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o-Thioquinones on [2.2]paracyclophanes: an example of totally stereocontrolled hetero Diels–Alder reactions

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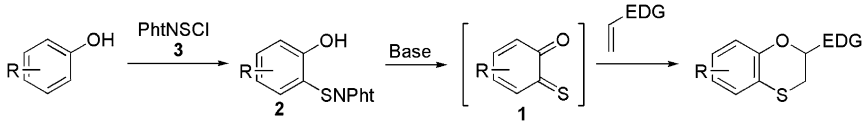
Abstract—The reaction of 4-hydroxy[2.2]paracyclophane with phthalimidesulfenyl chloride allowed the preparation of a suitable precursor for a paracyclophane-*o*-thioquinone. This species participates in an inverse electron demand hetero Diels–Alder reaction with different electron-rich alkenes to give the expected benzoxathiin cycloadducts with complete control of regio- and stereochemistry.

1. Introduction

Normal electron demand Diels–Alder reaction of [2.2]paracyclophane-based dienes is a well documented process that allowed the preparation of a variety of cyclophanes, especially chiral [2.2]paracyclophanes containing helical condensed aromatic subunits.[1] Helicenophanes, and more generally planar chiral cyclophanes are promising ligands to prepare catalysts for asymmetric processes, and are interesting for their potential applications as new materials.[2] There is now an increasing attention for paracyclophanes condensed with heterocyclic rings, and the hetero Diels–Alder reaction represents an useful tool for this task.[3] Mono-*o*-thioquinones,[4] of general formula **1**, are reactive intermediates potentially useful in this chemistry. As recently reported,[5] they can be obtained under very mild conditions by reacting the corresponding *o*-hydroxy-*N*-thiophthalimides **2** with bases (Scheme 1).

Compounds **2**, in turn, are the products of the *ortho* regiospecific S_EAr of phthalimidesulfenyl chloride **3** (PhtNSCl, Pht=Phthaloyl) with phenols, the key step of this procedure.[5] *o*-Thioquinones **1** are efficient electron-poor dienes with a plethora of electron-rich dienophiles[6] (Scheme 1), thus we envisaged their development with [2.2]paracyclophane substrates.

This paper reports the results of the study of (i) the sulfenylation reaction of 4-hydroxy[2.2]paracyclophane (**4**) with **3** (Scheme 2); (ii) the inverse electron demand Diels–Alder reaction of a [2.2]paracyclophane-*o*-thioquinone (**8**) obtained by this procedure.



Scheme 1. General procedure for the generation and trapping of *o*-thioquinones **1**.

Keywords: [2.2]Paracyclophanes; *o*-Thioquinones; Hetero Diels–Alder reactions; Stereoselectivity; Sulfur heterocycles.
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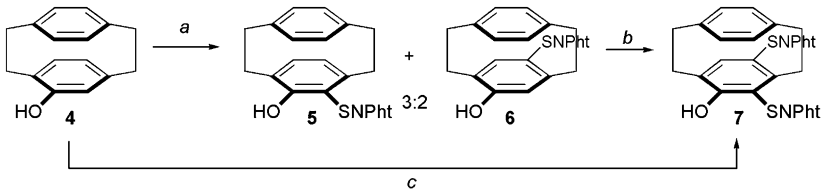


Scheme 2. Products formed on the phthalimide sulfenylation of 4-hydroxy[2.2]paracyclophane (**4**). Reagents: (a) **3** (1 equiv), $CHCl_3$, 0 °C, 2 h; (b) **3** (1 equiv), $CHCl_3$, rt, 1 h; (c) **3** (2.2 equiv), $CHCl_3$, rt, 2 h.

2. Results and discussion

2.1. Sulfenylation reaction of 4-hydroxy[2.2]paracyclophane (4)

The sulfenylation reaction of 4-hydroxy[2.2]paracyclophane (**4**) with **3** turned out to be a nontrivial extension of previously reported chemistry. After several attempts we realized that by carrying out the sulfenylation by adding 1 equiv of **3**, over 2 h at 0 °C, the expected *o*-hydroxy substituted derivative **5** could be isolated by flash chromatography on silica gel in 58% yield (Scheme 2). ^{1}H NMR spectroscopy of the crude reaction mixture showed (see Section 4) the contemporary formation of *para* isomer **6** (**5**:**6**=3:2), which was not isolated due to its poor stability and sensitivity to silica gel (Scheme 2).

