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Generation of 5,6-dimethylene-2(1*H*)-pyridinones from [3,4-*b*] sulfolene pyridinones and application in Diels–Alder reactions

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Abstract—2(1*H*)-Pyrazinones were converted into various [3,4-*b*] sulfolene pyridinones **19**–**21**, serving as precursors for thermolytic conversion into the corresponding 5,6-dimethylene 2(1*H*)-pyridinone *ortho*-quinodimethanes. These were trapped in situ by reaction with various dienophiles. Tethering of precursor **19** with a dienophilic side chain attached to the 7-position of the [3,4-*b*] sulfolene pyridinone also enabled intramolecular cycloaddition when no rearrangement by 1,5-H-shift was viable.

1. Introduction

During the last decade a vast number of publications have appeared on heteroaromatic *ortho*-quinodimethanes (*o*-QDM).[1] These highly reactive species are commonly generated in situ from various precursors,[2] e.g. by thermal extrusion of SO_2 from sulfolene-fused heterocyclic precursors.[3] In a preceding paper we described the use of [3,4-*c*] sulfolene pyridinones as precursors for generation of 3,4-dimethylene-2(1*H*)-pyridinone *o*-QDM and subsequent cycloaddition.[4,5] Here we present a study on the isomeric [3,4-*b*] sulfolene pyridinone precursor type. Upon extrusion of SO_2 the latter is transformed into the novel 5,6-dimethylene-2(1*H*)-pyridinone *o*-QDM system, which can be trapped in inter- and intramolecular Diels–Alder reactions to afford various unknown polycyclic pyridinones. In recent years, substituted pyridinones have regained interest, based on their biological and pharmacological properties.[6]

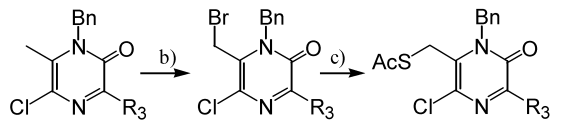
2. Results and discussion

2.1. Synthesis of the precursors

Our synthetic approach is depicted in Schemes 1 and 2. To generate the required 5,7-dihydrothieno[3,4-*b*]pyridin-2(1*H*)-one ring system, we envisaged bromination of the 6-methyl group of pyrazinones **2**–**4**, followed by functional group interconversion to introduce the 2-propynylsulfanyl group as a dienophilic side chain. The latter can undergo addition–elimination reaction with the pyrazinone azadiene to form the dihydrothiophene-fused bicyclic pyridinone. Oxidation of the ring sulfur atom finally can produce the desired [3,4-*b*] sulfolene pyridinone precursor.

The synthesis of the precursors started with nucleophilic substitution of the reactive imidoyl chloride function by treatment with sodium methoxide, sodium ethanethiolate, or tetraphenyltin to produce the 3-substituted pyrazinones **2**–**4**. Following bromination of the 6-methyl group the resulting bromides **5**–**7** were made to react with thiolacetic acid and triethylamine to give thioesters **8**–**10** (Scheme 1, Table 1).

Compounds **8**–**10** were converted into thioethers **11**–**13** by treatment with sodium methoxide to generate the thiolate anion followed by in situ reaction with propargyl bromide. Thioethers **11** and **13** were stable at room temperature but bis-thioether **12** had to be stored at low temperature. Internal cycloaddition of **11**–**13** was effected by heating in boiling toluene to afford dihydrothienopyridinones **16**–**18** exclusively. The preferred expulsion of cyanogen chloride from the intermediate cycloadducts **15** is in accord with our



1 R_3 = Cl

a) → **2** R_3 = OMe (95%), **3** R_3 = SEt (97%), **4** R_3 = Ph (69%); **5** R_3 = OMe (70%), **6** R_3 = SEt (89%), **7** R_3 = Ph (86%); **8** R_3 = OMe (80%), **9** R_3 = SEt (94%), **10** R_3 = Ph (90%)

Scheme 1. Synthesis of the thioesters **8**–**10**. *Reagents and conditions*: (a) **2**: 1.1 equiv. NaOMe, MeOH, room temperature; **3**: 1.2 equiv. NaSEt, THF, room temperature; **4**: 1.2 equiv. $SnPh_4$, 0.01 equiv. $Pd(P(Ph)_3)_4$, toluene, reflux, 1 week; (b) 1.2 equiv. NBS, CCl_4, reflux, cat. $(PhCOO)_2$; (c) 1.2 equiv. $HSCOCH_3$, Et_3N, THF, room temperature, 1 h.

