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INTRODUCING THE DIELS-ALDER REACTIVITY OF 2-FURANMETHANETHIOL WITH SELECTED MALEIC ACID DERIVATIVES

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Abstract – Surprising chemoselectivity is demonstrated in the reaction of 2-furanmethanethiol with maleic anhydride and with *N*-phenylmaleimide. These maleic acid derivatives demonstrate a predilection for Diels-Alder cycloaddition, forgoing both conjugate addition and initial carbonyl attack. *N*-Ethylmaleimide showed a preference for conjugate addition, whereas diethyl fumarate or dimethyl maleate proved unreactive. The cycloadduct of 2-furanmethanethiol and maleic anhydride was subjected to dehydration/aromatization conditions to create benzo[*c*]thiophen-1(3*H*)-one-7-carboxylic acid. An alkylation attempt also led to the formation of a thiolester.

This paper is dedicated to Prof. Victor Snieckus, a leader in organic chemistry, on the occasion of his 77th birthday.

The inhibition of the poly(ADP ribose polymerase) (PARP) family of enzymes has been tied to the treatment of cancer,[1] vascular disease[2] and the control of PARP overexpression, which can lead to necrotic cell death.[3] Many inhibitors of the PARP enzyme possess the benzamide core (**1**) and particular efficacy is observed when the amide takes the form of a lactam or related structure.[2-4] As such we have been pursuing synthetic approaches to the isoindolone ring system (**2**).[5] In addition to the inhibitory activity related to PARP enzymes,[4] the isoindolone core is present in compounds exhibiting substantial biological activity for a variety of therapeutic uses[6] including antiangiogenic activity,[7] inhibition of kinase enzymes,[8] detection of schizophrenia[9] and action as anti-inflammatory drugs.[10]

It was thought that a diverse and flexible library of inhibitors containing the compound **2** core could be accessed from compounds possessing the general structure **3**, in which the carbonyl groups are undefined

carboxylic acid derivatives, possibly in the form of an imide. Specifically, the plan is to attach the sulfur atom of **3** to the proximal carbonyl carbon, while also forming an additional 5-membered ring that incorporates the carbonyl carbons. Chemical adaptation thereafter, by way of sulfur oxidation and eventual fragmentation followed by Diels-Alder chemistry, would allow rapid construction of a library of compounds with diversity on the lower portion of the molecule.

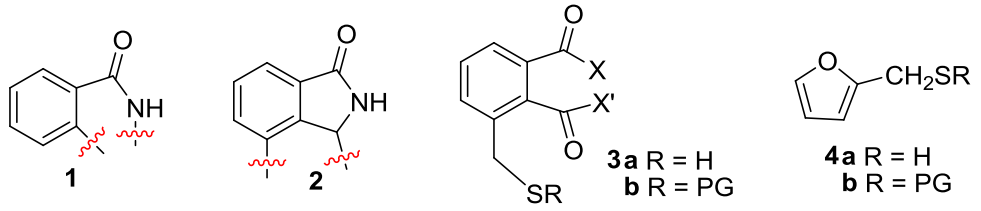
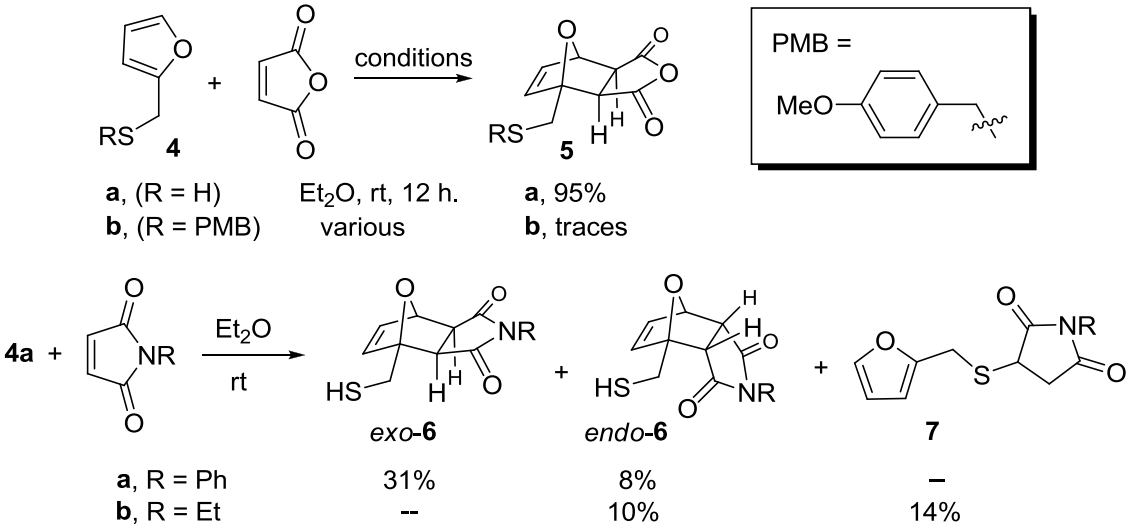


