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# Efficient access to novel hexahydro-chromene and tetrahydro-pyrano[2,3-*d*] pyrimidine-annulated benzo-*δ*-sultones via a domino Knöevenagel-hetero-Diels–Alder reaction in water

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ABSTRACT

An efficient catalyst-free, diastereosective synthesis of novel hexahydro-chromene and tetrahydro-pyrano[2,3-*d*]pyrimidine-annulated benzo-*δ*-sultones is described. A number of 2-formyl-4-phenyl (*E*)-2-phenylethenesulfonates were synthesized and underwent a one-pot domino Knöevenagel-hetero-Diels–Alder reaction, respectively, with dimedone and *N*,*N*-dimethylbarbituric acid in water, affording the desired products in moderate to excellent yields.



## 1. Introduction

The synthesis of complex organic molecules needs to rely on methods that provide maximum efficiency in modern research in organic chemistry. Combinatorial chemistry has emerged as a powerful synthetic procedure in this area. Obtaining scaffolds from the combination of multiple transformations in a single-pot designated as domino reactions, is a highly efficient means for improvement of the reaction efficiency.[1] The domino Knöevenagel-hetero-Diels–Alder reaction, which was developed widely by Tietze and Rackelman, is an efficient process in organic synthesis, especially in the area of heterocycles and natural products.[2] Transformation of the precursors into the desired products including two or more rings at once, avoiding sequential chemical steps is the main advantage of this reaction. However, such processes could be implemented efficiently provided that activating groups are to be built up into dienophiles to achieve the desired reactivity.[3]

The internal esters of hydroxy sulfonic acids or sulfur analogues of lactones, sultones, constitute a class of heterocyclic compounds whose chemistry continues to be of interest.[4] Most of the literature on biological properties of sultones is concerned with toxicological properties. However, the β-keto-γ-sultones and their enol ethers, as well as the analogous sultams, are claimed in a 1976 patent to have cellular immunosuppressive properties, which could make them useful therapeutic agents for inhibiting transplant rejection and in treating autoimmune disorders.[5] The biological activities of sultones consist of skin sensitization,[6] and antiviral activities.[7] However, in 1992, Camarasa and co-workers discovered a new class of specific human immunodeficiency virus type 1 (HIV-1) inhibitors, called TSAO derivatives containing a sultone moiety.[8] Sultones are considered as sulfoalkylating agents due to their easily reaction with a variety of nucleophiles for the synthesis of alkylsulfonic acids.[9]

To the best of our knowledge, there has been no report in the literature on the intramolecular hetero-Diels–Alder reaction of a dienophile tethered to a diene moiety by a sulfonate link. As a part of our own interest in cycloaddition reactions,[10] herein we report our one-pot synthetic approach for the preparation of benzo-*δ*-sultones bearing hexahydro-chromene and tetrahydro-pyrano[2,3-*d*]pyrimidine motifs. Since water is an easily available and environmentally friendly matter in nature, a number of processes including Diels–Alder reactions have been carried out in aqueous media.[3f,11] Therefore, we decided to use it as a safe solvent in our new procedure. We were also intended to work under catalyst-free conditions in order to develop an eco-friendly benign synthetic method.

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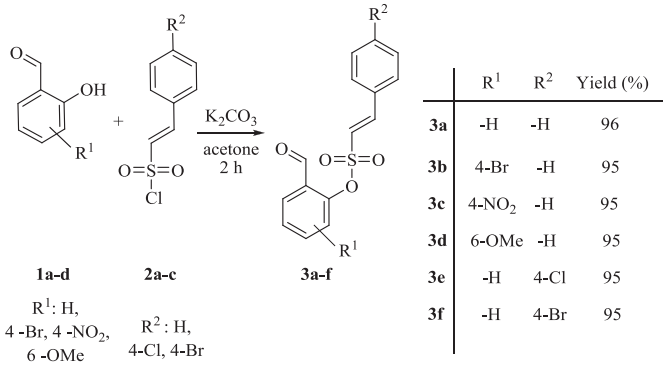
## 2. Results and discussion

### 2.1. Preparation of 2-formylphenyl-(*E*)-2-phenylethenesulfonates 3a–f

Compounds **3a**–**f** were prepared by condensation of (*E*)-2-phenylethenesulfonyl chloride **2a**–**c** with 2-hydroxybenzaldehydes **1a**–**d** (Scheme 1). The structures of **3a**–**f** were confirmed from analytical data. For example, appearing of two doublets at $\delta$ 7.00 and 7.63 with $J$=15.5 Hz for $SO_2CH{=}C$ and $Ph{-}CH{=}C$ and a singlet at $\delta$ 10.37 in the $^1$H NMR spectrum of **2a** is consistent with the (*E*)-configuration of the olefin protons and the presence of an aldehyde group.



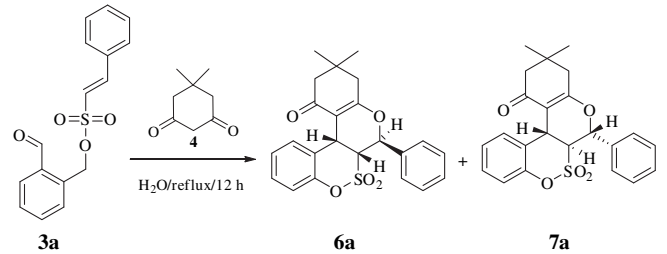

| | $R^1$ | $R^2$ | Yield (%) |
|---|---|---|---|
| **3a** | -H | -H | 96 |
| **3b** | 4-Br | -H | 95 |
| **3c** | 4-$NO_2$ | -H | 95 |
| **3d** | 6-OMe | -H | 95 |
| **3e** | -H | 4-Cl | 95 |
| **3f** | -H | 4-Br | 95 |

**Scheme 1.** Synthesis of **3a**–**f** from condensation of **1a**–**d** with **2a**–**c**.

### 2.2. Preparation of domino Knöevenagel-hetero-Diels–Alder cycloadducts of 6a–f and 7a–f

To optimize the reaction conditions, we screened several solvents and catalysts. Changing the ratio of aldehyde to 1,3-dione counterpart (**3a**/**4**) was also found to have a considerable effect on the reaction yield (Table 1). The hetero-Diels–Alder reaction was sluggish and inefficient in the presence of ethylenediamine *N*,*N*′-diacetic acid (EDDA)[12] as catalyst in toluene (entry 1). Interestingly, piperidine,[12] a commonly used base in Knöevenagel condensations in ethanol, afforded the corresponding cycloadduct in 48–60% yields (entries 2, 3, and 4). Surprisingly, 62% of the product was obtained under catalyst-free condition when we used water as solvent (entry 5). Finally, changing the ratio of **3a**/**4** from 1/1 to 1/1.2 and 1/1.4 was also found to have a determining effect on the product yields (entries 6 and 7). An inseparable mixture of **6a** (*cis*–*trans*) and **7a** (*trans*–*trans*) was obtained when the crude product was subjected to column chromatography on silica gel (Table 1). Attempts to separate the diastereoisomers were unsuccessful due to the similar polarities of **6a** and **7a**. The diastereoselectivity of **6a** and **7a** was determined as 89/11 from the corresponding $^1$H NMR spectrum and comparison of the relevant characteristic signals. All analytical data including IR, $^1$H and $^{13}$C NMR of **6a** and **7a** were in agreement with the proposed structures. For example, the *cis*–*trans* and *trans*–*trans* annealation of **6a** and **7a** were determined by coupling patterns for $H_{6a}$, which showed medium-small and large/large coupling constants, respectively. Thus, though the $H_{6a}$ of **6a** resonates at $\delta$ 4.21 a**s** a doublet of a doublet with $J$=10.8 and 5.5 Hz, the $H_{6a}$ of **7a** appears at $\delta$ 3.63 as a doublet of doublet with $J$=12.0 and 10.2 Hz (Fig. 1).

