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Synthesis and cycloaddition reactions of sulfur-substituted quinolizidine dienes

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ABSTRACT

Synthesis of sulfur-substituted quinolizidine dienes via ring-closing enyne metathesis (RCEYM) of the corresponding enynes has been achieved. The cycloaddition reactions of these dienes with electron-deficient dienophiles give tricyclic and tetracyclic nitrogen-containing products.

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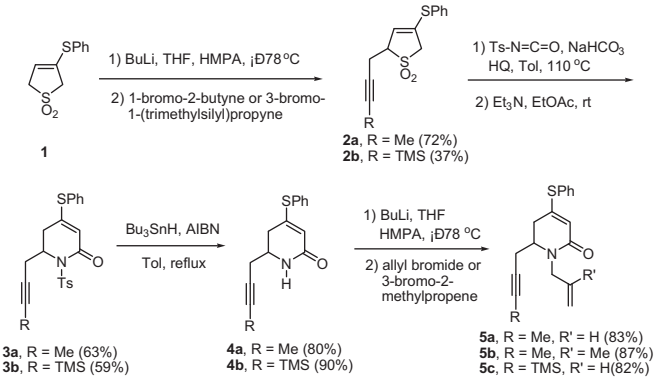
1. Introduction

Enyne metathesis is a bond reorganization of an alkene and an alkyne to produce a conjugated diene.[1] If carried out intramolecularly, this reaction is often referred to as ring-closing enyne metathesis (RCEYM) because an additional ring is formed during this process. RCEYM is a powerful tool for the synthesis of carbocycles[2] and various heterocycles[3] bearing a conjugated diene moiety, which can further undergo Diels–Alder reactions with dienophiles to form more complex structures.

We have previously developed a new aza-Diels–Alder reaction of thio-substituted 3-sulfolenes with *p*-toluenesulfonyl isocyanate (PTSI) to synthesize sulfur-substituted piperidine derivatives,[4] and have used this method to prepare some indolizidines and quinolizidines,[5] which often show interesting biological activities.[6] We now report our studies using this method in combination with the RCEYM strategy to make sulfur-substituted quinolizidine dienes, and our results of their cycloaddition reactions with electron-deficient dienophiles to provide a rapid synthesis of tricyclic and tetracyclic nitrogen-containing compounds.

2. Results and discussion

Preparation of the enyne precursors **5** for the RCEYM is shown in Scheme 1. Treatment of 3-(phenylthio)-3-sulfolene (**1**)[7] with BuLi in THF at −78 °C in the presence of hexamethylphosphoric amide (HMPA) followed by reaction with1-bromo-2-butyne or 3-bromo-1-(trimethylsilyl)propyne gave the alkylated products **2a** and **2b**, respectively. The yield of **2b** was considerably lower than that of **2a**, probably due to steric hindrance of the electrophile. Heating the 3-sulfolenes **2** with *p*-toluenesulfonyl isocyanate (PTSI) in toluene gave the aza-Diels–Alder reaction products,[4] which were directly treated with triethylamine in ethyl acetate to provide the conjugated dihydropyridones **3a** and **3b**. Cleavage of the *N*-tosyl group by Bu_3SnH/AIBN[8] afforded the secondary amides **4a** and **4b** in good yield. Treatment of amides **4** with BuLi in THF at −78 °C in the presence of HMPA followed by reaction with allyl bromide or 3-bromo-2-methylpropene gave the *N*-allylated products **5a**–**c**.



Scheme 1.

The results of ring-closing enyne metathesis (RCEYM) of compounds **5** under various conditions are shown in Table 1. Reaction of compound **5a** with Grubbs' I catalyst (**G1**) in CH_2Cl_2 at room temperature gave the diene **6a** in high yield (entry 1). However, the

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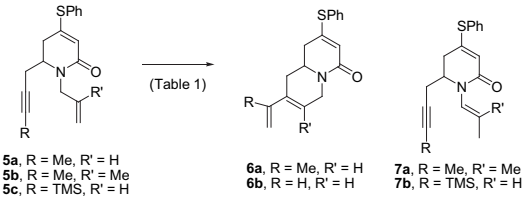
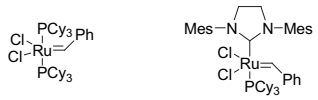
Table 1
RCEYM reaction of compounds **5** with Grubbs' catalysts



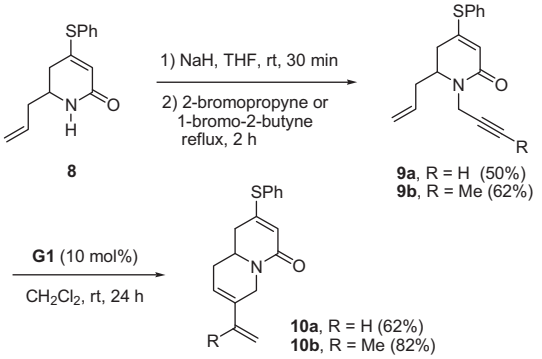
Entry	Reactant	Catalyst	Conditions	Product (%)
1	**5a**	**G1** (10 mol %)	CH_2Cl_2, rt, 18 h	**6a** (80)
2	**5b**	**G1** (10 mol %)	CH_2Cl_2, rt, 18 h	NR[a]
3	**5b**	**G1** (10 mol %)	CH_2Cl_2, reflux, 18 h	**7a** (21)[b]
4	**5b**	**G1** (10 mol %)	Tol, 85 °C, 25 h	**7a** (11)[c]
5	**5b**	**G2** (5 mol %)	CH_2Cl_2, reflux, 24 h	NR[a]
6	**5b**	**G2** (5 mol %)	Tol, reflux, 21 h	NR[a]
7	**5c**	**G1** (10 mol %)	CH_2Cl_2, rt, 18 h	NR[a]
8	**5c**	**G1** (10 mol %)	CH_2Cl_2, reflux, 9 h	**6b** (66)
9	**5c**	**G2** (5 mol %)	CH_2Cl_2, reflux, 22 h	**7b** (14)[d]

[a] No reaction was observed.
[b] Compound **5b** was recovered in 67%.
[c] Compound **5b** was recovered in 63%.
[d] Compound **5c** was recovered in 62%.

reaction of compound **5b** with **G1** in CH_2Cl_2 at room temperature (entry 2) gave only the recovered starting material. The lower reactivity of compound **5b** than **5a** is probably due to the steric effect. Heating compound **5b** with **G1** in refluxing CH_2Cl_2 (entry 3) or in toluene at 85 °C (entry 4) gave the alkene-isomerized product **7a** in low yield, together with some unreacted starting material. If compound **5b** was treated with **G2** in refluxing CH_2Cl_2 (entry 5) or in refluxing toluene (entry 6), only the unreacted starting material was obtained. The reaction of compound **5c** with **G1** in CH_2Cl_2 (entry 7) did not proceed at room temperature, but yielded the diene **6b** in good yield in refluxing CH_2Cl_2 (entry 8). It should be noted that compound **6b** has lost the TMS group in compound **5c** during the RCEYM. The reaction of compound **5c** with **G2** in refluxing CH_2Cl_2 (entry 9) gave the alkene-isomerized product **7b** in 14% besides the recovered starting material.

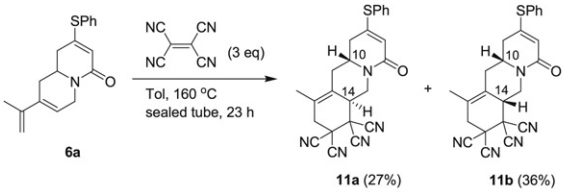


We have also developed another route for constructing the sulfur-substituted quinolizidine dienes **10** (Scheme 2). Treatment of compound **8**[5a] with sodium hydride in THF at room temperature followed by reaction with 2-bromopropyne or 1-bromo-2-butyne gave the *N*-alkylated products **9a** and **9b**. RCEYM of compounds **9a** and **9b** with **G1** in CH_2Cl_2 at room temperature afforded the corresponding dienes **10a** and **10b** in fair to good yield.



Scheme 2.

The reaction of diene **6a** with tetracyanoethene (TCNE) was carried out in toluene in a sealed tube at 160 °C to give a mixture of two cycloaddition products **11a** and **11b**, which were separated by column chromatography. The X-ray crystal structure of compound **11a** (Fig. 1)[9] shows that the two hydrogens at the ring junction (H-10 and H-14) are trans to each other, and that the quinolizidine ring has a cis conformation. The major product **11b** is an oil; its structure was established by the NOESY spectrum (see the Supplementary data), which shows cross signals between the H-10 and H-14 (Fig. 2). On the other hand, compound **11a** does not show cross signals between the H-10 and H-14 in its NOESY spectrum. Compounds **11a** and **11b** are facial stereoisomers. The major isomer **11b** results from the approach of TCNE opposite to the H-10 of diene **6a**. This mode of reaction is different from that with *N*-phenyl- or *N*-methylmaleimide (vide infra), which prefers *endo* addition. For the reaction with TCNE, there is no distinction between *endo* and *exo* addition. We speculate that the cyano group of TCNE may have some dipole or orbital interaction with the carbonyl group of the diene **6a**.



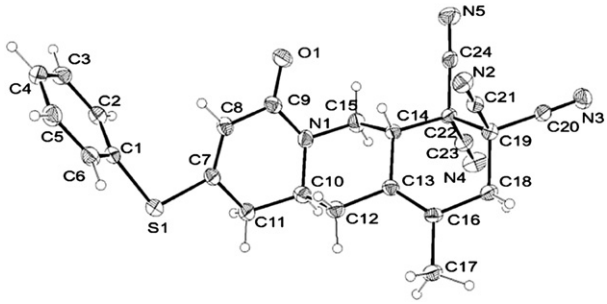


Fig. 1. X-ray crystal structure of compound **11a**.