Figure 1. Benzamide and isoindolone derivatives and precursors

Retrosynthetic analysis indicates that a logical approach to synthesizing **3** could be by Diels-Alder cycloaddition of furan **4a** with maleic anhydride and aromatization of the cycloadduct. However, the direct Diels-Alder reaction of maleic anhydride and furan **4a** was not expected to proceed, due to the well-established use of thiols and structurally related maleimides as linking agents by way of Michael addition chemistry.[11] Hence, a protected form was employed, wherein *p*-methoxybenzyl (PMB) was chosen for its anticipated involvement in future transformations.[12] As a starting point, sulfide **4b** (PG = PMB) and maleic anhydride were reacted under a variety of conditions, but there were only traces of product that appeared to form, under selected situations, and the product was not pursued. Presuming that steric factors brought on by the presence of the protecting group were hindering the reaction, on a whim, the unprotected thiol (**4a**) was reacted with maleic anhydride. Surprisingly, a clean Diels-Alder reaction occurred in ether at room temperature and **5a** was obtained as the lone product in 95% yield after recrystallization, and there was no evidence of conjugate addition. The *exo* nature of **5a** was confirmed through analysis of the bridgehead to α-carbonyl ^{1}H-^{1}H coupling constant ($J \sim 0$ Hz).

Given the observed of maleic anhydride and **4a**, the reaction of **4a** with *N*-phenylmaleimide was investigated, in order to get more rapid access to target compound **3**. Stirring furan **4a** with *N*-phenyl-maleimide also brought about a cycloaddition and no conjugate addition was observed. Attempts to separate the two isomers were challenging as the reaction mixture was only partially tractable; presumably the reversibility of the system caused some problems. Modifications to the reaction conditions, including reactant ratios, solvent and temperature did not make the mixture more manageable. A pair of isomeric cycloadducts was eventually prepared in a total isolated yield of 39%. The difference in reactivity between furans **4a** and **4b** may be traced to the larger steric substituent on the 2-position of **4b**; presumably the

tenuous thermodynamic preference for furan-based cycloadduct formation vs. reversion to starting materials[13] is negatively affected by the presence of the large group at the 2-position.



Scheme 1. Diels-Alder reactions of furan **4a** with maleic acid derivatives

The Diels-Alder chemistry of furfuryl alcohol[14] and furfuryl amine[15] with maleic anhydride has already been established. Furfuryl alcohol can undergo cycloaddition directly with the furan diene without intervention of the alcohol.[14] In contrast, furfuryl amines appear to initially open maleic anhydride through carbonyl attack by the nitrogen, thereby facilitating an intramolecular cycloaddition.[15b] On the other hand, the literature indicates 2-furanmethanethiol and it S-alkylated derivatives have never been employed in simple bimolecular Diels-Alder reactions. The only related Diels-Alder involvement of the 2-furfurylthio backbone has been the IMDA of sulfides derived from 2-furanmethanethiol.[16] Moreover, given the vast literature on the use of maleimides for labelling thiols via a conjugate addition reaction[11a,b] under neutral (aqueous) conditions,[17] the tendency of 2-furanmethanethiol to preferentially participate in the Diels-Alder reaction is remarkable.

