.5, 13.5 Hz, HC-1′), 2.10 (1H, dt, J = 4.5, 13 Hz, HC-2′), 1.90 (1H, dt, J = 3, 13.5 Hz, HC-1′), 1.72 (1H, dt, J = 3, 13 Hz, HC-2′), 1.42 (3H, s, H_3CC-2″), 1.20–1.00 (21H, m, $(CH_3)_2CHSi$); ^{13}C NMR δ: 176.6 (s, C═O), 176.0 (s, C═O), 156.7 (s, C-8), 110.2 (s, C-2″), 101.7 (d, C-9), 64.8 (t, CH_2O), 64.7 (t, OCH_2), 51.2 (d, C-3a), 45.4 (d, C-7a), 43.7 (s, C-7), 35.6 (t, C-6), 35.1 (d, C-4), 33.3 (t, C-2″), 26.4 (t, C-1″), 23.9 (q, CH_3C-2″), 17.9 (q, CH_3CHSi), 12.6 (d, CHSi); LRMS (EI), *m/z* (relative intensity): 481 ($[M]^+$, 27), 394 (11), 348 (13), 264 (23), 171 (13), 115 (21), 87 (100), 59 (48).

*(3a*R*, 4*R*, 7*R*, 7a*R*)-3a,4,7,7a-Tetrahydro-7-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-8-[(tris(1-methylethyl)silyl)oxy]-1,3-dioxo-2-phenyl-4,7-ethenothiopyrano[3,4-c]pyrrole-1,3(2H,-6H)-dione (**21**a)* (5% from thermal reaction of **19** with *N*-phenylmaleimide): IR ν_{max}: 1778, 1712, 1625, 1499 cm^{-1}; ^1H NMR δ: 7.26–7.50 (5H, m, Ar-H), 5.52 (1H, d, J = 7.5 Hz, HC-9), 3.99 (1H, dd, J = 3.5, 7.5 Hz, HC-4), 3.94 (4H, m, H_2CO), 3.25 (1H, dd, J = 3.5, 10 Hz, HC-3a), 3.10 (1H, dd, J = 2, 10 Hz, HC-7a), 3.00 (1H, d, J = 11 Hz, HC-6_{syn}), 2.56 (1H, dd, J = 2, 11 Hz, HC-6_{anti}), 2.30 (1H, dt, J = 5, 13 Hz, HC-1′), 2.03 (3H, m, HC-1′, HC-2′), 1.38 (3H, s, H_3CC-2″), 1.09 (21H, m, $(CH_3)_2CHSi$); ^{13}C NMR δ: 176.0 (s, C═O), 175.5 (s, C═O), 157.6 (s, C-8), 132.1 (s, C_6H_5), 129.2 (d ×2, C_6H_5), 128.8 (d, C_6H_5), 126.6 (d ×2, C_6H_5), 110.0 (s, C-2″), 104.3 (d, C-9), 64.7 (t ×2, OCH_2), 49.6 (d, C-3a), 44.0 (d, C-7a), 43.6 (s, C-7), 36.8 (d, C-4), 35.7 (t, C-6), 35.3 (t, C-2′), 27.5 (t, C-1′), 23.8 (q, CH_3C-2″), 18.0 (q, CH_3CHSi), 12.9 (d, CHSi); LRMS (EI), *m/z* (relative intensity): 557 ($[M]^+$, 14), 383 (15), 282 (13), 115 (27), 87 (100), 73 (36), 59 (60).

*(3a*S*, 4*R*, 7*R*, 7a*S*)-3a,4,7,7a-Tetrahydro-1,3,8-trioxo-7-(3-oxobutyl)-2-phenyl-4,7-ethanothiopyrano[3,4-c]pyrrole-1,3(2H,6H)-dione (**22**a)* (72% from $EtAlCl_2$ mediated reaction of **19** with *N*-phenylmaleimide): IR ν_{max}: 1776, 1712, 1664 cm^{-1}; ^1H NMR δ: 7.49–7.12 (5H, m, Ar-H), 3.82 (1H, ddd, J = 2, 3, 9.5 Hz, HC-3a), 3.69 (1H, ddd, J = 3, 3, 6 Hz, HC-4), 3.36 (1H, d, J = 9.5 Hz, HC-7a), 3.06 (1H, d, J = 12 Hz, HC-6_{syn}), 2.92 (1H, ddd, J = 2, 2, 18.5 Hz, HC-9_{exo}), 2.87 (1H, d, J = 12 Hz, HC-6_{anti}), 2.78–2.65 (2H, m, HC-2′, HC-9_{endo}), 2.50 (1H, ddd, J = 5.5, 10, 15.5 Hz, HC-2′), 2.35 (1H, ddd, J = 5.5, 10, 15.5 Hz, HC-1′), 2.29–2.15 (1H, m, HC-1′), 2.20 (3H, s, H_3C-4′); ^{13}C NMR δ: 207.7 (s, C═O), 207.4 (s, C═O), 174.5 (s, C═O), 174.1 (s, C═O), 131.1 (s, C_6H_5), 129.3 (d ×2, C_6H_5), 129.2 (d, C_6H_5), 126.3 (d ×2, C_6H_5), 47.7 (s, C-7), 47.4 (d, C-3a), 45.0 (t, C-9), 44.1 (d, C-7a), 38.2 (t, C-2′), 34.0 (d, C-4), 29.9 (q, C-4′), 29.9 (t, C-6), 25.4 (t, C-1′); LRMS (EI), *m/z* (relative intensity): 357 ($[M]^+$, 6), 339 (100), 300 (33), 183 (60), 174 (35), 165 (22), 141 (30), 126 (36). Elemental anal. calcd. for $C_{19}H_{19}NO_4S$: C 63.85, H 5.36, N 3.92; found: C 63.71, H 5.50, N 3.83.

*(3a*S*, 4*R*, 7*R*, 7a*S*)-3a,4,7,7a-Tetrahydro-2-methyl-1,3,8-trioxo-7-(3-oxobutyl)-4,7-ethanothiopyrano[3,4-c]pyrrole-1,3(2H,6H)-dione (**22**b)* (71% from $EtAlCl_2$ mediated reaction of **19** with *N*-methylmaleimide): IR ν_{max}: 1775, 1721, 1692 cm^{-1}; ^1H NMR δ: 3.67–3.57 (2H, m, HC-3a, HC-4), 3.19 (1H, d, J = 9 Hz, HC-7a), 3.00 (1H, d, J = 12 Hz, HC-6_{syn}), 2.95 (3H, s, H_3CN), 2.81 (1H, d, J = 12 Hz, HC-6_{anti}), 2.82

(1H, ddd, J = 2.5, 2.5, 20 Hz, HC-9$_{exo}$), 2.67 (1H, ddd, J = 6, 10, 17 Hz, HC-2′), 2.55–2.43 (2H, m, HC-2′, HC-9$_{endo}$), 2.33–2.15 (2H, m, HC-1′), 2.21 (3H, s, H_3C-4′); ^{13}C NMR δ: 207.7 (s, C=O), 207.4 (s, C=O), 175.0 (s, C=O), 174.9 (s, C=O), 47.6 (s, C-7), 47.4 (d, C-3a), 44.8 (t, C-9), 44.1 (d, C-7a), 38.2 (t, C-2′), 33.7 (d, C-4), 30.1 (t, C-6), 29.8 (q, C-4′), 25.4 (t, C-1′), 25.1 (q, CH_3N); LRMS (EI), *m/z* (relative intensity): 295 ([M]$^+$, 6), 277 ([M−H_2O]$^+$, 100), 262 (21), 238 (42), 210 (15), 183 (77), 141 (39), 126 (46).