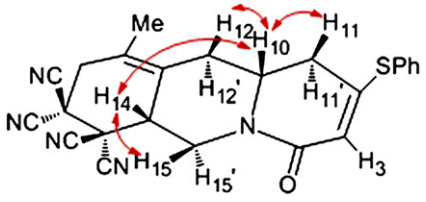
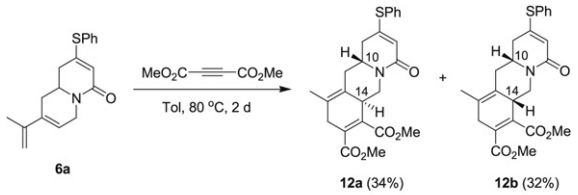


Fig. 2. NOESY correlations of compound **11b**.

The reaction of diene **6a** with dimethyl acetylenedicarboxylate (DMAD) in toluene at 80 °C yielded a mixture of cycloaddition products **12a** and **12b** in about equal amounts. These two compounds were separated by column chromatography. The X-ray crystal structure of compound **12a** (Fig. 3)[9] shows that the two hydrogen atoms at the ring junction (H-10 and H-14) are trans to each other, and that the quinolizidine ring has the trans conformation. The other product **12b** is a liquid, whose structure was established by its NOESY spectrum (see the Supplementary data), which shows cross signals between the H-10 and H-14. As compared to the reaction of diene **6a** with TCNE, the reaction of diene



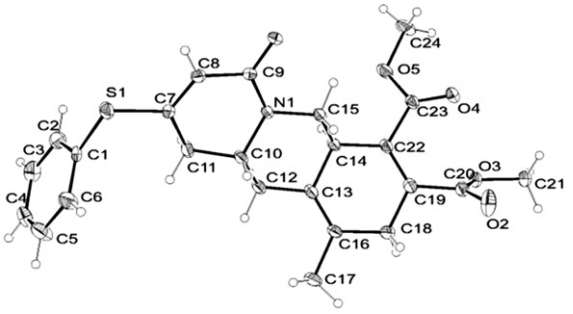
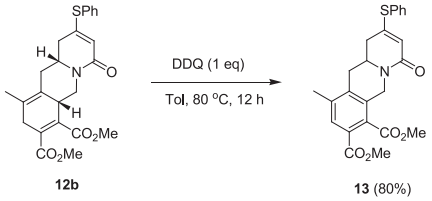


Fig. 3. X-ray crystal structure of compound **12a**.

6a with DMAD showed no facial selectivity. This is probably because DMAD is a linear molecule and has less steric hindrance. We also found that compound **12b** could be oxidized by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to the aromatic compound **13** in good yield. It should be noted that compound **12b** was considerably less stable than compound **12a**; the former was partially oxidized to compound **13** in the air.



Reactions of diene **6a** with *N*-phenylmaleimide and *N*-methylmaleimide in toluene in a sealed tube at 160 °C yielded a mixture of steroid-like skeleton products **14a**/**14b** and **15a**/**15b**, respectively. These products were separated by column chromatography as viscous liquids. The structures of these compounds were determined by NMR spectroscopic methods (see the Supplementary data). The NOESY spectrum of compound **14a** shows cross signals between H-6a and H-12, and between H-12′, H-12a and H-12b (Fig. 4). On the other hand, the NOESY spectrum of compound **14b** has cross signals between H-6′ and H-12′, and between H-12, H-12a and H-12b (Fig. 5).

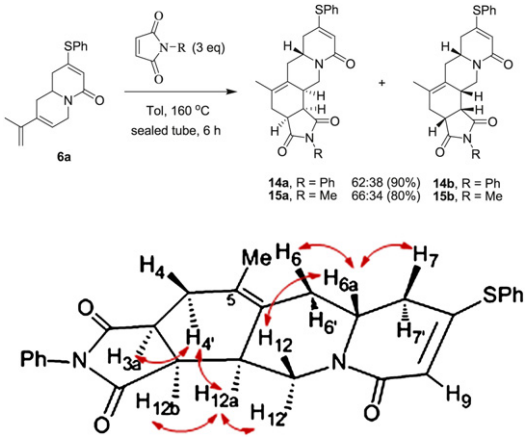


Fig. 4. NOESY correlations of compound **14a**.

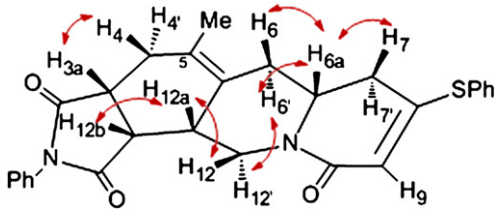


Fig. 5. NOESY correlations of compound **14b**.

It should be noted that both compounds **14a**/**14b** and **15a**/**15b** were the *endo* addition products, probably favored by secondary orbital interactions. Furthermore, the major products **14a** and **15a** resulted from approach of the maleimides from the same side as the H_{6a} of diene **6a**. A molecular model for the *endo* addition of maleimides from the opposite side of H_{6a} of diene **6a** shows a severe steric repulsion with the H-6′ of diene **6a** (Fig. 6). Also, the approach of the dienophiles from the less hindered convex face seems to be more favorable than from the concave face.

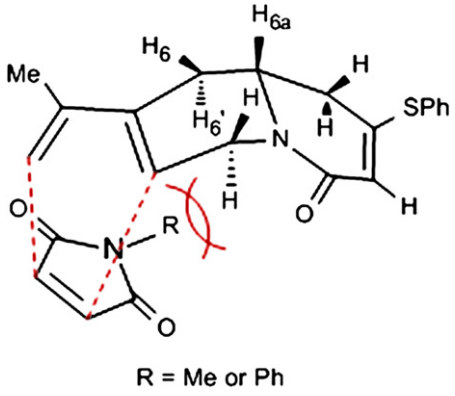
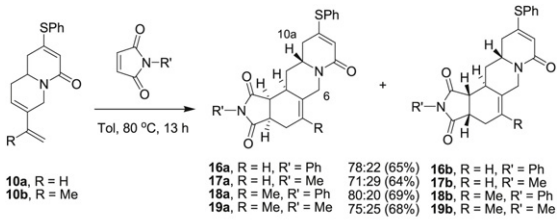


Fig. 6. Steric repulsion of maleimides with diene **6a**.

Reactions of dienes **10a** and **10b** with *N*-phenylmaleimide and *N*-methylmaleimide proceeded much faster than those of diene **6a**, and were carried out by heating in toluene at 80 °C for 13 h to give a mixture of *endo* products **16a**–**19a** and *exo* products **16b**–**19b**. The ratios of these isomers were estimated from the ^{1}H NMR integrations of the H-6 doublets. The stereochemistry proposed for compound **16a** was based on a literature report for a related case, which was confirmed by X-ray diffraction.[3d] The structure of compound **16b** was determined by NOESY spectra (see the Supplementary data) and comparison with the NMR spectrum of a similar compound reported in the literature.[3d] The NOESY correlations of the major products **17a** (Fig. 7) and **18a** (Fig. 8) show that these are the *endo* addition products with the *N*-phenyl- or *N*-methylmaleimide approaching from the less hindered side of the dienes **10a** and **10b**, i.e., the same side as the H-10a.

The reaction of diene **10b** with 4-(phenylsulfonyl)-1-tosyl-5,6-dihydro-2-pyridone (**20**)[4b] in toluene in a sealed tube at 160 °C yielded the cycloaddition product **21**. However, diene **10a** did not react under this condition; heating at 180 °C resulted only in the decomposition of diene **10a**. The structure of the *exo* addition product **21** was confirmed by X-ray crystallography (Fig. 9),[9] which also shows that the quinolizidine ring has a cis conformation. We propose that the dienophile **20** approaches diene **10b** from the less hindered side (the same side as the H-10a) to give product **21**. The steric bulkiness of the phenylsulfonyl group of dienophile **20** would disfavor the *endo* addition. We have previously shown that compound **20** can react with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene, 2,3-dimethylbutadie-ne, or cyclopentadiene at 140–160 °C.[10]



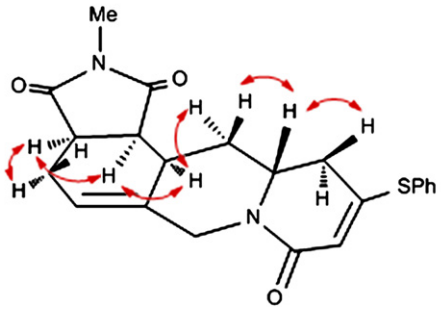


Fig. 7. NOESY correlations of compound **17a**.

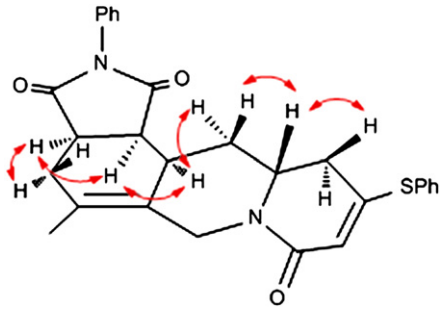


Fig. 8. NOESY correlations of compound **18a**.

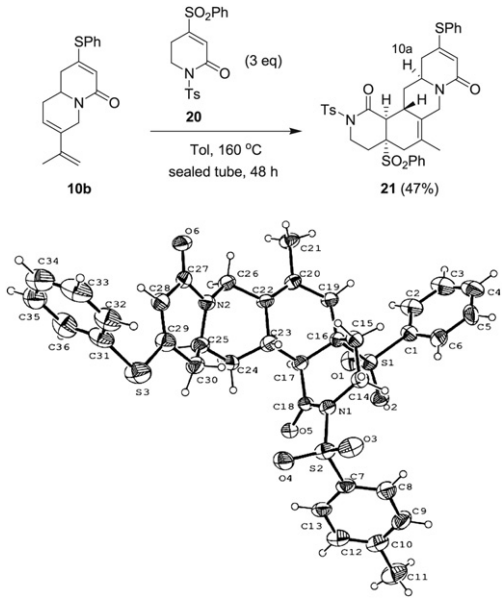
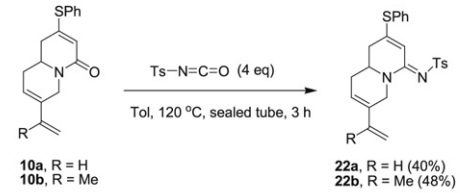


Fig. 9. X-ray crystal structure of compound **21**.