Keywords: *ortho*-Quinodimethane; Pyridinone; Diels–Alder reaction.
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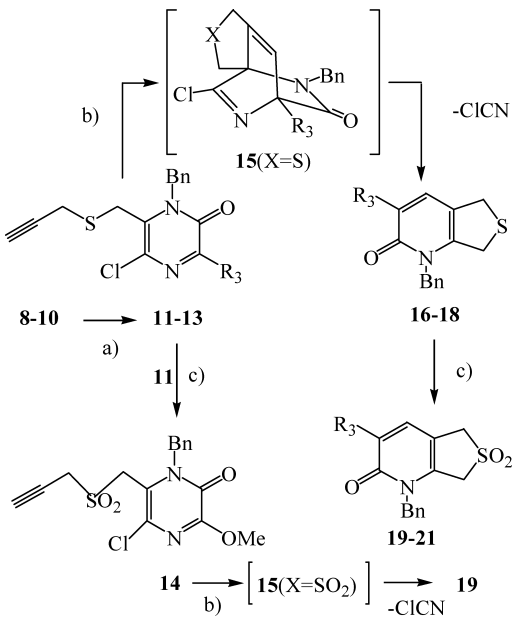


Scheme 2. Synthesis of sulfolene pyridinones. *Reagents and conditions*: (a) (i) 1.3 equiv. NaOMe, MeOH, room temperature, (ii) 3 equiv. propargyl bromide, room temperature; (b) toluene, reflux; (c) 3 equiv. *m*-CPBA, CH_2Cl_2, room temperature.

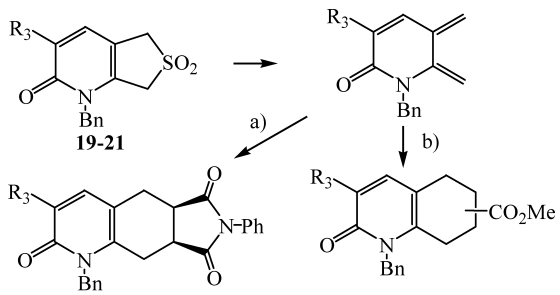
previous findings, which indicated that concurrent loss of benzyl isocyanate is a less favourable process.[7,8] The reaction times required for conversion of **11**–**13** into cyclic sulfides **16**–**18** were largely different. For instance, compound **12** (R_3=SEt) underwent Diels–Alder reaction already at room temperature, but subsequent elimination of cyanogen chloride from cycloadduct **15** to form **17** required further heating in boiling toluene for 15 h. By contrast, compounds **11** and **13** were converted directly into the final products **16** and **18** after heating for 6 and 3 h, respectively. Clearly, the activation energy for cycloaddition of the azadiene system and subsequent cycloreversion is affected in a different way by substituents in position 3 of the pyrazinone. Final oxidation of the cyclic sulfides **16**–**18** using *meta*-chloroperoxybenzoic acid (*m*-CPBA) furnished the required sulfolene pyridinones **19**–**21** (note: R_3=SO_2Et in the case of **20**). In an alternative route, the cycloaddition/oxidation sequence was reversed: following oxidation of thioether **11** using *m*-CPBA, the resulting sulfone **14** was heated in toluene for 2 h to produce *o*-QDM precursor **19** (Scheme 2). The latter route is less preferred, mainly because the yield of the cycloaddition–elimination reaction is significantly lower.