**Table 1**
Results obtained for the domino Knöevenagel-hetero-Diels–Alder reaction of **3a** with **4**




| Entry | Solvent | Catalyst | **3a**/**4** Ratio | Time (h) | Yield (%) |
|---|---|---|---|---|---|
| 1 | Toluene | EDDA | 1.0/1.0 | 46 | 23 |
| 2 | EtOH | Piperidine | 1.0/1.0 | 12 | 48 |
| 3 | EtOH | Piperidine | 1.0/1.2 | 12 | 60 |
| 4 | EtOH | Piperidine | 1.0/1.4 | 12 | 60 |
| 5 | $H_2O$ | — | 1.0/1.0 | 12 | 62 |
| 6 | $H_2O$ | — | 1.0/1.2 | 12 | 78 |
| 7 | $H_2O$ | — | 1.0/1.4 | 12 | 78 |

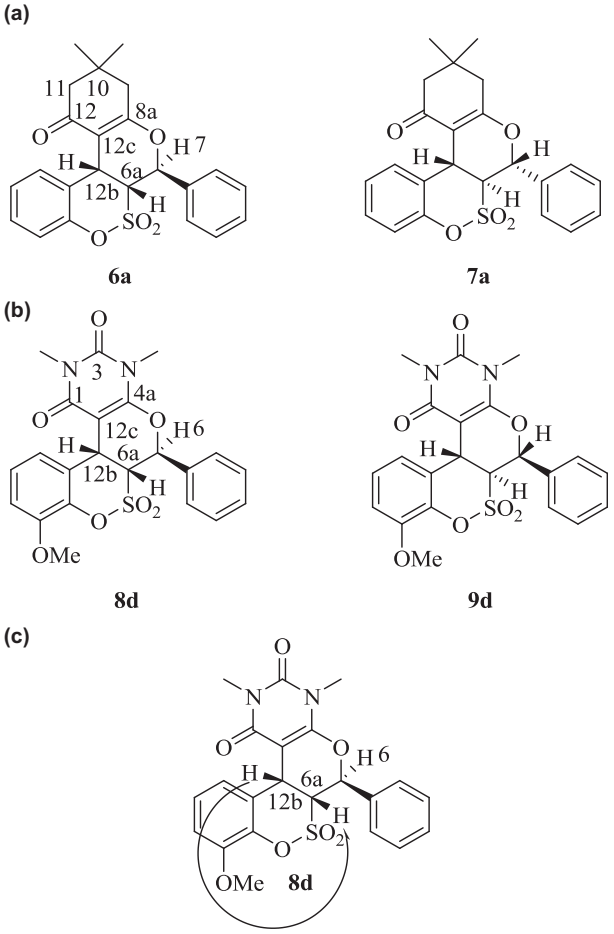
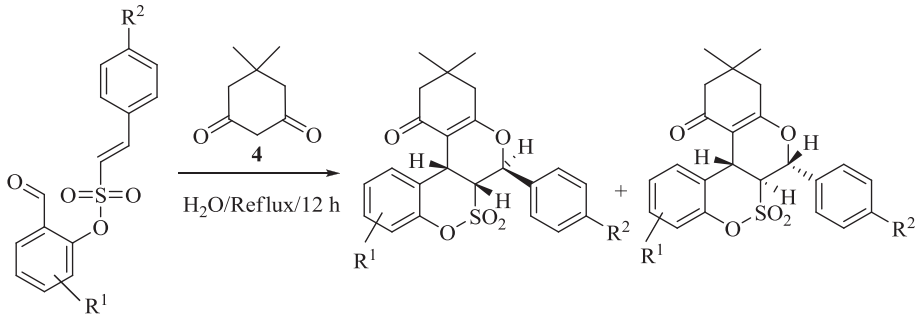



**Fig. 1.** Structures of (a) **6a** and **7a**, (b) **8d** and **9d**, (c) characteristic NOE of **8d**.

We next examined the substrate scope under optimal conditions with a variety of sulfonates **3a**–**f** and dimedone **4** (Scheme 2, Table 2). Inseparable mixtures of **6a**–**f** and **7a**–**f** were obtained with all analytical data including IR, $^1$H and $^{13}$C NMR consistent with the proposed structures.

### 2.3. Preparation of domino Knöevenagel-hetero-Diels–Alder cycloadducts of 8a–f and 9a–f

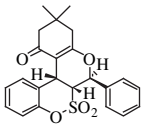
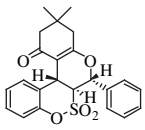
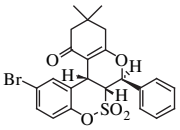
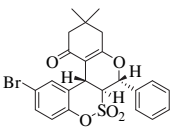
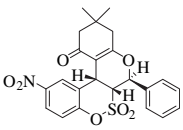
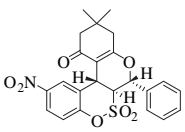
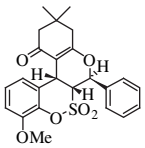
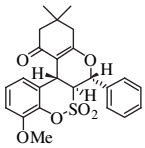
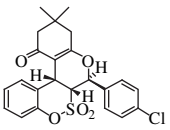
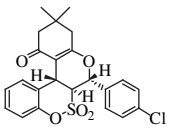
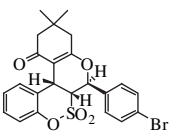
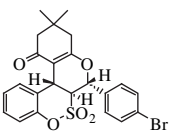
Sulfonates **3a**–**f** smoothly underwent domino Knöevenagel-hetero-Diels–Alder reactions with *N*,*N*-dimethylbarbituric acid (**5**) under optimal conditions affording a mixture of **8a**–**f** and **9a**–**f**




3a-f 6a-f 7a-f

**Scheme 2.** Synthesis of hexahydro-chromene-annulated benzo-δ-sultones **6a**–**f** and **7a**–**f**.

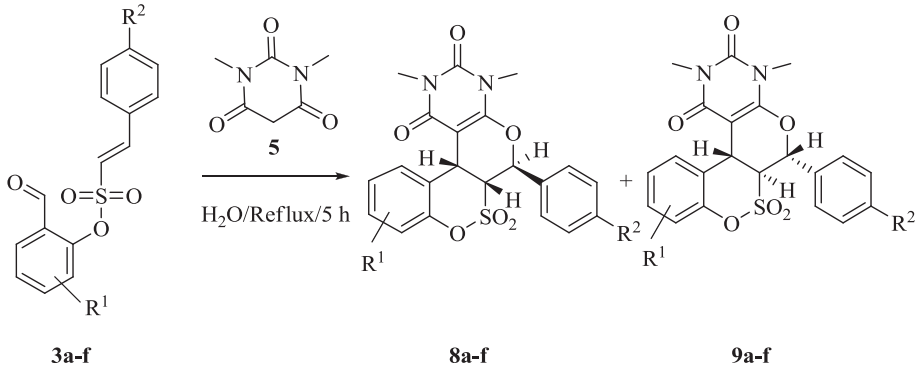
**Table 2**
Results obtained for the domino Knöevenagel-hetero-Diels–Alder reaction of **3a**–**f** with **4**

| Entry | $R^1$ | $R^2$ | Products | | Yield (%) | Ratio of **6**/**7** |
|---|---|---|---|---|---|---|
| | | | **6** | **7** | | |
| 1 | –H | –H |  **6a** |  **7a** | 78 | 89/11 |
| 2 | 4-Br | –H |  **6b** |  **7b** | 60 | 84/16 |
| 3 | 4-$NO_2$ | –H |  **6c** |  **7c** | 56 | 85/15 |
| 4 | 6-OMe | –H |  **6d** |  **7d** | 75 | 88/12 |
| 5 | –H | -4-Cl |  **6e** |  **7e** | 46 | 87/13 |
| 6 | –H | -4-Br |  **6f** |  **7f** | 42 | 91/9 |

after column chromatography with silica gel (Scheme 3, Table 3). All analytical data including IR, $^1H$ and $^{13}C$ NMR of **8a**–**f** and **9a**–**f** were in agreement with the proposed structures. For example, the *cis–trans* and *trans–trans* annealations of **8d** and **9d** were determined by coupling patterns for $H_{6a}$, which showed medium/small and large/large coupling constants with $H_{12b}$ and $H_6$, respectively. Thus, though the $H_{6a}$ of **8a** resonates at $\delta$ 4.34 as a doublet of a doublet with $J$=10.8 and 5.8 Hz, the $H_{6a}$ of **9a** appears at