It is interesting to note that cyclopentadiene reacts with compound **20** to give only the *endo* addition product. Apparently, diene **10b** is much more sterically hindered than cyclopentadiene.

The reaction of dienes **10a** and **10b** with *p*-toluenesulfonyl isocyanate (PTSI) did not undergo the expected Diels–Alder reaction. Instead, the imine products **22a** and **22b** were obtained, respectively. We propose that PTSI first undergoes a [2+2] cycloaddition reaction with the C=O of the dienes **10** followed by elimination of CO_2 to give the C=N products **22**.[10] The X-ray crystal structure of compound **22b** (Fig. 10)[9] shows that the C=N has the *E*-configuration, and the quinolizidine ring has a cis conformation.



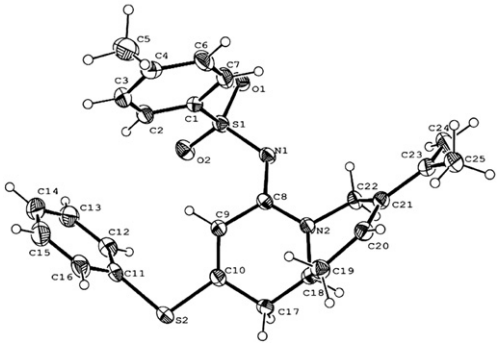
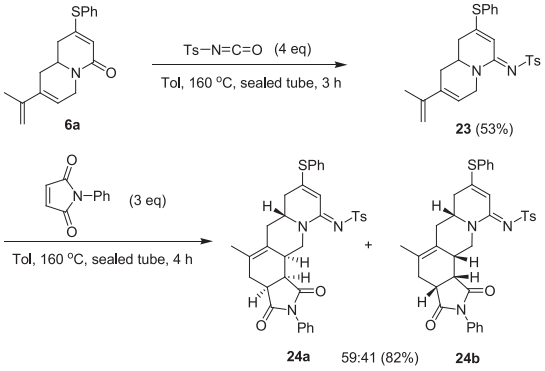


Fig. 10. X-ray crystal structure of compound **22b**.

Similar reaction of diene **6a** with PTSI also produced the imine product **23**. The similarity of its NMR spectral data with those of compound **22b** led us to propose that compound **23** also has the *E*-configuration of the C=N bond. Further reaction of compound **23** with *N*-phenylmaleimide in toluene in a sealed tube at 160 °C gave a mixture of cycloaddition products **24a** and **24b**. The stereoselectivity of this reaction was similar to that obtained for diene **6a**.



3. Conclusions

In summary, we have developed two facile routes (Schemes 1 and 2) to prepare the enynes **5** and **9**, which could be converted, respectively, to the quinolizidine dienes **6** and **10** via ring-closing enyne metathesis (RCEYM). We have also studied the cycloaddition reactions of dienes **6a**, **10a**, and **10b** with various electron-deficient dienophiles to give tricyclic and tetracyclic nitrogen-containing products, which could have some biological activities. The stereochemistry of these reactions is affected by the structures of the dienes and dienophiles.

4. Experimental section

4.1. General

Melting points were determined with a SMP3 melting apparatus. Infrared spectra were recorded with a Perkin Elmer 100 series FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 300 or 600 spectrometer operating at 300 or 600, and at 75 or 150 MHz, respectively, unless specified otherwise. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (J) are given in hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf–Nonius FR-590 diffractometer (CAD4, Kappa CCD). Elemental analyses were carried out with Heraeus Vario III-NCSH, Heraeus CHN–O–S-Rapid Analyzer or Elementar Vario EL III. Flash column chromatographic purifications were performed using Merck 60H silica gel.

*4.1.1. 2-(But-2-ynyl)-4-(phenylthio)-3-sulfolene (**2a**).* To a solution of compound **1** (565 mg, 2.50 mmol) in THF (8 mL) and HMPA (1.74 mL, 10 mmol) under nitrogen at −78 °C was added dropwise a solution of BuLi in hexane (2.5 M, 1.2 mL, 3.00 mmol). After stirring at −78 °C for 30 min, 1-bromo-2-butyne (0.9 mL, 10.00 mmol) was added in one portion. The mixture was slowly warmed to −40 °C, and was maintained at this temperature for 3 h before it was poured into a saturated ammonium chloride solution. The aqueous solution was extracted three times with ethyl acetate, and the combined organic layers were dried ($MgSO_4$) and evaporated under vacuum. The crude product was purified by flash chromatography using ethyl acetate/hexanes (1:8) as eluent to give compound **2a** (500 mg, 72%) as a yellow oil: IR (film) 3060, 2227, 1583, 1313, 1123 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.47–7.36 (5H, m), 5.92–5.90 (1H, m), 3.95–3.90 (1H, m), 3.72 (2H, t, J=1.5 Hz), 2.79–2.69 (1H, m), 2.60–2.51 (1H, m), 1.78 (3H, t, J=2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 133.3, 132.5, 129.7, 129.6, 129.1, 124.8, 79.1, 73.1, 65.7, 57.7, 19.5, 3.5; FAB-MS m/z 279 (M^++H, 4); FAB-HRMS calcd for $C_{14}H_{14}O_2S_2$ 278.0435, found 278.0436.

*4.1.2. 4-(Phenylthio)-2-(3-(trimethylsilyl)prop-2-ynyl)-3-sulfolene (**2b**).* Using a similar condition as for compound **2a** except for warming the reaction mixture to −60 °C for 2.5 h, compound **2b** was isolated as a yellow oil (124 mg, 37%): IR (film) 3058, 2179, 1583, 1316, 1126 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.48–7.37 (5H, m), 5.77 (1H, dt, J=3.0, 1.5 Hz), 3.94–3.89 (1H, m), 3.73 (2H, t, J=1.5 Hz), 2.78 (1H, dd, J=17.1, 5.4 Hz), 2.62 (1H, dd, J=17.1, 8.1 Hz), 0.14 (9H, t, J=3.3 Hz); ^{13}C NMR ($CDCl_3$) δ 133.5, 133.0, 129.6, 129.1, 129.0, 122.8, 100.4, 88.2, 64.9, 57.4, 20.4, −0.2; FAB-MS m/z 337 (M^++H, 6); FAB-HRMS calcd for $C_{16}H_{20}O_2S_2Si$ 336.0674, found 336.0675.

*4.1.3. 6-(But-2-ynyl)-4-(phenylthio)-1-tosyl-5,6-dihydropyridin-2(1H)-one (**3a**).* A mixture of compound **2a** (568 mg, 2.04 mmol), $NaHCO_3$ (171 mg, 2.04 mmol), hydroquinone (11.2 mg, 0.10 mmol), and PTSI (1.25 mL, 8.16 mmol) in toluene (10 mL) was heated at reflux under nitrogen for 6 h. After cooling in an ice bath, 5% aq NaOH was slowly added to decompose the excess PTSI. The solvent was removed under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:6) containing 5% Et_3N as eluent to give compound **3a** (533 mg, 63%) as a white solid: mp 154–155 °C (recryst from EA/hexanes); IR (film) 3053, 2232, 1660, 1594, 1344, 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.92 (2H, d, J=8.1 Hz), 7.46–7.27 (5H, m), 7.25 (2H, d, J=8.1 Hz), 5.20 (1H, s), 4.93–4.87 (1H, m), 2.90 (2H, d, J=3.3 Hz), 2.59–2.55 (2H, m), 2.37 (3H, s), 1.77 (3H, t, J=2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 160.2, 157.5, 144.5, 136.4, 135.2, 130.2, 129.8, 129.1, 128.7, 127.3, 113.2, 79.4, 74.1, 53.7, 31.9, 23.3, 21.4, 3.4; FAB-MS m/z 412 (M^++H, 100); FAB-HRMS calcd for $C_{22}H_{21}NO_3S_2$ 411.0963, found 411.0969.

*4.1.4. 4-(Phenylthio)-1-tosyl-6-(3-(trimethylsilyl)prop-2-ynyl)-5,6-dihydropyridin-2(1H)-one (**3b**).* Using a similar condition as for compound **3a**, product **3b** (91 mg, 59%) was obtained as a white solid: mp 114–116 °C (recryst from EA/hexanes); IR (film) 3058, 2240, 1678, 1597, 1374 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.92 (2H, d, J=8.0 Hz), 7.48–7.37 (5H, m), 7.27 (2H, d, J=8.0 Hz), 5.18 (1H, s), 4.97–4.91 (1H, m), 2.93 (2H, d, J=3.3 Hz), 2.67 (2H, d, J=7.5 Hz), 2.39 (3H, s), 0.18 (9H, s); ^{13}C NMR ($CDCl_3$) δ 160.4, 157.6, 144.7, 136.5, 135.3, 130.5, 130.0, 129.3, 129.0, 127.5, 113.5, 101.4, 89.1, 53.4, 32.2, 24.5, 21.6, -0.1; FAB-MS m/z 470 (M^++H, 90); FAB-HRMS calcd for $C_{24}H_{27}NO_3S_2Si$ 469.1202, found 469.1195.

