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Domino Reactions of Bis-Diazo Compounds: Rhodium(II) Acetate Catalyzed Diastereoselective Synthesis of Epoxy- and Epithio-Bridged Heterocycle-Fused Quinolizinone Analogues

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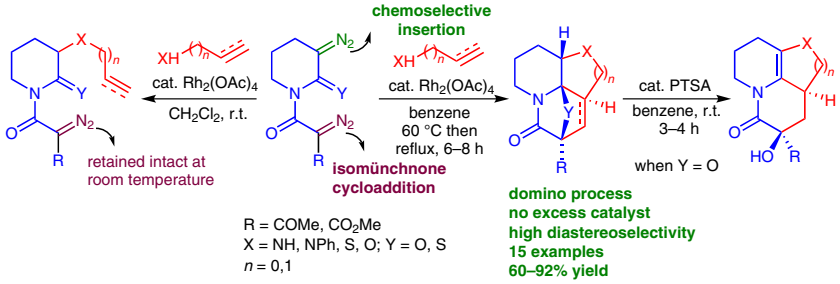

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Abstract Rhodium(II) acetate catalyzed domino reactions of bis-diazo compounds afford epoxy- and epithio-bridged heterocycle-fused quinolizinone systems in a stereoselective manner. The presence of an acceptor diazo functionality leads to a selective intermolecular X–H insertion reaction in a chemoselective manner, and the acceptor/acceptor diazo functionality subsequently participates in the formation of isomünchnone/thioisomünchnone 1,3-dipoles followed by intramolecular cycloaddition in a diastereoselective manner. This domino reaction is capable of constructing epoxy- and epithio-bridged heterocycle-fused quinolizinone ring systems with four stereogenic centers. The Brønsted acid induced reactions of oxa-bridged tricyclic compounds furnish ring-opened alcohol products in a regioselective manner.

Key words bis-diazo compounds, domino reactions, diastereoselectivity, X–H insertion, isomünchnones, rhodium(II) acetate

The construction of fused heterocycles through selective multiple-bond formation in a single synthetic step is of particular interest in organic synthesis. Quinolizines constitute a significant part of heterocyclic chemistry due to their biological properties and their presence as structural features of numerous alkaloids and drug candidates.[1] For example, quinolizine-fused carbo- and heterocyclic systems such as allomatridine,[1g,h] frog alkaloid (–)-205B,[1a] lycopodine,[1d] hydrojulolidine,[1e] and indoloquinolizine[1f] (Figure 1) are existing alkaloids having potent biological activities with utility of the lycopodine family of alkaloids in Chinese folk medicine for the treatment of skin disorders.[1d] The synthetic utilization of diazocarbonyl compounds has been demonstrated to explore an array of reactions[2] such as cyclopropanation, C–H insertion, heteroatom–H insertion and ylide formation toward the synthesis of a wide range of polycyclic systems and natural products. The multifarious transformations of carbonyl ylides derived from diazocarbonyl compounds catalyzed by transition metals have received significant attention.[3] The chemistry of such interesting mesoionic oxazolium ylides (isomünchnones) and their cycloaddition reactions with various dipolarophiles or trapping with different nucleophiles to achieve a variety of heterocycles have been documented.[4] Other interesting '*masked*' thiocarbonyl ylides (thioisomünchnones), generated from thioamides, undergo 1,3-dipolar cycloaddition reactions.[5] The decomposition of diazo compounds bearing a sulfur atom requires higher temperature because the metal catalyst activity is generally poisoned by sulfur.[6]

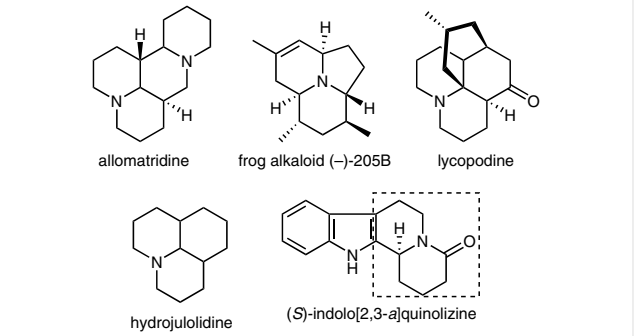
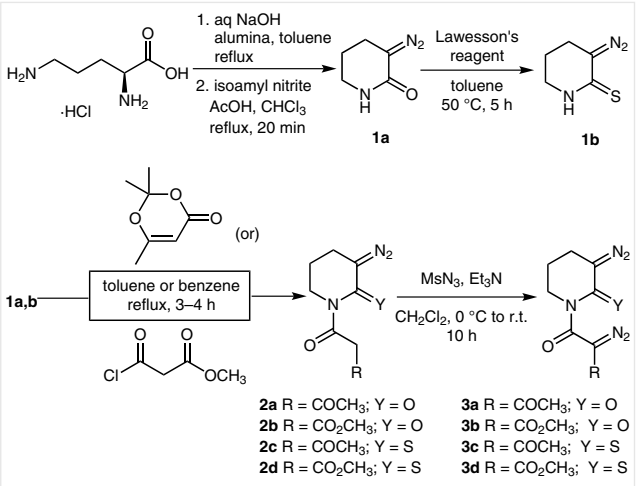


Figure 1 Examples of fused quinolizine alkaloids

However, the synthetic applications of bis-diazocarbonyl compounds are scarce, with reported methods utilizing photolysis, thermolysis, ring contraction and metal catalysis.[7] Taking advantage of our interest in the chemistry of bis-diazocarbonyl compounds,[7f–h] we herein report the domino reactions of acceptor (A) and acceptor/acceptor (A/A) substituted bis-diazo compounds in the presence of rhodium(II) acetate for the construction of a range of epoxy- and epithio-bridged heterocycle-fused quinolizinone systems having different ring sizes. The reactions proceed

via X–H insertion/dipolar cycloaddition of isomünchnones and thioisomünchnones in a regio-, chemo- and diastereoselective manner.

In continuation of our earlier work[7f–h] on bis-diazocarbonyl compounds, we were motivated to investigate the domino reactions of differently substituted bis-diazo compounds **3** (Scheme 1). The required starting material, diazo compound **1a**, was synthesized[8] from L-ornithine monohydrochloride. Thionation of the carbonyl group of **1a** was carried out using Lawesson's reagent to furnish **1b**. The bis-diazo compounds were obtained quite conveniently by acylation of **1a**,**b** with 2,2,6-trimethyl-1,3-dioxin-4(*H*)-one or methylmalonyl chloride in dry toluene under reflux conditions. The second diazo functionality was introduced at the active methylene group, with or without isolating the acylated product, to furnish the bis-diazo compounds **3a**–**d** (Scheme 1). The various bifunctional reaction partners used for the insertion/cycloaddition study are shown in Figure 2.



Scheme 1 Synthesis of the mono- and bis-diazo compounds

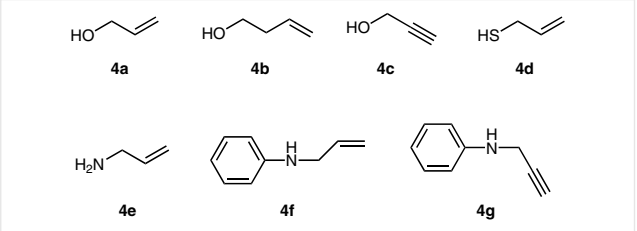
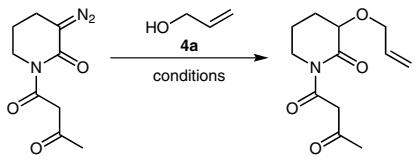


Figure 2 Various bifunctional reaction partners for the study

To study the reactions of the bis-diazocarbonyl compounds, it was necessary to develop mild reaction conditions in order to prevent uncontrolled thermal decomposition of the diazo functionalities. We began our study with N-substituted mono-diazo compound **2a** in order to optimize the insertion reaction conditions and to ascertain the chemical behavior of the acceptor diazo functionality with a bifunctional reaction partner in order to avoid the potential interference of the second A/A diazo functionality present in bis-diazo compounds **3**. Prior to assessing the reactivity of bis-diazo compound **3**, compound **2a** was initially utilized for the insertion reactions. Thus, diazo compound **2a** was allowed to react with allyl alcohol **4a** under mild reaction conditions with a range of catalysts at different temperatures. As diazo compounds are known to be potentially explosive, and so as to ensure the complete conversion, the reaction was performed by adding N-substituted diazo compound **2a** to allyl alcohol **4a** over a period of 30 minutes (flow rate of 0.1 mL/min via a syringe pump) in the presence of $Cu(OTf)_2$ at room temperature to furnish the corresponding product **5a** in 21% yield (Table 1, entry 1). Under similar conditions, the reaction catalyzed by $Cu(acac)_2$ gave a yield of only 17% (Table 1, entry 2). As the O–H insertion reaction of α-diazocarbonyl compounds was feasible using mild Lewis acids,[9] the reaction of diazo compound **2a** with **4a** was performed in the presence $In(OTf)_3$ to afford the desired product in 34% yield (Table 1, entry 3). However, the reaction using $InCl_3$ as the catalyst failed to give the insertion product, even after 12 hours (Table 1, entry 4). The reaction of **2a** and allyl alcohol **4a** under similar conditions using $Rh_2(OAc)_4$ as the catalyst afforded the insertion product **5a** in 76% yield (Table 1, entry 5). The product was obtained in 54% yield when dichloroethane was used as the solvent (Table 1, entry 6). The insertion reaction was preferred in benzene, as it was found to be a more suitable solvent than dichloromethane for the dipole formation/cycloaddition reactions in the second step. Thus, diazo compound **2a** was added slowly with the insertion partner, allyl alcohol **4a**, in the presence of $Rh_2(OAc)_4$ at 25 °C to furnish the product **5a** in 46% yield (Table 1, entry 7), when the reaction was carried out in benzene. Next, the reaction was repeated at 60 °C to furnish product **5a** in 72% yield (Table 1, entry 8).