The isolation of exclusively the *exo* isomer of **5a** is uncommon given that furan cycloadditions usually give a mixture of *endo* and *exo* isomers. To investigate this, a low temperature ^{1}H NMR study was performed. Before beginning, it was determined that the cycloadditions have the same single product in $CHCl_3$, permitting an NMR analysis in $CDCl_3$. A reaction vessel containing $CDCl_3$ held at –78 °C was charged with equimolar amounts of maleic anhydride and furan **4a**, in concentrations comparable to the reaction conditions. About 0.5 mL of the solution was transferred to an NMR tube and the tube was inserted in the NMR probe which was previously precooled to -10 °C.

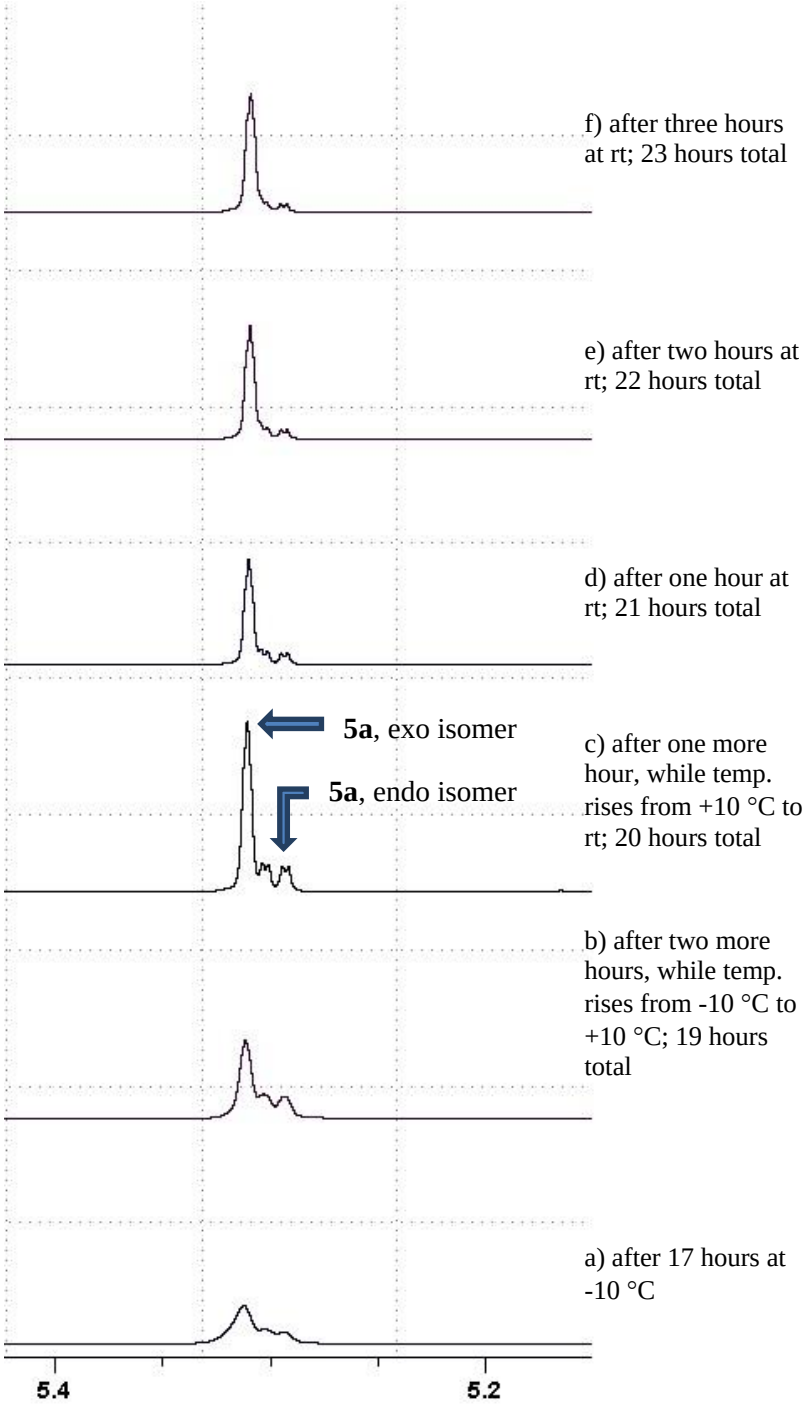


Figure 2. Partial 600 MHz variable temperature ^{1}H NMR spectra for the reaction of maleic anhydride and 2-furanmethanethiol