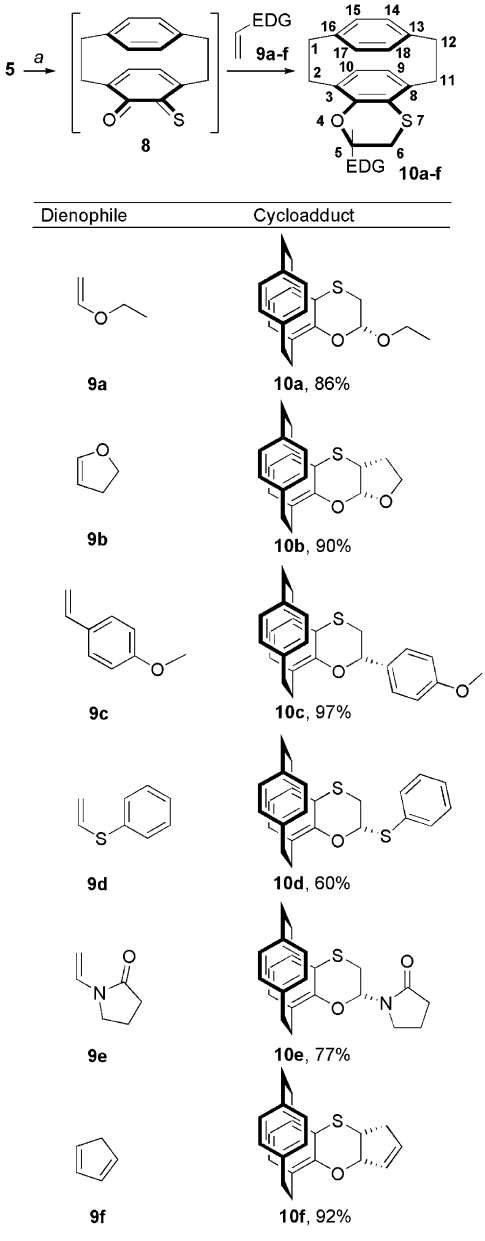
Carrying out the sulfenylation at rt, and/or using 2.2 equiv of **3**, led to the bis-sulfenylated thiophthalimide **7**, isolated as the sole reaction product in 82% yield (Scheme 2).

The sulfenylation of more than 50 different substituted phenols reported in the last decade,[5,6] afforded the *o*-monosubstituted *N*-thiophthalimide as the sole reaction product. However, the reaction of **3** with 2,5-dimethyl phenol, chosen as a simplified model of **4**, gave, after 3 h at rt, a 2:1 mixture of the corresponding *o*- and *p*-*N*-thiophthalimides indicating that a 2,5-dialkyl substitution can cause the lack of *ortho* regioselectivity. On the other hand, the possibility of bis-sulfenylation, with formation of **7**, is peculiar of this system. It has been demonstrated that a *N*-thiophthalimide substituent strongly depletes the nucleophilicity of aromatic rings[7] avoiding poly-substitution even with high reactive aromatics, like resorcin or 2,7-dihydroxynaphthalene. The isolation of **7**, that is formed even under very mild conditions, suggested that the paracyclophane system, due to the particular stereo-electronic situation offered by the proximity of the two aromatic rings, is able to overcome the withdrawing effect of the first thiophthalimide group. As a matter of fact, 2,5-dimethyl phenol or the corresponding *o*- and *p*-thiophthalimides, did not undergo bis-substitution neither using excess amounts of **3**, nor carrying out the reaction at 60 °C for several hours.

2.2. Inverse electron demand Diels–Alder reaction of the [2.2]paracyclophane-*o*-thioquinone (8)

Having derivative **5** in hand we decided to verify the possibility to generate the corresponding *o*-thioquinone **8** as a new interesting electron-poor diene possessing diastereotopic faces.

Reacting *o*-hydroxy-*N*-thiophthalimide **5** with 1 equiv of Et_3N in the presence of 5 equiv of ethyl vinyl ether (**9a**), after 20 h at 60 °C in $CHCl_3$, the expected benzoxathiin **10a** was obtained in 86% yield (Scheme 3).



Scheme 3. Generation and [4+2] cycloadditions of *o*-thioquionone **8**. Reagents: (a) Et_3N (1 equiv), dienophile **9** (2–5 equiv), $CHCl_3$, 60 °C, 20 h.