*4.1.5. 6-(But-2-ynyl)-4-(phenylthio)-5,6-dihydropyridin-2(1H)-one (**4a**).* To a refluxing solution of compound **3a** (360 mg, 0.88 mmol) in degassed toluene (15 mL) was added dropwise a solution of Bu_3SnH (0.28 mL, 1.06 mmol) and AIBN (86 mg, 0.52 mmol) in toluene (5 mL). The reaction mixture was refluxed for another 2 h. The solvent was then evaporated under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) containing 5% Et_3N as eluent to give compound **4a** (180 mg, 80%) as a white solid: mp 136–137 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3053, 1656, 1590, 1265 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.52–7.38 (5H, m), 5.77 (1H, br s), 5.28 (1H, s), 3.75–3.65 (1H, m), 2.51–2.43 (2H, m), 2.42–2.30 (2H, m), 1.79 (3H, t, J=2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 165.7, 154.6, 135.4, 130.0, 129.9, 128.1, 114.2, 79.5, 73.8, 50.2, 34.0, 25.2, 3.5; EI-MS m/z 257 (M^+, 2); EI-HRMS calcd for $C_{15}H_{15}NOS$ 257.0874, found 257.0870. Anal. Calcd for $C_{15}H_{15}NOS$: C, 70.01; H, 5.87; N, 5.44. Found: C, 70.03; H, 5.93; N, 5.56.

*4.1.6. 4-(Phenylthio)-6-(3-(trimethylsilyl)prop-2-ynyl)-5,6-dihydropyridin-2(1H)-one (**4b**).* Using a similar condition as for compound **4a**, product **4b** (500 mg, 90%) was isolated as a white solid: mp 164–166 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3180, 3053, 2181, 1662, 1244, 1047 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.50–7.36 (5H, m), 6.18 (1H, br s), 5.27 (1H, s), 3.75–3.69 (1H, m), 2.55 (1H, dd, J=16.5, 5.4 Hz), 2.49–2.39 (3H, m), 0.13 (9H, s); ^{13}C NMR ($CDCl_3$) δ 165.6, 154.3, 135.3, 130.0, 129.8, 128.1, 114.3, 101.3, 88.4, 49.8, 33.6, 26.1, −0.1; EI-MS m/z 316 (M^++1, 1); EI-HRMS calcd for $C_{17}H_{21}NOSSi$ 315.1113, found 315.1119.

*4.1.7. 1-Allyl-6-(but-2-ynyl)-4-(phenylthio)-5,6-dihydropyridin-2(1H)-one (**5a**).* To a solution of compound **4a** (300 mg, 1.17 mmol) in THF (7 mL) and HMPA (0.81 mL, 4.68 mmol) under nitrogen at −78 °C was added dropwise a solution of BuLi in hexane (2.5 M, 1.2 mL, 3.00 mmol). After stirring at −78 °C for 30 min, allyl bromide (0.4 mL, 4.68 mmol) was added in one portion. The mixture was slowly warmed to room temperature, and was stirred for another 2 h before it was poured into a saturated ammonium chloride solution. The aqueous solution was extracted three times with ethyl acetate, and the combined organic layers were dried ($MgSO_4$) and evaporated under vacuum. The crude product was purified by flash chromatography using ethyl acetate/hexanes (1:5) as eluent to give compound **5a** (288 mg, 83%) as a white solid: mp 89–90 °C (recryst from EA/hexanes); IR (film) 3053, 1639, 1595, 1455, 1253 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.53–7.39 (5H, m), 5.78 (1H, dddd, J=17.1, 10.2, 6.6, 4.8 Hz), 5.38 (1H, d, J=2.1 Hz), 5.22–5.15 (2H, m), 4.59 (1H, ddt, J=15.6, 4.8, 1.5 Hz), 3.63–3.56 (1H, m), 3.46 (1H, dd, J=15.6, 6.6 Hz), 2.79 (1H, ddd, J=17.1, 6.3, 2.1 Hz), 2.65 (1H, dd, J=17.1, 2.1 Hz), 2.46–2.41 (2H, m), 1.79–1.76 (3H, m); ^{13}C NMR ($CDCl_3$) δ 162.1, 150.7, 135.1, 133.6, 129.6, 129.5, 128.4, 116.9, 115.0, 78.3, 74.9, 53.9, 46.8, 31.7, 21.3, 3.3; EI-MS m/z 297 (M^+, 14); EI-HRMS calcd for $C_{18}H_{19}NOS$ 297.1187, found

297.1184. Anal. Calcd for $C_{18}H_{19}NOS$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.68; H, 6.31; N, 4.95.

*4.1.8. 6-(But-2-ynyl)-1-(2-methylallyl)-4-(phenylthio)-5,6-dihydropyridin-2(1H)-one (**5b**).* Using a similar condition as for compound **5a**, product **5b** (126 mg, 87%) was obtained as a yellow oil: IR (film) 3068, 1642, 1596, 1454, 1440, 1248 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54–7.38 (5H, m), 5.39 (1H, d, J=2.4 Hz), 4.89–4.85 (2H, m), 4.65 (1H, d, J=15.6 Hz), 3.59–3.52 (1H, m), 3.29 (1H, d, J=15.6 Hz), 2.79 (1H, ddd, J=17.1, 6.3, 1.8 Hz), 2.65 (1H, dd, J=17.1, 1.8 Hz), 2.51–2.35 (2H, m), 1.77 (3H, t, J=2.4 Hz), 1.70 (3H, s); ^{13}C NMR ($CDCl_3$) δ 162.2, 150.8, 140.9, 135.1, 129.6, 129.5, 128.2, 114.7, 112.2, 78.2, 75.0, 53.4, 49.4, 31.5, 20.8, 19.8, 3.3; FAB-MS m/z 312 (M^++H, 100); FAB-HRMS calcd for $C_{19}H_{21}NOS$ 311.1344, found 311.1335.

*4.1.9. 1-Allyl-4-(phenylthio)-6-(3-(trimethylsilyl)prop-2-ynyl)-5,6-dihydropyridin-2(1H)-one (**5c**).* Using a similar condition as for compound **5a**, product **5c** (83 mg, 82%) was obtained as a yellow oil: IR (film): IR (film) 3053, 2175, 1642, 1454, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.39 (5H, m), 5.78 (1H, dddd, J=17.1, 10.2, 6.9, 4.8 Hz), 5.39 (1H, d, J=2.4 Hz), 5.24–5.16 (2H, m), 4.61 (1H, ddt, J=15.6, 4.8, 1.8 Hz), 3.70–3.63 (1H, m), 3.49 (1H, dd, J=15.6, 6.9 Hz), 2.81 (1H, ddd, J=17.1, 6.3, 2.4 Hz), 2.61 (1H, dd, J=17.1, 1.8 Hz), 2.54 (1H, s), 2.52 (1H, s), 0.16 (9H, s); ^{13}C NMR ($CDCl_3$) δ 162.3, 151.0, 135.3, 133.8, 130.0, 129.9, 128.5, 117.3, 115.2, 102.8, 87.9, 53.9, 47.2, 32.2, 22.7, 0.0; EI-MS m/z 355 (M^+, 2); EI-HRMS calcd for $C_{20}H_{25}NOSSi$ 355.1426, found 355.1425.

*4.1.10. 2-(Phenylthio)-8-(prop-1-en-2-yl)-1,6,9,9a-tetrahydroquinolizin-4-one (**6a**).* A mixture of compound **5a** (86 mg, 0.29 mmol) and **G1** (24.0 mg, 0.029 mmol) in CH_2Cl_2 (5 mL) was stirred under nitrogen at room temperature for 16 h. The solvent was then evaporated under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:5) as eluent to give compound **6a** (69 mg, 80%) as a yellow oil: IR (film) 3054, 1634, 1596, 1424, 1265 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53–7.40 (5H, m), 5.82 (1H, br s), 5.34 (1H, s), 4.96–4.94 (2H, m), 4.66 (1H, br d, J=19.8 Hz), 3.79–3.69 (2H, m), 2.83 (1H, dd, J=17.1, 6.6 Hz), 2.50–2.38 (3H, m), 1.90 (3H, s); ^{13}C NMR ($CDCl_3$) δ 164.1, 151.5, 142.0, 135.4, 134.4, 130.0, 129.9, 128.4, 121.2, 115.2, 111.3, 51.4, 42.9, 34.2, 31.7, 20.3; FAB-MS m/z 298 (M^++H, 100); FAB-HRMS calcd for $C_{18}H_{19}NOS$ 297.1187, found 297.1183.

*4.1.11. 2-(Phenylthio)-8-vinyl-1,6,9,9a-tetrahydroquinolizin-4-one (**6b**).* Using a similar condition as for compound **6a**, product **6b** (28 mg, 66%) was obtained as a yellow oil: IR (film) 3093, 1652, 1375, 1240, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.38 (5H, m), 6.35 (1H, dd, J=17.7, 10.8 Hz), 5.73 (1H, br s), 5.34 (1H, t, J=0.9 Hz), 5.14–5.00 (2H, m), 4.67 (1H, br d, J=19.8 Hz), 3.82–3.73 (1H, m), 3.67 (1H, dd, J=19.8, 2.4 Hz), 2.84 (1H, ddd, J=17.1, 6.6, 0.9 Hz), 2.46 (1H, ddd, J=17.1, 6.6, 0.9 Hz), 2.35–2.27 (2H, m); ^{13}C NMR ($CDCl_3$) δ 163.9, 151.3, 137.7, 135.2, 133.5, 129.9, 129.7, 128.2, 125.2, 115.0, 111.7, 51.0, 42.6, 33.9, 29.9; ESI-MS m/z 283 (M^+, 100); ESI-HRMS m/z calcd for $C_{17}H_{17}NOS$ 283.1031, found 283.1038.

*4.1.12. 6-(But-2-ynyl)-1-(2-methylprop-1-enyl)-4-(phenylthio)-5,6-dihydropyridin-2(1H)-one (**7a**).* A mixture of compound **5b** (100 mg, 0.32 mmol) and **G1** (28 mg, 0.03 mmol) in CH_2Cl_2 (4 mL) was refluxed under nitrogen for 18 h. The solvent was then evaporated under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:5) as eluent to give compound **7a** (21 mg, 21%) as a yellow oil: IR (film) 3058, 1645, 1420, 1243 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54–7.40 (5H, m), 5.95–5.94 (1H, m), 5.40 (1H, d, J=2.1 Hz), 3.68–3.60 (1H, m), 2.91 (1H, ddd, J=17.1, 6.3, 2.1 Hz), 2.72 (1H, dd, J=17.1, 2.1 Hz), 2.47–2.40 (2H, m), 1.78 (3H, t, J=2.4 Hz), 1.76 (3H, d, J=1.2 Hz), 1.64 (3H, d, J=1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 162.8, 151.8, 135.5, 133.1, 130.0, 129.9, 128.5, 122.2, 115.2, 78.6, 75.3, 57.6, 31.6, 22.5, 21.6, 18.2, 3.6; EI-MS m/z 311 (M^+, 3); EI-HRMS calcd for $C_{19}H_{21}NOS$ 311.1344, found 311.1347.