In the early stages of the analysis, the NMR acquisitions were of poor resolution because the maleic anhydride was not completely soluble (Figure 2, a & b). As time progressed, the resolution improved and the peaks could be interpreted and assigned. As such, the singlet due to the bridgehead H of *exo*-**5a** was recognizable, but was accompanied by a doublet of doublets (J = 1.5, 5.6 Hz) at slightly lower ppm (Figure 2 c), which was assigned to be the bridgehead H of the *endo* isomer of **5a**, based on the larger coupling

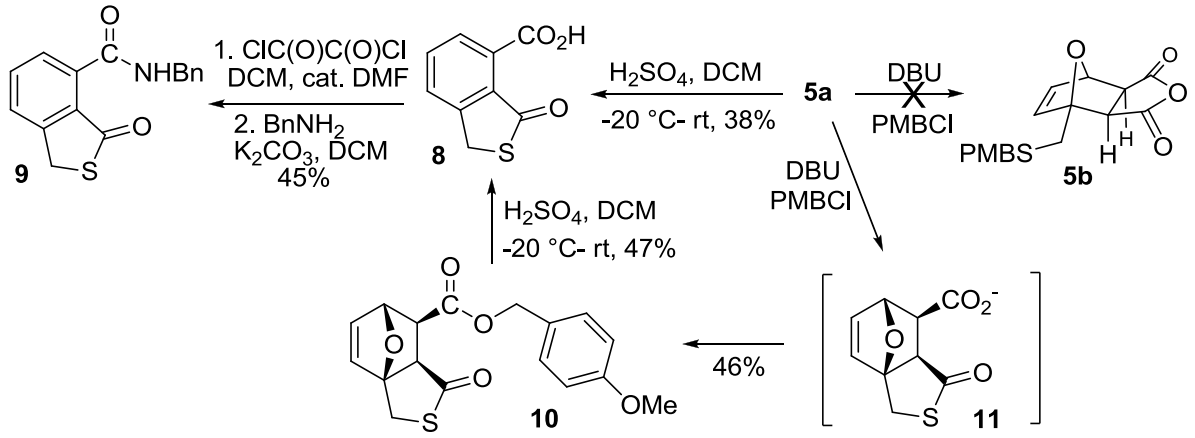
constant. The relative ratio of the *exo*:*endo* isomers was roughly estimated to be 60:40 (Figure 2, a). As time progressed and the temperature rose to rt, the intensity of the minor isomer decreases, indicating the slow conversion to the thermodynamically preferred *exo* product (Figure 2 d-f). After several more hours at rt, there was exclusive formation of the *exo* adduct. Clearly, the two isomers form at similar rates, but with warming cycloreversion and formation of the thermodynamically more stable *exo* isomer occurs.[18]

The reaction of *N*-ethylmaleimide with the unprotected thiol (**4a**) gave both Michael addition and a single Diels-Alder adduct (*endo*-**6b)** with the preference of the conjugate addition product **7b**. The reaction was then done at cold temperature (-5 to 0 ºC) in attempt to change the ratio of products but no significant change was observed. The literature suggests that *N*-alkyl and *N*-phenyl substituents impart similar contributions to the kinetics of maleimide cycloadditions to furans.[19] As such, the observed reactivity differences of *N*-ethyl and *N*-phenylmaleimides may be attributable to the higher activity of the nitrogen lone electron pair of the *N*-ethyl group, which may better facilitate some of the proton transfers[20] required for the conjugate addition. Finally, to probe other dienophiles, the reaction chemistry of diethyl fumarate and dimethyl maleate with **4a** was evaluated but neither Diels-Alder chemistry nor conjugate addition reactions were evident in diethyl ether at room temperature or in refluxing toluene.