A similar reaction was performed in dichloroethane to furnish the product in 51% yield (Table 1, entry 9). To our delight, the insertion reaction of N-substituted diazo compound **2a** with allyl alcohol **4a** in the presence of $Rh_2(OAc)_4$ at 60 °C in benzene proved to be suitable conditions for the insertion reactions as they could be used for further transformations. Under these reaction conditions, other insertion partners were reacted with the appropriate diazo compounds yielding the corresponding products **5b**–**e** in good yields via O–H or S–H insertion reactions (Scheme 2). It was observed that the unsubstituted diazo compound **1** afforded the corresponding insertion products **5c**–**e** in lower yields; this might be due to the relatively poor solubility of **1** in benzene. It should be noted that S–H, N–H insertion reactions are generally less studied due to a reduction[6b,10] in

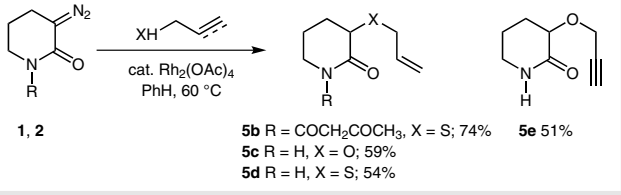
Table 1 Insertion Reactions[a] of Diazo Compound **2a**



Entry	Catalyst	Solvent	Temp (°C)	Time (h)	Yield (%)[c]
1	$Cu(OTf)_2$	CH_2Cl_2	25	4	21
2	$Cu(acac)_2$	CH_2Cl_2	25	4	17
3	$In(OTf)_3$[b]	CH_2Cl_2	25	4	34
4	$InCl_3$[b]	CH_2Cl_2	25	12	–
5	$Rh_2(OAc)_4$	CH_2Cl_2	25	3	76
6	$Rh_2(OAc)_4$	DCE	25	3	54
7	$Rh_2(OAc)_4$	benzene	25	3	46
8	$Rh_2(OAc)_4$	benzene	60	2	72
9	$Rh_2(OAc)_4$	DCE	60	3	51

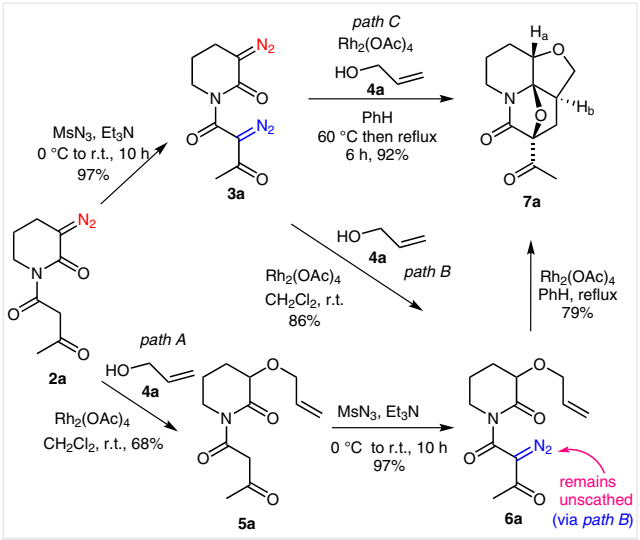
[a] *Reaction conditions*: slow addition of **2a** (0.42 mmol, 0.1 mL/min), **4a** (0.42 mmol), catalyst (1 mol% of copper or rhodium catalyst), solvent (3 mL).
[b] 10 mol% of the indium catalyst was used.
[c] Yield of isolated product.

the activity of the rhodium catalyst, and there was no formation of the corresponding cyclopropane[11] derivative with olefinic alcohols **4**.



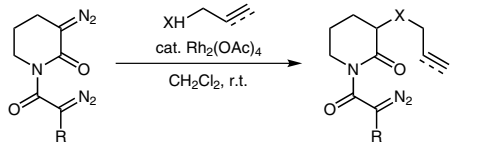
Scheme 2 Survey of bifunctional reaction partners

In continuation of the above insertion reactions of diazo compounds **1** and **2**, our ultimate aim was to develop a process utilizing bis-diazo compounds **3** in the presence of $Rh_2(OAc)_4$ as the catalyst, avoiding the isolation of any intermediates. Hence, the possibility of subsequent ylide-forming reactions was explored. Reaction of the N-substituted mono-diazo compound **2a** with **4a** in the presence of $Rh_2(OAc)_4$ afforded the corresponding product **5a** (Table 1 and Scheme 3, path A). To continue the sequence, the second A/A diazo functionality was introduced by subjecting compound **5a** to the diazo transfer reaction using MsN_3/Et_3N. The presence of a diazo functionality in **6a** was confirmed based on the characteristic peak at 2137 cm^{-1} in the IR spectrum. Utilizing compound **6a** for possible 1,3-dipole formation, the reaction in the presence of $Rh_2(OAc)_4$ was performed to afford the epoxy-bridged furan-fused quinolizinone system **7a** in 79% yield. Alternatively, bis-diazo compound **3a**, synthesized from compound **2a** using MsN_3/Et_3N, was subjected to an insertion reaction with allyl alcohol **4a** in CH_2Cl_2 at room temperature catalyzed by $Rh_2(OAc)_4$ to afford the clean O–H insertion product **6a** in 86% yield (Scheme 3, path B). Interestingly, the IR spectrum of compound **6a** confirmed the presence of a second diazo group without any decomposition. Next, it was intended to investigate the chemical behavior of the second diazo group for the formation of isomünchnone dipoles toward synthetic applications. In order to utilize the chemistry of the second diazo functionality, the reaction of **6a** in the presence of $Rh_2(OAc)_4$ as the catalyst was performed in benzene at reflux temperature. Based on the TLC analysis, the reaction mixture was concentrated and purified by column chromatography to afford product **7a** in 79% yield (Scheme 3). The ^1H NMR spectrum of compound **7a** exhibited two multiplets for H_a and H_b in the range of 3.67–3.61 ppm and 3.49–3.44 ppm, respectively. The high-resolution mass spectrum showed the required molecular ion peak.



Scheme 3 Stepwise and one-pot insertion/cycloaddition sequences

Other insertion reactions of bis-diazo compounds **3a**,**b** with bifunctional partners **4c**,**d** were carried out to furnish the corresponding products **6b**–**f** (Scheme 4). Following the stepwise reaction of compound **3a**, bis-diazo compound **3b** was reacted with allyl alcohol **4a** to give product **6b** in 64% yield. The insertion product **6c** was obtained in 89% yield when bis-diazo compound **3a** was reacted with propargyl alcohol (**4c**). Similarly, propargyl alcohol (**4c**) and bis-diazo compound **3b** underwent the insertion reaction to yield product **6d**. The insertion product **6e** was obtained from the reaction of **3a** with **4d**. In addition, the reaction of bis-diazo compound **3b** and allyl mercaptan (**4d**) yielded the insertion product **6f**.

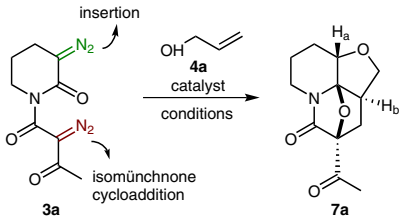


Scheme 4 Insertion reactions of other bifunctional partners with bis-diazo compounds

The successful O–H insertion reaction of an acceptor carbenoid followed by 1,3-dipolar cycloaddition reactions of an acceptor/acceptor carbenoid prompted us to investigate the domino reaction of bis-diazo compounds **3**. Thus, we next planned to test the feasibility of the one-pot reaction of **3a** with allyl alcohol **4a** by coupling both the above reaction processes. Hence, the reaction of bis-diazo compound **3a** and allyl alcohol **4a** in the presence of $Rh_2(OAc)_4$ in anhydrous benzene, initially at 60 °C and then at reflux temperature, until complete conversion of the starting material furnished product **7a** in 92% yield (Scheme 3, path C). The lower yield obtained in the stepwise reaction may be due to the involvement of the isolation of two compounds, **5a** and **6a**. The optimization of the intermolecular X–H insertion and the subsequent intramolecular cycloaddition reactions of bis-diazo compound **3a** and bifunctional partner **4a** was carried out with various metal catalysts and the obtained results are summarized in Table 2. The use of ruthenium-based catalysts, effective in cyclopropanation and ylide formation,[12] failed to yield the desired product (Table 2, entries 11 and 12).

Under the above optimized conditions, the reaction of bis-diazo compound **3b** with chosen partner **4a** furnished the epoxy-bridged furan-fused quinolizinone **7b** in 83% yield via O–H insertion followed by isomünchnone cycloaddition. The reaction of **3a** with propargyl alcohol (**4c**) yielded the expected furan-fused quinolizinone **7c**, having a double bond, in 67% yield. Subsequently, bis-diazo compound **3b** was reacted with propargyl alcohol (**4c**) to yield 62% of product **7d**. The reaction of homoallyl alcohol **4b** and bis-diazo compound **3a** afforded the epoxy-bridged pyran-fused quinolizinone **7e** in 73% yield. Having successfully demonstrated the domino reaction of O–H insertion and isomünchnone cycloaddition, it was next planned to exploit the N–H and S–H insertion and cycloaddition reactions using bifunctional reaction partners for this synthetic study. Thus, reaction of **3a** with *N*-allylaniline (**4f**) afforded the desired pyrrolidine-fused quinolizinone **7f** in 85% yield. The reaction of *N*-propargyl aniline (**4g**) with bis-diazo compound **3a** yielded the expected product **7g** in 60% yield. Next, the reaction of allyl mercaptan (**4d**) with **3a** was performed using the optimized conditions to afford epoxy-bridged tetrahydrothiophene-fused quinolizinone **7h** in 76% yield. Similar reaction conditions were employed for the reaction of **3b** and allyl mercaptan (**4d**), which afforded the product **7i** in 70% yield (Scheme 5).