General procedure for aldol cyclodehydration of 1,5-diones

A solution of dione and *p*-TsOH (0.05–0.15 equiv.) in C_6H_6 (ca. 20 mL/mmol of dione) was heated under reflux. When the reaction was complete (TLC), the cooled (rt) mixture was diluted with C_6H_6, washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (25–50% ethyl acetate in hexane or ether) to provide the product.

*3a*S*, *4*R*, *9a*R* *9b*S*)-3a,4,5,8,9,9b-Hexahydro-3-oxo-2-phenyl-1*H*,7*H*-9a,4-(epithiomethano)benz[e]indole-1,3(2*H*),-7-trione (**23**a)* (30 mg, 88% from aldol cyclodehydration of **22***a* for 41 h): IR ν_{max}: 1774, 1710, 1671, 1496 cm^{-1}; ^{1}H NMR δ: 7.17–7.50 (5H, m, Ar-H), 6.04 (1H, br s, HC-6), 3.75 (1H, ddd, J = 2, 5, 9.5 Hz, HC-3a), 3.47 (1H, ddd, J = 2.5, 2.5, 5 Hz, HC-4), 3.41 (1H, m, HC-9), 3.27 (1H, d, J = 11 Hz, HC-10), 3.09 (1H, d, J = 9.5 Hz, HC-9b), 2.98 (1H, d, J = 19.5 Hz, HC-5$_{endo}$), 2.87 (1H, d, J = 11 Hz, HC-10), 2.79 (1H, ddd, J = 2, 2.5, 19.5 Hz, HC-5$_{exo}$), 2.53 (2H, m, HC-8), 1.88 (1H, ddd, J = 5, 14.5, 14.5 Hz, HC-9); ^{13}C NMR δ: 196.5 (s, C-7), 175.3 (s, C=O), 175.1 (s, C=O), 158.2 (s, C-5a), 131.2 (s, C_6H_5), 129.4 (d ×2, C_6H_5), 129.1 (d, C_6H_5), 126.2 (d ×2, C_6H_5), 129.0 (d, C-6), 48.1 (d, C-3a), 46.3 (d, C-9b), 37.3 (s, C-9a), 35.3 (t, C-8), 33.9 (t, C-5), 33.5 (t, C-10), 32.8 (d, C-4), 29.3 (t, C-9); LRMS (EI), *m/z* (relative intensity): 339 ([M]$^+$, 10), 175 (100), 165 (22).

*3a*S*, *4*R*, *9a*R* *9b*S*)-3a,4,5,8,9,9b-Hexahydro-2-methyl-3-oxo-1*H*,7*H*-9a,4-(epithiomethano)benz[e]indole-1,3(2*H*),-7-trione (**23**b)* (10 mg, 70% from aldol cyclodehydration of **22***b* for 45 h): IR ν_{max}: 1773, 1693, 1667, 1434, 1381, 1284 cm^{-1}; ^{1}H NMR δ: 5.97 (1H, dd, J = 2, 2 Hz, HC-6), 3.59 (1H, ddd, J = 2, 2.5, 9.5 Hz, HC-3a), 3.48–3.35 (2H, m, HC-4, HC-9), 3.24 (1H, d, J = 11 Hz, HC-10), 2.99 (3H, s, H_3CN), 2.94 (1H, d, J = 6 Hz, HC-9b), 2.91–2.84 (1H, m, HC-5), 2.82 (1H, d, J = 11 Hz, HC-10), 2.60–2.45 (3H, m, HC-5, H_2C-8), 1.85 (1H, ddd, J = 5, 14.5, 14.5 Hz, HC-9); ^{13}C NMR δ: 196.5 (s, C-7), 176.0 (s ×2, C=O), 158.3 (s, C-5a), 128.9 (d, C-6), 48.1 (d, C-3a), 46.2 (d, C-9b), 37.1 (s, C-9a), 35.2 (t), 33.9 (t), 33.4 (t), 32.6 (d, C-4), 29.2 (t), 25.1 (q, CH_3N); LRMS (CI, NH_3), *m/z* (relative intensity): 295 ([M+18]$^+$, 47), 278 ([M+1]$^+$, 100), 113 (54).

*(1′*R*, *4′*R*, *6′*R*)-3-[(8-Oxo-4-(3-oxobutyl)-2-thiabicyclo-[2.2.2]oct-6-yl)carbonyl]-2-oxazolidinone (**24**)*

To a stirred solution of 3-propenoyl-2-oxazolidinone (40 mg, 0.03 mmol) in CH_2Cl_2 (2 mL) at −20°C was added $TiCl_4$ (0.2 M solution in CH_2Cl_2; 1 mL, 0.2 mmol). A solution of **19** (92 mg, 0.24 mmol) in CH_2Cl_2 (2 mL) was added to the mixture. After 1 h, the reaction was quenched by addition of 1 N HCl. The mixture was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$, dried over Na_2SO_4, concentrated, and fractionated by FCC (50% ethyl acetate in hexane) to give **12** (9 mg, 20%), the Michael adduct 3-[3,4-dihydro-3-(3-oxobutyl)-4-oxo-2*H*-thiopyran-3-yl]propanoyl-2-oxazolidinone (5 mg, 6%):[7] IR ν_{max}: 1775, 1707, 1698, 1652, 1560, 1388 cm^{-1}; ^{1}H NMR δ: 7.30 (1H, dd, J = 1, 10 Hz, HC-6″), 6.03 (1H, d, J = 10 Hz, HC-5″), 4.41 (2H, ap t, J = 8 Hz, H_2C-5), 4.00 (2H, ap t, J = 8 Hz, H_2C-4), 3.27 (1H, d, J = 13.5 Hz, HC-2″), 3.03 (1H, dd, J = 1, 13.5 Hz, HC-2″), 2.98–2.75 (2H, m, H_2C-2′), 2.56–2.28 (2H, m, H_2C-2‴), 2.17–2.05 (2H, m, H_2C-1‴), 2.13 (3H, s, H_3C-4‴), 1.99–1.82 (2H, m, H_2C-1′); ^{13}C NMR δ: 207.7 (s, C-3‴), 196.4 (s, C-4″), 172.7 (s, C-1′), 153.5 (s, C-2), 144.9 (d, C-6″), 122.8 (d, C-5″), 62.1 (t, C-5), 44.9 (s, C-3″), 42.6 (t, C-4), 38.0 (t, C-2‴), 36.1 (t, C-2′), 30.0 (t, C-2″), 27.7 (t, C-1‴ or C-3′), 26.3 (t, C-1‴ or C-3′); LRMS (CI, NH_3), *m/z* (relative intensity): 343 ([M+18]$^+$, 25), 326 ([M+1]$^+$, 100), 254 (29), 239 (28), 183 (71); and the *exo* Diels–Alder adduct **24** (43 mg, 55%): IR ν_{max}: 2919, 1775, 1768, 1721, 1692, 1650 cm^{-1}; ^{1}H NMR δ: 4.47 (2H, ap t, J = 8.5 Hz, H_2C-5), 4.22–4.00 (3H, m, H_2C-4, HC-6′), 3.52 (1H, ddd, J = 3, 3, 6.5 Hz, HC-1′), 2.93 (1H, d, J = 11 Hz, HC-3′$_{syn}$), 2.85 (2H, d, J = 3 Hz, HC-7′), 2.71 (1H, dd, J = 3, 11 Hz, HC-3′$_{anti}$), 2.61 (1H, dd, J = 5, 14 Hz, HC-5′$_{exo}$), 2.51 (2H, ap t, J = 8 Hz, HC-2″), 2.16 (3H, s, H_3C-4″), 1.93–1.80 (2H, m, HC-1″), 1.73 (1H, ddd, J = 3, 10.5, 14 Hz, HC-5′$_{endo}$); ^{13}C NMR δ: 211.8 (s, C-8′), 207.8 (s, C-3″), 172.0 (s, O=CC-6′), 153.4 (s, C-2), 62.4 (t, C-5), 48.5 (t, C-4), 44.2 (s, C-4′), 43.8 (d, C-6′), 43.1 (t, C-7′), 38.4 (t, C-2″), 36.7 (d, C-1′), 31.6 (t, C-3′), 29.9 (q, CH_3), 28.3 (t, C-1′), 28.1 (t, C-5); LRMS (EI), *m/z* (relative intensity): 325 ([M]$^+$, 44), 307 ([M−H_2O]$^+$, 11), 267 (46), 191 (28), 88 (39), 43 (100).