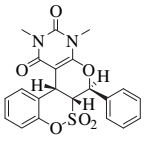
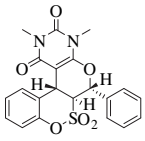
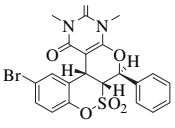
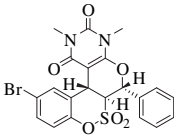
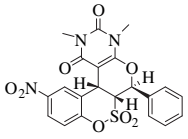
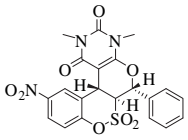
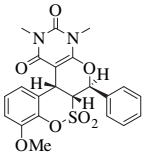
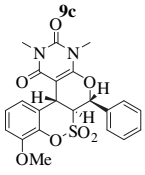
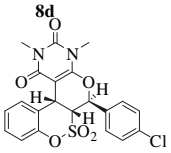
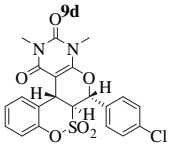
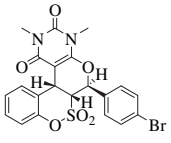
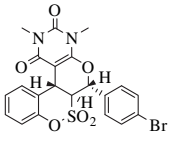
$\delta$ 3.68 as a doublet of doublet with $J$=11.9 and 10.3 Hz (Fig. 1b). The $^1$H NMR data agreed with their assignment and were further supported by $^1$H NMR NOESY experiment, which confirmed that the ring junction stereochemistry is cis (Fig. 1c).

Overall, the hexahydro-chromene and tetrahydro-pyrano[2,3-d] pyrimidine-annulated benzo-$\delta$-sultones **6a**–**f**/**8a**–**f** were obtained via highly diastreoselective processes in good yields. When benzaldehyde bearing an electron-donating group, such as methoxyl




**Scheme 3.** Synthesis of tetrahydro-pyrano[2,3-*d*]pyrimidine-annulated benzo-$\delta$-sultones **8a**–**f** and **9a**–**f**.

**Table 3**
Results obtained for the domino Knöevenagel-hetero-Diels–Alder reaction of **3a**–**f** with **5**

| Entry | $R^1$ | $R^2$ | Product | | Yield (%) | Ratio of **8**/**9** |
|---|---|---|---|---|---|---|
| | | | **8** | **9** | | |
| 1 | –H | –H |  **8a** |  **9a** | 93 | 90/10 |
| 2 | 4-Br | –H |  **8b** |  **9b** | 64 | 90/10 |
| 3 | 4-$NO_2$ | –H |  **8c** |  **9c** | 75 | 75/25 |
| 4 | 6-OMe | –H |  **8d** |  **9d** | 86 | 93/7 |
| 5 | –H | -4-Cl |  **8e** |  **9e** | 48 | 91/9 |
| 6 | –H | -4-Br |  **8f** |  **9f** | 46 | 85/15 |

was used, modest yields of the corresponding benzo-δ-sultones were obtained (entry 4, Tables 2 and 3). Aldehydes bearing electron-withdrawing groups, such as bromine or nitro also provided benzo-δ-sultones in lower yields (entries 2–3, Tables 2 and 3). The domino Knöevenagel-hetero-Diels–Alder reactions afforded the corresponding benzo-δ-sultones in lowest yields when the condensed products of unsubstituted aldehydes with (*E*)-2-phenylethenesulfonyl chlorides bearing electron-withdrawing groups were used as the starting materials (entries 5 and 6, Tables 2 and 3). Rationalization of the obtained results may not be an easy task. Changing the substituents on either phenyl ring has simultaneous effects on the diene HOMO and the dienophile LUMO energies since these moieties are directly tethered to the phenyl group. Therefore, one may not expect to observe the results in agreement either with normal or inverse electron demand behavior, which has been extensively reviewed in frontier molecular orbital theory.[13]

Comparison of the results depicted in Table 3 with those of Table 2 shows that the domino-hetero-Diels–Alder of **3a**–**f** with *N*,*N*-dimethylbarbituric acid (**5**) has afforded the corresponding cycloadducts in higher product yields. The lower $Pk_a$ of **5** (4.40)[14] than that of dimedone (**4**), which is 5.23,[15] seems to be responsible for the higher efficiency of **5** in the formation of the corresponding Knöevenagel products.

It is generally accepted that the cycloaddition is concerted with both carbon–carbon σ-bonds being formed at the same time, although not necessarily to the same extent. The cycloaddition of a heterodiene generated from Knöevenagel condensation of an aldehyde either with dimedone or *N*,*N*-dimethylbarbituric acid and an (*E*)-2-phenylethenesulfonate as a dienophile could lead to a mixture of stereoisomers. The stereochemical outcome of the cycloaddition is dependent on the geometries of the diene as well as the dipolarophile. For example, while the trans stereochemistry of the resultant pyran $C_{6a}$–$C_7$ bond emerges from the trans geometry of the dipolarophile, the stereochemistry of the sultone $C_{6a}$–$C_{12b}$ bond depends on the transition state structure of the cycloadditions. It seems justified that the *cis*–*trans* and *trans*–*trans* annulated products are formed via *endo-E-syn* transition state **I** and *exo-E-anti* transition state **II** (Fig. 2), respectively, if aromatic α,β-unsaturated aldehydes are used in the Knöevenagel step.[1b] The investigated hetero-Diels–Alder reactions showed high diastereoselectivity, according to similar intramolecular processes.[16] The high stereocontrol in all cases has been attributed to the Knöevenagel products containing a trisubstituted double bond with a geminal substitution at the $sp^2$ terminus.[17] The *endo-E-syn* transition state leading to the *cis*–*trans* annulated cycloadducts must have been more favorable than the *exo-E-anti* transition state due to an $sp^2$-geminal effect based on the phenomenon of 1,3-allylic strain.[18]

## 3. Conclusion

In conclusion, a number of synthesized bifunctional starting materials containing an aldehyde and an unsaturated sulfonate groups underwent a one-pot domino Knöevenagel-hetero-Diels–Alder reaction, respectively, with dimedone and *N*,*N*-dimethylbarbituric acid in water, affording novel hexahydro-chromene and -pyrano[2,3-*d*]pyrimidine-annulated benzo-δ-sultones in moderate to high yields. These new structures broaden the scaffolds that are accessible through domino-hetero-Diels–Alder reactions and many of them may represent interesting pharmacophores.