Table 2 Optimization of the Reaction Conditions[a]



Entry	Catalyst[b]	Solvent	Time (h)	Yield (%)[c]
1[d]	$Cu(OTf)_2$	CH_2Cl_2	14	13
2[d]	$CuCl_2$	CH_2Cl_2	24	–
3[d]	$Cu(acac)_2$	CH_2Cl_2	11	trace
4	$Cu(OTf)_2$	DCE	10	21
5	$Cu(OAc)_2$	DCE	36	–
6	$Cu(OTf)_2$	benzene	16	26
7[d]	$Rh_2(OAc)_4$	CH_2Cl_2	12	29
8	$Rh_2(OAc)_4$	DCE	7	53
9	$Rh_2(OAc)_4$	benzene	6	92
10	$Rh_2(CF_3CF_2CO_2)_4$	benzene	7	81
11	$Ru(PPh_3)_3Cl_2$	benzene	24	–
12	$RuCl_3$	benzene	24	–

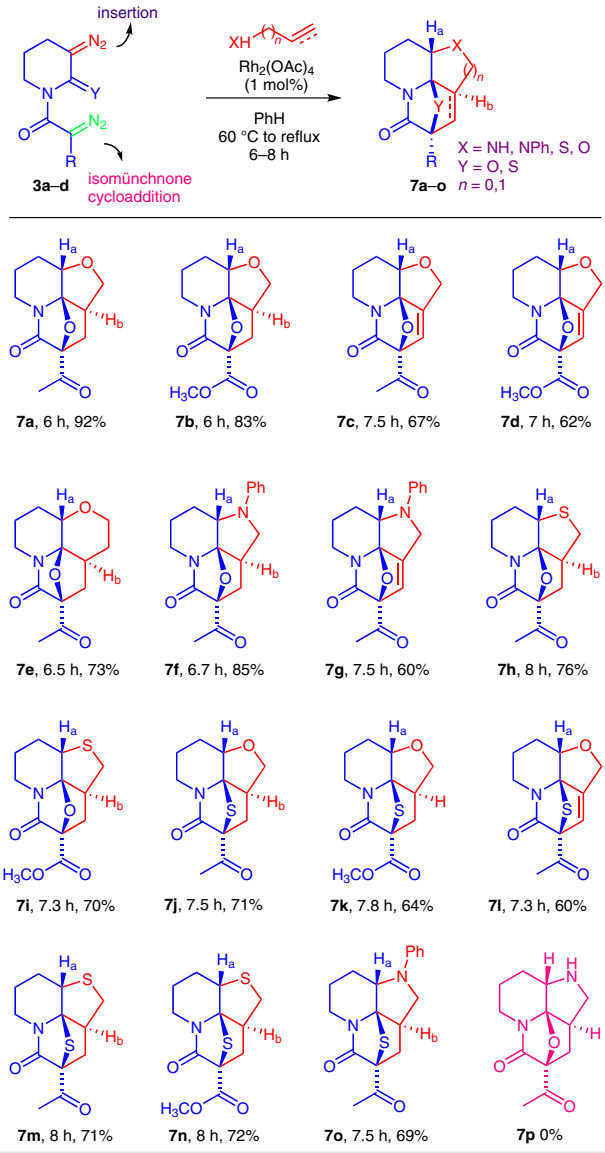
[a] *Reaction conditions*: **3a** (0.42 mmol), **4a** (0.42 mmol), catalyst, solvent (3 mL), 60 °C then reflux.
[b] 1 mol% of copper, rhodium or ruthenium catalyst was used.
[c] Yield of isolated product.
[d] Reflux conditions.

Thioisomünchnones generated from diazothioamides[13] have also proved to be interesting precursors to sulfur-containing heterocyclic compounds. The successful intramolecular 1,3-dipolar cycloaddition reactions of isomünchnones formed in the presence of rhodium(II) acetate as the catalyst motivated us to envisage the tandem process of bis-diazo compounds **3c**,**d** owing to their potential to generate less studied thioisomünchnone dipoles, the reactions of which would result in epithio-bridged heterocyclic compounds. The bis-diazo compound **3c** was subjected to reaction with allyl alcohol **4a** under similar reaction conditions to furnish the epithio-bridged furan-fused quinolizinone system **7j** in 71% yield via an O–H insertion, subsequent thioisomünchnone formation and cycloaddition. Similarly, the bifunctional reaction partner **4a** reacted with the appropriate bis-diazo compound **3d** to give the epithio-bridged heterocyclic system **7k**. The reaction of **3c** with bifunctional propargyl alcohol (**4c**) gave the epithio-bridged product **7l**, having a double bond, in 60% yield. In continuation, the possible S–H or N–H insertion reactions followed

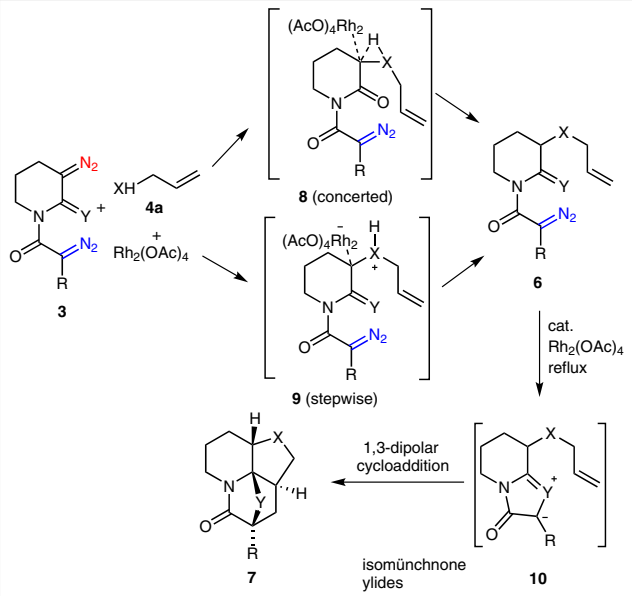
by cycloadditions of bis-diazo compounds were further planned. Toward this goal, the reaction of allyl mercaptan (**4d**) with **3c** furnished epithio-bridged tetrahydrothiophene-fused quinolizinone product **7m**, having two sulfur atoms, in 71% yield (Scheme 5) via S–H insertion, subsequent thioisomünchnone formation and cycloaddition. Similarly, the reaction of **3d** and bifunctional partner **4d** was performed to furnish the corresponding thiophene-fused quinolizinone **7n**, again having two sulfur atoms, in 72% yield.

Toward N–H insertion/cycloaddition reactions, the representative reaction of **3c** with *N*-allylaniline (**4f**) furnished epithio-bridged pyrrole-fused quinolizinone **7o** in 69% yield. However, the use of allylamine (**4e**) did not yield the desired product **7p** (Scheme 5), even with an excess amount of catalyst; instead we observed unidentified products. The structures and stereochemistries of products **7b** and **7h** were determined unequivocally by single-crystal X-ray analysis (Figure 3). The H_a and H_b protons of the epoxy- and epithio-bridged heterocycle-fused quinolizinones **7** are *anti* to each other due to *endo*-cycloaddition during the second step with regard to the tethered pendent dipole. This observation is in full accord with molecular mechanics calculations[14] that indicate that *endo*-products **7b**,**h** are more stable than the corresponding *exo*-isomers. The stereochemistry of the other products was assigned based upon analogy with products **7b**,**h**.

Mechanistically, the rhodium(II) carbenoid derived from bis-diazo compounds **3** undergoes intermolecular insertion into the polar X–H bond of the alcohol, thiol or amine **4** in a concerted or stepwise fashion to give the insertion products **6** in a chemoselective manner. Next, the second diazo functionality present in the same molecule forms the reactive isomünchnone dipoles **10** in the presence of the $Rh_2(OAc)_4$ catalyst in the reaction mixture. Subsequent intramolecular 1,3-dipolar cycloaddition reaction with the tethered pendent olefin unit affords heterocycle-fused quinolizinones **7** with complete diastereoselectivity (Scheme 6).



Scheme 5 Scope of the insertion/cycloaddition reactions of bis-diazo compounds



Scheme 6 Mechanistic pathway for the domino insertion/[3+2] cycloaddition reactions

We were further interested in carrying out the ring-opening reactions of the synthesized tricyclic systems **7** to give hydroxy compounds. To this end, a representative ring-opening reaction of epoxy-bridged furan-fused quinolizinone **7a** in the presence of *p*-toluenesulfonic acid was car-

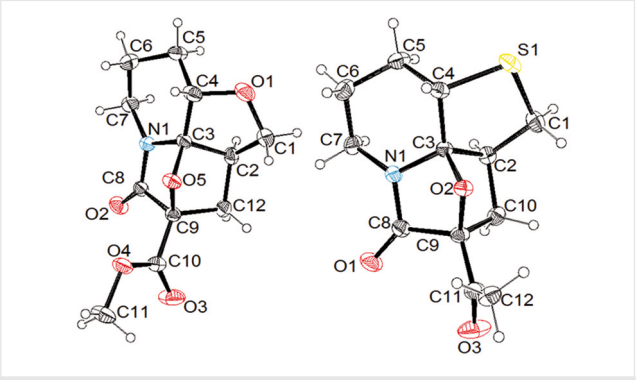
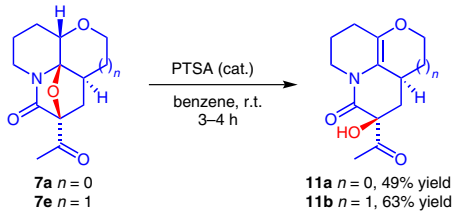


Figure 3 X-ray crystal structures (ORTEP views) of compounds **7b** (left) and **7h** (right)

ried out in benzene at room temperature. Interestingly, the reaction furnished smoothly the furan-fused quinolizinone **11a** in moderate yield and in a regioselective manner. Under similar conditions, the reaction of compound **7e** afforded pyran-fused quinolizinone **11b** in 63% yield (Scheme 7). The ring-opening reaction might occur via initial protonation of the ethereal oxygen by the catalytic acid, followed by cleavage of the C–O bond in a regioselective manner.



Scheme 7 Ring-opening reactions of tricyclic systems **7a**,**e**

In conclusion, the rhodium(II) acetate catalyzed transformations of bis-diazo compounds have been demonstrated to proceed via an intermolecular X–H insertion reaction, without affecting other diazo functionality present in the same molecule, in a chemoselective manner. Subsequently, the dipole formation–cycloaddition reaction furnished the corresponding epoxy- or epithio-bridged heterocycle-fused quinolizinone systems with complete diastereoselectivity via isomünchnone or thioisomünchnone dipoles. In addition, representative ring-opening reactions afforded fused heterocyclic alcohols in a regioselective manner. No excess catalyst was required for these domino reactions of bis-diazo compounds. Further investigation of these interesting bis-diazo compounds is currently in progress in our laboratory and the results will be reported in due course.

All reactions were carried out in oven-dried glassware under an atmosphere of argon. Dry dichloromethane (dried over phosphorus pentoxide) and dry benzene (stored over sodium wire) were freshly prepared for each reaction. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F_{254} silica gel plates and the components of mixtures were made visual by observation under iodine or UV light, or by sulfuric acid charring. Column chromatography was performed on Merck silica gel (100–200 mesh). Melting points were obtained using a Veego VMP-D instrument and are uncorrected. FT-IR spectra were recorded using a Bruker Alpha-T spectrophotometer using the ATR technique. ^{1}H and ^{13}C NMR spectra (400 MHz and 100 MHz, respectively) were obtained using a Bruker Avance 400 spectrometer and are referenced to TMS. Multiplicities are indicated as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), or variants thereof. Coupling constants (*J*) are reported in hertz (Hz). Carbon types were determined from DEPT ^{13}C NMR experiments. Low- and high-resolution mass spectra were determined on Thermofisher LTQ XL and Waters QTof Micromass spectrometers, respectively, using the ESI method. Elemental analyses were determined using a Vario Micro Cube instrument.