Cycloadduct **5a** was subjected to conditions to effect aromatization of the [2.2.1]-bicyclic ring.[21] Employing **5a**, low mass recoveries were observed when established harsh H_2SO_4 conditions were employed,[22] but using the milder two-phase combination of H_2SO_4 and CH_2Cl_2[23] brought about a single, nearly pure product with moderate mass recovery. Spectral analysis of the purified product revealed aromatization, which was also accompanied by thiol attack of the proximal anhydride carbonyl; a heretofore unknown thiophthalide (benzo[*c*]thiophen-1(3*H*)-one-7-carboxylic acid**, 8**) was isolated in 38% purified yield. Compound **8** is the first thiophthalide possessing a carboxylic acid at the 7-position on the aromatic ring. Thiophthalides are garnering increased attention for their value as useful intermediates in organic synthesis.[24] As an additional adaptation, were we able to convert acid **8** to its *N*-benzylamide **9** (45%, two steps, unoptimized), while keeping the thiolester linkage intact (Scheme 2).

Thiophthalides **8** and **9** represent successfully synthesized versions of **3**, wherein the R and X' groups are identified by, and indeed eliminated through, the formation of the thiolester linkage. Nevertheless we sought to see if the thiol functionality could be alkylated to create a different form of **3**. As such, **5a** was reacted with *p*-methoxybenzyl chloride (PMBCl) in the presence of DBU, but although the PMB unit was incorporated, **5b** was not formed. Instead the product obtained had lost the anhydride functionality (IR, ^{13}C NMR) but the oxabicyclic framework remained in place (^{1}H NMR). The product exhibited two new

carbonyl stretches at 1735 and 1698 cm^{-1} and the new benzyl protons appear at 5.12 ppm, indicative of attachment to an ester oxygen. A ^{13}C NMR resonance was also evident near 204 ppm. The new product was assigned the structure **10**, which is consistent with the characterization data. Although base was used for this transformation, the original stereochemistry of the ring substituents appears intact, based on ^{1}H-^{1}H coupling constants of the hydrogens adjacent to the carbonyl groups.[14b,25] Thiolactone formation is not surprising in light of the chemistry of the corresponding furfuryl alcohol chemistry. Compound **10** is presumably formed through intermediate **11** which undergoes *O*-alkylation with *in situ* PMB-Cl.[14] Aromatization attempts on **10** using the milder conditions also led to the isolation of thiophthalide **8** in 47% yield.



Scheme 2. Aromatization and functionalization of bicyclic anhydrides

To summarize, a Diels-Alder approach has permitted the construction of a 3-thiomethylated 1,2-dicarboxyl benzene derivative. Specifically, thiophthalide **8**, a novel benzo[*c*]thiophen-1(3*H*)-one, was created in two steps from 2-furanmethanethiol and maleic anhydride. 2-Furanmethanethiol demonstrates surprising chemoselectivity with maleic anhydride and with *N*-phenylmaleimide, favoring cycloaddition over conjugate addition and carbonyl attack. The current study suggests that 2-furanmethanethiol or its derivatives could be developed into new bifunctional cross-linking reagents possessing thiol vs diene selectivity for various fluorescent maleic acid derivatives.[26] Exploration of the chemistry of thiophthalides **8** and **9** is underway for eventual creation of new isoindolones.

EXPERIMENTAL

Preparation of furfuryl *p*-methoxybenzyl sulfane (4b). 2-Furylmethanethiol (1 eq, 5.68 g, 49.7 mmol) and Et_3N (1 eq, 7.0 mL, 49.7 mmol) together with 25 mL of DCM were set to stir at room temperature,

under a constant stream of nitrogen gas. *p*-Methoxybenzyl bromide (1.1 eq, 11 g, 5.50 mmol) was dissolved in 5 mL of DCM and added to the above mixture dropwise. The reaction was stirred at room temperature for 2 h during which time a precipitate formed. The precipitate was redissolved in DCM and 30 mL of 0.1 M HCl was added. The aqueous layer was extracted with DCM and washed with brine, and the combined organics were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was further concentrated under high vacuum and purified by silica gel flash chromatography (9:1, hexanes/EtOAc) to yield **4b** as a white solid (60%). R_f = 0.24 (9:1, hexanes/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (1H, dd, *J* = 1.9 & 0.9 Hz, 1H), 7.23 (m, 2H), 6.85 (m, 2H), 6.32 (dd, *J* = 3.1 & 0.9 Hz, 1H), 6.15 (dd, *J* = 1.9 & 3.1 Hz, 1H), 3.80 (s, 3H), 3.66 (s, 2H), 3.58 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 151.8, 142.1, 130.1, 129.8, 113.9, 110.4, 107.5, 55.3, 35.2, 27.3; IR (neat): υ 2954, 2912, 2834, 1609, 1175 cm^{-1}. Anal. Calcd for $C_{13}H_{14}O_2S$: C, 66.64 H, 6.02. Found: C, 66.71 H, 6.00.