*4.1.13. (E)-4-(Phenylthio)-1-(prop-1-enyl)-6-(3-(trimethylsilyl)prop-2-ynyl)-5,6-dihydropyridin-2(1H)-one (**7b**).* A mixture of compound **5c** (218 mg, 0.61 mmol) and **G2** (30 mg, 0.03 mmol) in CH_2Cl_2 (6 mL) was refluxed under nitrogen for 22 h. The solvent was then evaporated under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:5) as eluent to give compound **7b** (31 mg, 14%) as a yellow oil: IR (film) 3053, 2176, 1651, 1596, 1417, 1249 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54–7.39 (5H, m), 7.10 (1H, dq, J=14.7, 1.8 Hz), 5.39 (1H, d, J=2.1 Hz), 5.06 (1H, dq, J=14.7, 6.6 Hz), 4.09–4.02 (1H, m), 2.86 (1H, ddd, J=17.1, 6.3, 2.1 Hz), 2.75 (1H, dd, J=17.1, 2.1 Hz), 2.54–2.51 (2H, m), 1.74 (3H, dd, J=6.6, 1.8 Hz), 0.18 (9H, t, J=3.3 Hz); ^{13}C NMR ($CDCl_3$) δ 159.9, 152.5, 135.4, 130.1, 129.9, 128.2, 125.0, 114.6, 105.3, 102.6, 87.9, 51.9, 30.9, 21.6, 15.5, 0.1; EI-MS m/z 355 (M^+, 11); EI-HRMS calcd for $C_{20}H_{25}NOSSi$ 355.1426, found 355.1421.

*4.1.14. 6-Allyl-4-(phenylthio)-1-propargyl-1,2,5,6-tetrahydropyridin-2-one (**9a**).* A mixture of compound **8** (200 mg, 0.82 mmol) and NaH (60%, 58.7 mg, 1.48 mmol) in THF (4 mL) was stirred at room temperature for 45 min. Propargyl bromide (0.29 mL, 3.28 mmol) was then added, and the reaction mixture was refluxed for 2 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:5) as eluent to give compound **9a** (114 mg, 50% yield) as a yellow oil: IR (film) 3291, 3062, 2118, 1642, 1590, 1454, 1251 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.49–7.39 (5H, m), 5.75–5.68 (1H, m), 5.34 (1H, d, J=2.1 Hz), 5.19–5.17 (1H, m), 5.13 (1H, s), 4.71 (1H, dd, J=2.4, 17.7 Hz), 3.88–3.78 (2H, m), 2.83 (1H, ddd, J=2.1, 6.3, 16.8 Hz), 2.48–2.34 (3H, m), 2.23 (1H, t, J=2.7 Hz); ^{13}C NMR ($CDCl_3$) δ 162.5, 152.0, 135.4, 133.7, 130.0, 129.8, 128.4, 119.5, 114.6, 79.3, 72.1, 54.2, 35.7, 33.8, 32.0; FAB-MS m/z 284 (M^++H, 100); FAB-HRMS calcd for $C_{17}H_{18}NSO$ 284.1109, found 284.1113.

*4.1.15. 6-Allyl-1-(2-butynyl)-4-(phenylthio)-1,2,5,6-tetrahydropyridin-2-one (**9b**).* Using a similar condition as for compound **9a**, product **9b** (380 mg, 62% yield) was obtained as a yellow oil: IR (film) 3077, 2221, 1642, 1594, 1447, 1251 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51–7.39 (5H, m), 5.75–5.68 (1H, m), 5.34 (1H, d, J=2.2 Hz), 5.17–5.15 (1H, m), 5.11 (1H, s), 4.71 (1H, dq, J=17.4, 2.4 Hz), 3.86–3.74 (2H, m), 2.81 (1H, ddd, J=2.2, 6.3, 16.8 Hz), 2.44–2.34 (3H, m), 1.81 (3H, t, J=2.4 Hz); ^{13}C NMR ($CDCl_3$) δ 162.5, 151.5, 135.4, 133.9, 130.0, 129.8, 128.5, 118.9, 114.9, 79.8, 74.3, 54.0, 35.7, 34.2, 32.0, 3.6; FAB-MS m/z 298 (M^++H, 96); FAB-HRMS calcd for $C_{18}H_{20}NSO$ 298.1266, found 298.1259.

*4.1.16. 2-(Phenylthio)-7-vinyl-1,6,9,9a-tetrahydroquinolizin-4-one (**10a**).* Using a similar condition as for compound **6a**, product **10a** (46 mg, 62% yield) was obtained as a light yellow liquid: IR (film) 3070, 1635, 1598, 1417, 1251 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52–7.38 (5H, m), 6.27 (1H, dd, J=11.1, 17.7 Hz), 5.77 (1H, d, J=5.1 Hz), 5.36 (1H, s), 5.16 (1H, d, J=17.7 Hz), 5.00 (1H, d, J=11.1 Hz), 4.81 (1H, d, J=17.7 Hz), 3.77–3.65 (2H, m), 2.81 (1H, ddd, J=0.9, 6.6, 17.1 Hz), 2.51–2.33 (2H, m), 2.14 (1H, br d, J=17.7 Hz); ^{13}C NMR ($CDCl_3$) δ 164.0, 151.1, 136.4, 135.3, 134.2, 130.0, 129.9, 128.3, 125.1, 115.3, 112.1, 51.3, 41.9, 33.7, 31.4; FAB-MS m/z 284 (M^++H, 62); FAB-HRMS calcd for $C_{17}H_{18}NSO$ 284.1109 (M^++H), found 284.1107.

*4.1.17. 7-Isopropenyl-2-(phenylthio)-1,6,9,9a-tetrahydroquinolizin-4-one (**10b**).* Using a similar condition as for compound **6a**, product **10b** (112 mg, 82%) was obtained as a light yellow liquid: IR (film) 3092, 1642, 1598, 1417, 1255 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.52–7.27 (5H, m), 5.87 (1H, t, J=2.4 Hz), 5.36 (1H, s), 5.0 (1H, s), 4.91 (1H, s), 4.88

(1H, d, J=19.2 Hz), 3.77–3.67 (2H, m), 2.84 (1H, ddd, J=1.2, 6.6, 17.1 Hz), 2.49–2.43 (1H, m), 2.37 (1H, dd, J=5.7, 17.1 Hz), 2.16 (1H, br d, J=17.1 Hz), 1.88 (3H, s); ^{13}C NMR ($CDCl_3$) δ 163.8, 150.8, 135.3, 135.2, 129.95, 129.85, 128.4, 121.2, 115.4, 111.3, 51.3, 42.9, 33.6, 31.3, 20.5; FAB-MS m/z 298 (M^++H, 100); FAB-HRMS calcd for $C_{18}H_{20}NSO$ 298.1266, found 298.1270.

*4.1.18. trans-10-Methyl-4-oxo-2-(phenylthio)-6,6a-dihydro-1H-pyrido[1,2-b]isoquinoline-7,7,8,8(4H,9H,11H,11aH)-tetracarbonitrile (**11a**) and cis-10-methyl-4-oxo-2-(phenylthio)-6,6a-dihydro-1H-pyrido[1,2-b]isoquinoline-7,7,8,8(4H,9H,11H,11aH)-tetracarbonitrile (**11b**).* A mixture or compound **6a** (110 mg, 0.37 mmol) and TCNE (142 mg, 1.11 mmol) in degassed toluene (3 mL) in a sealed tube was heated at 160 °C for 23 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give compound **11a** (42 mg, 27%) as a white solid and compound **11b** (57 mg, 36%) as a yellow oil. Compound **11a**: mp 193–195 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3055, 2306, 1648, 1422, 1266 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51–7.44 (5H, m), δ 5.34 (1H, s), δ 5.03 (1H, dd, J=12.6, 4.8 Hz), 3.59–3.54 (1H, m), 3.18 (1H, d, J=18.6 Hz), 3.09–3.07 (1H, m), 2.96–2.91 (2H, m), 2.79–2.72 (2H, m), 2.42 (1H, dd, J=17.4, 6.0 Hz), 2.20 (1H, dd, J=13.8 Hz), 1.88 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.8, 153.5, 135.4, 130.3, 130.0, 127.5, 124.9, 122.9, 113.8, 110.8, 110.3, 110.1, 108.8, 54.0, 44.9, 41.9, 40.3, 38.0, 37.3, 33.8, 33.5, 18.8; EI-MS m/z 425 (M^+, 53); EI-HRMS calcd for $C_{24}H_{19}N_5OS$ 425.1310, found 425.1305. Compound **11b**: IR (film) 3055, 2306, 1647, 1423, 1266 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49–7.43 (5H, m), 5.39 (1H, d, J=1.8 Hz), 4.42 (1H, dd, J=13.2, 4.8 Hz), 4.04–3.99 (1H, m), 3.75 (1H, dd, J=13.2, 8.4 Hz), 3.39 (1H, br s), 3.16 (1H, d, J=18.6 Hz), 3.05 (1H, d, J=18.6 Hz), 2.69 (1H, br d, J=16.2 Hz), 2.57–2.51 (2H, m), 2.35 (1H, dd, J=16.2, 4.2 Hz), 1.82 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 153.1, 135.2, 130.2, 129.9, 127.8, 124.1, 123.1, 114.8, 110.7, 110.5, 110.3, 108.1, 50.8, 41.5, 40.8, 39.2, 38.7, 37.6, 35.2, 32.0, 18.1; EI-MS m/z 425 (M^+, 50); EI-HRMS calcd for $C_{24}H_{19}N_5OS$ 425.1310, found 425.1306.