3-Diazopiperidine-2-one (1a)[8a]

To a stirred solution of 3-aminopiperidin-2-one (1.6 g, 14.0 mmol) in anhydrous $CHCl_3$ (30 mL) were added dropwise isoamyl nitrite (1.98 g, 16.8 mmol) and glacial AcOH (126 mg, 2.1 mmol) sequentially under an Ar atm. The reaction mixture was then heated at reflux temperature for 20 min, cooled in ice-bath and washed with sat. $NaHCO_3$ solution (10 mL). The organic layer was separated, dried over $MgSO_4$, and the solvent was evaporated under vacuum. The red solid was purified by column chromatography using alumina to give **1a** as an orange solid (1.07 g, 60%).

Mp 117–120 °C.

IR (ATR): 3270, 3181, 3033, 2949, 2879, 2087, 1638, 1480, 1461, 1413, 1293, 1177, 1077, 993 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (br s, 1 H, NH), 2.78 (s, 2 H, NCH_2), 2.76 (t, *J* = 6.7 Hz, 2 H, CH_2), 1.89–1.84 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.2 (C=O), 68.7 (C=N_2), 41.2 (CH_2), 21.8 (CH_2), 20.9 (CH_2).

3-Diazopiperidine-2-thione (1b)

To a stirred solution of 3-diazopiperidin-2-one (**1a**) (1 g, 8.0 mmol) in anhydrous toluene (20 mL) was added Lawesson's reagent (1.6 g, 4 mmol) under an Ar atm. The yellow reaction mixture was heated at 50 °C for 5 h. After completion of the reaction (monitored by TLC), the mixture was concentrated under reduced pressure and the residue purified by flash column chromatography to afford **1b** as a yellow solid (710 mg, 63%).

Mp 124–126 °C.

IR (ATR): 3209, 3124, 3021, 2936, 2281, 2025, 1638, 1472, 1428, 1293, 1119, 1098, 985 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (br s, 1 H, NH), 2.74 (s, 2 H, NCH_2), 2.69 (t, *J* = 6.4 Hz, 2 H, CH_2), 1.87–1.83 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8 (C=O), 69.4 (C=N_2), 41.5 (CH_2), 21.6 (CH_2), 20.5 (CH_2).

MS (ESI): *m*/*z* = 142.0 $[M + H]^+$.

Anal. Calcd for $C_5H_7N_3S$: C, 42.53; H, 5.00; N, 29.76. Found: C, 42.33; H, 5.02; N, 29.79.

1-(3-Diazo-2-oxopiperidin-1-yl)butane-1,3-dione (2a)[8b]

To an oven-dried 25 mL round-bottom flask fitted with a reflux condenser was added a solution of **1a** (300 mg, 2.4 mmol) in anhydrous toluene (15 mL) under an N_2 atm and the mixture was heated to reflux temperature. 2,2,6-Trimethyl-1,3-dioxin-(4*H*)-one (340 mg, 2.4 mmol) was added and the mixture stirred for 3 h. After completion of the reaction as indicated by TLC, the mixture was cooled to r.t. and the solvent was evaporated to dryness. The residue was purified via column chromatography to furnish compound **2a** as a pale yellow oil (410 mg, 81%).

IR (ATR): 3119, 2089, 1711, 1659, 1631, 1374, 1356, 1320, 1251, 1143, 936 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.05 (s, 2 H, OCH_2), 3.69–3.66 (m, 2 H, CH_2), 2.81 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.45 (s, 3 H, CH_3), 2.03–1.97 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.3 (C=O), 169.3 (C=O), 168.9 (C=O), 64.9 ($C=N_2$), 47.8 (CH_2), 44.4 (CH_2), 33.3 (CH_2), 29.9 (CH_3), 21.3 (CH_2).

Methyl 3-(3-Diazo-2-oxopiperidin-1-yl)-3-oxopropanoate (2b)

To a flame-dried 25 mL round-bottom flask fitted with a reflux condenser was added anhydrous benzene (15 mL) followed by **1a** (300 mg, 2.4 mmol). The mixture was heated to reflux temperature and then methylmalonyl chloride (360 mg, 2.6 mmol) was added and the mixture allowed to stir at reflux temperature for 4 h. The mixture was cooled to r.t. and the solvent was removed under vacuum to dryness. The residue was purified via column chromatography to give **2b** as a yellow oil (418 mg, 77%).

IR (ATR): 3111, 2096, 1729, 1692, 1656, 1374, 1341, 1329, 1240, 1136, 928 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.04–4.00 (m, 2 H, CH_2), 3.99–3.90 (m, 2 H, CH_2), 3.65 (s, 3 H, CH_3), 2.83 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.07–1.99 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.1 (C=O), 169.9 (C=O), 169.7 (C=O), 65.7 ($C=N_2$), 51.2 (CH_3), 44.6 (CH_2), 33.5 (CH_2), 29.9 (CH_2), 21.2 (CH_2).

MS (ESI): *m*/*z* = 226.1 $[M + H]^+$.

Anal. Calcd for $C_9H_{11}N_3O_4$: C, 48.00; H, 4.92; N, 18.66. Found: C, 47.85; H, 4.90; N, 18.70.

1-(3-Diazo-2-thioxopiperidin-1-yl)butane-1,3-dione (2c)

The title compound was synthesised using the procedure described for **2a**. Yield: 390 mg (78%); viscous yellow oil.

IR (ATR): 2197, 2103, 1718, 1661, 1627, 1374, 1355, 1342, 1237, 1129, 974 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.07 (s, 2 H, OCH_2), 3.66–3.62 (m, 2 H, CH_2), 2.83 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.37 (s, 3 H, CH_3), 1.99–1.95 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.0 (C=O), 169.6 (NC=O), 167.7 (C=S), 64.9 ($C=N_2$), 47.8 (CH_2), 44.0 (CH_2), 33.7 (CH_2), 30.0 (CH_3), 21.1 (CH_2).

MS (ESI): *m*/*z* = 226.1 $[M + H]^+$.

Anal. Calcd for $C_9H_{11}N_3O_2S$: C, 47.99; H, 4.92; N, 18.65. Found: C, 47.83; H, 4.89; N, 18.68.

Methyl 3-(3-diazo-2-thioxopiperidin-1-yl)-3-oxopropanoate (2d)

The title compound was synthesised using the procedure described for **2b**. Yield: 403 mg (76%); thick, deep-yellow oil.

IR (ATR): 3201, 2089, 1719, 1698, 1686, 1594, 1341, 1327, 1238, 1136, 961 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.11–4.08 (m, 2 H, CH_2), 3.92–3.87 (m, 2 H, CH_2), 3.52 (s, 3 H, CH_3), 2.79 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.09–1.89 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.4 (C=O), 169.3 (NC=O), 168.1 (C=S), 66.2 ($C=N_2$), 51.3 (CH_3), 44.6 (CH_2), 33.8 (CH_2), 29.4 (CH_2), 20.8 (CH_2).

MS (ESI): *m*/*z* = 242.1 $[M + H]^+$.

Anal. Calcd for $C_9H_{11}N_3O_3S$: C, 44.80; H, 4.60; N, 17.42. Found: C, 43.84; H, 4.58; N, 17.44.

2-Diazo-1-(3-diazo-2-oxopiperidin-1-yl)butane-1,3-dione (3a)

To a stirred solution of **2a** (100 mg, 0.47 mmol) in anhydrous CH_2Cl_2 (30 mL) under an Ar atm were added methanesulfonyl azide (MsN_3) (57 mg, 0.47 mmol) and anhydrous Et_3N (52 mg, 0.51 mmol) sequentially via a syringe at 0 °C. The reaction mixture was allowed to stir at r.t. for 10 h. After completion of the reaction (monitored by TLC), the mixture was quenched with ice-cold H_2O, the organic layer was separated and dried over anhydrous Na_2SO_4, and the solvent was evaporated to dryness under vacuum. The crude residue was purified by flash column chromatography to give **3a** as a deep red solid (218 mg, 97%).

Mp 147–149 °C.

IR (ATR): 3178, 2095, 2089, 1726, 1689, 1638, 1385, 1351, 1316, 1269, 1152, 939 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.40–3.33 (m, 2 H, CH_2), 2.43 (s, 3 H, CH_3), 2.16–2.13 (m, 1 H, CH_2), 1.99–1.82 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.4 (C=O), 173.2 (C=O), 168.7 (C=O), 64.9 ($C=N_2$), 54.3 ($C=N_2$), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 236.0 $[M + H]^+$.

Anal. Calcd for $C_9H_9N_5O_3$: C, 45.96; H, 3.86; N, 29.78. Found: C, 46.07; H, 3.88; N, 29.71.

Methyl 2-Diazo-3-(3-diazo-2-oxopiperidin-1-yl)-3-oxopropanoate (3b)

The title compound was synthesized using the procedure described for **3a**.

Yield: 102 mg (92%); yellow oil.

IR (ATR): 3270, 2137, 1659, 1363, 1316, 1289, 1264, 1164, 735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.77–3.66 (m, 2 H, CH_2), 3.28 (s, 3 H, CH_3), 3.15–3.07 (m, 1 H, CH), 2.23–1.87 (m, 4 H, CH_2), 1.49–1.18 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3 (C=O), 173.0 (C=O), 169.0 (C=O), 75.2 ($C=N_2$), 75.0 (CH_2), 64.9 ($C=N_2$), 54.3 (CH_2), 30.1 (CH_2), 19.1 (CH_3).

MS (ESI): *m*/*z* = 252.0 $[M + H]^+$.

Anal. Calcd for $C_9H_9N_5O_4$: C, 43.03; H, 3.61; N, 27.88. Found: C, 43.12; H, 3.59; N, 27.96.

2-Diazo-1-(3-diazo-2-thioxopiperidin-1-yl)butane-1,3-dione (3c)

The title compound was synthesized using the procedure described for **3a**.

Yield: 97 mg (87%); orange solid; mp 136–138 °C.