General procedure for the Diels-Alder cycloaddition of 2-furanmethanethiol (4a) with various dienophiles. The dienophile 1.2 eq was dissolved in 2 mL dry Et_2O and 2-furylmethanethiol (1.00 g, 1 eq, 8.8 mmol) were added and the solution stirred overnight at room temperature. The crude was dried and purified by flash column chromatography (hexanes/EtOAc) unless otherwise mentioned.

Reaction of thiol 4a with maleic anhydride. The reaction of maleic anhydride (1.2 eq, 1.03 g, 10.5 mmol) and **4a** (1.00 g, 1 eq, 8.8 mmol) provided crude 2.0 g of **5a** which was recrystallized from DCM to provide pure **5a** (1.76 g, 95%) as white plates. mp 69-71 ºC. ^{1}H NMR (400 MHz, acetone-d_6) δ 6.70-6.67 (m, 2H), 5.36 (1H, d, *J* = 1.5 Hz), 3.62 (1H, d, *J* = 6.7 Hz), 3.53 (1H, d, *J* = 6.7 Hz), 3.16 (ABX pattern, J_{AB} = 14.4 Hz, J_{AB} = 9.1 Hz, J_{AB} = 8.4 Hz, 2.22 (dd, *J* = 9.1 & 8.4 Hz, 1H); ^{13}C NMR (150 MHz Acetone-d_6) δ 170.8, 169.8, 138.0, 137.62, 93.1, 82.4, 52.7, 50.5, 23.1; IR (neat): υ 3090, 3006, 2582, 1841, 1775, 1227 cm^{-1}. Anal. Calcd for $C_9H_8O_4S$: C, 50.94 H, 3.80. Found: C, 50.92 H, 3.90.

Variable temperature ^{1}H NMR study of the reaction of thiol 4a with maleic anhydride. Quantities of maleic anhydride and **4a** as employed above were placed in a vessel with $CDCl_3$ (2 mL), precooled to -78 ºC. Approximately 0.5 mL of this solution was transferred to a precooled NMR tube which was then quickly placed in the probe (precooled to -10 ºC) of a Bruker 600 MHz NMR. ^{1}H NMR spectra were acquired hourly for 23 h. The temperature was held at -10 ºC for 17 h and then allowed to warm to +10 ºC and then to rt. Selected data are shown in Figure 2. A final ^{1}H NMR spectrum was obtained after 16 h at rt and showed only the *exo* isomer of **5a**.

Reaction of thiol 4a with *N*-phenylmaleimide. The reaction of *N*-phenylmaleimide (1.2 eq, 1.82 g, 10.5 mmol) and **4a** (1.00 g, 1eq, 8.8 mmol) provided a mixture which was subjected to flash chromatography to