## 4. Experimental section

### 4.1. General information

All commercially available chemicals and reagents were purchased from Merck Chemical Company and used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected. IR spectra were recorded on a Shimadzu 4300 spectrophotometer, in $cm^{-1}$. $^1H$ and $^{13}C$ NMR spectra were recorded on a Bruker DRX-500-AVANCE spectrometer at 500 ($^1H$) and 125 MHz ($^{13}C$) using $CDCl_3$ as solvent and with the residual solvent signal as internal reference ($CDCl_3$, 7.24 and 77.0 ppm). Mass spectra of the products were obtained with a HP (Agilent technologies) 5937 Mass Selective Detector. Elemental analyses were carried out by a CHN-Rapid Heraeus elemental analyzer (Wellesley, MA).

### 4.2. General procedure for the preparation of 3a–f

To a solution of a 2-hydroxybenzaldehyde (610 mg, 5 mmol) and (*E*)-2-phenylethenesulfonyl chloride (1010 mg, 5 mmol) in acetone

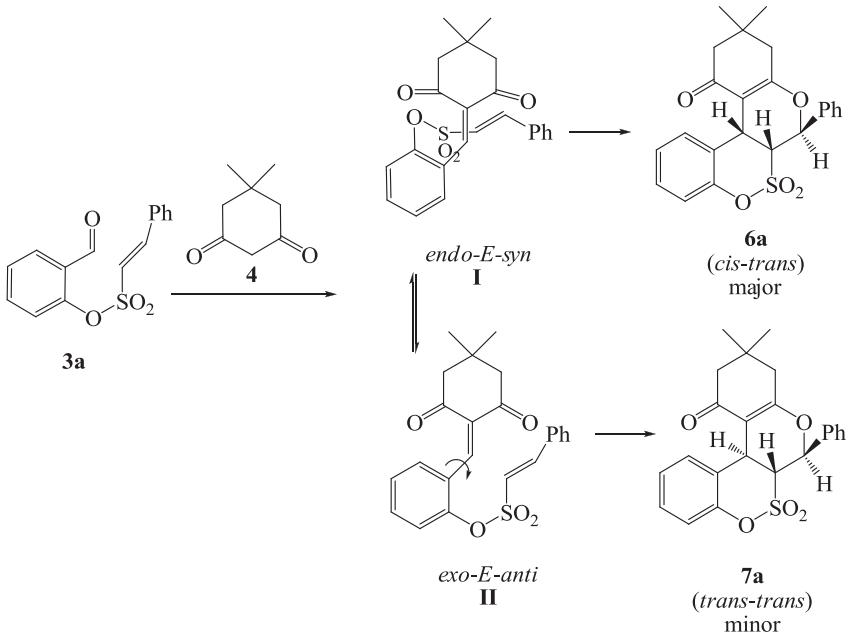



**Fig. 2.** Transition state model evoked for the formation of **6a** and **7a**.

(30 mL) was added $K_2CO_3$ (690 mg, 5 mmol) and the mixture was stirred for 2 h at room temperature. After evaporation of the solvent at reduced pressure, 30 mL of $H_2O$ was added and the organic compound was extracted with $CH_2Cl_2$ (30 mL). The solvent was then evaporated under reduced pressure and the crude products were recrystallized from $C_2H_5OH$ to afford **3a**–**f**.

*4.2.1. 2-Formylphenyl-(E)-2-phenylethenesulfonate (**3a**).* Colorless solid; (276 mg, 96%); mp: 59–62 °C; Found: C, 62.32; H, 4.12. $C_{15}H_{12}O_4S$ requires C, 62.49; H, 4.20%. $\nu_{max}$ (KBr): 3059; 2885; 1690 (C=O); 1604, 1361 ($OSO_2$), 1147 ($OSO_2$) $cm^{-1}$. $\delta_H$ (500 MHz, $CDCl_3$) 7.00 (1H, d, *J* 15.5 Hz, $SO_2CH$=CH); 7.44–7.53 (7H, m, Ar); 7.63 (1H, d, *J* 15.5 Hz, ArCH=CH); 7.66 (1H, t, *J* 7.6 Hz, Ar); 7.96 (1H, d, *J* 7.6 Hz, Ar); 10.37 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 120.3, 124.2, 128.1, 129.2, 129.6, 129.7, 129.8, 130.0, 132.6, 135.9, 147.8, 151.1, 188.3 (C=O); *m*/*z* (EI, 70 eV) 287 (10, $M^+-1$), 167 (88), 120 (25), 103 (100), 77 (36%).

*4.2.2. 2-Formyl-4-bromophenyl-(E)-2-phenylethenesulfonate (**3b**).* Colorless solid; (351 mg, 96%); mp: 69–70 °C; Found: C, 49.01; H, 3.00. $C_{15}H_{11}BrO_4S$ requires C, 49.06; H, 3.02%. $\nu_{max}$ (KBr): 3064, 2877, 1693 (C=O), 1607, 1380 ($OSO_2$), 1165 ($OSO_2$) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 6.94 (1H, d, *J* 15.5 Hz, $SO_2CH$=CH), 7.33 (1H, d, *J* 8.7 Hz, Ar), 7.46–7.54 (5H, m, Ar), 7.63 (1H, d, *J* 15.5 Hz, ArCH=CH), 7.75 (1H, d, *J* 8.7 Hz, Ar), 8.07 (1H, s, Ar), 10.37 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 119.8, 121.8, 126.0, 129.3, 129.8, 131.0, 131.6, 132.5, 132.8, 138.6, 148.4, 149.9, 186.9 (C=O); *m*/*z* (EI, 70 eV) 367 (1, $M^++1$), 200 (8), 167 (90), 103 (100), 77 (29%).

*4.2.3. 2-Formyl-4-nitrophenyl (E)-2-phenylethenesulfonate (**3c**).* Cream solid; (316 mg, 95%); mp: 104–107 °C; Found: C, 54.00; H, 3.29; N, 4.14. $C_{15}H_{11}NO_6S$ requires C, 54.05; H, 3.33; N, 4.20%. $\nu_{max}$ (KBr): 3062, 2896, 1693 (C=O), 1609, 1344 ($OSO_2$), 1162 ($OSO_2$) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 7.02 (1H, d, *J* 15.4 Hz, $SO_2CH$=CH), 7.48–7.67 (6H, m, Ar), 7.71 (1H, d, *J* 15.4 Hz, ArCH=CH), 8.50 (1H, d, *J* 7.9 Hz, Ar), 8.79 (1H, s, Ar), 10.37 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 119.5, 125.4, 125.6, 129.5, 129.9, 130.1, 130.3, 131.3, 133.2, 146.9, 149.2, 154.7, 186.1 (C=O); *m*/*z* (EI, 70 eV) 334 (10, $M^++1$), 316 (53), 273 (100), 183 (27), 151 (49%).

*4.2.4. 2-Formyl-6-methoxyphenyl-(E)-2-phenylethenesulfonate (**3d**).* Colorless solid; (302 mg, 95%); mp: 96–98 °C; Found: C, 60.29; H, 4.38. $C_{16}H_{14}O_5S$ requires C, 60.37; H, 4.43%. $\nu_{max}$ (KBr): 3065, 2898, 1690 (C=O), 1614, 1576, 1362 ($OSO_2$), 1144 ($OSO_2$) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 3.82 (3H, s, MeO), 7.07 (1H, d, *J* 15.6 Hz, $SO_2CH$=CH), 7.21 (1H, d, *J* 8.2 Hz, Ar), 7.37 (1H, t, *J* 7.9 Hz, Ar), 7.45–7.56 (6H, m, Ar), 7.55 (1H, d, *J* 15.6 Hz, ArCH=CH), 10.41 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 56.9, 118.6, 120.4, 121.6, 128.1, 128.4, 129.7, 129.9, 131.8, 132.2, 140.8, 146.0, 152.0, 188.7 (C=O); *m*/*z* (EI, 70 eV) 301 (1, $M^+-1$), 167 (83), 151 (53), 103 (100), 77 (42%).