IR (ATR): 2095, 2089, 1726, 1689, 1638, 1385, 1351, 1316, 1269, 1152, 939 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.40–3.33 (m, 2 H, CH), 2.43 (s, 3 H, CH_3), 2.16–2.13 (m, 1 H, CH_2), 1.99–1.82 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.4 (C=O), 168.7 (C=S), 173.2 (C=O), 64.9 (C=N_2), 54.3 (C=N_2), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 252.0 $[M + H]^+$.

Anal. Calcd for $C_9H_9N_5O_2S$: C, 43.02; H, 3.61; N, 27.87. Found: C, 42.90; H, 3.59; N, 27.80.

Methyl 2-Diazo-3-(3-diazo-2-thioxopiperidin-1-yl)-3-oxopropanoate (3d)

The title compound was synthesized using the procedure described for **3a**.

Yield: 93 mg (84%); yellow oil.

IR (ATR): 3270, 2137, 1659, 1363, 1316, 1289, 1264, 1164, 735 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.77–3.66 (m, 2 H, CH_2), 3.28 (s, 3 H, CH_3), 3.15–3.07 (m, 1 H, CH), 2.23–1.87 (m, 2 H, CH_2), 1.49–1.18 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3 (C=O), 173.0 (C=O), 169.0 (C=S), 75.2 (C=N_2), 75.0 (CH_2), 64.9 (C=N_2), 54.3 (CH_2), 30.1 (CH_2), 19.1 (CH_3).

MS (ESI): *m*/*z* = 268.0 $[M + H]^+$.

Anal. Calcd for $C_9H_9N_5O_3S$: C, 40.45; H, 3.39; N, 26.20. Found: C, 40.54; H, 3.37; N, 26.16.

1-[2-Oxo-3-(prop-2-en-1-yloxy)piperidin-1-yl]butane-1,3-dione (5a); Typical Procedure

N-Substituted diazo compound **2a** (40 mg, 3.2 mmol) and allyl alcohol **4a** (18 mg, 3.2 mmol) were dissolved in anhydrous benzene (20 mL) and stirred for 5 min at r.t. To this stirred solution was added $Rh_2(OAc)_4$ (1 mol%) and the resulting mixture was stirred at 60 °C for 2 h. After cooling, the mixture was concentrated under reduced pressure. Purification of the residue by column chromatography on silica gel gave the title compound **5a** as a pale yellow oil (31 mg, 72%).

IR (ATR): 2815, 1685, 1691, 1495, 1455, 1420, 1384, 1354, 965 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85–5.80 (m, 1 H, CH), 5.24 (ddd, J_1 = 8.2 Hz, 1 H, J_2 = 5.4 Hz, J_3 = 4.0 Hz, CH), 5.13 (ddd, J_1 = 8.0 Hz, J_2 = 5.8 Hz, J_3 = 3.8 Hz, 1 H, CH), 4.24–4.19 (m, 1 H, CH), 4.05 (dd, J_1 = 3.2 Hz, J_2 = 2 Hz, 4 H, CH_2), 3.98–3.94 (m, 1 H, CH_2), 3.92–3.81 (m, 1 H, CH_2), 2.20 (s, 3 H, CH_3), 2.09 (d, *J* = 5.6 Hz, 1 H, CH_2), 1.96–1.78 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.4 (C=O), 173.2 (C=O), 168.7 (NC=O), 134.0 (CH), 117.9 (CH_2), 75.9 (CH), 71.7 (CH_2), 54.3 (C=N_2), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 240.0 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.13; H, 7.14; N, 5.83.

1-[2-Oxo-3-(prop-2-en-1-ylsulfanyl)piperidin-1-yl]butane-1,3-dione (5b)

Yield: 36 mg (74%); yellow oil.

IR (ATR): 1723, 1685, 1634, 1391, 1294, 1152, 990, 922 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85–5.80 (m, 1 H, CH), 5.18 (ddt, J_1 = 38.8 Hz, J_2 = 17.2 Hz, J_3 = 1.6 Hz, 2 H, CH_2), 4.21 (ddt, J_1 = 12.4 Hz, J_2 = 5.2 Hz, J_3 = 1.6 Hz, 1 H, CH), 4.09–3.81 (m, 5 H, CH_2), 3.61–3.55 (m, 1 H, CH), 3.58 (t, *J* = 5.2 Hz, 1 H, CH), 2.20 (s, 3 H, CH_3), 2.10–1.85 (m, 1 H, CH_2), 1.84–1.78 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3 (C=O), 173.2 (C=O), 168.7 (NC=O), 134.0 (CH), 117.9 (CH_2), 75.9 (SCH), 71.7 (SCH_2), 54.3 (CH_2), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 256.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{17}NO_3S$: C, 56.45; H, 6.71; N, 5.49. Found: C, 56.55; H, 6.69; N, 5.47.

3-(Prop-2-en-1-yloxy)piperidin-2-one (5c)

Yield: 24 mg (59%); colorless solid; mp 114–116 °C.

IR (ATR): 2953, 2822, 1730, 1495, 1437, 1416, 1210, 1172, 735, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (s, 1 H, NH), 5.88–5.83 (m, 1 H, CH), 5.11 (ddd, J_1 = 4.6 Hz, J_2 = 3.2 Hz, J_3 = 2.0 Hz, 2 H, CH_2), 4.33–4.28 (m, 1 H, CH), 4.15–4.10 (m, 1 H, CH), 3.77–3.73 (m, 1 H, CH_2), 3.25–3.19 (m, 2 H, CH_2), 1.87–1.83 (m, 4 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.2 (C=O), 131.7 (CH), 115.8 (CH_2), 85.1 (CH), 71.3 (CH_2), 38.2 (CH_2), 32.1 (CH_2), 19.3 (CH_2).

MS (ESI): *m*/*z* = 156.0 $[M + H]^+$.

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.79; H, 8.42; N, 9.06.

3-(Prop-2-en-1-ylsulfanyl)piperidin-2-one (5d)

Yield: 32 mg (54%); yellowish-green solid; mp 157–159 °C.

IR (ATR): 2953, 2822, 1730, 1495, 1437, 1416, 1210, 1172, 735, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (s, 1 H, NH), 5.88–5.83 (m, 1 H, CH), 5.11 (ddd, J_1 = 4.6 Hz, J_2 = 3.2 Hz, J_3 = 1.4 Hz, 2 H, CH_2), 4.33–4.28 (m, 1 H, CH), 4.15–4.10 (m, 1 H, CH), 3.77–3.73 (m, 1 H, CH_2), 3.25–3.19 (m, 2 H, CH_2), 1.87–1.83 (m, 4 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.7 (C=O), 133.1 (CH), 117.2 (CH_2), 51.7 (CH), 37.5 (CH_2), 37.3 (CH_2), 31.6 (CH_2), 21.9 (CH_2).

MS (ESI): *m*/*z* = 172.0 $[M + H]^+$.

Anal. Calcd for $C_8H_{13}NOS$: C, 56.11; H, 7.65; N, 8.18. Found: C, 56.19; H, 7.67; N, 8.15.

3-(Prop-2-yn-1-yloxy)piperidin-2-one (5e)

Yield: 24 mg (51%); colorless liquid.

IR (ATR): 3416, 2931, 1718, 1651, 1601, 1389, 1322, 1035, 815, 753 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.01 (s, 1 H, NH), 4.57–4.48 (m, 2 H, CH_2), 4.03–4.00 (m, 1 H, CH), 3.33–3.24 (m, 2 H, CH_2), 2.44 (t, *J* = 2.4 Hz, 1 H, CH), 2.12–1.88 (m, 3 H, CH_2), 1.80–1.75 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0 (C=O), 80.0 (quat-C), 75.0 (CH), 73.0 (CH), 58.2 (CH_2), 42.0 (CH_2), 28.0 (CH_2), 20.0 (CH_2).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_8H_{11}NO_2Na$: 176.0687; found: 176.0680.

2-Diazo-1-[2-oxo-3-(prop-2-en-1-yloxy)piperidin-1-yl]butane-1,3-dione (6a)

Yield: 73 mg (86%); yellow viscous oil.

IR (ATR): 2137, 1723, 1687, 1638, 1385, 1351, 1316, 1269, 1152, 931 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.74–5.69 (m, 1 H, CH), 5.22–5.12 (m, 2 H, CH_2), 3.62–3.60 (m, 2 H, CH), 3.40–3.33 (m, 2 H, CH), 3.19 (dd, J_1 = 6.4 Hz, J_2 = 2.7 Hz, 1 H, CH_2), 2.43 (s, 3 H, CH_3), 2.16–2.13 (m, 1 H, CH_2), 1.99–1.82 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.4 (C=O), 173.2 (C=O), 168.7 (NC=O), 134.0 (CH), 117.9 (CH_2), 75.9 (CH), 71.7 (CH_2), 54.3 (C=N_2), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 266.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.70; N, 15.84. Found: C, 54.21; H, 5.68; N, 15.81.

3-(3-Allyloxy-2-oxo-piperidin-1-yl)-2-diazo-3-oxo-propionic Acid Methyl Ester (6b)

Yield: 68 mg (64%); yellow oil.

IR (ATR): 3270, 2137, 1659, 1363, 1316, 1289, 1264, 1164, 735 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.97–5.87 (m, 1 H, CH), 5.35–5.13 (m, 2 H, CH_2), 4.38 (q, *J* = 6.4 Hz, 1 H, CH), 4.11–3.81 (m, 1 H, CH), 3.77–3.66 (m, 2 H, CH_2), 3.28 (s, 3 H, CH_3), 3.15–3.07 (m, 1 H, CH), 2.23–1.87 (m, 4 H, CH_2), 1.49–1.18 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.3 (C=O), 173.0 (C=O), 169.0 (C=O), 79.0 (quat-C), 75.2 (C=N_2), 75.0 (CH_2), 58.0 (CH_2), 54.3 (CH_2), 42.0 (CH_2), 30.1 (CH_2), 26.4 (CH_2), 19.1 (CH_3).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{16}N_3O_5$: 282.1090; found: 282.1092.

2-Diazo-1-[2-oxo-3-(prop-2-yn-1-yloxy)piperidin-1-yl]butane-1,3-dione (6c)

Yield: 76 mg (89%); yellow oil.