provide *exo*-**6a** (0.78 g, 31%) as a white solid and *endo*-**6a** (0.21g, 8%) as a pale yellow solid.
Data for *exo*-**6a**: mp 130-132 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.42 (m, 3H), 7.30–7.27 (m, 2H), 6.67 (d, *J* = 5.7 Hz, 1H), 6.62 (d, *J* = 5.7 Hz, 1H), 5.39 (s, 1H), 3.26-3.17 (m, 3H), 3.08 (dd, *J* = 14.4 & 9.5 Hz, 1H), 2.20 (dd, *J* = 9.5 & 8.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 174.1, 138.6, 137.2, 131.5, 129.2, 128.9, 126.5, 92.6, 81.7, 50.9, 48.4, 24.0; IR (neat): υ 2567, 1776, 1709, 1499, 1386, 1195 cm^{-1}; HRMS (TOF, ESI) Calcd for $[C_{15}H_{13}O_3S + H]^+$ 288.6089. Found: 288.0684.
Data for *endo*-**6a**: mp 72-74 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.43 (m, 3H), 7.28–7.12 (m, 2H), 6.62 (dd, *J* = 1.7, 5.7 Hz, 1H), 6.50 (d, *J* = 5.7 Hz, 1H), 5.41 (dd, *J* = 1.6, 5.5 Hz, 1H), 3.87 (dd, *J* = 7.7 & 5.5 Hz, 1H), 3.66 (d, *J* = 7.7 Hz, 1H), 3.46 (dd, *J* = 14.6 & 8.0 Hz, 1H), 3.27 (dd, *J* = 14.6 & 8.7 Hz, 1H) 1.80 (dd, *J* = 8.7 & 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 173.8, 136.1, 135.6, 131.3, 129.3, 128.9, 126.3, 92.2, 79.5, 48.9, 47.9, 26.3; IR (neat): υ 2569, 1776, 1710, 1498, 1383, 1186 cm^{-1}; HRMS (TOF, ESI) Calcd for $[C_{15}H_{13}O_3S + H]^+$ 288.0689. Found: 288.0692.

Reaction of thiol 4a with *N*-ethylmaleimide. The reaction of *N*-ethylmaleimide (1.2 eq, 1.31 g, 10.5 mmol) and **4a** (1.00 g, 1eq, 8.8 mmol) provided a mixture which was subjected to flash chromatography to provide **7b** (0.29 g, 14%) as a brown oil and *endo*-**6b** (0.20 g, 10%) as a white solid.
Data for **7b**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (dd, *J* = 1.8 & 0.7 Hz, 1H), 6.33 (dd, *J* = 3.2 & 1.8 Hz, 1H), 6.29 (dd, *J* = 3.2 & 0.7 Hz, 1H), 4.31 (d, *J* = 14.9 Hz, 1H), 3.84 (d, *J* = 14.9 Hz, 1H), 3.66 (dd, *J* = 9.2 & 4.0 Hz, 1H), 3.56 (q, *J* = 7.2 Hz, 2H), 3.03 (dd, *J* = 18.8 & 9.2 Hz, 1H), 2.40 (dd, *J* = 18.8 & 4.0 Hz, 1H), 1.18 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.8, 174.6, 135.8, 135.3, 91.7, 79.1, 48.9, 47.9, 33.5, 26.3, 12.7; IR (neat): υ 3119, 2980, 2879, 1774, 1720, 1591, 1503, 1398, 1351, 1227 cm^{-1}; Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21 H, 5.48. Found: C, 54.99 H, 5.37.
Data for *endo*-**6b**: mp 93-95 ºC (EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.36 (dd, *J* = 5.8 & 1.4 Hz, 1H), 6.25 (d, *J* = 5.8 Hz, 1H)5.21 (dd, *J* = 5.4 & 1.4 Hz, 1H), 3.59 (dd, *J* = 7.6 & 5.4 Hz, 1H), 3.37 (d, *J* = 8.7 Hz, 1H), 3.34-3.29 (m, 3H), 3.13 (dd, *J* = 14.4 & 8.7 Hz, 1H), 1.68 (t. *J* = 8.3 Hz, 1H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.5, 174.5, 149.9, 142.7, 110.6, 108.7, 37.8, 35.4, 34.0, 28.1, 12.9; IR (neat): υ 3084, 2979, 2937, 2570, 1768, 1698, 1444, 1399, 1341, 1283, 1225, 1135 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NO_3S$: C, 55.21 H, 5.48. Found: C, 55.40 H, 5.48.