This confirms that *o*-thioquinone **8** is formed in situ and participates in an inverse electron demand cycloaddition with **9a** to give cycloadduct **10a** with complete regio- and stereocontrol (Scheme 3).

The cycloadditions occurred with different electron-rich alkenes **9b–e** and with cyclopentadiene (**9f**). In all cases, the expected cycloadducts **10b–f** were isolated in very good yield as single regio- and stereoisomers (Scheme 3).[8]

Although the Diels–Alder reactions were highly diastereoselective and occurred with good to high yields, we also tried to carry out the cycloadditions under high pressure conditions. It is well-known that pressure not only accelerates the cycloadditions, but also can affect the diastereoselectivity and the regioselectivity of the reactions. Surprisingly, when we performed the cycloadditions under high pressure (7–9 kbar) at 25–60 °C the reaction yield dropped dramatically.

2.3. Structure analysis

The structures of the isolated benzoxathiins were assigned by analysis of their ^{1}H and ^{13}C NMR spectra, in some cases confirmed by X-ray analysis. In all cycloadducts **10a–e**, the proton on C-5 appears as a doublet of doublets with a small and a high ^{3}J coupling constant with the diastereotopic C(6)H protons (see Section 4). This clearly indicates that the C(5)H proton lies in the pseudo-axial position and the EDG lies in the pseudo-equatorial position. However, this is not enough to attribute the relative stereochemistry to the diastereoisomer achieved from the cycloaddition.

For example oxathiin **10a**, isolated in the reaction of **8** with vinyl ether **9a**, could possess either structure ***A*** or ***B*** as reported in Figure 1. The attribution of the structure ***A*** to **10a** was determined by extensive ^{1}H and ^{13}C NMR investigations, especially ^{1}H–{^{1}H} NOE experiments.

Selective pre-irradiation of the C(17)H resonance resulted in signal enhancement of the resonances attributed to C(5)H, C(18)H, and C(1)H. This indicated a cis-relationship between C(5)H and the unsubstituted benzene ring of the paracyclophane unit (i.e., structure ***A***), confirming either a totally *anti* (with respect to the unsubstituted benzene ring of the paracyclophane unit)–*endo*- or *syn*–*exo*-diastereoselectivity in the cycloaddition reaction between **8** and **9a** (Fig. 1). Further support for such assignment was given by the NOE's observed between C(6)H and C(18)H, C(10)H and C(15)H, and C(9)H and C(14). Definitive confirmation for the structure ***A*** of oxathiin **10a** was obtained by X-ray analysis as showed in Figure 1.

The complete stereoselectivity[8] obtained in these reactions can be probably justified considering the matching situation of the *anti*-approach, favorite for the lack of steric interaction between the dienophile and the paracyclophane bridge, and the *endo* mode, preferred for the possibility of secondary orbital interactions. Similar considerations and spectroscopic evidences were convincing for the attribution of the same relative structure to oxathiins **10b–e**.

However, NMR considerations were less helpful for the attribution of the structure to derivative **10f**, first of all since the unique ^{3}J coupling constant is less supportive, and secondly for the modifications of the twisted-chair conformations produced on such oxathiin by the cis-fused cyclopentene ring.

Gratifyingly, it was possible to obtain an X-ray structure of derivative **10f**. As reported in Figure 2 the oxathiin ring of **10f** adopts an almost boat conformation and, as in the case of derivative **10a**, it is formed through a complete regio- and stereoselective *endo–anti* (or *exo–syn*) cycloaddition between paracyclophane derived *o*-thioquinone **8** and dienophile **9f** (Fig. 2).