IR (ATR): 3270, 2955, 2139, 1718, 1653, 1437, 1331, 1160, 1128 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.48–4.37 (m, 2 H, CH_2), 4.23 (q, *J* = 6.0 Hz, 1 H, CH), 3.68 (q, *J* = 7.6 Hz, 2 H, CH_2), 2.51 (t, *J* = 5.6 Hz, 1 H, CH), 2.45 (s, 3 H, CH_3), 2.23–2.18 (m, 1 H, CH_2), 2.06–2.00 (m, 1 H, CH_2), (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.1 (C=O), 169.1 (NC=O), 102.0 (quat-C), 95.0 (quat-C), 72.0 (CH_2), 70.2 (CH), 46.2 (CH), 39.0 (CH_2), 31.0 (CH_2), 30.0 (CH_2), 27.2 (CH_3), 20.0 (CH_2).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{14}N_3O_4$: 264.0984; found 264.0981.

Methyl 2-Diazo-3-oxo-3-[2-oxo-3-(prop-2-yn-1-yloxy)piperidin-1-yl]propanoate (6d)

Yield: 76 mg (89%); yellow oil.

IR (ATR): 2093, 1723, 1687, 1638, 1384, 1351, 1314, 1150, 728 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.49 (dd, J_1 = 16 Hz, J_2 = 6.1 Hz, 1 H, CH), 4.43–4.35 (m, 2 H, CH_2), 4.32–4.21 (m, 2 H, CH_2), 3.87 (d, *J* = 5.6 Hz, 1 H, CH), 3.78 (s, 3 H, CH_3), 2.56–2.54 (m, 2 H, CH_2), 2.31–2.19 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.1 (C=O), 169.1 (NC=O), 102.0 (quat-C), 95.0 (quat-C), 72.0 (CH_2), 70.2 (CH), 46.2 (CH), 39.0 (CH_2), 31.0 (CH_2), 30.0 (CH_2), 27.2 (CH_3), 20.0 (CH_2).

MS (ESI): *m*/*z* = 280.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{13}N_3O_5$: C, 51.61; H, 4.69; N, 15.06. Found: C, 51.48; H, 4.66; N, 15.03.

2-Diazo-1-[2-oxo-3-(prop-2-en-1-ylsulfanyl)piperidin-1-yl]butane-1,3-dione (6e)

Yield: 253 mg (91%); yellow oil.

IR (ATR): 2095, 1723, 1687, 1638, 1385, 1351, 1316, 1269, 1152, 931 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.74–5.69 (m, 1 H, CH), 5.22–5.12 (m, 2 H, CH_2), 3.62–3.60 (m, 2 H, CH), 3.40–3.33 (m, 2 H, CH), 3.19 (dd, J_1 = 5.8 Hz, J_2 = 1.8 Hz, 1 H, CH_2), 2.43 (s, 3 H, CH_3), 2.16–2.13 (m, 1 H, CH_2), 1.99–1.82 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 201.4 (C=O), 173.2 (C=O), 168.7 (NC=O), 134.0 (=CH), 117.9 (=CH_2), 75.9 (SCH), 71.7 (SCH_2), 54.3 (C=N_2), 41.7 (CH_2), 30.1 (CH_3), 26.4 (CH_2), 19.1 (CH_2).

MS (ESI): *m*/*z* = 282.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{15}N_3O_3S$: C, 51.23; H, 5.37; N, 14.94. Found: C, 51.09; H, 5.34; N, 14.92.

Methyl 2-Diazo-3-oxo-3-[2-oxo-3-(prop-2-en-1-ylsulfanyl)piperidin-1-yl]propanoate (6f)

Yield: 173 mg (64%); yellow viscous oil.

IR (ATR): 2133, 1654, 1357, 1314, 1288, 1082, 1160, 964 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.93–5.90 (m, 1 H, =CH), 5.35–5.13 (m, 2 H, C=CH_2), 4.39–4.08 (m, 1 H, CH), 3.89–3.58 (m, 3 H, CH_2), 3.27 (s, 3 H, OCH_3), 3.08–2.93 (m, 1 H, CH), 2.23–2.03 (m, 1 H, CH), 2.00–1.87 (m, 2 H, CH_2), 1.22 (td, J_1 = 5.6 Hz, J_2 = 1.3 Hz, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1 (CH_2), 26.4 (CH_2), 30.1 (CH_3), 41.7 (CH_2), 54.3 (C=N_2), 71.7 (SCH_2), 75.9 (SCH), 117.9 (=CH_2), 134.0 (=CH), 168.7 (NC=O), 173.2 (C=O), 201.4 (C=O).

MS (ESI): *m*/*z* = 298.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{15}N_3O_4S$: C, 48.47; H, 5.08; N, 14.13. Found: C, 48.33; H, 5.05; N, 14.11.

Epoxy- and Epithio-Bridged Heterocycle-Fused Quinolizinones 7a–o; General Procedure

In an oven-dried flask, a solution containing the appropriate bis-diazo compound **3** (100 mg, 0.42 mmol) and the selected bifunctional reaction partner **4** (0.42 mmol), rhodium(II) acetate dimer (1 mol%) in anhydrous benzene (dried over Na wire) was degassed under Ar. After loading the catalyst, the reaction was kept stirring under reflux for the appropriate amount of time (see Scheme 5) until complete consumption of starting material had occurred as monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure and the resulting crude residue was purified by flash column chromatography (hexanes–EtOAc) to afford epoxy- or epithio-bridged heterocycle-fused quinolizinones **7a–o**.

4-Acetyloctahydro-5*H*-4,9b-epoxyfuro[2,3,4-*ij*]quinolizin-5-one (7a)

Yield: 93 mg (92%); colorless solid; mp 140–142 °C.

IR (ATR): 1733, 1719, 1415, 1361, 1265, 1148, 1083, 953, 889 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.17–4.09 (m, 2 H, OCH_2), 3.67–3.61 (m, 1 H, OCH), 3.49–3.44 (m, 1 H, CH), 2.84 (ddd, J_1 = 15.2 Hz, J_2 = 11.2 Hz, J_3 = 3.6 Hz, 1 H, CH_2), 2.67–2.61 (m, 1 H, CH_2), 2.33 (s, 3 H, CH_3), 2.29–2.25 (m, 1 H, CH_2), 2.16–2.11 (m, 1 H, CH_2), 1.85 (dd, J_1 = 12.4 Hz, J_2 = 3.6 Hz, 1 H, CH), 1.82–1.76 (m, 1 H, CH_2), 1.61–1.50 (m, 1 H, CH_2), 1.37–1.27 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.1 (C=O), 169.1 (NC=O), 102.0 (quat-C), 94.5 (quat-C), 72.0 (OCH_2), 70.2 (OCH), 46.2 (CH), 38.7 (CH_2), 30.7 (CH_2), 29.5 (CH_2), 27.3 (CH_3), 19.7 (CH_2).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{16}NO_4$: 238.1079; found: 238.1078.

Methyl 5-Oxohexahydro-2*H*-4,9b-epoxyfuro[2,3,4-*ij*]quinolizine-4(5*H*)-carboxylate (7b)

Yield: 83 mg (83%); colorless solid; mp 149–151 °C.

IR (ATR): 2944, 2816, 2779, 1687, 1454, 1382, 1353, 1317, 1297, 1243, 1153, 964 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.17–4.12 (m, 2 H, OCH_2), 3.85 (s, 3 H, OCH_3), 3.67–3.62 (m, 1 H, OCH), 3.49 (dd, J_1 = 10.4 Hz, J_2 = 3.7 Hz, 1 H, CH), 2.89–2.82 (m, 1 H, CH), 2.66–2.62 (m, 1 H, CH), 2.28–2.16 (m, 2 H, CH_2), 2.00 (dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, 1 H, CH), 1.81–1.76 (m, 1 H, CH), 1.57–1.53 (m, 1 H, CH_2), 1.34–1.30 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (C=O), 165.7 (NC=O), 102.0 (quat-C), 89.9 (quat-C), 71.9 (OCH_2), 70.2 (OCH), 53.2 (CH), 46.3 (OCH_3), 38.9, (CH_2), 31.0 (CH_2), 29.6 (CH_2), 19.7 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_5$: 254.1028; found: 254.1025.

Crystal Data for Compound 7b

The product was recrystallized using EtOAc and hexanes. $C_{12}H_{15}NO_5$, *M* = 254.10, crystal size 0.8 × 0.15 × 0.10 mm, orthorhombic, space group *P*-$2_12_12_1$, with *a* = 8.203(1) Å, *b* = 10.630(2) Å, *c* = 13.417(2) Å, *a* = 90°, *b* = 90°, *g* = 90°, *V* = 1170.0(3) Å^3; *T* = 296 K, R_1 = 0.0357, wR_2 = 0.1112 on observed data, *Z* = 4, D_{calcd} = 1.438 g cm^{-3}, *F*(000) = 536, absorption coefficient = 0.113 mm^{-1}, *l* = 0.71073 Å, 1418 reflections were collected on a Smart Apex CCD single-crystal diffractometer, 2131 observed reflections [$I \geq 2\sigma(I)$]. The largest difference peak and hole was 0.18 and –0.19 eÅ^{-3}, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL-97 software (CCDC 1432164).

4-Acetyl-2,4,7,8,9,9a-hexahydro-5*H*-4,9b-epoxyfuro[2,3,4-*ij*]quinolizin-5-one (7c)

Yield: 67 mg (67%); pale white solid; mp 143–145 °C.

IR (ATR): 2952, 2926, 1730, 1437, 1416, 1361, 1209, 1171, 1008, 957 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.92 (s, 1 H, CH), 5.11 (t, *J* = 0.8 Hz, 2 H, CH_2), 4.79–4.73 (m, 1 H, CH), 4.13 (ddd, J_1 = 14.4 Hz, J_2 = 6.8 Hz, J_3 = 2.0 Hz, 1 H, CH), 3.74–3.66 (m, 1 H, CH_2), 2.67 (s, 3 H, CH_3), 2.47–2.34 (m, 2 H, CH_2), 2.29–2.22 (m, 1 H, CH), 1.98–1.86 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.3 (C=O), 159.8 (NC=O), 147.7 (quat-C), 133.4 (quat-C), 118.8 (CH_2), 112.7 (CH), 96.1 (CH), 43.0 (CH_2), 32.0 (CH_2), 30.0 (CH_2), 27.2 (CH_3), 20.0 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_4$: 236.0923; found: 236.0912.

Methyl 5-Oxo-7,8,9,9a-tetrahydro-2*H*-4,9b-epoxyfuro[2,3,4-*ij*]quinolizine-4(5*H*)-carboxylate (7d)

Yield: 63 mg (62%); pale yellow semi-solid; mp 158–160 °C.