Table 1. Synthesis of the sulfolene pyridinones

Starting compound	Product	R_3	Yield (%)
8	**11**	OMe	90
9	**12**	SEt	88
10	**13**	Ph	70
11	**14**	OMe	70
11	**16**	OMe	74
12	**17**	SEt	93
13	**18**	Ph	65
14	**19**	OMe	64
16	**19**	OMe	80
17	**20**	SO_2Et	50
18	**21**	Ph	57

2.2. Intermolecular Diels–Alder reactions

To study the reactivity of the pyridinone *o*-QDM generated from precursors **19**–**21** and the regioselectivity in subsequent cycloaddition reactions, different types of dienophiles were applied in the thermolysis experiments. These were carried out by heating a mixture of precursor **19**–**21** and *N*-phenylmaleimide (NPMA) or methyl acrylate in *o*-dichlorobenzene (*o*-DCB) in a sealed glass tube at 150 to 160 °C (Scheme 3).



Scheme 3. Intermolecular Diels–Alder reactions. *Reagents and conditions*: (a) 3 equiv. NPMA, 150–160 °C, *o*-DCB; (b) 10 equiv. methyl acrylate, 150–160 °C, *o*-DCB.

The cycloadducts **22**–**24** formed with NPMA were isolated in good yields. The structure and conformational behaviour of these adducts were determined on the basis of coupling constants and NOESY as illustrated for adduct **24** (Fig. 1). Proton H-4 exhibits a strong NOE-correlation (dashed lines) with an *ortho*-proton of the phenyl group and with the coplanar equatorial proton H-5eq (δ 3.12, dd, 1H, $^2J_{5eq-5ax}$=15.0 Hz, $^3J_{5eq-5a}$=1.7 Hz). Obviously H-5eq can be connected to H-5ax (δ 2.75, dd, 1H, $^2J_{5ax-5eq}$=15.0 Hz, $^3J_{5ax-5a}$=5.0 Hz), which in turn shows a strong NOE with the angular proton H-5a. Since such a correlation is not observed for H-5eq, the latter must have a *trans*-relationship with H-5a. This, in turn, implies an equatorial orientation of H-5a, according with the conformational structure proposed in Figure 1 and the small coupling constant values observed for $^3J_{5eq-5a}$ (1.7 Hz) and $^3J_{5ax-5a}$ (5.0 Hz). For the analogous cycloadducts **22** and **23** a comparable conformational structure was inferred, based on similar coupling patterns and NOE-correlations.

In spite of the different electronic nature of the substituents introduced in 3-position of the pyridinone precursors **19**–**21**, reaction of the corresponding *o*-QDM with methyl acrylate failed to show a clear-cut effect on the regioselectivity of the

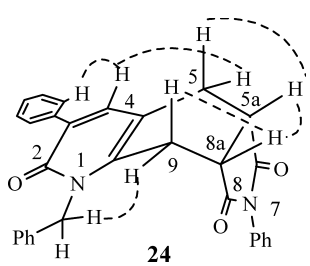


Figure 1. NOE-couplings in adduct **24**.

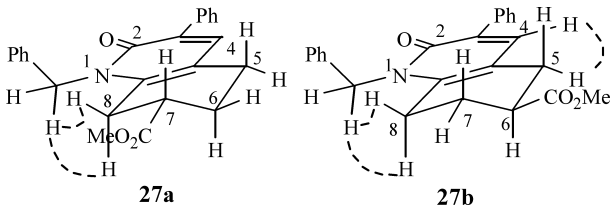


Figure 2. Mixture of regiomeric adducts **27**.

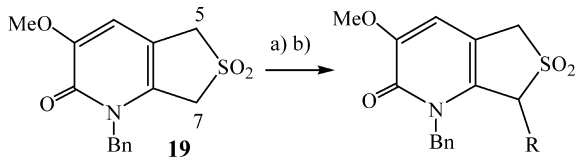
cycloaddition as the product ratio invariably approached a value 1:1. For the determination of the isomeric ratio we again relied on ^{1}H NMR analysis as exemplified for the adduct mixture **27a**,**b** (R_3=Ph, Fig. 2).