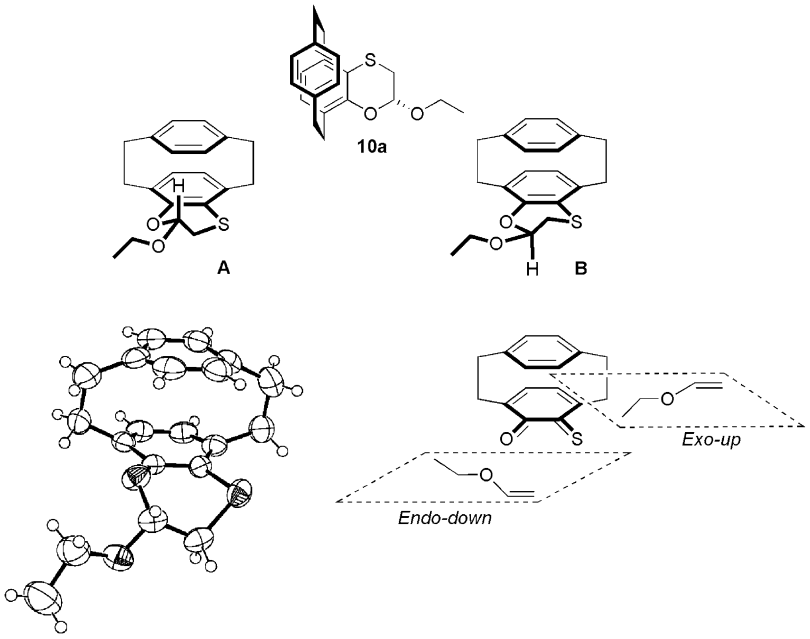


Figure 1. Relative structures ***A*** and ***B*** for **10a**, front view X-ray ORTEP of **10a**, and possible approaches leading to structure ***A***.

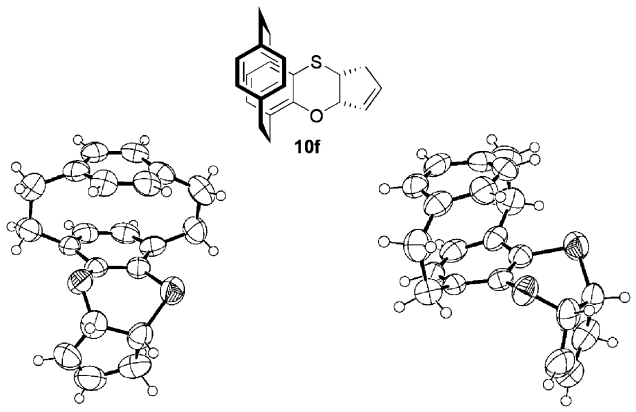


Figure 2. Front and side view of X-ray ORTEP of **10f**.

3. Conclusions

The application of the phthalimidesulfenyl chloride chemistry to 4-hydroxy-[2.2]paracyclophane **4** allowed the preparation of the precursor for the new chiral *o*-thioquinone **8** as well as furnished the first example of bis-sulfenylation. The cycloaddition of several electron-rich alkenes with the heterodiene **8** generated in situ occurred with a complete stereo differentiation between the diastereotopic faces of diene **8**. Further application of this chemistry as well as the opportunities disclosed by the preparation of **7** are under investigations in these labs.

4. Experimental

4.1. General

All reactions were monitored by TLC on commercially available precoated plates (silica gel 60 F_{254}) and the products were visualized with acid vanillin solution. Silica gel 60, 230–400 mesh, was used for column chromatography. Petrol refers to light petroleum, bp 40–60 °C. Melting points were measured on a microscopic apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, in $CDCl_3$ solutions. Residual $CHCl_3$ was used as reference at 7.26 and 77.00 ppm, respectively. FTIR spectra were recorded in KBr pellets. Mass spectra were measured with a Shimadzu QP5050. Phthalimidesulfenyl chloride[6c] (**3**) and 4-hydroxy[2.2]paracyclophane[9] (**4**) were prepared as reported elsewhere.

4.1.1. X-ray crystallography. These were carried out with a Goniometer Oxford Diffraction KM4 Xcalibur2 at rt. In both cases KM4 CCD/SAPPHIRE detectors were used for cell parameter determination and data collection; in the case of cycloadduct **10a**, a graphite-monochromated Cu Kα radiation (40 mA/−40 KV) was used, whereas for cycloadduct **10f** a graphite-monochromated Mo Kα radiation (40 mA/−40 KV) was used. The integrated intensities, measured using the ω scan mode, were corrected for Lorentz and polarization effects.[10] The substantial redundancy in data allows empirical absorption corrections (SADABS[11]) to be applied using multiple measurements of symmetry-equivalent reflections. These structures were solved by direct methods of SIR97[12] and refined using the full-matrix least squares on F^2 provided by SHELXL97.[13] The nonhydrogen atoms were refined anisotropically, whereas hydrogen atoms were refined as isotropic. In both cases hydrogens were assigned in calculated positions.

The X-ray CIF files for these structures have been deposited at the Cambridge Crystallographic Data Center and allocated with the deposition numbers *CCDC 294833* for cycloadduct **10a** and *CCDC 294834* for cycloadduct **10f**. Copies of the data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (e-mail: deposit@ccdc.cam.ac.uk; internet: www.ccdc.cam.ac.uk).