*(3′*R*, *8a′*R*, *10′*R*)-3-[(3,4,7,8-Tetrahydro-6-oxo-6*H*-3,8a-ethano-1*H*-2-benzothiopyran-10-yl)carbonyl]-2-oxazolidinone (**25**)* (135 mg, 90% from aldol cyclodehydration of **24** for 33 h): IR ν_{max}: 2921, 1774, 1770, 1703, 1665, 1631 cm^{-1}; ^{1}H NMR δ: 5.97 (1H, br s, HC-5′), 4.47 (2H, ap t, J = 7 Hz, H_2C-5), 4.20–4.00 (3H, m, H_2C-4, HC-10′), 3.39 (1H, ddd, J = 3, 3, 3 Hz, HC-3′), 3.05–3.00 (2H, m, H_2C-4′), 2.95 (1H, dd, J = 3, 10 Hz, HC-1′$_{anti}$), 2.83 (1H, d, J = 10 Hz, HC-1′$_{syn}$), 2.55–2.38 (3H, m, H_2C-7′, HC-9′$_{exo}$), 1.97–1.89 (2H, m, H_2C-8′), 1.67 (1H, ddd, J = 3, 10.5, 13.5 Hz, HC-9′$_{endo}$); ^{13}C NMR δ: 197.5 (s, C-6′), 172.6 (s, C-2), 165.0 (s, O=CC-10′), 153.4 (s, C-4a), 126.2 (d, C-5′), 62.4 (t, C-5), 44.6 (d, C-10′), 43.1 (t, C-4), 39.7 (t, C-7′), 34.6 (d, C-3′), 33.7 (t, C-1′), 33.7 (s, C-8a), 33.4 (t, C-4′), 32.6 (t), 31.1 (t); LRMS (EI), *m/z* (relative intensity): 307 ([M]$^+$, 69), 260 (40), 220 (43), 192 (43), 173 (100), 166 (55), 146 (23), 117 (32).

*Methyl (1*R*, *4*R*, *6*R*)-8-oxo-4-(3-oxobutyl)-2-thiabicyclo[2.2.2]octane-6-carboxylate (**26**)* (64% from $EtAlCl_2$ mediated reaction of **19** with methyl acrylate): IR ν_{max}: 1721, 1662, 1435, 1357, 1204, 1167 cm^{-1}; ^{1}H NMR δ: 3.78 (3H, s, H_3CO), 3.51 (1H, ddd, J = 3, 3, 6.5 Hz, HC-1), 3.09 (1H, ddd, J = 3.5, 5.5, 11 Hz, HC-6), 2.86 (1H, dd, J = 3, 20 Hz, HC-7$_{exo}$), 2.85 (1H, d, J = 11 Hz, HC-3$_{syn}$), 2.73 (1H, dd, J = 2.5, 11 Hz, HC-3$_{anti}$), 2.71 (1H, dd, J = 3, 20 Hz, HC-7$_{endo}$), 2.52-

[7] This is the first occasion where we have isolated a Michael adduct from a Lewis acid mediated reaction of a 2*H*-thiopyran diene with a dienophile (cf. refs. 3*d* and 10).

2.45 (3H, m, H_2C-2′, HC-5_{exo}), 2.15 (3H, s, H_3C-4′), 1.90–1.75 (3H, m, HC-1′, HC-5_{endo}); ^{13}C NMR δ: 211.7 (s, C-8), 207.8 (s, C-3′), 172.7 (s, O═CO), 52.5 (q, CH_3O), 48.1 (t, C-7), 44.1 (d, C-6), 38.4 (t, C-2′), 36.6 (d, C-1), 31.3 (t, C-3), 29.9 (q, C-4′), 29.2 (t, C-5), 28.3 (t, C-1′); LRMS (EI), *m/z* (relative intensity): 270 ($[M]^+$, 56), 252 ($[M-H_2O]^+$, 16), 212 (65), 199 (31), 184 (28), 183 (26), 125 (25), 43 (100).

*Methyl (1*R**, 4*R**, 6*S**)-8-oxo-4-(3-oxobutyl)-2-thiabicyclo[2.2.2]octane-6-carboxylate (**27**)* (17% from $EtAlCl_2$ mediated reaction of **19** with methyl acrylate): IR ν_{max}: 2952, 1721, 1224, 1174 cm^{-1}; ^1H NMR δ: 3.73 (3H, s, CH_3O), 3.46–3.37 (2H, m, HC-1, HC-6), 2.87 (1H, d, J = 11 Hz, HC-3_{syn}), 2.78 (1H, dd, J = 2.5, 11 Hz, HC-3_{anti}), 2.72 (2H, br s, H_2C-7), 2.60–2.46 (2H, m, H_2C-2′), 2.20–2.15 (2H, m, HC-5_{endo}), 2.16 (3H, s, H_3C-4′), 2.00 (1H, dd, J = 11, 14 Hz, HC-5_{exo}), 1.92 (1H, ddd, J = 6.5, 9, 14 Hz, HC-1′), 1.70 (1H, ddd, J = 6.5, 9, 14 Hz, HC-1′); ^{13}C NMR δ: 211.2 (s, C-8), 207.9 (s, C-3′), 173.3 (s, O═CO), 52.4 (q, CH_3O), 45.2 (t, C-7), 45.0 (s, C-4), 44.7 (d, C-6), 38.5 (t, C-2′), 35.5 (d, C-1), 32.0 (t, C-3), 29.9 (t, C-5), 29.9 (q, C-4′), 28.3 (t, C-1′); LRMS (EI), *m/z* (relative intensity): 270 ($[M]^+$, 72), 212 (55), 184 (29), 183 (27), 165 (20), 125 (30), 91 (25), 43 (100).