IR (ATR): 3417, 2935, 1717, 1653, 1601, 1466, 1440, 1369, 1252, 1088, 815 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.52–6.48 (m, 1 H, CH), 4.69–4.51 (m, 3 H, CH_2), 3.94 (s, 3 H, CH_3), 3.33–3.28 (m, 2 H, CH_2), 2.03–1.99 (m, 1 H, CH_2), 1.94–1.86 (m, 1 H, CH_2), 1.84–1.76 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7 (C=O), 164.1 (C=O), 159.7 (quat-C), 123.0 (CH), 103.6 (CH_2), 97.7 (CH), 71.0 (CH), 63.8 (CH_2), 53.3 (CH_3), 39.5 (CH_2), 25.8 (CH_2), 17.1 (CH_2).

MS (ESI): *m*/*z* = 252.0 [M + H]$^+$.

Anal. Calcd for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.22; N, 5.58. Found: C, 57.48; H, 5.20; N, 5.56.

5-Acetyloctahydro-5,10b-epoxypyrano[2,3,4-*ij*]quinolizin-6(2*H*)-one (7e)

Yield: 78 mg (73%); colorless solid; mp 163–165 °C.

IR (ATR): 3328, 2967, 1719, 1656, 1624, 1479, 1438, 1321, 1211, 1074, 866 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.18–4.13 (m, 1 H, CH), 3.72–3.68 (m, 1 H, CH), 3.65–3.61 (m, 2 H, CH_2), 2.59 (td, J_1 = 13.2 Hz J_2 = 3.6 Hz, 1 H, CH), 2.34 (s, 3 H, CH_3), 2.24–2.13 (m, 2 H, CH_2), 1.93–1.79 (m, 4 H, CH_2), 1.65–1.56 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.7 (NC=O), 170.0 (C=O), 91.2 (quat-C), 90.5 (quat-C), 70.5 (CH), 59.7 (CH_2), 38.5 (CH_2), 36.0 (CH_2), 35.2 (CH_3), 31.7 (CH_2), 27.4 (CH), 24.6 (CH_2), 22.0 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{18}NO_4$: 252.1236; found: 252.1230.

4-Acetyl-1-phenyloctahydro-4,9b-epoxypyrrolo[2,3,4-*ij*]quinolizin-5(1*H*)-one (7f)

Yield: 115 mg (85%); white solid; mp 141–143 °C.

IR (ATR): 3319, 3127, 3064, 2987, 2130, 1826, 1612, 1509, 1394, 1104, 913 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.22 (m, 2 H, ArH), 6.74 (t, *J* = 7.2 Hz, 1 H, ArH), 6.59 (d, *J* = 8.0 Hz, 1 H, ArH), 3.94 (q, *J* = 6.0 Hz, 1 H, CH), 3.87–3.81 (m, 2 H, CH_2), 2.98–2.81 (m, 3 H, CH_2), 2.76–2.71 (m, 1 H, CH_2), 2.37 (s, 3 H, CH_3), 2.33–2.28 (m, 1 H, CH_2), 2.04 (dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, 1 H, CH), 1.94–1.91 (m, 1 H, CH_2), 1.76–1.71 (m, 1 H, CH_2), 1.34–1.24 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.3 (NC=O), 169.3 (C=O), 146.7 (CH), 129.5 (CH), 117.0 (CH), 111.7 (CH), 99.3 (quat-C), 93.7 (quat-C), 54.6 (CH), 52.6 (CH_2), 42.7 (CH_3), 39.0 (CH_2), 33.1 (CH_2), 29.1 (CH_2), 27.4 (CH_2), 20.8 (CH_2).

MS (ESI): *m*/*z* = 313.1 [M + H]$^+$.

Anal. Calcd for $C_{18}H_{20}N_2O_3$: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.04; H, 6.42; N, 8.95.

4-Acetyl-1-phenyl-2,4,7,8,9,9a-hexahydro-4,9b-epoxypyrrolo[2,3,4-*ij*]quinolizin-5(1*H*)-one (7g)

Yield: 79 mg (60%); colorless solid; mp 153–155 °C.

IR (ATR): 3416, 2931, 1718, 1651, 1601, 1466, 1440, 1369, 1252, 1088, 815 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.19 (m, 2 H, ArH), 6.74 (t, *J* = 7.6 Hz, 1 H, CH), 6.60 (d, *J* = 7.6 Hz, 2 H, ArH), 6.52 (t, *J* = 2.4 Hz, 1 H, CH), 4.53 (t, *J* = 4.0 Hz, 1 H, CH), 4.20 (t, *J* = 2.4 Hz, 2 H, CH_2), 3.38–3.31 (m, 1 H, CH_2), 3.21–3.18 (m, 1 H, CH_2), 2.31 (s, 3 H, CH_3), 2.17–2.11 (m, 1 H, CH_2), 2.01–1.67 (m, 3 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.3 (C=O), 169.3 (NC=O), 146.7 (quat-C), 129.4 (quat-C), 117.0 (CH_2), 111.6 (CH), 99.3 (CH_2), 93.7 (CH_2), 54.6 (CH_2), 52.6 (CH_3), 42.7 (CH_2), 39.0 (CH_2), 33.1 (CH_2), 29.1 (CH_2), 27.4 (CH), 20.7 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{19}N_2O_3$: 311.1396; found: 311.1387.

4-Acetyloctahydro-5*H*-4,9b-epoxythieno[2,3,4-*ij*]quinolizin-5-one (7h)

Yield: 81 mg (76%); pale yellow solid; mp 167–169 °C.

IR (ATR): 2813, 2776, 1661, 1485, 1483, 1455, 1435, 1357, 1318, 1112, 964 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 3.77 (dd, J_1 = 12.8 Hz, J_2 = 2 Hz, 1 H, CH), 3.44–3.41 (m, 1 H, CH), 3.10–3.05 (m, 1 H, CH), 2.81–2.75 (m, 2 H, CH_2), 2.68–2.63 (m, 1 H, CH), 2.32 (s, 3 H, CH_3), 2.28–2.16 (m, 2 H, CH_2), 1.91–1.80 (m, 2 H, CH_2), 1.59–1.52 (m, 2 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.2 (C=O), 169.1 (NC=O), 103.4 (quat-C), 92.6 (quat-C), 47.5 (CH), 40.3 (CH), 39.0 (CH_2), 35.0 (CH_2), 34.7 (CH_2), 33.3 (CH_2), 27.4 (CH_3), 22.3 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_3S$: 254.0851; found: 254.0886.

Crystal Data for Compound 7h

The product was recrystallized using EtOAc and hexanes. $C_{12}H_{15}NO_3S$, *M* = 253.31, crystal size 0.09 × 0.08 × 0.07 mm, orthorhombic, space group $Pna2_1$, with *a* = 15.716(3) Å, *b* = 8.797(2) Å, *c* = 8.520(2) Å, *a* = 90°, *b* = 90°, *g* = 90°, *V* = 1178.0(10) Å^3, *T* = 296 K, R_1 = 0.0415, wR_2 = 0.1080 on observed data, *Z* = 4, D_{calcd} = 1.428 g cm^{-3}, *F*(000) = 536, absorption coefficient = 0.270 mm^{-1}, *l* = 0.71073 Å, 4089 reflections were collected on a Smart Apex CCD single crystal diffractometer, 3326 observed reflections [$I > 2\sigma(I)$]. The largest difference peak and hole are 0.30 and –0.27 eÅ^{-3}, respectively. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXL-97 software (CCDC 1432165).

Methyl 5-Oxohexahydro-2*H*-4,9b-epoxythieno[2,3,4-*ij*]quinolizine-4(5*H*)-carboxylate (7i)

Yield: 74 mg (70%); white solid; mp 162–164 °C.

IR (ATR): 2955, 2924, 1752, 1719, 1440, 1398, 1333, 1268, 1203, 1160, 1076 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.17–4.12 (m, 2 H, SCH_2), 3.85 (s, 3 H, OCH_3), 3.64 (dt, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1 H, SCH), 3.49 (q, *J* = 2.0 Hz, 1 H, CH), 2.84 (dt, J_1 = 14.8 Hz, J_2 = 1.2 Hz, 1 H, CH), 2.67–2.61 (m, 1 H, CH), 2.29–2.16 (m, 2 H, CH_2), 2.00 (dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, 1 H, CH), 1.81–1.75 (m, 1 H, CH), 1.60–1.53 (m, 1 H, CH_2), 1.37–1.27 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (C=O), 165.7 (NC=O), 102.0 (quat-C), 89.9 (quat-C), 71.9 (OCH_2), 70.2 (OCH), 53.2 (CH), 46.3 (OCH_3), 38.9 (CH_2), 31.0 (CH_2), 29.6 (CH_2), 19.7 (CH_2).

MS (ESI): *m*/*z* = 270.1 [M + H]$^+$.

Anal. Calcd for $C_{12}H_{15}NO_4S$: C, 53.52; H, 5.61; N, 5.20. Found: C, 53.66; H, 5.58; N, 5.18.

4-Acetyloctahydro-5*H*-4,9b-epithiofuro[2,3,4-*ij*]quinolizin-5-one (7j)

Yield: 71 mg (71%); colorless solid; mp 144–146 °C.

IR (ATR): 1733, 1719, 1415, 1361, 1265, 1148, 1083, 953, 889 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.23–4.17 (m, 2 H, CH_2), 3.74–3.67 (m, 1 H, CH), 3.54 (q, *J* = 2.0 Hz, 1 H, CH), 2.91 (ddd, J_1 = 14.8 Hz, J_2 = 11.2 Hz, J_3 = 3.6 Hz, 1 H, CH), 2.74–2.67 (m, 1 H, CH), 2.35 (s, 3 H, CH_3), 2.35–2.31 (m, 1 H, CH_2), 2.13 (dd, J_1 = 12.8 Hz, J_2 = 7.6 Hz, 1 H, CH_2), 1.94–1.82 (m, 2 H, CH_2), 1.68–1.57 (m, 1 H, CH_2), 1.44–1.39 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.1 (C=O), 169.2 (C=O), 101.7 (quat-C), 94.6 (quat-C), 72.0 (CH_2), 70.3 (CH), 46.3 (CH), 38.8 (CH_2), 30.7 (CH_2), 29.6 (CH_2), 27.3 (CH_3), 19.7 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_3S$: 254.0851; found: 254.0852.