4.1.2. 5-*N*-Thiophthalimide-4-hydroxy[2.2]paracyclophane (5). To a solution of 4-hydroxy[2.2]paracyclophane (**4**) (0.400 g, 1.78 mmol) in dry $CHCl_3$ (25 mL), at 0 °C, a solution of sulfenyl chloride (**3**) (0.409 g, 1.78 mmol) in dry $CHCl_3$ (20 mL) was added dropwise. The mixture was stirred at 0 °C for 2 h, then diluted with CH_2Cl_2 (20 mL) and washed with saturated $NaHCO_3$ solution (2×100 mL) and H_2O (2×100 mL). The organic phase was dried over Na_2SO_4 and evaporated under reduced pressure to give *ortho-N*-thiophthalimide (**5**) and *para-N*-thiophthalimide substituted derivatives (**6**) in a 3:2 ratio (δ OH_{ortho}= 8.23 ppm, δ OH_{para}=5.59 ppm). After column chromatography (eluent: CH_2Cl_2), the major product **5** was isolated pure as a white solid (0.420 g, 1.05 mmol, 58% yield), mp 205–207 °C; ^{1}H NMR δ 8.23 (1H, s), 7.85–7.78 (2H, m), 7.73–7.67 (2H, m), 7.0 (1H, dd, *J*=7.8, 1.8 Hz), 6.58 (1H, dd, *J*=8.0, 1.8 Hz), 6.51 (1H, d, *J*=7.8 Hz), 6.43–6.35 (2H, m), 6.32 (1H, d, *J*=8.0 Hz), 4.40–4.27 (1H, m), 3.54–3.41 (1H, m), 3.27–3.06 (4H, m), 3.03–2.88 (1H, m), 2.68–2.53 (1H, m); ^{13}C NMR δ 168.2, 157.5, 146.7, 139.7, 138.9, 138.6, 134.6, 134.3, 132.7, 131.9, 129.5, 127.9, 127.54, 127.53, 125.1, 123.9, 120.6, 34.8, 34.7, 33.6, 30.9; MS *m*/*z* (%) 401 ($M^{\bullet+}$, 34), 297 (57), 254 (44), 150 (88), 104 (100); IR ν_{max} 3355 (O–H stretching), 1776+1731+1703 (C═O stretching PhtN), 1283 (C–OH stretching) cm^{-1}; Anal. Calcd for $C_{24}H_{19}NO_3S$: C 71.80, H 4.77, N 3.49. Found: C 71.64, H 4.75, N 3.42.

4.1.3. 5,7-Bis(*N*-thiophthalimide)-4-hydroxy[2.2]paracyclophane (7). To a solution of 4-hydroxy[2.2]paracyclophane (**4**) (0.100 g, 0.44 mmol) in dry $CHCl_3$ (4 mL), a solution of sulfenyl chloride (**3**) (0.215 g, 1.01 mmol) in dry $CHCl_3$ (4 mL) was added. The reaction mixture was stirred at rt for 2 h, then diluted with CH_2Cl_2 (15 mL), and washed with saturated $NaHCO_3$ solution (2×25 mL) and H_2O (2×25 mL). The organic phase was dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (eluent: CH_2Cl_2), to give compound **7** as a yellow solid (0.210 g, 0.36 mmol, 82% yield), mp 199 °C decomp.; ^{1}H NMR δ 8.63 (1H, s), 7.84–7.81 (2H, m), 7.79–7.77 (2H, m), 7.69–7.65 (4H, m), 7.12 (1H, s), 6.92 (1H, dd, *J*=8.0, 2.0 Hz), 6.61 (1H, dd, *J*=8.0, 2.0 Hz), 6.38 (1H, dd, *J*=8.0, 2.0 Hz), 6.34 (1H, dd, *J*=8.0, 2.0 Hz), 4.40–4.28 (2H, m), 3.43–3.34 (2H, m), 3.25–3.17 (1H, m), 3.15–3.05 (2H, m), 2.63–2.55 (1H, m); ^{13}C NMR δ 168.2, 167.8, 159.9, 151.3, 145.9, 139.6, 139.4, 134.8, 134.5, 133.9, 132.1, 131.9, 131.2, 129.5, 128.4, 128.3, 126.2, 124.2, 123.9, 122.2, 34.7, 33.4, 32.4, 30.6; IR ν_{max} 3344 (O–H stretching), 1781+1731+1703 (C═O stretching PhtN), 1278 (C–OH

stretching) cm^{-1}; Anal. Calcd for $C_{32}H_{22}N_2O_5S_2$: C 66.42, H 3.83, N 4.84. Found: C 66.30, H 3.70, N 4.71.