*Methyl (3*R**, 8a*R**, 10*R**)-3,4,7,8-tetrahydro-6-oxo-6*H*-3,8a-ethano-1*H*-2-benzothiopyran-10-carboxylate (**28**)* (80 mg, 95% from aldol cyclodehydration of **26** for 48 h): IR ν_{max}: 1736, 1667, 1630, 1200 cm^{-1}; ^1H NMR δ: 5.98 (1H, dd, J = 1.5, 1.5 Hz, HC-5), 3.78 (3H, s, H_3CO), 3.33 (1H, ddd, J = 3, 3.5, 3.5 Hz, HC-3), 3.10 (1H, ddd, J = 3.5, 4, 11 Hz, HC-10), 3.03 (1H, ddd, J = 1.5, 3.5, 18 Hz, HC-4), 2.94 (1H, dd, J = 3, 10.5 Hz, HC-1_{anti}), 2.91 (1H, ddd, J = 1.5, 3, 18 Hz, HC-4), 2.74 (1H, d, J = 10.5 Hz, HC-1_{syn}), 2.45 (3H, m, H_2C-7, HC-9_{exo}), 1.93 (2H, m, H_2C-8), 1.78 (1H, ddd, J = 3, 11, 14 Hz, HC-9_{endo}); ^{13}C NMR δ: 197.5 (s, C-6), 173.1 (s, OC═O), 164.9 (s, C-4a), 126.1 (d, C-5), 52.3 (q, CH_3O), 44.7 (d, C-10), 39.3 (t, C-7), 34.6 (d, C-3), 33.7 (t), 33.6 (s, C-8a), 33.4 (t), 31.9 (t), 31.3 (t); LRMS (EI), *m/z* (relative intensity): 252 ($[M]^+$, 100), 166 (72), 147 (45), 146 (83), 145 (94), 117 (68), 91 (67).

*Methyl (3*R**, 8a*R**, 10*S**)-3,4,7,8-tetrahydro-6-oxo-6*H*-3,8a-ethano-1*H*-2-benzothiopyran-10-carboxylate (**29**)* (25 mg, 72% from aldol cyclodehydration of **27** for 48 h): IR ν_{max}: 1730, 1667, 1631, 1434, 1196, 1171 cm^{-1}; ^1H NMR δ: 5.94 (1H, dd, J = 1.5, 2 Hz, HC-5), 3.71 (3H, s, H_3CO), 3.36 (1H, dddd, J = 2, 2, 3.5, 10 Hz, HC-10), 3.23 (1H, ddd, J = 2, 2.5, 3.5 Hz, HC-3), 3.07 (1H, dd, J = 2.5, 10.5 Hz, HC-1_{anti}), 2.94 (1H, ddd, J = 2, 2.5, 18.5 Hz, HC-4_{endo}), 2.81 (1H, dddd, J = 1.5, 2, 3.5, 18.5 Hz, H-4_{exo}), 2.73 (1H, d, J = 10.5 Hz, HC-1_{syn}), 2.55–2.35 (2H, m, H_2C-7), 2.00 (3H, m, H_2C-9, HC-8), 1.83 (1H, ddd, J = 4, 5.5, 14 Hz, HC-8); ^{13}C NMR δ: 201.5 (s, C-6), 173.4 (s, OC═O), 165.1 (s, C-4a), 126.1 (d, C-5), 52.3 (q, CH_3O), 45.5 (d, C-10), 36.0 (t), 34.3 (s, C-8a), 33.7 (t), 33.5 (t), 33.5 (d, C-3), 33.4 (t), 32.3 (t); LRMS (EI), *m/z* (relative intensity): 252 ($[M]^+$, 100), 205 (51), 166 (89), 147 (28), 146 (35), 145 (54), 117 (60), 91 (50).

*General procedure for preparation of bisketals **30**, **34**, and **35***
A solution of the dione, ethylene glycol (10–25 equiv.), and *p*-TsOH (0.05–0.15 equiv.) in benzene (ca. 25 mL/mmol of dione) was heated under reflux for 1.5–2 h. When the reaction was complete (TLC), the cooled (rt) mixture was diluted with C_6H_6, washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by FCC (10–20% ethyl acetate in hexane) to give product.

*(3a*S**, 4*R**, 7*R**, 7a*S**)-1,2,3,3a,4,6,7,7a-Octahydro-7-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-1,3-dioxo-2-phenylspiro-[4,7-ethanothiopyrano[3,4-c]pyrrole-8,2′-*[1,3]dioxolane] (**30**) (70 mg, 93% from **22***a*): IR ν_{max}: 2980, 1775, 1710, 1597, 1498, 1382, 1183 cm^{-1}; ^1H NMR δ: 7.48–7.20 (5H, m, C_6H_5), 3.95–3.83 (8H, m, H_2CO), 3.53 (1H, ddd, J = 1.5, 3, 10 Hz, HC-3a), 3.38 (1H, ddd, J = 3, 3, 3 Hz, HC-4), 3.08 (1H, d, J = 10 Hz, HC-7a), 2.99 (1H, d, J = 11.5 Hz, HC-6_{syn}), 2.84 (1H, d, J = 11.5 Hz, HC-6_{anti}), 2.45–2.10 (4H, m, H_2C-2′, H_2C-9), 1.65–1.55 (2H, m, H_2C-1′), 1.38 (3H, s, H_3C); ^{13}C NMR δ: 175.8 (s ×2, C═O), 132.3 (s, C_6H_5), 129.2 (d ×2, C_6H_5), 128.6 (d, C_6H_5), 126.6 (d ×2, C_6H_5), 110.2 (s, C-8 or C-2′), 108.5 (s, C-8 or C-2′), 65.5 (t, CH_2O), 65.0 (t, CH_2O), 64.6 (t ×2, CH_2O), 47.1 (d, C-3a), 43.6 (t, C-9), 42.7 (s, C-7), 41.9 (d, C-7a), 32.8 (t), 31.9 (d, C-4), 28.1 (t), 24.1 (t), 23.7 (q, CH_3); LRMS (EI), *m/z* (relative intensity): 445 ($[M]^+$, 63), 430 (23), 400 (65), 383 (100), 358 (20).

General procedure for Raney Ni desulfurization
A suspension of sulfide and W2 Raney Ni (21) (ca. 1–3 mL/mmol of sulfide) in methanol (ca. 20 mL/mmol of sulfide) was heated under reflux for 2–4 h. When the reaction was complete (TLC), the mixture was filtered through Celite and the combined filtrate and washings were concentrated and, if necessary, fractionated FCC (ethyl acetate in hexane or ether) to give the product.

*(3a*S**,4*S**,7a*S**)-3a,6, 7,7a-Tetrahydro-4-methyl-4-(3-oxobutyl)-2-phenylisoindole-1,3,5(2*H*,4*H*)-trione (**31**)* The crude product from desulfurization of **30** (55 mg, 0.12 mmol) was dissolved in CH_2Cl_2 (3 mL) containing TFA (several drops) and stirred at rt overnight. The mixture was concentrated and fractionated by FCC (10% ethyl acetate in ether) to give **31** (36 mg, 92%): IR ν_{max}: 2972, 1774, 1708, 1497, 1380, 1193 cm^{-1}; ^1H NMR δ: 7.53–7.26 (5H, m, Ar-H), 3.38–3.28 (1H, m, HC-7a), 3.12 (1H, d, J = 10 Hz, HC-3a), 2.70–2.40 (5H, m), 2.40–2.20 (1H, m), 2.20–2.05 (1H, m), 2.09 (3H, s, H_3C-4′), 1.70–1.60 (1H, m), 1.39 (3H, s, H_3CC-4); ^{13}C NMR δ: 211.5 (s, C-5), 209.0 (s, C-3′), 177.5 (s, C═O), 175.7 (s, C═O), 131.7 (s, C_6H_5), 129.3 (d ×2, C_6H_5), 128.9 (d, C_6H_5), 126.5 (d ×2, C_6H_5), 48.4 (s, C-4), 48.0 (d, C-3a), 38.6 (d, C-7a), 37.7 (t), 36.7 (t), 30.1 (q, C-4′), 27.4 (t), 21.5 (q, CH_3C-4), 19.7 (t); LRMS (EI), *m/z* (relative intensity): 327 ($[M]^+$, 21), 299 (17), 271 (20), 270 (21), 257 (33), 187 (44), 110 (46), 95 (29), 43 (100).