*4.1.19. trans-Dimethyl 10-methyl-4-oxo-2-(phenylthio)-4,6,6a,9,11,11a-hexahydro-1H-pyrido[1,2-b]isoquinoline-7,8-dicarboxylate (**12a**) and cis-dimethyl10-methyl-4-oxo-2-(phenylthio)-4,6,6a,9,11,11a-hexahydro-1H-pyrido[1,2-b]isoquinoline-7,8-dicarboxylate (**12b**).* A mixture of compound **6a** (50 mg, 0.17 mmol) and DMAD (0.13 mL, 1.02 mmol) in degassed toluene (2 mL) was heated under nitrogen at 80 °C for 48 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give compound **12a** (25 mg, 34%) as a white solid and compound **12b** (24 mg, 32%) as a yellow oil. Compound **12a**: mp 169–171 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3058, 1721, 1639, 1434, 1264 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51–7.40 (5H, m), 5.32 (1H, d, J=1.2 Hz), 4.64 (1H, dd, J=15.6, 3.9 Hz), 3.82 (3H, s), 3.77 (3H, s), 3.48–3.38 (1H, m), 3.17–3.13 (1H, m), 3.06 (1H, dd, J=23.1, 6.9 Hz), 2.87 (1H, dd, J=22.5, 6.0 Hz), 2.76 (1H, dd, J=13.5, 3.3 Hz), 2.65 (1H, dd, J=17.1, 5.7 Hz), 2.48 (1H, ddd, J=17.1, 9.6, 1.5 Hz), 2.33 (1H, dd, J=12.0, 11.7 Hz), 1.95 (1H, t, J=12.3 Hz), 1.72 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.8, 167.7, 164.7, 152.3, 135.3, 133.8, 132.6, 130.0, 129.8, 128.1, 125.0, 121.9, 114.9, 55.7, 52.5, 52.3, 47.9, 39.4, 35.5, 35.1, 33.7, 17.7; EI-MS m/z 439 (M^+, 6); EI-HRMS calcd for $C_{24}H_{25}NO_5S$ 439.1453, found 439.1447; Compound **12b**: IR (film) 3053, 1721, 1637, 1433, 1264 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.51–7.39 (5H, m), 5.36 (1H, d, J=1.2 Hz), 4.11 (1H, dd, J=12.3, 4.8 Hz), 4.05–3.94 (1H, m), 3.80 (3H, s), 3.76 (3H, s), 3.59–3.51 (1H, m), 3.20 (1H, t, J=12.3 Hz), 3.06 (1H, dd, J=22.8, 7.5 Hz), 2.87 (1H, dd, J=22.8, 9.0 Hz), 2.60 (1H, br d, J=15.0 Hz), 2.53–2.37 (3H, m), 1.67 (3H, s); ^{13}C NMR ($CDCl_3$) δ 167.8, 167.7, 164.7, 152.3, 135.3, 133.8, 132.6, 130.0, 129.8, 128.1, 125.0, 121.9, 114.9, 55.7, 52.5, 52.3, 47.9, 39.4, 35.5, 35.1, 33.7, 17.7; EI-MS m/z 439 (M^+, 6); EI-HRMS calcd for $C_{24}H_{25}NO_5S$ 439.1453, found 439.1447.

*4.1.20. Dimethyl 10-methyl-4-oxo-2-(phenylthio)-4,6,11,11a-tetrahydro-1H-pyrido[1,2-b]isoquinoline-7,8-dicarboxylate (**13**).* A mixture of compound **12b** (15 mg, 0.03 mmol) and DDQ (7 mg, 0.03 mmol) in degassed toluene (1 mL) was heated under nitrogen at 80 °C for 12 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give compound **13** (12 mg, 80%) as a yellow oil: IR (film) 3053, 1733, 1647, 1239, 1046 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.67 (1H, s), 7.53–7.40 (5H, m), 5.35 (1H, s), 5.13 (1H, d, J=17.4 Hz), 4.36 (1H, d, J=17.4 Hz), 3.94 (3H, s), 3.85 (3H, s), 2.97–2.85 (2H, m), 2.76 (1H, dd, J=16.5, 4.2 Hz), 2.50 (1H, dd, J=17.1, 6.0 Hz), 2.30 (3H, s); ^{13}C NMR ($CDCl_3$) δ 168.8, 166.3, 163.0, 151.3, 138.0, 137.7, 135.4, 131.7, 131.3, 130.1, 129.9, 129.4, 128.2, 126.2, 115.1, 52.9, 52.5, 51.3, 42.3, 33.7, 32.1, 19.4; EI-MS m/z 437 (M^+, 10); EI-HRMS calcd for $C_{24}H_{23}NO_5S$ 437.1297, found 437.1300.

*4.1.21. endo-trans-5-Methyl-2-phenyl-8-(phenylthio)-3a,4,6a,7,12,12a-hexahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinoline-1,3,10(2H,6H,12bH)-trione (**14a**) and endo-cis-5-methyl-2-phenyl-8-(phenylthio)-3a,4,6a,7,12,12a-hexahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinoline-1,3,10(2H,6H,12bH)-trione (**14b**).* A mixture of compound **6a** (100 mg, 0.34 mmol) and *N*-phenylmaleimide (175 mg, 1.02 mmol) in degassed toluene (3 mL) was heated at 160 °C for 4 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **14a** and **14b** (143 mg, 90%; 62:38 by ^{1}H NMR). With repeated separation by flash chromatography, pure samples of **14a** and **14b** were obtained. Compound **14a**: a yellow oil; IR (film) 3057, 1703, 1630, 1381, 1187 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48–7.36 (8H, m), 7.14–7.12 (2H, m), 5.34 (1H, d, J=1.8 Hz), 4.63 (1H, dd, J=13.8, 6.0 Hz), 4.03–4.01 (1H, m), 3.73 (1H, dd, J=13.8, 12.0 Hz), 3.30–3.24 (2H, m), 2.69 (1H, dd, J=15.0, 1.2 Hz), 2.56 (2H, br s), 2.49–2.40 (2H, m), 2.33 (1H, br d), 2.23 (1H, dd, J=16.8, 4.8 Hz), 1.78 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.5, 176.8, 163.0, 152.3, 135.2, 131.8, 130.6, 129.9, 129.8, 129.2, 128.7, 128.3, 127.7, 126.4, 115.2, 51.9, 42.2, 40.8, 38.2, 38.0, 35.5, 31.4, 29.1, 18.9; EI-MS m/z 470 (M^+, 4); EI-HRMS calcd for $C_{28}H_{26}N_2O_3S$ 470.1664, found 470.1664. Compound **14b**: a yellow oil; IR (film) 3058, 1737, 1709, 1639, 1374, 1239, 1046 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49–7.36 (8H, m), 7.16–7.15 (2H, m), 5.40 (1H, d, J=2.4 Hz), 4.64 (1H, dd, J=13.8, 5.4 Hz), 3.86 (1H, dd, J=13.8, 12.6 Hz), 3.68–3.64 (1H, m), 3.27–3.22 (2H, m), 2.70 (1H, dd, J=14.4, 1.2 Hz), 2.64 (1H, dd, J=14.4, 3.0 Hz), 2.63 (1H, br s), 2.51 (1H, ddd, J=16.2, 13.8, 2.1 Hz), 2.33–2.30 (2H, m), 2.24 (1H, dd, J=16.8, 3.6 Hz), 1.78 (3H, s); ^{13}C NMR (150 MHz, $CDCl_3$) δ 178.5, 176.5, 163.4, 152.4, 135.2, 131.8, 129.9, 129.8, 129.1, 128.6, 128.54, 128.45, 128.2, 126.4, 116.0, 53.1, 42.2, 40.0, 37.6, 36.1, 35.9, 31.0, 30.4, 19.1; EI-MS m/z 470 (M^+, 0.1); EI-HRMS calcd for $C_{28}H_{26}N_2O_3S$ 470.1664, found 470.1660.

*4.1.22. endo-trans-2,5-Dimethyl-8-(phenylthio)-3a,4,6a,7,12,12a-hexahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinoline-1,3,10(2H,6H,12bH)-trione (**15a**) and endo-cis-2,5-dimethyl-8-(phenylthio)-3a,4,6a,7,12,12a-hexahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinoline-1,3,10(2H,6H,12bH)-trione (**15b**).* A mixture of compound **6a** (111 mg, 0.37 mmol) and *N*-methylmaleimide (123 mg, 1.11 mmol) in degassed toluene (3 mL) was heated at 160 °C for 4 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **15a** and **15b** (121 mg, 80%; 66:34 by ^{1}H NMR). With repeated separation by flash chromatography, pure samples of **15a** and **15b** were obtained.

Compound **15a**: a yellow oil; IR (film) 3055, 1693, 1632, 1430 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.37 (5H, m), 5.33 (1H, d, J=2.1 Hz), 4.57 (1H, dd, J=13.5, 6.0 Hz), 4.02–3.94 (1H, m), 3.72 (1H, dd, J=13.5, 11.4 Hz), 3.14–3.05 (2H, m), 2.90 (3H, s), 2.59 (1H, dd, J=15.3, 1.5 Hz), 2.47–2.35 (4H, m), 2.26–2.19 (2H, m), 1.70 (3H, s); ^{13}C NMR ($CDCl_3$) δ 179.4, 177.8, 163.0, 152.2, 135.2, 130.4, 129.9, 129.8, 128.5, 127.4, 115.4, 52.0, 42.1, 40.7, 38.2, 37.9, 35.5, 30.9, 29.2, 24.9, 19.0; EI-MS m/z 408 (M^+, 100); EI-HRMS calcd for $C_{23}H_{24}N_2O_3S$ 408.1508, found 408.1504. Compound **15b**: a yellow oil; IR (film) 3055, 1693, 1632, 1431 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.39 (5H, m), 5.39 (1H, d, J=2.4 Hz), 4.62 (1H, dd, J=13.8, 5.4 Hz), 3.81 (1H, dd, J=13.8, 12.6 Hz), 3.68–3.60 (1H, m), 3.15–3.05 (2H, m), 2.91 (3H, s), 2.63–2.45 (4H, m), 2.31–2.19 (3H, m), 1.71 (3H, s); ^{13}C NMR ($CDCl_3$) δ 179.5, 177.5, 163.5, 152.2, 135.3, 129.9 (×2), 128.6, 128.3, 128.1, 116.3, 53.2, 42.0, 39.9, 37.7, 36.0, 35.9, 30.7, 30.6, 25.0, 19.2; EI-MS m/z 408 (M^+, 43); EI-HRMS calcd for $C_{23}H_{24}N_2O_3S$ 408.1508, found 408.1506.