4.1.4. General procedure for Diels–Alder cycloadditions of *o*-thioquinone 8 with dienophiles 9. To a solution of 5-*N*-thiophthalimide-4-hydroxy[2.2]paracyclophane (**5**) (0.40 g, 1.0 mmol) in dry $CHCl_3$ (10 mL), Et_3N (0.14 mL, 1.0 mmol) and dienophile **9a–f** (2–5 mmol) were added in sequence. The mixture was heated at 60 °C for 20 h and then concentrated under reduced pressure. The crude material was purified by column chromatography to give cycloadduct **10a–f**. Data are as it follows:

4.1.4.1. Cycloadduct 10a. General procedure was followed to afford, after column chromatography (eluent: CH_2Cl_2/petroleum ether 1:1), the title product **10a** as a yellow solid (86% yield), mp 108–110 °C (from acetone); ^1H NMR δ 7.05 (1H, ddd, J=7.9, 1.1, 1.1 Hz, H-18), 6.67 (1H, d, J=7.9, 1.1, 1.1 Hz, H-17), 6.51 (2H, t, J=1.1 Hz, H-14, H-15), 6.31 (1H, d, J=7.7 Hz, H-10), 6.14 (1H, d, J=7.7 Hz, H-9), 5.46 (1H, dd, J=4.9, 2.6 Hz, H-5), 3.88–3.70 (2H, m, OCH_2), 3.30 (1H, ddd, J=13.0, 9.9, 2.9 Hz, H-2), 3.15 (1H, m, H-11), 3.12 (1H, dd, J=12.7, 2.6 Hz, H-6), 3.08–2.94 (4H, m, H-1, H-12), 2.81 (1H, dd, J=12.7, 4.9 Hz, H-6), 2.71 (1H, m, H-11), 2.55 (1H, ddd, J=13.0, 10.4, 5.6 Hz, H-2), 1.22 (3H, t, J=7.1 Hz, CH_3). ^{13}C NMR δ148.2 (C-3), 139.7+138.4 (C-13, C-16), 138.2 (C-8), 133.4+132.9 (C-14, C-15), 130.9 (C-10), 128.8 (C-3), 128.0 (C-17), 127.4 (C-18), 126.5 (C-9), 119.9 (C-7a), 94.2 (C-5), 64.2 (OCH_2), 34.3+33.2 (C-1, C-12), 32.9 (C-3a), 30.5 (C-2), 28.4 (C-6), 15.2 (CH_3). MS m/z (%) 326 ($M^{\bullet+}$, 85), 222 (63), 176 (88), 163 (100); IR ν_{max} 2997, 2963, 2918, 1574, 1412, 1054, 1015 cm^{-1}; Anal. Calcd for $C_{20}H_{22}O_2S$: C 73.58, H 6.79. Found: C 73.88, H 6.91.

X-ray structural analysis of **10a**: formula $C_{20}H_{22}O_2S$, M_r=326.44, Monoclinic, space group Cc, a=9.165(1), b=23.026(2), c=8.052(1) Å, β=93.166(7), V=1696.6(3) Å^3, Z=4, D_c=1.278, μ=1.742 mm^{-1}, $F(000)$=696. Reflections (6201) were collected with a $7.38<\theta<58.68$ range with a completeness to theta 98.3%; 1783 were independent, the parameters were 284, and the final R index was 0.0388 for reflections having $I>2\sigma I$, and 0.0470 for all data.