*(3a*S**, 9a*S**, 9b*S**)-4,5,8,9,9a,9b-Hexahydro-9a-methyl-2-phenylbenz[e]isoindole-1,3,7(2*H*,3a*H*)-trione (**32**)* (5.1 mg, 45% from aldol cyclodehydration of **31** for 7 h): IR ν_{max}: 2949, 1776, 1708, 1664, 1496, 1381 cm^{-1}; ^1H NMR δ: 7.50–7.20 (5H, m, Ar-H), 5.84 (1H, br s, HC-6), 3.42 (1H, ddd, J = 3, 7, 8.5 Hz, HC-3a), 3.31 (1H, ddd, J = 5.5, 13.5, 13.5 Hz, HC-8), 3.06 (1H, d, J = 8.5 Hz, HC-9b), 2.67 (1H, ddd, J = 5, 13.5, 18 Hz, HC-9), 2.53 (1H, ddd, J = 3, 5.5, 18 Hz, HC-9), 2.43 (1H, ddd, J = 2, 5, 12 Hz, HC-5), 2.38–2.15 (3H, m, H_2C-4, HC-5), 1.92 (1H, ddd, J = 3, 5, 13.5 Hz, HC-8), 1.54 (3H, s,

H_3C); ^{13}C NMR δ: 198.0 (s, C-7), 177.8 (s, NC═O), 175.8 (s, NC═O), 164.4 (s, C-5a), 131.6 (s, C_6H_5), 129.3 (d ×2, C_6H_5), 128.9 (d, C_6H_5), 126.6 (d, C-1), 126.4 (d ×2, C_6H_5), 48.3 (d, C-9b), 39.6 (d, C-3a), 34.0 (s, C-9a), 34.0 (t), 33.6 (t), 28.2 (q, CH_3), 28.1 (t), 22.7 (t); LRMS (CI, NH_3), *m/z* (relative intensity): 327 ([M+18]$^+$, 81), 310 ([M+1]$^+$, 100).

(3aS, 4S*, 6S*, 7aS*)-3a,6,7,7a-Tetrahydro-4,8-dimethyl-2-phenyl-6,4-propeno-1H-isoindole-1,3,5(2H,4H)-trione (**33**)* (3.5 mg, 31% from aldol cyclodehydration of **31** for 7 h): IR ν_{max}: 1777, 1710, 1500, 1381, 1157 cm^{-1}; ^1H NMR δ: 7.53–7.26 (5H, m, Ar-H), 5.46 (1H, br d, J = 4.5 Hz, HC-9), 3.24 (1H, d, J = 9 Hz, HC-3a), 3.14 (1H, dd, J = 2.5, 14.5 Hz, HC-7), 3.01 (1H, dd, J = 8, 8.5 Hz, HC-7a), 2.80 (1H, br s, HC-6), 2.55 (1H, dd, J = 5, 19 Hz, HC-10), 2.20–2.19 (2H, m, HC-7, HC-10), 1.75 (3H, s, H_3CC-8), 1.38 (3H, s, H_3CC-4); LRMS (CI, NH_3), *m/z* (relative intensity): 327 ([M+18]$^+$, 100), 310 ([M+1]$^+$, 27), 187 (17).

(1R, 4R*, 7R*)-4-[2-(2-Methyl-1,3-dioxolan-2-yl)ethyl]-7-[(2-oxazolidinone-3-yl)carbonyl]spiro[2-thiabicyclo[2.2.2]-octane-5,2′-[1,3]dioxolane] (**34**)* (45 mg, 84% from bisketalization of **24**): IR ν_{max}: 1774, 1700, 1386 cm^{-1}; ^1H NMR δ: 4.39 (2H, ap t, J = 8 Hz, H_2COCO), 4.10–3.82 (11H, m, H_2CO (×4), H_2CN, HC-7), 3.16 (1H, ddd, J = 3, 3, 3 Hz, HC-1), 2.80 (1H, dd, J = 1.5, 11 Hz, HC-3$_{anti}$), 2.67 (1H, d, J = 11 Hz, HC-3$_{syn}$), 2.42–2.25 (3H, m), 1.70–1.45 (5H, m), 1.29 (3H, s, H_3C); ^{13}C NMR δ: 173.2 (s, O═CC-7), 153 (s, O═CO), 110.3 (s, C-5 or C-2″), 110.2 (s, C-5 or C-2″), 64.8 (t, CH_2O), 64.7 (t ×2, CH_2O), 64.4 (t, CH_2O), 62.2 (t, C-5), 46.1 (t, CH_2N), 43.2 (d, C-7), 43.1 (t, C-6), 37.8 (s, C-4), 35.3 (d, C-1), 33.2 (t), 28.4 (t), 27.0 (t), 26.8 (t), 23.9 (q, CH_3); LRMS (CI, NH_3), *m/z* (relative intensity): 414 ([M+1]$^+$, 61), 370 (12), 354 (12), 87 (100).

(6′S, 8′R*)-3-[(6-methyl-6-(2-(2-Methyl-1,3-dioxolan-2-yl)-ethyl)-1,4-dioxaspiro[4.5]decan-8-yl)carbonyl]-2-oxazolidinone (**36**)* (13 mg, 66% from desulfurization of **34**):[8] IR ν_{max}: 2967, 1777, 1697, 1388 cm^{-1}; ^1H NMR δ: 4.38 (2H, ap t, J = 8 Hz, HC-5), 4.01–3.80 (11H, m, H_2CO, H_2C-4), 1.92–1.55 (10H, m), 1.35 (3H, s, H_3CC-2‴), 0.84 (3H, s, H_3CC-6); LRMS (CI, NH_3), *m/z* (relative intensity): 401 ([M+18]$^+$, 16), 384 ([M+1]$^+$, 72), 357 (75), 340 (76), 322 (100), 227 (32), 105 (35), 99 (75).

Methyl (6S, 8R*)-6-methyl-6-[2-(2-methyl-1,3-dioxolan-2-yl)ethyl]-1,4-dioxaspiro[4.5]decan-8-carboxylate (**37**)*
Bisketalization of **26** (22 mg, 0.08 mmol) gave **35** (26 mg, 89%): ^1H NMR δ: 3.95–3.80 (8H, m, H_2CO (×4), H_2CN, HC-7), 3.19 (1H, ddd, J = 2.5, 3, 4 Hz, HC-1), 2.96 (1H, ddd, J = 2.5, 6, 10 Hz, HC-7), 2.80 (1H, dd, J = 2, 11 Hz, HC-3$_{anti}$), 2.60 (1H, d, J = 11 Hz, HC-3$_{syn}$), 2.30 (1H, dd, J = 3, 12 Hz, HC-6), 2.20 (1H, dd, J = 4, 12 Hz), 2.12 (1H, dd, J = 6, 14 Hz, HC-8$_{exo}$), 1.80 (1H, ddd, J = 2.5, 10, 14 Hz, HC-8$_{endo}$), 1.70-1.40 (4H, m), 1.28 (3H, s, H_3C). Desulfurization of **35** (26 mg, 0.073 mmol) gave **37** (21 mg, 88%): IR ν_{max}: 2953, 1735, 1202, 1168, 1087 cm^{-1}; ^1H NMR δ: 3.92 (8H, m, H_2CO), 3.65 (3H, s, H_3CO), 2.55–2.43 (1H, m, HC-8), 1.91–1.82 (1H, m), 1.80–1.65 (3H, m), 1.65–1.55 (6H, m), 1.33 (3H, s, H_3CC-2″), 0.83 (3H, s, H_3CC-6); LRMS (EI), *m/z* (relative intensity): 328 ([M]$^+$, 47), 313 (21), 297 (24), 285 (27), 284 (25), 243 (28), 253 (30), 241 (27), 227 (100).