Methyl 5-Oxooctahydro-2*H*-2a,1,4-epithiofuro[2,3,4-*ij*]quinolizine-4-carboxylate (7k)

Yield: 64 mg (64%); viscous oil.

IR (ATR): 3106, 2869, 1752, 1713, 1429, 1398, 1324, 1211, 1203, 1163, 968 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.17–4.12 (m, 2 H, CH_2), 3.85 (s, 3 H, CH_3), 3.64 (dt, J_1 = 12.8 Hz, J_2 = 4.0 Hz, 1 H, CH), 3.49 (q, *J* = 2.0 Hz, 1 H, CH), 2.89–2.82 (m, 1 H, CH), 2.68–2.61 (m, 1 H, CH), 2.29–2.16 (m, 2 H, CH_2), 2.00 (dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, 1 H, CH), 1.81–1.76 (m, 1 H, CH), 1.57–1.53 (m, 1 H, CH_2), 1.37–1.27 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.6 (C=O), 165.7 (C=O), 102.0 (quat-C), 89.9 (quat-C), 71.9 (CH_2), 70.2 (CH), 53.2 (CH), 46.3 (CH_3), 38.9, (CH_2), 31.4 (CH_2), 29.6 (CH_2), 19.7 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_4S$: 270.0800; found: 270.0812.

4-Acetyl-7,8,9,9a-tetrahydro-2*H*-2a,1,4-epithiofuro[2,3,4-*ij*]quinolizin-5(4*H*)-one (7l)

Yield: 64 mg (60%); viscous oil.

IR (ATR): 2955, 2924, 1752, 1719, 1440, 1398, 1333, 1268, 1203, 1160, 1074 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 5.92 (s, 1 H, CH), 5.11 (d, *J* = 3.6 Hz, 2 H, CH_2), 4.79–4.73 (m, 1 H, CH), 4.13 (ddd, J_1 = 14.8 Hz, J_2 = 6.8 Hz, J_3 = 2.4 Hz, 1 H, CH), 3.74–3.66 (m, 1 H, CH), 2.67 (s, 3 H, CH_3), 2.47–2.34 (m, 2 H, CH_2), 2.29–2.22 (m, 1 H, CH_2), 1.98–1.86 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0 (C=O), 159.3 (NC=O), 147.2 (quat-C), 133.0 (quat-C), 118.3 (CH_2), 112.2 (CH), 73.0 (quat-C), 72.8 (CH_2), 42.5 (CH_2), 31.5 (CH_2), 26.4 (CH_3), 19.1 (CH_2).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_3S$: 252.0694; found: 252.0642.

4-Acetyloctahydro-5*H*-4,9b-epithiothieno[2,3,4-*ij*]quinolizin-5-one (7m)

Yield: 76 mg (71%); fluffy solid; mp 140–142 °C.

IR (ATR): 2964, 2715, 1733, 1719, 1415, 1361, 1265, 1148, 1083, 953, 889 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.17–4.09 (m, 2 H, CH_2), 3.67–3.61 (m, 1 H, CH), 3.46 (q, *J* = 2.0 Hz, 1 H, CH), 2.84 (ddd, J_1 = 15.2 Hz, J_2 = 11.2 Hz, J_3 = 3.6 Hz, 1 H, CH_2), 2.68–2.61 (m, 1 H, CH_2), 2.33 (s, 3 H, CH_3), 2.31–2.23 (m, 1 H, CH_2), 2.14 (dd, J_1 = 12.8 Hz, J_2 = 7.6 Hz, 1 H, CH_2), 1.87–1.77 (m, 2 H, CH_2), 1.61–1.50 (m, 1 H, CH_2), 1.37–1.27 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.1 (C=O), 169.2 (NC=O), 101.6 (quat-C), 94.5 (quat-C), 72.0 (CH_2), 70.2 (CH), 46.2 (CH), 38.7 (CH_2), 30.7 (CH_2), 29.5 (CH_2), 27.3 (CH_3), 19.7 (CH_2).

MS (ESI): *m*/*z* = 270.1 [M + H]$^+$.

Anal. Calcd for $C_{12}H_{15}NO_2S_2$: C, 53.50; H, 5.61; N, 5.20. Found: C, 53.65; H, 5.59; N, 5.18.

Methyl 5-Oxooctahydro-2*H*-2a,1,4-epithiothieno[2,3,4-*ij*]quinolizine-4-carboxylate (7n)

Yield: 76 mg (72%); yellow solid; mp 162–164 °C.

IR (ATR): 2955, 2924, 1752, 1719, 1440, 1398, 1333, 1268, 1203, 1160, 1076 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.20 (q, *J* = 7.6 Hz, 2 H, CH_2), 3.91 (s, 3 H, CH_3), 3.72–3.69 (m, 1 H, CH), 3.55 (t, *J* = 10.0 Hz, 1 H, CH), 2.94–2.88 (m, 1 H, CH), 2.74–2.67 (m, 1 H, CH), 2.34–2.23 (m, 2 H, CH_2), 2.07 (dd, J_1 = 12.8 Hz, J_2 = 3.2 Hz, 1 H, CH), 1.86–1.83 (m, 1 H, CH), 1.66–1.56 (m, 2 H, CH_2), 1.38 (q, *J* = 12.4 Hz, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.7 (C=O), 165.7 (C=O), 102.0 (quat-C), 89.9 (quat-C), 71.9 (OCH_2), 70.2 (CH), 53.2 (CH), 46.3 (CH_3), 38.9, (CH_2), 31.0 (CH_2), 29.6 (CH_2), 19.7 (CH_2).

MS (ESI): *m*/*z* = 286.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{15}NO_3S_2$: C, 50.50; H, 5.30; N, 4.91. Found: C, 50.35; H, 5.29; N, 4.89.

4-Acetyl-1-phenyloctahydro-4,9b-epithiopyrrolo[2,3,4-*ij*]quinolizin-5(1*H*)-one (7o)

Yield: 90 mg (69%); pale yellow solid; mp 134–136 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.22 (m, 2 H, ArH), 6.74 (t, *J* = 7.2 Hz, 1 H, ArH), 6.59 (d, *J* = 8.0 Hz, 2 H, ArH), 2.98–2.81 (m, 3 H, CH_2), 2.76–2.71 (m, 1 H, CH), 2.37 (s, 3 H, CH_3), 2.33–2.28 (m, 1 H, CH), 2.06–2.02 (m, 1 H, CH), 2.04 (dd, J_1 = 12.8 Hz, J_2 = 3.6 Hz, 3 H, CH_2), 1.94–1.91 (m, 1 H, CH), 1.76–1.71 (m, 1 H, CH), 1.34–1.24 (m, 1 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.7 (C=O), 166.8 (NC=O), 144.1 (quat-C), 127.0 (CH), 114.5 (CH), 109.1 (CH), 96.8 (CH_2), 91.1 (CH_2), 52.0 (CH), 50.0 (CH_2), 40.1 (CH), 36.5 (CH_2), 30.5 (CH_2), 26.5 (CH_2), 24.8 (CH_3), 18.2 (CH_2).

MS (ESI): *m*/*z* = 329.1 $[M + H]^+$.

Anal. Calcd for $C_{18}H_{20}N_2O_2S$: C, 65.83; H, 6.14; N, 8.53. Found: C, 65.70; H, 6.12; N, 8.55.

4-Acetyl-4-hydroxy-2a,3,4,6,7,8-hexahydro-2*H*-1-oxa-5a-aza-acenaphthylen-5-one (11a)

PTSA (10 mol%) was added portionwise (in three intervals) to a solution of epoxy-bridged tricyclic compound **7a** (60 mg, 0.25 mmol) in benzene (2 mL). The reaction mixture was allowed to stir at r.t. for 3 h. After completion of the reaction (monitored by TLC), H_2O (4 mL) was added and the mixture was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine (3 × 10 mL), dried over Na_2SO_4 and evaporated. The crude residue was purified by column chromatography to give **11a** as a thick, pale yellow oil (33 mg, 49%).

IR (ATR): 3547, 3301, 2974, 2834, 1756, 1721, 1438, 1392, 1328, 1257, 1211, 1181, 1069 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.77 (s, 1 H, OH), 4.57–4.52 (m, 1 H), 4.39–4.35 (m, 1 H), 4.09–4.03 (m, 1 H), 3.44–3.37 (m, 1 H), 2.95–2.88 (m, 1 H), 2.54 (s, 3 H), 2.51–2.41 (m, 2 H), 2.20–2.04 (m, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 207.0 (C=O), 164.0 (NC=O), 135.3 (quat-C), 111.5 (quat-C), 76.7 (quat-C), 38.6 (CH_2), 33.3 (CH_2), 27.4 (CH_2), 24.4 (CH_2), 23.1 (CH), 22.5 (CH_3), 18.5 (CH).

MS (ESI): *m*/*z* = 238.1 $[M + H]^+$.

Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.61; H, 6.35; N, 5.88.

5-Acetyl-5-hydroxy-2,3,3a,4,5,7,8,9-octahydro-1-oxa-6a-aza-phenalen-6-one (11b)

The title product was synthesized from **7e** in 4 h based on the procedure described for the preparation of compound **11a**.

Yield: 38 mg (63%); thick greenish oil.

IR (ATR): 3312, 3178, 2964, 1739, 1721, 1430, 1384, 1321, 1257, 1211, 1065 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.48 (s, 1 H, OH), 4.25 (dt, J_1 = 13.2 Hz, J_2 = 4.0 Hz, 1 H, CH), 4.08 (dq, J_1 = 11.2 Hz, J_2 = 4 Hz, J_3 = 2.4 Hz, 1 H, CH), 3.80–3.74 (m, 1 H, CH), 3.15–3.08 (m, 1 H, CH), 2.66–2.60 (m, 1 H, CH), 2.25 (s, 3 H, CH_3), 2.22–2.15 (m, 2 H, CH_2), 1.91–1.82 (m, 2 H, CH_2), 1.65–1.51 (m, 4 H, CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 209.0 (C=O), 166.1 (NC=O), 137.4 (quat-C), 113.6 (quat-C), 79.0 (quat-C), 65.0 (CH_2), 41.0 (CH_2), 35.3 (CH_2), 29.5 (CH_2), 26.4 (CH), 25.1 (CH_3), 24.6 (CH), 21.0 (CH_2).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{17}NO_4Na$: 274.1055; found: 274.1050.

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Supporting Information

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