4.1.4.2. Cycloadduct 10b. General procedure was followed to afford, after column chromatography (eluent: petroleum ether/EtOAc 15:1), the title product **10b** as a yellow solid (90% yield), mp 108–110 °C; ^1H NMR δ 6.96 (1H, d, J=8.0 Hz), 6.72 (1H, d, J=8.0 Hz), 6.49 (2H, s), 6.38 (1H, d, J=8.0 Hz), 6.24 (1H, d, J=7.6 Hz), 5.91 (1H, d, J=6.0 Hz), 3.81–3.70 (2H, m), 3.64 (1H, dt, J=9.0, 5.6 Hz), 3.38 (1H, ddd, J=13.0, 9.8, 3.2 Hz), 3.09–2.91 (5H, m), 2.83–2.76 (1H, m), 2.56 (1H, ddd, J=15.6, 10.4, 5.1 Hz), 2.20–2.11 (1H, m), 1.69–1.58 (1H, m); ^{13}C NMR δ 150.2, 139.5, 139.4, 137.6, 132.7, 132.3, 131.1, 129.1, 128.1, 127.4, 126.6, 122.8, 101.6, 68.1, 41.7, 34.1, 33.6, 32.3, 31.4, 30.2; MS m/z (%) 324 ($M^{\bullet+}$, 68), 220 (100), 104 (78), 70 (60); IR ν_{max} 3000, 2924, 2845, 1567, 1409, 1040, 1006 cm^{-1}; Anal. Calcd for $C_{20}H_{20}O_2S$: C 74.04, H 6.21. Found: C 73.84, H 6.49.

4.1.4.3. Cycloadduct 10c. General procedure was followed to afford, after column chromatography (eluent: petroleum ether/EtOAc 100:1), the title product **10c** as a yellow solid (97% yield), mp 98–100 °C; ^1H NMR δ 7.38–7.34 (2H, m), 7.31 (1H, d, J=7.4 Hz), 6.98–6.94 (2H, m), 6.67 (1H, d, J=8.0 Hz), 6.56 (2H, s), 6.36 (1H, d, J=7.6 Hz), 6.19 (1H, d, J=7.6 Hz), 5.41 (1H, dd, J=9.4, 2.2 Hz), 3.85 (3H, s), 3.43–3.36 (1H, m), 3.17–3.08 (3H, m), 3.06–3.01 (3H, m), 2.95 (1H, dd, J=13.4, 9.4 Hz), 2.83–2.75 (1H, m), 2.62–2.55 (1H, m); ^{13}C NMR δ 159.4, 149.5, 139.9, 138.3, 138.1, 133.4, 133.0, 132.4, 130.5, 128.8, 128.5, 127.2, 127.0, 126.0, 118.7, 113.9, 74.3, 55.3, 34.2, 33.0, 32.5, 31.6, 30.3; MS m/z (%) 388 ($M^{\bullet+}$, 39), 163 (62), 134 (62), 121 (100); IR ν_{max} 3008, 2918, 2840, 1608, 1580, 1513, 1250, 1020 cm^{-1}; Anal. Calcd for $C_{25}H_{24}O_2S$: C 77.28, H 6.23. Found: C 77.22, H 6.25.

4.1.4.4. Cycloadduct 10d. General procedure was followed to afford, after column chromatography (eluent: petroleum ether/CH_2Cl_2 7:3), the title product **10d** as a white solid (60% yield), mp 130–132 °C; ^1H NMR δ 7.53 (2H, m, H-2′+H-6′), 7.34 (3H, m, H-3′, H-4′, H-5′), 7.02 (1H, dd, J=8.0, 1.6 Hz, H-18), 6.58 (1H, dd, J=8.0, 1.6 Hz, H-17), 6.51 (2H, d, J=1.6 Hz, H-14, H-15), 6.34 (1H, d, J=7.7 Hz, H-10), 6.21 (1H, d, J=7.7 Hz, H-9), 5.86 (1H, dd, J=5.2, 3.1 Hz, H-5), 3.47 (1H, dd, J=13.0, 3.1 Hz, H-6), 3.25–3.16 (3H, m, H-2, H-12, H-11), 3.06 (1H, dd, J=13.0, 5.2 Hz, H-6), 3.02–2.95 (2H, m, H-1, H-12), 2.85 (1H, ddd, J=13.1, 10.3, 5.1 Hz, H-1), 2.72 (1H, m, H-11), 2.55 (1H, ddd, J=13.0, 11.0, 5.5 Hz, H-2). ^{13}C NMR δ 147.7 (C-3a), 139.8+138.4+138.3 (C-8, C-16, C-13), 133.7 (C-1′), 133.3 (C-2′, C-6′), 133.4+133.0 (C-15, C-14), 131.25 (C-2), 129.6 (C-1), 129.2 (C-3′, C-5′), 128.2 (C-4′), 127.9 (C-17), 127.6 (C-18), 127.0 (C-9), 119.2 (C-7a), 81.3 (C-5), 34.2+33.1 (C-1, C-12), 32.9 (C-11), 30.5 (C-2), 29.3 (C-6); MS m/z (%) 390 ($M^{\bullet+}$, 100), 281 (38), 177 (93), 163 (66), 136 (29); IR ν_{max} 3042, 2918, 2851, 1580, 1401, 1048 cm^{-1}; Anal. Calcd for $C_{24}H_{22}OS_2$: C 73.81, H 5.68. Found: C 73.87, H 5.67.