(2′R, 8a′S*)-3-[1,2,3,4,6,7,8,8a-Octahydro-8a-methyl-6-oxonaphthalene-2-carbonyl]-2-oxazolidinone (**38**)* (7 mg, 83% from aldol cyclodehydration of **40**): IR ν_{max}: 2929, 1775, 1693, 1666, 1388, 1225 cm^{-1}; ^1H NMR δ: 5.80 (1H, br s, HC-5′), 4.46-4.37 (2H, m, HC-5), 4.12–3.94 (2H, m, HC-4), 3.75–3.65 (1H, m, HC-2′), 2.84–2.72 (1H, m, HC-4′), 2.53 (1H, ddd, J = 5, 14, 17.5 Hz, HC-7′), 2.39 (1H, ddd, J = 2, 4.5, 17.5 Hz, HC-7′), 2.31–2.20 (2H, m, H_2C-3′), 2.11 (1H, ddd, J = 5, 13.5, 14 Hz, HC-8′), 1.98 (1H, dd, J = 7.5, 14 Hz, HC-1′), 1.88–1.75 (1H, m, HC-4′), 1.75 (1H, dd, J = 4.5, 14 Hz, HC-1′), 1.69 (1H, ddd, J = 2.5, 5, 13.5 Hz, HC-8′); ^{13}C NMR δ: 199.1 (s, C-6′), 176.2 (s, O═CC-2′), 170.3 (s, C-4′a), 153.0 (s, C-2), 125.1 (d, C-5′), 62.1 (t, C-5), 43.0 (t, C-4), 41.6 (t, C-1′), 36.3 (t, C-7′), 36.1 (s, C-8a), 35.9 (d, C-2′), 34.1 (t), 28.7 (t), 26.2 (t), 23.6 (q, CH_3); LRMS (CI, NH_3), *m/z* (relative intensity): 295 ([M+18]$^+$, 21), 278 ([M+1]$^+$, 100).

Methyl (2R, 8aS*)-1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-oxonaphthalene-2-carboxylate* (**39**) (9 mg, 78% from aldol-cyclodehydration of **41**): IR ν_{max}: 2948, 1730, 1672, 1619, 1437, 1208 cm^{-1}; ^1H NMR δ: 5.76 (1H, br s, HC-5), 3.73 (3H, s, H_3CO), 2.75–2.63 (2H, m, HC-2, HC-4), 2.50 (1H, ddd, J = 6, 13.5, 17.5 Hz, HC-7), 2.40–2.28 (2H, m, HC-1, HC-7), 2.28–2.15 (2H, m, HC-3, HC-4), 1.82 (1H, ddd, J = 5, 13.5, 13.5 Hz, HC-8), 1.79 (1H, ddd, J = 3, 6, 13.5 Hz, HC-8), 1.72–1.58 (2H, m, HC-1, HC-3), 1.14 (3H, s, H_3CC); ^{13}C NMR δ: 199.2 (s, C-6), 175.4 (s, OC═O), 169.7 (s, C-4a), 124.7 (d, C-5), 51.9 (q, CH_3O), 41.7 (t), 37.4 (t), 37.1 (d, C-2), 36.0 (s, C-8a), 33.8 (t), 29.1 (t), 26.7 (t), 22.6 (q, CH_3C); LRMS (EI), *m/z* (relative intensity): 222 ([M]$^+$, 49), 194 (37), 180 (50), 163 (36), 121 (100).

(1′R, 3′S*)-3-[(3-Methyl-3-(3-oxobutyl)-4-oxo-cyclohexan-1-yl)carbonyl]-2-oxazolidinone (**40**)* A solution of **36** (13 mg, 0.034 mmol) and 5% HF (0.1 mL) in CH_3CN (2 mL) was stirred at rt for 30 min. The mixture was diluted with CH_2Cl_2, washed with 5% $NaHCO_3$ and water, dried over Na_2SO_4, concentrated, and fractionated by PTLC (10% ethyl acetate in ether) to give **40** (9 mg, 90%): IR ν_{max}: 2964, 1773, 1700, 1388, 1224 cm^{-1}; ^1H NMR δ: 4.44 (2H, ap t, J = 8 Hz, HC-5), 4.17 (1H, dddd, J = 3.5, 3.5, 12.5, 12.5 Hz, HC-1′), 4.02 (2H, m, HC-4), 2.66 (1H, ddd, J = 6, 14.5, 14.5 Hz, HC-5′), 2.55–2.40 (1H, m, HC-2″), 2.34 (1H, ddd, J = 2.5, 4.5, 14.5 Hz, HC-5′), 2.28–2.00 (4H, m), 2.12 (3H, s, H_3C-4″), 1.91 (1H, dddd, J = 4.5, 12.5, 13, 14.5 Hz, HC-6′), 1.74 (2H, m, HC-1″, HC-2′); ^{13}C NMR δ: 213.5 (s, C-4′), 207.6 (s, C-3″), 174.8 (s, O═CC-1′), 153.2 (s, C-2), 62.1 (t, C-5), 47.3 (s, C-3′), 42.8 (t, C-4), 41.6 (t), 37.8 (t), 37.3 (t), 37.0 (d, C-1′), 30.5 (t), 30.1 (q, C-4″), 28.9 (t), 21.9 (q, CH_3C-3′); LRMS (CI, NH_3), *m/z* (relative intensity): 313 ([M+18]$^+$, 84), 296 ([M+1]$^+$, 100), 183 (80).

Methyl (1R, 3S*)-3-methyl-3-(3-oxobutyl)-4-oxo-cyclohexan-1-carboxylate (**41**)*
A solution of **37** (21 mg, 0.064 mmol) and 5% HF (0.1 mL) in

[8] This reaction also gave **37** (2 mg, 13%).

CH_3CN (2 mL) was stirred at rt for 30 min. The mixture was diluted with CH_2Cl_2, washed with 5% Na_2CO_3 and water, dried over Na_2SO_4, concentrated, and fractionated by PTLC (10% ethyl acetate in ether) to give **41** (14 mg, 94%): IR ν_{max}: 2954, 1732, 1709, 1435, 1200 cm^{-1}; ^1H NMR δ: 3.68 (3H, s, J = 3.5, 12.5 Hz, H_3CO), 3.00 (1H, dddd, J = 3.5, 3.5, 12.5, 12.5 Hz, HC-1), 2.60–2.00 (7H, m), 2.11 (3H, s, H_3C-4′), 1.90–1.70 (2H, m), 1.66–1.54 (1H, m), 1.00 (3H, s, H_3CC-3); ^{13}C NMR δ: 213.5 (s, C-4), 207.6 (s, C-3′), 174.9 (s, OC═O), 52.0 (q, CH_3O), 47.1 (s, C-3), 42.0 (t), 37.9 (t), 37.8 (d, C-1), 37.2 (t), 30.7 (t), 30.1 (q, C-4′), 29.2 (t), 21.9 (q, CH_3C-3′); LRMS (CI, NH_3), *m/z* (relative intensity): 258 ($[M+18]^+$, 33), 241 ($[M+1]^+$, 100).