Dehydration/aromatization of cycloadduct 5a. Compound **5a** (1.00 g, 3.00 mmol) was added portion wise to a cold (-30 ºC) mixture of H_2SO_4/DCM (1:2 v/v, 10 mL), the solution was allowed to warm to room temperature over 4 h and then was poured in crushed ice. The mixture was extracted with DCM (3 X 10 mL), washed with water and dried over $MgSO_4$. Concentration *in vacuo* gave thiophthalide **8** (0.22 g, 38%) as a white solid. mp 138-140 °C ($CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.57 (dd, *J* = 7.3, 1.4 Hz, 1H),

7.86-7.81 (m, 2H), 4.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.7, 164.4, 149.7, 133.2, 129.7, 128.0, 126.4, 123.9, 35.3; IR (neat): υ 3200-2500, 2962, 2934, 1721, 1577, 1465, 1439, 1291, cm^{-1}. GS/MS (CI): 194 (M^+, 87), 177($(M-OH)^+$, 100); Anal. Calcd for $C_9H_6O_3S$: C, 55.66 H, 3.11. Found: C, 55.80 H, 3.31.

Conversion of thiophthalide 8 to *N*-benzylamide 9. Compound **8** (500 mg, 2.6 mmol) was dissolved in dry DCM (10 mL) in a flame dried flask purged with argon. Oxalyl chloride (0.26 ml, 3.1 mmol) and a catalytic amount of DMF were added to the mixture. After stirring at room temperature for 3 h, the solvent and unreacted oxalyl chloride were evaporated under high vacuum. The yellow residue was dissolved in dry DCM (10 mL) and the solution cooled in an ice bath. K_2CO_3 (400 mg, 2.8 mmol) and a solution of benzylamine (0.31 mL, 2.8 mmol) in DCM (3 mL) were then added. After stirring for 8 h the reaction mixture was extracted with water (20 mL), 5% HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL) and water (20 mL). After drying over $MgSO_4$, the solvent was evaporated the solid remained was rinsed with EtOAc to give 330 mg (45%) of white solid in pure form. A recrystallized sample (DCM) gave white needles, mp 166-168 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (br s, 1H), 8.09 (d, *J* = 7.5 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.44 (d, *J* = 7.4 Hz, 2H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.30 (m, 1H), 4.70 (d, *J* = 5.5 Hz, 2H), 4.51 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 165.7, 148.8, 138.0, 134.0, 133.1, 132.0, 130.5, 128.7, 138.6, 128.1, 127.5, 44.5, 34.2; IR (neat): υ 3271, 1688, 1643, 1546, 1453, 1221, 1170, 996. HRMS (TOF, ESI) Calcd for $[C_{16}H_{13}NO_2S]^+$ 284.0740. Found: 284.0749.

Alkylation of cycloadduct 5a. Thiol **5a** (0.21 g, 1 eq, 1.0 mmol) was dissolved in dry DCM (3 mL) under Ar. To this solution was added DBU (0.17 g, 1.1 eq, 1.1 mmol) followed by *p*-methoxybenzyl chloride (0.17 g, 1.1 eq, 1.1 mmol) and the reaction was stirred overnight at room temperature. Water was added and the reaction was extracted with DCM (3 X 10 mL) and the combined organics were dried over $MgSO_4$, filtered and concentrated. The crude product was purified by flash column chromatography (hexanes/EtOAc) to provide **10** (0.15 g, 46%) as a pale yellow solid. mp 110-113 °C ($CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$ δ 7.36 (m, 2H), 6.90 (m, 2H), 6.55 (m, 1H), 6.47 (1H, d, *J* = 5.7 Hz, 1H), 5.16 (s, 1H), 5.12 (AB pattern, *J* = 12.0 Hz, 2H), 4.03 (d, *J* = 12.7 Hz, 1H), 3.83 (d, *J* = 12.7 Hz, 1H), 3.82 (s, 3H), 2.97 (d, *J* = 8.8 Hz, 1H), 2.83 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (150 MHz $CDCl_3$) δ 203.7, 171.4, 159.7, 138.3, 136.5, 130.5, 127.7, 113.9, 92.7, 81.4, 67.1, 58.1, 55.3, 48.8, 33.0; IR (neat) υ 3003, 2954, 2837, 1735, 1697, 1613, 1515, 1250, 1166 cm^{-1}; HRMS (TOF, ESI) Calcd for $[C_{17}H_{16}O_5S + NH_4]^+$ 350.1057. Found: 350.1046.

Dehydration/aromatization of compound 10. The chemistry was carried out as above using 200 mg (0.60 mmol) to give 55.4 mg (47%) of **8**.

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