*4.2.5. (E)-2-Formylphenyl 2-(4-chlorophenyl)ethenesulfonate (**3e**).* Yellow solid; (305 mg, 95%); mp: 113–116 °C; Found: C, 55.76; H, 3.38. $C_{15}H_{11}ClO_4S$ requires C, 55.82; H, 3.44%. $\nu_{max}$ (KBr): 3058, 2887, 1691 (C=O), 1595, 1350 ($OSO_2$), 1176 ($OSO_2$) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 6.96 (1H, d, *J* 15.5 Hz, $SO_2CH$=CH), 7.44–7.48 (6H, m, Ar), 7.57 (1H, d, *J* 15.5 Hz, ArCH=CH), 7.96 (1H, t, *J* 6.6 Hz, Ar), 7.97 (1H, d, *J* 6.7 Hz, Ar), 10.35 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 120.9, 124.3, 128.2, 129.8, 130.1, 130.2, 130.3, 130.4, 135.9, 138.8, 146.3, 150.9, 188.3 (C=O); *m*/*z* (EI, 70 eV) 324 (1, $M^++2$), 322 (3, $M^+$), 201 (74), 137 (100), 120 (41), 102 (54%).

*4.2.6. (E)-2-Formylphenyl 2-(4-bromophenyl)ethenesulfonate (**3f**).* White solid; (348 mg, 95%); mp: 101–104 °C; Found: C, 48.98; H, 3.03. $C_{15}H_{11}BrO_4S$ requires C, 49.06; H, 3.02%. $\nu_{max}$ (KBr): 3054, 2894, 1690 (CO), 1676, 1601, 1341 ($OSO_2$), 1161 ($OSO_2$) $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 6.98 (1H, d, *J* 15.5 Hz, $SO_2CH$=CH), 7.39 (2H, d, *J* 8.4 Hz, Ar), 7.45 (1H, d, *J* 8.2 Hz, Ar), 7.48 (1H, t, *J* 7.5 Hz, Ar), 7.55 (1H, d, *J* 15.5 Hz, ArCH=CH), 7.61 (2H, d, *J* 8.4 Hz, Ar), 7.68 (1H, t, *J* 7.7 Hz, Ar), 7.97 (1H, t, *J* 7.7 Hz, Ar), 10.35 (1H, s, CHO); $\delta_C$ (125 MHz, $CDCl_3$): 121.1, 124.3, 127.3, 128.2, 129.7, 130.1, 130.5, 130.7, 133.1, 135.9, 146.3, 150.9, 188.3 (C=O); *m*/*z* (EI, 70 eV) 369 (2, $M^++2$), 367 (3, $M^+$), 247 (54), 183 (94), 120 (60), 102 (100%).

### 4.3. General procedure for domino Knoevenagel-hetero-Diels–Alder reaction

A mixture of (*E*)-2-formylphenyl-2-phenylethenesulfonate **3** (1 mmol) and active methylene compounds **4** or **5** (1.2 mmol) in water (15 mL) was heated to reflux whilst stirring. The progress of the reaction was monitored by TLC. After completion (See Tables 2 and 3), the solid precipitate was filtered, washed with hot water (5 mL), and dried in air. The products were separated by column chromatography (ethyl acetate/hexane, 1:3). A mixture of two diastereomers was obtained in each case. All attempts to separate these two isomers were unsuccessful due to their similar polarities. The diastereomeric ratios were determined based on their $^1H$ NMR using the characteristic signals.

*4.3.1. 10,10-Dimethyl-7-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6a**, **7a**).* White solid (89:11 dr 320 mg, 78%), mp 174–177 °C. Found: C, 67.23; H, 5.37. $C_{23}H_{22}O_5S$ requires C, 67.30; H, 5.40%. $\nu_{max}$ (KBr): 1653, 1629, 1384, 1162 $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$) 1.18 (s, 3H, Me) {for **7a**, 1.20 (3H, s, Me)}, 1.22 (s, 3H, Me) {for **7a**, 1.23 (3H, s, Me)}, 2.46 (s, 2H, $CH_2C$=C) {for **7a**, 2.45 (s, 2H, $CH_2C$=C)}, 2.43 (1H, d, *J* 16.3 Hz, CHHC=O), part of $AB_q$, 2.54 (1H, d, *J* 16.3 Hz, CHHC=O) part of $AB_q$ {for **7a**, 2.45–2.50 (2H, m, $CH_2C$=O)}, 4.21 (1H, dd, *J* 10.8, 5.5 Hz, $H_{6a}$) {for **7a**, 3.63 (1H, dd, *J* 12.0, 10.2 Hz, $H_{6a}$)}, 4.97 (1H, d, *J* 10.8 Hz, PhCHO) {for **7a**, 4.60 (1H, d, *J* 12.0 Hz, PhCHO)}, 5.02 (1H, d, *J* 5.5 Hz, $H_{12b}$) {for **7a**, 5.19 (1H, d, *J* 10.2 Hz, $H_{12b}$)}, 7.13 (1H, d, *J* 7.8 Hz, Ar), 7.18 (1H, d, *J* 8.0 Hz, Ar), 7.24–7.49 (7H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 28.9 (Me), 32.6 ($CMe_2$), 33.6 ($C_{12b}$), 42.7 (*C*C=C), 51.0 (*C*C=O), 60.4 ($C_{6a}$), 76.5 (PhC–O), 108.7 ($C_{12a}$), 120.1, 126.4, 127.4, 128.6, 129.3, 129.8, 129.9, 130.4, 136.0, 149.8 (C–Ar), 171.1 ($C_{8a}$), 196.9 (C=O); *m*/*z* (EI, 70 eV) 410 (3, $M^+$), 346 (100, $M^+-SO_2$), 330 (63, $M^+-SO_3$), 239 (28), 207 (30%).

*4.3.2. 2-Bromo-10,10-dimethyl-7-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6b**,**7b**).* White solid (84:16 dr 293 mg, 60%); mp: 218–220 °C. Found: C, 56.35; H, 4.23. $C_{23}H_{21}BrO_5S$ requires C, 56.45; H, 4.33%. $\nu_{max}$ (KBr): 1658, 1628, 1380, 1162 $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$): 1.18 (3H, s, Me) {for **7b**, 1.22 (3H, S, Me)}, 1.24 (3H, s, Me) {for **7b**, 1.33 (3H, s, Me)}, 2.48 (2H, s, $CH_2C$=C) {for **7b**, 2.47 (s, 2H, $CH_2C$=C)}, 2.43 (1H, d, *J* 16.3 Hz, $CH_2C$=O), part of $AB_q$, 2.57 (1H, d, *J* 16.3 Hz, $CH_2C$=O), part of $AB_q$, {for **7b**, 2.43–2.52 (2H, m, $CH_2C$=O)}, 4.21 (1H, dd, *J* 10.8, 5.5 Hz, $H_{6a}$) {for **7b**, 3.61 (1H, dd, *J* 12.3, 10.1 Hz, $H_{6a}$)}, 4.94 (1H, d, *J* 10.8 Hz, PhCHO) {for **7b**, 4.57 (1H, d, *J* 12.3 Hz, PhCHO)}, 4.99 (1H, d, *J* 5.5 Hz, $H_{12b}$) {for **7b**, 5.17 (1H, d, *J* 10.1 Hz, $H_{12b}$)}, 7.07 (1H, d, *J* 8.6 Hz, Ar), 7.21 (1H, s, Ar), 7.38–7.53 (6H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.7 (Me), 28.9 (Me), 32.7 ($CMe_2$), 33.5 ($C_{12b}$), 42.7 (*C*C=C), 51.0 (*C*C=O), 60.4 ($C_{6a}$), 76.4 (PhC–O), 107.9 ($C_{12a}$), 118.8, 121.8, 128.6, 128.8, 129.3, 130.5, 132.9, 133.1, 136.5, 148.5 (C–Ar), 171.5 ($C_{8a}$), 197.0 (C=O); *m*/*z* (EI, 70 eV) 489 (2, $M^+$), 425 (16, $M^+-SO_2$), 409 (33, $M^+-SO_3$), 256 (100), 144 (93%).