*Methyl (2*R**, 6*R**, 8a*S**)-1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-[(dimethyl(1,1-dimethylethyl)silyl)oxy]naphthalene-2-carboxylate (**43**)*

Method A: $NaBH_4$ (2 mg, 0.05 mmol) was added to a solution of **39** (2 mg, 0.009 mmol) in 50% CH_3OH – CH_2Cl_2 (0.8 mL) and the mixture was stirred at rt for 30 min. The mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, and concentrated to give the crude alcohol (2 mg). A solution of the alcohol, TBDMSCl (3.4 mg, 0.022 mmol), and imidazole (1.2 mg, 0.018 mmol) in CH_2Cl_2 (0.6 mL) was stirred at rt for 16 h. The mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, and concentrated to give the crude TBDMS ether (3 mg), which was identical by TLC and by ^1H NMR with the product obtained from **45** as described below.

Method B: (16 mg, 85% from desulfurization of **45**): IR ν_{max}: 2932, 1735, 1471, 1204, 1158, 1130 cm^{-1}; ^1H NMR δ: 5.26 (1H, br s, HC-5), 4.25–4.18 (1H, m, HC-6), 3.69 (3H, s, H_3CO), 2.65–2.58 (1H, m, HC-2), 2.52–2.38 (1H, m, HC-4), 2.26 (1H, dddd, J = 2.5, 2.5, 2.5, 13 Hz, HC-3), 2.14 (1H, ddd, J = 2.5, 2.5, 13.5 Hz, HC-1), 1.95–1.85 (1H, m, HC-4), 1.81–1.70 (1H, m, HC-7), 1.60–1.25 (5H, m), 0.98 (3H, s, H_3CC), 0.90 (9H, s, $(H_3C)_3$), 0.08 (3H, s, H_3CSi), 0.07 (3H, s, H_3CSi); ^{13}C NMR δ: 176.1 (s, C═O), 144.2 (s, C-4a), 125.3 (d, C-5), 69.0 (d, C-6), 51.5 (q, CH_3O), 42.9 (t, C-1), 37.8 (d, C-2), 37.4 (t), 35.0 (s, C-8a), 29.0 (t), 28.8 (t), 28.0 (t), 26.0 (q, $(CH_3)_3$), 23.9 (q, CH_3C), 18.4 (s, CSi), −4.4 (q, CH_3Si), −4.5 (q, CH_3Si); LRMS (EI), *m/z* (relative intensity): 338 ($[M]^+$, 14), 281 (54), 207 (20), 147 (100), 105 (36), 91 (35), 75 (54).

*Methyl (3*R**, 6*S**, 8a*R**, 10*R**)-3,4,7,8-tetrahydro-6-hydroxy-6H-3,8a-ethano-1H-2-benzothiopyran-10-carboxylate (**44**a)*

$NaBH_4$ (ca. 10 mg, 0.26 mmol) was added in one portion to a stirred solution of **26** (32 mg, 0.13 mmol) in 50% CH_3OH in CH_2Cl_2 (3 mL) at rt. The mixture was stirred for 30 min and then was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by MPC (40% ethyl acetate in hexane) to give **44***b* (17.5 mg, 54%) and **44***a* (12 mg, 37%): IR ν_{max}: 3388, 2930, 1736, 1666, 1434, 1203, 1180 cm^{-1}; ^1H NMR δ: 5.63 (1H, ddd, J = 2, 2, 3.5 Hz, HC-5), 4.21–4.15 (1H, m, HC-6), 3.74 (3H, s, CH_3O), 3.21 (1H, ddd, J = 3, 3, 3 Hz, HC-3), 2.96 (1H, ddd, J = 3, 6, 11 Hz, HC-10), 2.85–2.75 (2H, m, H_2C-4), 2.70 (1H, dd, J = 2.5, 10.5 Hz, HC-1_{anti}), 2.56 (1H, d, J = 10.5 Hz, HC-1_{syn}), 2.23 (1H, dd, J = 6, 13.5 Hz, HC-9_{exo}), 1.90 (1H, m, HC-7), 1.79 (1H, ddd, J = 3, 11, 13.5 Hz, HC-9_{endo}), 1.68–1.54 (2H, m, HC-7, HC-8), 1.47–1.34 (1H, m, HC-8); ^{13}C NMR δ: 173.8 (s, OC═O), 141.1 (s, C-4a), 125.3 (d, C-5), 65.2 (d, C-6), 52.1 (q, CH_3O), 44.9 (d, C-10), 38.5 (t, C-4), 34.9 (d, C-3), 34.4 (t, C-1), 33.3 (t), 32.3 (s, C-8a), 31.2 (t), 28.8 (t); LRMS (EI), *m/z* (relative intensity): 254 ($[M]^+$, 52), 223 (11), 192 (12), 175 (21), 147 (100), 134 (76), 131 (38), 91 (74).

*Methyl (3*R**, 6*R**, 8a*R**, 10*R**)-3,4,7,8-tetrahydro-6-hydroxy-6H-3,8a-ethano-1H-2-benzothiopyran-10-carboxylate (**44**b)*: IR ν_{max}: 3383, 2931, 1731, 1666, 1433, 1201, 1012 cm^{-1}; ^1H NMR δ: 5.62 (1H, br s, HC-5), 4.22–4.13 (1H, m, HC-6), 3.74 (3H, s, H_3CO), 3.20 (1H, ddd, J = 3, 3, 3 Hz, HC-3), 2.97 (1H, ddd, J = 3, 5, 11 Hz, HC-10), 2.85 (1H, br d, J = 17.5 Hz, HC-4), 2.70–2.65 (2H, m, HC-1_{anti}, HC-4), 2.61 (1H, d, J = 10 Hz, HC-1_{syn}), 2.21 (1H, dd, J = 5.5,13.5 Hz, HC-5_{exo}), 1.95–1.84 (1H, m, HC-7), 1.58 (4H, m, HC-5_{endo}, HC-7, H_2C-8); ^{13}C NMR δ: 173.8 (s, OC═O), 140.9 (s, C-4a), 125.7 (d, C-5), 65.9 (d, C-6), 52.0 (q, CH_3O), 45.0 (d, C-10), 38.5 (t), 34.7 (d, C-3), 34.6 (t), 33.2 (t), 32.2 (s, C-8a), 32.0 (t), 29.0 (t); LRMS (EI), *m/z* (relative intensity): 254 ($[M]^+$, 70), 236 (78), 223 (19), 147 (87), 129 (93), 91 (100).

*Methyl (3*R**, 6*R**, 8a*R**, 10*R**)-3,4,7,8-tetrahydro-6-[(dimethyl(1,1-dimethylethyl)silyl)oxy]-6H-3,8a-ethano-1H-2-benzothiopyran-10-carboxylate (**45**)*

A solution of **44***b* (17 mg, 0.067 mmol), TBDMSCl (25 mg, 0.17 mmol), and imidazole (9 mg, 0.13 mmol) in CH_2Cl_2 (3 mL) was stirred at rt for 20 h. The mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by FCC (10% ether in hexane) to give **45** (21.5 mg, 87%). IR ν_{max}: 2949, 1741, 1666, 1434, 1213, 1109, 1071 cm^{-1}; ^1H NMR δ: 5.49 (1H, br s, HC-5), 4.22–4.13 (1H, m, HC-6), 3.74 (3H, s, H_3CO), 3.17 (1H, ddd, J = 3, 3, 3 Hz, HC-3), 2.99 (1H, ddd, J = 3, 5, 11 Hz, HC-10), 2.90–2.80 (2H, m, HC-1_{anti}, HC-4), 2.69 (1H, ddd, J = 3, 5, 17 Hz, HC-4), 2.58 (1H, d, J = 10 Hz, HC-1_{syn}), 2.23 (1H, dd, J = 5, 13.5 Hz, HC-9_{exo}), 1.85–1.74 (1H, m, HC-7), 1.65–1.38 (4H, m, HC-7, H_2C-8, HC-9_{endo}), 0.89 (9H, s, $(H_3C)_3C$), 0.07 (3H, s, H_3CSi), 0.07 (3H, s, H_3CSi); ^{13}C NMR δ: 173.9 (s, OC═O), 138.8 (s, C-4a), 127.1 (d, C-5), 67.1 (d, C-6), 52.1 (q, CH_3O), 45.3 (d, C-10), 38.4 (t), 34.8 (d, C-4), 34.7 (t), 33.6 (t), 32.8 (t), 32.0 (t, C-8a), 29.4 (t), 26.0 (q, $(CH_3)_3$), 18.3 (s, $C(CH_3)_3$), −4.5 (q, CH_3Si); LRMS (EI), *m/z* (relative intensity): 368 ($[M]^+$, 17), 353 (32), 337 (100).