*4.1.23. 2-Phenyl-9-(phenylthio)-3a,4,6,10,10a,11,11a,11b-octahydro-2,6a-diaza-cyclopenta[a]anthracene-1,3,7-trione (**16**).* A mixture of compound **10a** (58 mg, 0.20 mmol) and *N*-phenylmaleimide (106 mg, 0.60 mmol) in degassed toluene (3 mL) was heated at 80 °C for 13 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **16a** and **16b** (61 mg, 65%; 78:22 by ^1H NMR) as a light yellow solid: mp 97–99 °C; IR (film) 3062, 1705, 1631, 1583, 1380, 1185 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40–7.35 (8H, m), 7.20–7.14 (2H, m), 5.84 (1H, d, J=6.9 Hz), 5.35 (1H, d, J=1.4 Hz), 4.74 (0.22H, d, J=15.9 Hz), 4.60 (0.78H, d, J=15.0 Hz), 4.08–3.98 (1H, m), 3.67 (1H, d, J=15.6 Hz), 3.33–3.25 (2H, m), 2.85 (1H, dd, J=7.5, 15.6 Hz), 2.79–2.58 (3H, m), 2.28–2.21 (2H, m), 2.09–1.91 (1H, m); FAB-MS m/z 457 (M^++H, 53); FAB-HRMS calcd for $C_{27}H_{25}N_2SO_3$ 457.1586, found 457.1590. Compound **16a**: ^{13}C NMR ($CDCl_3$) δ 178.4, 176.9, 163.0, 152.6, 136.7, 135.3, 131.8, 130.0, 129.9, 129.3, 128.8, 128.5, 126.5, 121.6, 115.7, 51.0, 43.1, 41.7, 40.0, 34.5, 30.7, 28.6, 24.1.

*4.1.24. 2-Methyl-9-(phenylthio)-3a,4,6,10,10a,11,11a,11b-octahydro-2,6a-diaza-cyclopenta[a]anthracene-1,3,7-trione (**17**).* A mixture of compound **10a** (62 mg, 0.22 mmol) and *N*-methylmaleimide (73 mg, 0.66 mmol) in degassed toluene (2 mL) was heated at 80 °C for 13 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **17a** and **17b** (55 mg, 64%; 71:29 by ^1H NMR) as a light yellow solid: mp 95–96 °C; IR (film) 3062, 1694, 1635, 1587, 1432 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.49–7.38 (5H, m), 5.76 (1H, br), 5.34 (1H, d, J=2.1 Hz), 4.69 (0.29H, d, J=15.9 Hz), 4.53 (0.71H, d, J=15.0 Hz), 4.04–3.97 (1H, m), 3.63 (1H, d, J=13.5 Hz), 3.15–3.12 (2H, m), 2.94 (2H, s), 2.92 (1H, s), 2.81–2.67 (2H, m), 2.63–2.55 (2H, m), 2.35–2.12 (2H, m), 2.05–1.92 (1H, m); FAB-MS m/z 395 (M^++H, 76); FAB-HRMS calcd for $C_{22}H_{23}N_2SO_3$ 395.1429, found 395.1433. The mixture of **17a** and **17b** was recrystallized from CH_2Cl_2/hexanes to give some pure compound **17a**: ^1H NMR ($CDCl_3$) δ 7.50–7.40 (5H, m), 5.75 (1H, br), 5.33 (1H, d, J=2.1 Hz), 4.53 (1H, d, J=15.0 Hz), 4.05–3.98 (1H, m), 3.63 (1H, d, J=15 Hz), 3.15–3.13 (2H, m), 2.95 (3H, s), 2.81–2.71 (2H, m), 2.68–2.58 (2H, m), 2.23 (1H, dd, J=4.5, 16.5 Hz), 2.17–2.12 (1H, m), 1.76 (1H, dt, J=4.5, 14.4 Hz); ^{13}C NMR ($CDCl_3$) δ 179.4, 177.9, 163.0, 152.4, 136.6, 135.3, 130.0, 129.9, 128.7, 121.5, 115.8, 51.0, 43.0, 41.7, 39.9, 34.6, 30.6, 28.7, 25.1, 23.8.

*4.1.25. 5-Ethyl-2-phenyl-9-(phenylthio)-3a,4,6,10,10a,11,11a,11b-octahydro-2,6a-diaza-cyclopenta[a]anthracene-1,3,7-trione (**18**).* A mixture of compound **10b** (112 mg, 0.37 mmol) and *N*-phenylmaleimide (196 mg, 1.11 mmol) in degassed toluene (5 mL) was heated at 80 °C for 13 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **18a** and **18b** (123 mg, 69%; 80:20 by ^1H NMR) as a light yellow solid: mp 137–139 °C; IR (film) 3062, 1708, 1635, 1587, 1384, 1185 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43–7.35 (8H, m), 7.17–7.09 (2H, m), 5.36 (1H, d, J=2.1 Hz), 5.11 (0.2H, d, J=15.9 Hz), 5.00 (0.8H, d, J=15 Hz), 4.11–4.04 (1H, m), 3.42 (1H, d, J=15 Hz), 3.32–3.19 (2H, m), 2.78–2.57 (4H, m), 2.35–2.21 (2H, m), 2.04–1.94 (1H, m), 1.81 (3H, s); FAB-MS m/z 471 (M^++H, 98); FAB-HRMS calcd for $C_{28}H_{27}N_2SO_3$ 471.1742, found 471.1736. The mixture of **18a** and **18b** was recrystallized from CH_2Cl_2/hexanes to give some pure compound **18a**: ^1H NMR ($CDCl_3$) δ 7.50–7.36 (8H, m), 7.17–7.14 (2H, m), 5.36 (1H, d, J=2.1 Hz), 5.00 (1H, d, J=15.3 Hz), 4.10–4.06 (1H, m), 3.42 (1H, d, J=15.3 Hz), 3.32–3.20 (2H, m), 2.79–2.58 (4H, m), 2.34–2.21 (2H, m), 2.03–1.96 (1H, m), 1.80 (3H, s); ^{13}C NMR ($CDCl_3$) δ 178.4, 177.1, 163.0, 152.5, 135.3, 131.9, 130.0, 129.9, 129.4, 129.3, 128.8, 128.6, 128.0, 126.5, 115.8, 50.8, 43.7, 40.1, 37.6, 34.3, 31.6, 30.8, 28.8, 19.3.

*4.1.26. 2,5-Dimethyl-9-(phenylthio)-3a,4,6,10,10a,11,11a,11b-octahydro-2,6a-diaza-cyclopenta[a]anthracene-1,3,7-trione (**19**).* A mixture of compound **10b** (60 mg, 0.20 mmol) and *N*-methylmaleimide (67 mg, 0.60 mmol) in degassed toluene (3 mL) was heated at 80 °C for 13 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **19a** and **19b** (56 mg, 68%; 75:25 by ^1H NMR) as a light yellow solid: mp 157–159 °C; IR (film) 3055, 1697, 1635, 1587, 1432 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50–7.38 (5H, m), 5.34 (1H, d, J=1.2 Hz), 5.03 (0.25H, d, J=15.9 Hz), 4.88 (0.75H, d, J=15.3 Hz), 4.10–4.02 (1H, m), 3.41 (1H, d, J=15.3 Hz), 3.11–3.02 (2H, m), 2.93 (2.3H, s), 2.91 (0.8H, s), 2.74–2.54 (4H, m), 2.26–2.18 (2H, m), 1.97–1.89 (1H, m), 1.80–1.73 (4H, m); FAB-MS m/z 409 (M^++H, 100); FAB-HRMS calcd for $C_{23}H_{25}N_2SO_3$ 409.1586, found 409.1579. Compound **19a**: ^{13}C NMR ($CDCl_3$) δ 179.3, 178.0, 163.0, 152.4, 135.3, 129.9, 129.8, 129.1, 128.6, 127.7, 115.8, 50.7, 43.3, 39.9, 37.4, 34.4, 31.2, 30.3, 28.8, 25.1, 19.3.

*4.1.27. exo-trans-6-Methyl-4a-(phenylsulfonyl)-10-(phenylthio)-2-tosyl-3,4,4a,5,7,11,11a,12,12a,12b-decahydro-2,7a-diaza-cyclohexa[a]anthracene-1,8-dione (**21**).* A mixture of compound **10b** (40 mg, 0.13 mmol) and compound **20** (158 mg, 0.40 mmol) in degassed toluene (2 mL) was heated at 160 °C for 48 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give compound **21** (43 mg, 47% yield) as a white solid: mp 242–244 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3062, 1697, 1642, 1590, 1358, 1144 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00 (2H, d, J=8.2 Hz), 7.79–7.55 (5H, m), 7.52–7.40 (5H, m), 7.36 (2H, d, J=8.2 Hz), 5.29 (1H, d, J=2.4 Hz), 4.89 (1H, d, J=17.1 Hz), 4.36–4.31 (1H, m), 4.20–4.10 (1H, m), 3.84–3.78 (1H, m), 3.41 (1H, d, J=17.1 Hz), 2.66–2.54 (2H, m), 2.45 (3H, s), 2.41–2.26 (4H, m), 2.17 (1H, dd, J=4.5, 17.1 Hz), 2.00–1.94 (2H, m), 1.71–1.64 (1H, m), 1.55 (3H, s); ^{13}C NMR ($CDCl_3$) δ 170.5, 164.3, 153.7, 144.8, 135.6, 135.5, 134.7, 134.2, 130.7, 130.1, 130.0 (x2), 129.4, 128.9, 128.4, 124.0, 121.6, 114.8, 64.2, 50.8, 47.0, 44.4, 39.8, 36.5, 34.9, 34.4, 31.8, 23.7, 21.9, 18.2; FAB-MS m/z 689 (M^++H, 100); FAB-HRMS calcd for $C_{36}H_{37}N_2S_3O_6$ 689.1814, found 689.1819.