4.1.4.5. Cycloadduct 10e. General procedure was followed to afford, after column chromatography (eluent: petroleum ether/EtOAc 1:1), the title product **10e** as a white solid (77% yield), mp 175–177 °C; ^1H NMR δ 7.22 (1H, dd, J=8.0, 1.6 Hz), 6.87 (1H, dd, J=8.0, 1.6 Hz), 6.52–6.47 (2H, m), 6.33 (1H, d, J=7.6 Hz), 6.25 (1H, dd, J=7.6, 4.0 Hz), 6.17 (1H, d, J=7.6 Hz), 3.52–3.46 (1H, m), 3.36–3.30 (1H, m), 3.25 (1H, ddd, J=12.8, 9.2, 3.2 Hz), 3.10–2.97 (5H, m), 2.94–2.92 (2H, m), 2.80–2.71 (1H, m), 2.57–2.47 (3H, m), 2.12–2.0 (2H, m); ^{13}C NMR δ 175.5, 149.7, 139.7, 138.4, 137.6, 133.2, 132.3, 130.8, 128.9, 128.5, 127.3, 126.2, 118.9, 75.9, 42.2, 33.9, 33.0, 32.4, 31.2, 30.4, 27.2, 18.1; MS m/z (%) 365 ($M^{\bullet+}$, 32), 280 (12), 176 (100), 56 (25); IR ν_{max} 3002, 2918, 2851, 1686 (C=O str.), 1401, 1283, 1032 cm^{-1}; Anal. Calcd for $C_{22}H_{23}NO_2S$: C 72.30, H 6.34, N 3.83. Found: C 71.97, H 6.37, N 3.64.

4.1.4.6. Cycloadduct 10f. General procedure was followed to afford, after column chromatography (eluent: petroleum ether/CH_2Cl_2 7:3), the title product **10f** as a white solid (92% yield), mp 105–107 °C (from $CHCl_3$); ^1H NMR δ 6.92 (1H, dd, J=7.6, 1.6 Hz), 6.74 (1H, dd, J=7.8, 1.8 Hz), 6.51–6.45 (2H, m), 6.33 (1H, d, J=8.0 Hz), 6.21 (1H, d, J=7.6 Hz), 5.77–5.73 (1H, m), 5.67–5.62 (1H, m),

5.56–5.51 (1H, m), 3.94 (1H, dt, J=8.4, 5.6 Hz), 3.26 (1H, ddd, J=13.0, 9.8, 3.4 Hz), 3.13–3.03 (1H, m), 3.02–2.89 (4H, m), 2.80–2.73 (1H, m), 2.66 (1H, ddt, J=17.6, 8.4, 2.4 Hz), 2.54 (1H, ddd, J=15.6, 10.3, 5.4 Hz), 2.20–2.12 (1H, m); ^{13}C NMR δ 152.2, 140.0, 139.3, 137.8, 136.4, 132.6, 132.2, 130.7, 130.2, 129.7, 128.2, 127.7, 127.2, 126.4, 86.3, 42.3, 41.9, 34.3, 33.9, 32.3, 29.9; MS m/z (%) 320 ($M^{\bullet+}$, 64), 216 (100), 183 (39), 104 (42), 66 (26); IR ν_{max} 3036, 2924, 2845, 1611, 1577, 1404, 1029 cm^{-1}; Anal. Calcd for $C_{21}H_{20}OS$: C 78.71, H 6.29. Found: C 78.65, H 6.13.

X-ray structural analysis of cycloadduct **10f**: formula $C_{21}H_{20}OS$, M_r=320.43, Orthorhombic, space group $Pc2_1b$, a=8.020(2), b=11.423(3), c=17.745(3) Å, V=1625.7(6) Å^3, Z=4, D_c=1.309, μ=0.201 mm^{-1}, $F(000)$=680. Reflections (13,642) were collected with a $4.24<\theta<25.78$ range with a completeness to theta 88.9%; 2692 were independent, the parameters were 208, and the final R index was 0.0590 for reflections having $I>2\sigma I$.

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