*4.3.3. 2-Nitro-10,10-dimethyl-7-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6c**,**7c**).* Yellow solid (85:15 dr 255 mg, 56%); mp: 202–205 °C. Found: C, 60.65; H, 4.59. $C_{23}H_{21}NO_7S$ requires C, 60.65; H, 4.65%. $\nu_{max}$ (KBr): 1662, 1627, 1383, 1165 $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$): 1.20

(3H, s, Me) {for **7c**, 1.24 (3H, s, Me)}, 1.26 (3H, s, Me) {for **7c**, 1.38 (3H, s, Me)}, 2.50 (2H, s, $CH_2C{=}C$) {for **7c**, 2.49 (2H, s, $CH_2C{=}C$)}, 2.46 (1H, d, *J* 16.4 Hz, $CH_2C{=}O$), part of $AB_q$, 2.60 (1H, d, *J* 16.4 Hz, $CH_2C{=}O$), part of $AB_q$ {for **7c**, 2.44–2.57 (2H, m, $CH_2C{=}O$)}, 4.30 (1H, dd, *J* 10.7, 5.7 Hz, $H_{6a}$) {for **7c**, 3.68 (1H, dd, *J* 12.0, 10.1 Hz, $H_{6a}$)}, 4.96 (1H, d, *J* 10.7 Hz, PhC*H*O) {for **7c**, 4.65 (1H, d, *J* 12.0 Hz, PhC*H*O)}, 5.05 (1H, d, *J* 5.7 Hz, $H_{12b}$) {for **7c**, 5.22 (1H, d, *J* 10.1 Hz, $H_{12b}$)}, 7.33 (1H, d, *J* 8.9 Hz, Ar), 7.36–7.49 (5H, m, Ar), 8.04 (1H, s, Ar), 8.28 (1H, dd, *J* 8.6, 2.4 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.7 (Me), 28.8 (Me),32.7 ($CMe_2$), 33.8 ($C_{12b}$), 42.7 (*C*C=C), 50.9 (*C*C=O), 60.2 ($C_{6a}$), 76.4 (PhC–O), 107.8 ($C_{12b}$), 121.2, 125.6, 126.1, 128.2, 128.5, 129.4, 130.7, 135.3, 146.6, 153.8 (C–Ar), 171.8 ($C_{8a}$), 196.8 (C=O); *m*/*z* (EI, 70 eV) 455 (9, $M^+$), 391 (43, $M^+-SO_2$), 375 (100, $M^+-SO_3$), 344 (24), 103 (28%).

*4.3.4. 4-Methoxy-10,10-dimethyl-7-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6d**, **7d**).* White solid (88:12 dr 330 mg, 75%); mp: 222–225 °C. Found: C, 65.40; H, 5.48. $C_{24}H_{24}O_6S$ requires C, 65.44; H, 5.49%. $\nu_{max}$ (KBr): 1650, 1635, 1378, 1162 $cm^{-1}$; $\delta_H$ (500 MHz, $CDCl_3$): 1.18 (3H, s, Me) {for **7d**, 1.20 (3H, s, Me)}, 1.24 (3H, s, Me) {for **7d**, 1.32 (3H, s, Me)}, 2.46 (2H, s, $CH_2C{=}C$) {for **7d**, 2.45 (2H, s, $CH_2C{=}C$)}, 2.42 (1H, d, *J* 16.3 Hz, $CH_2C{=}O$), part of $AB_q$, 2.53 (1H, d, *J* 16.3 Hz, $CH_2C{=}O$) part of $AB_q$ {for **7d**, 2.40–2.47 (2H, m, $CH_2C{=}O$)}, 3.91 (3H, s, OMe) {for **7d**, 3.90 (3H, s, OMe)}, 4.25 (1H, dd, *J* 10.8, 5.7 Hz, $H_{6a}$) {for **7d**, 3.64 (1H, dd, *J* 12.0, 10.1 Hz, $H_{6a}$)}, 4.92 (1H, d, *J* 10.8 Hz, PhC*H*O) {for **7d**, 4.58 (1H,d, *J* 12.0 Hz, PhC*H*O)}, 4.99 (1H, d, *J* 5.7 Hz, $H_{12b}$) {for **7d**, 5.18 (1H, d, *J* 10.2 Hz, $H_{12b}$)}, 6.65 (1H, d, *J* 7.8 Hz, Ar), 6.99 (1H, d, *J* 8.3 Hz, Ar), 7.23 (1H, t, *J* 8.1 Hz, Ar), 7.39–7.50 (5H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 29.0 (Me), 32.6 (*C*Me$_2$), 33.7 ($C_{12b}$), 42.7 (*C*C=C), 51.0 (*C*C=O), 56.8 (MeO), 61.0 ($C_{6a}$), 76.4 (PhC–O), 108.2 ($C_{12a}$), 113.1, 120.6, 127.4, 128.4, 128.7, 129.2, 130.3, 136.1, 138.8, 150.6 (C–Ar), 170.9 ($C_{8a}$), 196.7 (C=O); *m*/*z* (EI, 70 eV) 440 (6, $M^+$), 376 (15, $M^+-SO_2$), 360 (100, $M^+-SO_3$), 269 (65), 178 (20%).

*4.3.5. 10,10-Dimethyl-7-(4-chloro)-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6e**,**7e**).* White solid (87:13 dr 204 mg, 46%); mp: 202–205 °C. Found: C, 62.01; H, 4.74. $C_{23}H_{21}ClO_5S$ requires C, 62.09; H, 4.76%. $\nu_{max}$ (KBr): 1663, 1625, 1383, 1162 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 1.19 (3H, s, Me) {for **7e**, 1.22 (3H, s, Me)},1.23 (3H, s, Me) {for **7e**, 1.29 (3H, s, Me)}, 2.45 (2H, s, $CH_2C{=}C$) {for **7e**, 2.44 (2H, s, $CH_2C{=}C$)}, 2.43 (1H, d, *J* 11.6 Hz, $CH_2C{=}O$) part of $AB_q$, 2.58 (1H, d, *J* 11.6 Hz, $CH_2C{=}O$) part of $AB_q$, {for **7e**, 2.43–2.50 (2H, m, $CH_2C{=}O$)}, 4.14 (1H, dd, *J* 10.8, 5.5 Hz, H6a) {for **7e**, 3.57 (1H, dd, *J* 12.0, 10.2 Hz, H6a)}, 4.93 (1H, d, *J* 10.8 Hz, PhCHO){for **7e**, 4.58 (1H, d, *J* 12.0 Hz, PhCHO)}, 5.02 (1H, d, *J* 5.5 Hz, H12b) {for **7e**, 5.17 (1H, d, *J* 10.2 Hz, H12b)}, 7.11(1H, d, *J* 7.7 Hz, Ar), 7.18 (1H, d, *J* 8.0 Hz, Ar), 7.35–7.43 (6H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 28.9 (Me), 32.6 ($CMe_2$), 33.5 (C12b), 42.6 (*C*C=C), 51.0 (*C*C=O), 60.5 ($C_{6a}$), 75.7 (PhC–O), 107.0 (C12a), 120.1, 126.3, 127.5, 129.5, 129.8, 130.0, 130.0, 130.3, 136.0.149.7 (C–Ar), 170.7 (C8a), 196.0 (C=O); *m*/*z* (EI, 70 eV) 446 (10, $M^+$+1), 381 (100, $M^+-SO_2$), 365 (63, $M^+-SO_3$), 256 (79), 296 (19%).