*4.1.28. 2-(Phenylthio)-7-vinyl-1,6,9,9a-tetrahydroquinolizin-4-N-tosyl-imine (**22a**).* A mixture of compound **9a** (84 mg, 0.31 mmol) and PTSI (0.18 mL, 1.24 mmol) in toluene (1.5 mL) was heated in a sealed tube at 120 °C for 6 h. After cooling in an ice bath, 5% aq NaOH was slowly added to decompose the excess PTSI. The reaction mixture was extracted with ethyl acetate (50 mL×3), and the organic solution was washed with 5% aq NaOH (30 mL×3). The solvent was removed under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluent

to give compound **22a** (54 mg, 40%) as a light yellow solid: mp 144–146 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3062, 1734, 1601, 1502, 1461, 1439 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55–7.51 (5H, m), 7.48 (2H, d, J=8.1 Hz), 7.11 (2H, d, J=8.1 Hz), 6.44 (1H, s), 6.25 (1H, dd, J=11.1, 17.8 Hz), 5.77 (1H, d, J=5.1 Hz), 5.13 (1H, d, J=17.8 Hz), 5.02 (1H, d, J=11.1 Hz), 4.88 (1H, d, J=17.9 Hz), 3.83 (1H, d, J=17.9 Hz), 3.75–3.68 (1H, m), 2.76 (1H, dd, J=6.6, 17.1 Hz), 2.49–2.34 (2H, m), 2.36 (3H, s), 2.18 (1H, dt, J=17.7, 4.8 Hz); ^{13}C NMR ($CDCl_3$) δ 157.4, 152.9, 141.6, 141.1, 135.9, 135.3, 133.8, 130.4, 130.1, 129.0, 127.5, 126.3, 124.6, 112.7, 109.9, 51.5, 44.5, 33.2, 31.1, 21.5; FAB-MS m/z 437 (M^++H, 67); FAB-HRMS calcd for $C_{24}H_{25}N_2S_2O_2$ 437.1357, found 437.1367.

*4.1.29. 7-Isopropenyl-2-(phenylthio)-1,6,9,9a-tetrahydroquinolizin-4-N-tosyl-imine (**22b**).* Using a similar condition as for compound **22a**, product **22b** (79 mg, 48% yield) was obtained as a yellow solid: mp 143–145 °C (recryst from CH_2Cl_2/hexanes); IR (film) 3062, 1730, 1601, 1505, 1461, 1439 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.55–7.52 (5H, m), 7.48 (2H, d, J=8.1 Hz), 7.11 (2H, d, J=8.1 Hz), 6.45 (1H, s), 5.86 (1H, d, J=4.8 Hz), 4.98–4.92 (3H, m), 3.87 (1H, d, J=17.7 Hz), 3.74–3.67 (1H, m), 2.77 (1H, dd, J=6.9, 17.4 Hz), 2.51–2.33 (2H, m), 2.36 (3H, s), 2.19 (1H, dt, J=17.1, 4.5 Hz), 1.87 (3H, s); ^{13}C NMR ($CDCl_3$) δ 157.3, 152.7, 141.5, 141.2, 140.1, 135.3, 135.0, 130.4, 130.1, 129.0, 127.6, 126.3, 120.8, 111.8, 110.0, 51.3, 45.5, 33.1, 31.1, 21.5, 20.6; FAB-MS m/z 451 (M^++H, 83); FAB-HRMS calcd for $C_{25}H_{27}N_2S_2O_2$ 451.1514, found 451.1522. Anal. Calcd for $C_{25}H_{26}N_2S_2O_2$: C, 66.63; H, 5.82; N, 6.22. Found: C, 66.39; H, 5.51; N, 6.24.

*4.1.30. (E)-4-Methyl-N-(2-(phenylthio)-8-(prop-1-en-2-yl)-1H-quinolizin-4(6H,9H,9aH)-ylidene)benzenesulfonamide (**23**).* A mixture of compound **6a** (100 mg, 0.34 mmol) and PTSI (0.21 mL, 1.36 mmol) in degassed toluene (3 mL) was heated in a sealed tube at 160 °C for 3 h. The solvent was removed under vacuum, and the residue was purified by flash chromatography using ethyl acetate/hexanes (1:3) as eluent to give compound **23** (81 mg, 53%) as a yellow liquid: IR (film) 3048, 1604, 1507, 1462, 1435 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–7.50 (5H, m), 7.46 (2H, d, J=8.1 Hz), 7.12 (2H, d, J=8.1 Hz), 6.42 (1H, s), 5.76 (1H, d, J=1.2 Hz), 4.95 (2H, s), 4.71 (1H, br d, J=20.1 Hz), 3.88 (1H, br d, J=20.1 Hz), 3.77–3.72 (1H, m), 2.74 (1H, dd, J=17.1, 6.3 Hz), 2.52–2.46 (1H, m), 2.42–2.39 (2H, m), 2.37 (3H, s), 1.89 (3H, s); ^{13}C NMR ($CDCl_3$) δ 157.4, 153.4, 141.6, 141.5, 141.1, 135.4, 134.3, 130.5, 130.1, 129.0, 127.5, 126.4, 120.3, 111.8, 109.8, 51.4, 45.3, 33.8, 31.6, 21.5, 20.2; FAB-MS m/z 451 (M^++H, 100); FAB-HRMS calcd for $C_{25}H_{26}N_2O_2S_2$ 450.1436, found 450.1428.

*4.1.31. endo-trans-(E)-4-Methyl-N-(5-methyl-1,3-dioxo-2-phenyl-8-(phenylthio)-1,2,3,3a,4,6a,7,12,12a,12b-decahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinolin-10(6H)-ylidene)benzenesulfonamide (**24a**) and endo-cis-(E)-4-methyl-N-(5-methyl-1,3-dioxo-2-phenyl-8-(phenylthio)-1,2,3,3a,4,6a,7,12,12a,12b-decahydropyrido[1,2-b]pyrrolo[3,4-h]isoquinolin-10(6H)-ylidene)benzenesulfonamide (**24b**).* A mixture of compound **23** (30 mg, 0.07 mmol) and *N*-phenylmaleimide (35 mg, 0.21 mmol) in degassed toluene (2.5 mL) was heated in a sealed tube at 160 °C for 4 h. The solvent was removed under vacuum, and the crude product was purified by flash chromatography using ethyl acetate/hexanes (1:1) as eluent to give a mixture of compounds **24a** and **24b** (34 mg, 82%; 59:41 by ^1H NMR) as a yellow oil. With repeated separation by flash chromatography, pure samples of **24a** and **24b** were obtained. Compound **24a**: a yellow oil; IR (film) 3057, 1707, 1599, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.51–7.35 (10H, m), 7.13–7.09 (4H, m), 6.24 (1H, d, J=1.8 Hz), 4.95 (1H, dd, J=13.8, 6.0 Hz), 3.97–3.91 (1H, m), 3.81 (1H, t, J=12.0 Hz), 3.34–3.25 (2H, m), 2.70 (1H, dd, J=15.6, 1.2 Hz), 2.64–2.43 (4H, dd, J=13.8, 6.0 Hz), 2.39–2.32 (4H, m), 2.23 (1H, dd, J=16.8, 4.8 Hz), 1.77 (3H, s); ^{13}C NMR ($CDCl_3$) δ 178.4, 176.8, 157.2, 154.8, 141.6, 141.1, 135.4, 131.8, 131.4, 130.5, 130.1, 129.3, 129.1, 128.8, 127.6, 126.8, 126.5, 126.4, 110.1, 52.3, 42.1, 40.9 (×2), 37.8, 34.8, 31.6, 29.0, 21.5, 19.0; FAB-MS m/z 624 (M^++H, 33); FAB-HRMS calcd for $C_{35}H_{33}N_3O_4S_2$ 623.1912, found 623.1907. Compound **24b**: a yellow oil; IR (film) 3063, 1707, 1599, 1499 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.48–7.35 (10H, m), 7.15–7.09 (4H, m), 6.46 (1H, d, J=2.4 Hz), 4.98 (1H, dd, J=14.4, 5.4 Hz), 3.95 (1H, t, J=13.2 Hz), 3.62–3.53 (1H, m), 3.32–3.25 (2H, m), 2.73–2.68 (1H, m), 2.64–2.55 (2H, m), 2.51–2.45 (1H, m), 2.37–2.33 (4H, m), 2.31 (1H, s), 2.23 (1H, dd, J=16.5, 3.9 Hz), 1.77 (3H, s); ^{13}C NMR ($CDCl_3$) δ 178.4, 176.5, 157.7, 154.6, 141.6, 141.1, 135.3, 131.8, 130.5, 130.1, 129.2, 129.0, 128.8, 128.6, 127.8, 127.6, 126.5, 126.4, 110.7, 53.5, 42.0, 40.2, 39.9, 35.8, 35.2, 31.3, 30.2, 21.5, 19.1; FAB-MS m/z 624 (M^++H, 20); FAB-HRMS calcd for $C_{35}H_{33}N_3O_4S_2$ 623.1912, found 623.1914.

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Supplementary data

^1H and ^{13}C NMR spectra for all compounds reported in this article. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2011.04.106.

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