*Methyl (2*S**, 6*R**, 8a*S**)-1,2,3,4,6,7,8,8a-octahydro-8a-methyl-6-[(dimethyl(1,1-dimethylethyl)silyl)oxy]naphthalene-2-carboxylate (**46**)* (5 mg, 87% from desulfurization of **48**): IR ν_{max}: 2933, 1738, 1471, 1435, 1251, 1160, 1078 cm^{-1}; ^1H NMR δ: 5.26 (1H, br s, HC-5), 4.26–4.18 (1H, m, HC-6), 3.66 (3H, s, H_3CO), 2.67 (1H, dddd, J = 3.5, 3.5, 12.5, 12.5 Hz, HC-2), 2.28–2.12 (1H, m, HC-4), 2.10–1.95 (2H, m, HC-1, HC-4), 1.85–170 (2H, m, HC-1, HC-3), 1.65–1.30 (5H, m), 1.12 (3H, s, H_3CC), 0.90 (9H, s, $(H_3C)_3$), 0.09 (3H, s, CH_3Si), 0.08 (3H, s, CH_3Si); ^{13}C NMR δ: 176.2 (s, C═O), 142.8 (s, C-4a), 125.8 (d, C-5), 68.9 (d, C-6), 51.6 (q, CH_3O), 44.4 (t, C-1), 39.4 (d, C-2), 37.4 (t), 34.7 (s, C-8a), 31.1 (t), 30.6 (t), 29.2 (t), 26.0 (q, $(CH_3)_3$), 23.8 (q, CH_3C), 18.4 (s, CSi), −4.4 (q, CH_3Si), −4.6 (q, CH_3Si); LRMS (CI, NH_3), *m/z* (relative intensity): 339 ($[M+1]^+$, 2), 282 (5), 208 (100).

Methyl (3R, 6R*, 8aR*, 10S*)-3,4,7,8-tetrahydro-6-hydroxy-6H-3,8a-ethano-1H-2-benzothiopyran-10-carboxylate (**47**b)*

$NaBH_4$ (ca. 5 mg, 0.13 mmol) was added in one portion to a stirred solution of **29** (20 mg, 0.079 mmol) in 50% CH_3OH in CH_2Cl_2 (2 mL) at rt. The mixture was stirred for 30 min and then was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by MPC (40% ethyl acetate in hexane) to give **47***a* (5 mg, 25%) and **47***b* (13 mg, 65%): IR ν_{max}: 3384, 2930, 1732, 1450, 1433, 1226, 1196 cm^{-1}; ^1H NMR δ: 5.55 (1H, br s, HC-5), 4.22–4.14 (1H, m, HC-6), 3.69 (3H, s, H_3CO), 3.28 (1H, dddd, J = 2, 2, 7, 10.5 Hz, HC-10), 3.12 (1H, ddd, J = 3, 3, 3 Hz, HC-3), 2.90 (1H, dd, J = 2.5, 10.5 Hz, HC-1_{anti}), 2.75–2.58 (2H, m, H_2C-4), 2.60 (1H, d, J = 10.5 Hz, HC-1_{syn}), 2.20–1.95 (1H, m, HC-7), 1.94 (1H, ddd, J = 2.5, 7, 13.5 Hz, HC-9_{exo}), 1.80 (1H, dd, J = 10.5, 13.5 Hz, HC-9_{endo}), 1.54 (3H, m, HC-7, H_2C-8); ^{13}C NMR δ: 173.9 (s, OC=O), 140.3 (s, C-4a), 126.0 (d, C-5), 66.6 (d, C-6), 52.1 (q, CH_3O), 45.8 (d, C-10), 34.8 (t), 34.5 (t), 34.4 (t), 33.6 (d, C-3), 32.8 (s, C-8a), 32.6 (t), 29.3 (t); LRMS (EI), *m/z* (relative intensity): 254 ([M]$^+$, 38), 236 (38), 195 (23), 150 (40), 147 (84), 129 (55), 91 (100).

Methyl (3R, 6R*, 8aR*, 10S*)-3,4,7,8-tetrahydro-6-[(dimethyl(1,1-dimethylethyl)silyl)oxy]-6H-3,8a-ethano-1H-2-benzothiopyran-10-carboxylate (**48**)*

A solution of **47***b* (10 mg,0.039 mmol), TBDMSCl (15 mg, 0.098 mmol), and imidazole (3.4 mg, 0.05 mmol) in CH_2Cl_2 (3 mL) was stirred at rt for 20 h. The mixture was diluted with CH_2Cl_2, washed with water, dried over Na_2SO_4, concentrated, and fractionated by FCC (5% ether in hexane) to give **48** (12.8 mg, 89%): IR ν_{max}: 2950, 2930, 1735, 1471, 1434, 1094, 1068 cm^{-1}; ^1H NMR δ: 5.42 (1H, br s, HC-5), 4.22–4.13 (1H, m, HC-6), 3.69 (3H, s, H_3CO), 3.28 (1H, br dd, J = 7, 10 Hz, HC-10), 3.10 (1H, ddd, J = 2.5, 3, 3 Hz, HC-3), 2.95 (1H, dd, J = 2, 10 Hz, HC-1_{anti}), 2.72–2.58 (2H, m, H_2C-4), 2.58 (1H, d, J = 10 Hz, HC-1_{syn}), 1.90 (1H, ddd, J = 2, 7, 13.5 Hz, HC-9_{endo}), 1.83–1.74 (2H, m, HC-4, HC-9_{exo}), 1.65–1.40 (3H, m, H_2C-7, HC-8), 0.89 (9H, s, $(H_3C)_3C$), 0.07 (6H, s, H_3CSi); ^{13}C NMR δ: 174.0 (s, OC=O), 138.4 (s, C-4a), 127.3 (d, C-5), 67.7 (d, C-6), 52.1 (q, CH_3O), 46.0 (d, C-10), 34.9 (t), 34.6 (t), 34.4 (t), 33.6 (d, C-3), 33.2 (t), 32.6 (s, C-8a), 29.5 (t), 26.0 (q, $(CH_3)_3C$), 18.3 (s, CSi), −4.5 (q, CH_3Si); LRMS (EI), *m/z* (relative intensity): 368 ([M]$^+$, 2), 312 (64), 280 (17), 238 (29), 237 (81), 178 (26), 162 (63), 143 (54), 75 (100).

Acknowledgements

Financial support from the Natural Sciences and Engineering Research Council of Canada is gratefully acknowledged.

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