*4.3.6. 10,10-Dimethyl-7-(4-boromo)-phenyl-6a,7,9,10,11,12b-hexahydro-5,8-dioxa-6-thia-benzo[c]phenanthren-12-one-6,6-dioxide (**6f**, **7f**).* White solid (91:9 dr 205 mg, 42%); mp: 196–200 °C. Found: C, 56.70; H, 4.23. $C_{23}H_{21}BrO_5S$ requires C, 56.54; H, 4.33%. $\nu_{max}$ (KBr): 1655, 1625, 1373, 1158 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 1.18 (3H, s, Me) {for **7f**, 1.21 (3H, s, Me)}, 1.23 (3H, s, Me) {for **7f**, 1.27 (3H, s, Me)}, 2.45 (2H, s, $CH_2C{=}C$) {for **7f**, 2.44 (s, 2H, $CH_2C{=}C$) }, 2.43 (1H, d, *J* 16.2 Hz, $CH_2C{=}O$), part of $AB_q$, 2.54 (1H, d, *J* 16.2 Hz, $CH_2C{=}O$), part of $AB_q$, {for **7f**, 2.41–2.56 (2H, m, $CH_2C{=}O$)}, 4.16 (1H, dd, *J* 10.8, 5.5 Hz, $H_{6a}$) {for **7f**, 3.48 (1H, dd, *J* 12.0, 10.1 Hz, $H_{6a}$)}, 4.91 (1H, d, *J* 10.8 Hz, PhCHO) {for **7f**, 4.58 (1H, d, *J* 12.0 Hz, PhCHO)}, 5.01 (1H, d, *J* 5.5 Hz, $H_{12b}$) {for **7f**, 5.15 (1H, d, *J* 10.1 Hz, $H_{12b}$)}, 7.11 (1H, d, *J* 7.7 Hz, Ar), 7.18 (1H, d, *J* 8.1 Hz, Ar), 7.27 (2H, d, *J* 8.1 Hz, Ar), 7.39 (2H, t, *J* 7.7 Hz, Ar), 7.58 (2H, d, *J* 8.1 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 28.9 (Me), 32.6 ($CMe_2$), 33.5 ($C_{12b}$), 42.6 (*C*C=C), 51.0 (*C*C=O), 60.0 ($C_{6a}$), 75.8 (PhCHO), 108.8 ($C_{12a}$), 120.1, 124.7, 126.3, 127.5, 129.8, 130.0, 130.3, 132.5, 135.1149.7 (C–Ar), 170.8 ($C_{8a}$), 196.8 (C=O); *m*/*z* (EI, 70 eV) 489 (5, $M^+$), 425 (100, $M^+-SO_2$), 409 (69, $M^+-SO_3$), 227 (80), 171 (33%).

*4.3.7. 2,4-Dimethyl-6-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione-7,7-dioxide (**8a**, **9a**).* White solid (90:10 dr 396 mg, 93%); mp: 225–227 °C. Found: C, 59.34; H, 4.37; N, 6.24. $C_{21}H_{18}N_2O_6S$ requires: C, 59.15; H, 4.25; N, 6.57%. $\nu_{max}$ (KBr): 1699, 1635, 1380, 1156 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.31 (3H, s, Me) {for **9a**, 3.39 (3H, s, Me)}, 3.47 (3H, s, Me) {for **9a**, 3.46 (3H, s, Me)}, 4.29 (1H, dd, *J* 10.7, 5.5 Hz, $H_{6a}$) {for **9a**, 3.68 (1H, dd, *J* 12.0, 10.2 Hz, $H_{6a}$)}, 5.12 (1H, d, *J* 5.5 Hz, $H_{12b}$) {for **9a**, 5.42 (1H, d, *J* 10.2 Hz, $H_{12b}$)}, 5.19 (1H, d, *J* 10.7 Hz, PhC*H*O) {for **9a**, 5.43 (1H, d, *J* 12.0 Hz, PhC*H*O)}, 7.19 (1H, d, *J* 8.0 Hz, Ar), 7.32–7.51 (8H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.9 (Me), 29.5 (Me), 34.5 ($C_{12b}$), 60.0 ($C_{6a}$), 78.8 (PhC–O), 85.5 ($C_{12c}$), 120.1, 125.8, 127.7, 128.6, 129.5, 130.0, 130.3, 130.9, 134.8, 149.6 (C–Ar), 151.1 (C=O), 156.7 ($C_{4a}$), 162.7 (C=O); *m*/*z* (EI, 70 eV) 426 (2, $M^+$), 362 (43, $M^+-SO_2$), 346 (33, $M^+-SO_3$), 243 (100), 207 (53%).

*4.3.8. 11-Bromo-2,4-dimethyl-6-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione-7,7-dioxide (**8b**, **9b**).* White solid (90:10 dr 323 mg, 64%); mp: 234–237 °C. Found: C, 49.59; H, 3.26; N, 5.50. $C_{21}H_{17}BrN_2O_6S$ requires C, 49.91; H, 3.39; N, 5.54%. $\nu_{max}$ (KBr): 1709, 1638, 1380, 1163 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.33 (3H, s, Me) {for **9b**, 3.39 (3H, s, Me)}, 3.48 (3H,s, Me) {for **9b**, 3.49 (3H, s, Me)}, 4.29 (1H, dd, *J* 10.7, 5.7 Hz, $H_{6a}$) {for **9b**, 3.65 (1H, dd, *J* 12.0, 10.3 Hz, $H_{6a}$)}, 5.10 (1H, d, *J* 5.7 Hz, $H_{12b}$) {for **9b**, 5.41 (1H, d, *J* 10.3 Hz, $H_{12b}$)}, 5.15 (1H, d, *J* 10.7 Hz, PhCHO) {for **9b**, 5.41 (1H, d, *J* 12.0 Hz, PhCHO)}, 7.09 (1H, d, *J* 8.6 Hz, Ar), 7.42–7.52 (6H, m, Ar), 7.56 (1H, dd, *J* 8.5, 1.8 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 29.0 (Me), 29.5 (Me), 34.6 ($C_{12b}$), 60.0 ($C_{6a}$), 78.6 (PhC–O), 84.6 ($C_{12c}$), 121.0, 121.8, 128.2, 128.6, 129.5, 130.1, 132.8, 133.5, 134.5, 148.6 (C–Ar), 151.0 (C=O), 156.8 ($C_{4a}$), 162.4 (C=O); *m*/*z* (EI, 70 eV) 506 (4, $M^+$+2), 441(50, $M^+-SO_2$), 425 (90, $M^+-SO_3$), 323 (90), 103 (100%).

*4.3.9. 11-Nitro-2,4-dimethyl-6-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione-7,7-dioxide (**8c**, **9c**).* Yellow solid (75:25 dr 353 mg, 75%); mp: 162–163 °C. Found: C, 53.52; H, 3.60; N, 8.88. $C_{21}H_{17}N_3O_8S$ requires C, 53.50; H, 3.63; N, 8.91%. $\nu_{max}$ (KBr): 1704, 1651, 1394, 1165 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.25 (3H, s, Me) {for **9c**, 3.32 (3H, s, Me)}, 3.40 (3H, s, Me) {for **9c**, 3.37 (3H, s, Me)}, 4.48 (1H, dd, *J* 10.7, 6.0 Hz, $H_{6a}$) {for **9c**, 3.74 (1H, dd, *J* 12.0, 10.2 Hz, $H_{6a}$)}, 5.07 (1H, d, *J* 6.0 Hz, $H_{12b}$) {for **9c**, 5.41 (1H, d, *J* 10.2 Hz, $H_{12b}$)}, 5.09 (1H, d, *J* 10.7 Hz, PhCHO) {for **9c**, 4.75 (1H, d, *J* 12.0 Hz, PhCHO)}, 7.33–7.47 (6H, m, Ar), 8.20 (1H, s, Ar), 8.23 (1H, dd, *J* 8.8, 2.4 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.9 (Me), 29.5 (Me), 35.4 ($CH_{12b}$), 59.3 ($CH_{6a}$), 78.5 (PhC–O), 84.5 ($C_{12b}$), 121.2, 125.8, 126.3, 127.6, 128.6, 129.5, 131.4, 134.1, 146.7 (C–Ar), 150.8 (C=O), 153.5 (C–Ar), 157.1 ($C_{4a}$), 162.6 (C=O); *m*/*z* (EI, 70 eV) 471 (3, $M^+$), 407 (16, $M^+-SO_2$), 391 (39, $M^+-SO_3$), 103 (58), 66 (100%).

*4.3.10. 9-Methoxy-2,4-dimethyl-6-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione-7,7-dioxide (**8d**, **9d**).* White solid (93:7 dr 392 mg, 86%); mp: 240–243 °C. Found: C, 57.91; H, 4.45; N, 5.96. $C_{22}H_{20}N_2O_7S$ requires C, 57.89; H, 4.42; N, 5.95%. $\nu_{max}$ (KBr): 1703, 1655, 1380, 1148 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.32 (3H, s, Me) {for **9d**, 3.38 (3H, s, Me)}, 3.45 (3H, s, Me) {for **9d**, 3.46 (3H, s, Me)}, 3.92 (3H, s, OMe) {for **9d**, 3.90 (3H, s, OMe)}, 4.34 (1H, dd, *J* 10.8, 5.8 Hz, $H_{6a}$) {for **9d**, 3.68 (1H, dd, *J*

11.9, 10.3 Hz, $H_{6a}$)}, 5.08 (1H, d, *J* 5.8 Hz, $H_{12b}$) {for **9d**, 5.41 (1H, d, *J* 10.3 Hz, $H_{12b}$)}, 5.14 (1H, d, *J* 10.8 Hz, PhCHO) {for **9d**, 4.75 (1H, d, *J* 11.9 Hz, PhCHO)}, 6.83 (1H, d, *J* 7.8 Hz, Ar), 7.01 (1H, d, *J* 8.3 Hz, Ar), 7.26 (1H, t, *J* 8.1 Hz, Ar), 7.41–7.51 (5H, m, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 29.5 (Me), 34.6 ($C_{12b}$), 56.8 (MeO), 60.6 ($C_{6a}$), 78.6 (PhC–O), 84.9 ($C_{12c}$), 113.4, 120.5, 127.6, 127.8, 128.7, 129.5, 130.9, 134.8, 138.6 (C–Ar), 150.6 (C=O), 151.1 (C–Ar), 156.7 ($C_{4a}$), 162.5 (C=O); *m*/*z* (EI, 70 eV) 456 (1, $M^+$), 392 (12, $M^+-SO_2$), 376 (40, $M^+-SO_3$), 268 (53), 255 (28), 253 (100%).

*4.3.11. 2,4-Dimethyl-6-(4-chloro)-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione,7,7-dioxide (**8e**, **9e**).* White solid (91:9 dr 221 mg, 48%); mp: 232–235 °C. Found: C, 54.69; H, 3.76; N, 6.06. $C_{21}H_{17}ClN_2O_6S$ requires C, 54.73; H, 3.72; N, 6.08%. $\nu_{max}$ (KBr): 1701, 1651, 1377, 1152 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.25 (3H, s, Me) {for **9e**, 3.32 (3H, s, Me)}, 3.40 (3H, s, Me) {for **9e**, 3.90 (3H, s, Me)}, 4.30 (1H, dd, *J* 10.8, 5.7 Hz, $H_{6a}$) {for **9e**, 3.68 (1H, dd, *J* 11.7, 10.3 Hz, $H_{6a}$)}, 5.06 (1H, d, *J* 5.7 Hz, $H_{12b}$) {for **9e**, 5.37 (1H, d, *J* 10.3 Hz, $H_{12b}$)}, 5.09 (1H, d, *J* 10.8 Hz, PhCHO) {for **9e**, 4.73 (1H, d, *J* 11.7 Hz, PhCHO)}, 7.14 (1H, d, *J* 8.1 Hz, Ar), 7.28 (2H, d, *J* 4.5 Hz, Ar), 7.34 (2H, d, *J* 8.5 Hz, Ar), 7.35–7.39 (1H, m, Ar), 7.40 (2H, d, *J* 8.5 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 29.5 (Me),34.5 ($C_{12b}$), 59.7 ($C_{6a}$), 77.9 (PhC–O), 85.5 ($C_{12c}$), 119.9, 125.6, 127.7, 129.7, 130.0, 130.1, 130.3, 133.3, 136.9, 149.4 (C–Ar), 152.0 (C=O), 156.5 ($C_{4a}$), 162.6 (C=O); *m*/*z* (EI, 70 eV) 460 (2, $M^+$), 396 (19, $M^+-SO_2$), 380 (8, $M^+-SO_3$), 299 (63), 243 (100%).

*4.3.12. 2,4-Dimethyl-6-(4-boromo)-phenyl-2,4,6,6a,12b-pentahydro-5,8-dioxa-7-thia-2,4-diaza-benzo[c]phenanthrene-1,3-dione,7,7-dioxide (**8f**, **9f**).* White solid (85:15 dr 231 mg, 46%); mp: 212–215 °C. Found: C, 49.90; H, 3.37; N, 5.49. $C_{21}H_{17}BrN_2O_6S$ requires C, 49.91; H, 3.39; N, 5.54%. $\nu_{max}$ (KBr): 1701, 1616, 1378, 1158 $cm^{-1}$, $\delta_H$ (500 MHz, $CDCl_3$): 3.32 (3H, s, Me) {for **9f**, 3.39 (3H, s, Me)}, 3.48 (3H, s, Me) {for **9f**, 3.52 (3H, s, Me)}, 4.24 (1H, dd, *J* 10.8, 5.7 Hz, $H_{6a}$) {for **9f**, 3.63 (1H, dd, *J* 12.1, 10.3 Hz, $H_{6a}$)}, 5.13 (1H, d, *J* 5.7 Hz, $H_{12b}$) {for **9f**, 5.39 (1H, d, *J* 10.3 Hz, $H_{12b}$)}, 5.14 (1H, d, *J* 10.8 Hz, PhCHO) {for **9f**, 4.78 (1H,d, *J* 12.1 Hz, PhCHO)}, 7.21 (1H, d, *J* 8.3 Hz, Ar), 7.30–7.45 (5H, m, Ar), 7.63 (2H, d, *J* 8.5 Hz, Ar); $\delta_C$ (125 MHz, $CDCl_3$): 28.8 (Me), 29.4 (Me), 34.5 ($C_{12b}$), 59.4 ($C_{6a}$), 75.2 (PhC–O), 85.5 ($C_{12b}$), 119.8, 125.0, 125.5, 127.6, 130.0, 130.2, 130.3, 132.5, 133.9, 149.4 (C–Ar), 151.0 (C=O), 156.5 ($C_{4a}$), 162.6 (C=O); *m*/*z* (EI, 70 eV) 505 (13, $M^+$+1), 441 (8, $M^+-SO_2$), 425 (83, $M^+-SO_3$), 285 (63), 243 (100%).

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.09.010. These data include MOL files and InChiKeys of the most important compounds described in this article.

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