The ^{1}H spectrum of **27a**,**b** run in $CDCl_3$ was unresolved; hence C_6D_6 was used as a solvent to unravel the signals corresponding to the aliphatic protons H-5 and H-8 (Aromatic Solvent Induced Shift). For regioisomer **27b** the geminal protons H-5 appeared as two dd signals: the signal at 2.52 ppm (^2J=15.9 Hz, ^3J=9.8 Hz) was assigned to H-5ax and that at 3.90 ppm (^2J=15.9 Hz, ^3J=5.1 Hz) to H-5eq. The assignment of H-5eq was confirmed by a NOE with H-4. For regioisomer **27a** protons H-8ax and H-8eq were identified as two dd absorptions at 2.63 and 2.30 ppm (^2J=17.5 Hz, ^3J=8.8, 5.6 Hz, respectively), both of which showed a NOE with the benzylic protons as in **27b**. The ratio **27a/27b** (43/57) was based on integration values. The isomeric products in other adduct mixtures were attributed in a similar way: **25a/25b** (47/53) and **26a/26b** (55/45).

Precursor **19** (R_3=OMe) also was thermolysed in the presence of other dienophiles; the results of these experiments are shown in Table 2. The cycloaddition with dimethyl maleate yielded the *cis*-substituted diester **28** (77%) as shown by NMR-analysis. When precursor **19** was thermolysed with 1,4-naphthoquinone the fully aromatised compound **29** was isolated as the only product. In the reaction with dimethyl acetylenedicarboxylate, the intermediate adduct also readily underwent aromatisation to produce quinolone **30**. The reaction with *p*-toluenesulfonyl cyanide furnished a separable mixture of naphthyridines **31** and **32**. The structural assignment of the regioisomers again was based on their ^{1}H NMR and NOE-diff spectra. In the spectrum of compound **31**, H-4 was identified as a singlet at 6.97 ppm; presaturation of this proton resulted in a NOE-enhancement of the signal due to H-5 (δ 8.30). The $^1J_{CH}$ values (184 and 170 Hz) corresponding to coupling of C-8 with H-8 (δ 8.63) and C-5 with H-5 respectively, clearly show that the nitrogen atom is in position 7. In the spectrum of adduct **32**, a similar NOE was observed between H-4 (δ 6.92) and H-5 (δ 8.70). The $^1J_{CH}$ values (185 and 169 Hz) corresponding to coupling with H-5 and H-8 (δ 8.10) respectively, now reveal the 6-position of the nitrogen atom. Thermolysis in presence of dihydrofuran led to a complex mixture of regioisomers and decomposition products, the adducts were not isolated and thus not characterized. The existence of **33** was demonstrated via mass spectral analysis.

2.3. Substitution of precursor 19

One advantage of a sulfolene precursor is the ability to abstract a proton at an acidic α-position of the sulfone to generate an anion that can be submitted to reaction with various electrophiles. Starting from sulfolene pyridinone **19** (R_3=OMe), we applied this strategy to attach some dienophilic side chains (Scheme 4, Table 3).



Scheme 4. Substitution of sulfolene pyridinone **19**. *Reagents and conditions*: (a) 1.1 equiv. NaH, DMF, 0 °C; (b) 1.5 equiv. RX.

To effect substitution at the more acidic α-position 7, a solution of **19** in dry DMF was treated at 0 °C with 1.1 equiv. of NaH. After 15 min 2 equiv. of electrophile were added to the reaction mixture. When tetrabutylammonium fluoride was used as a base, the reaction had to proceed at room temperature and the yields were appreciably lower. Attempts to substitute the less acidic α-position 5 by treatment of **19** with 2.1 equiv. of KH or BuLi followed by addition of an electrophile, met with failure. Hence no dianion could be generated from the [3,4-*b*] type precursor **19** even under strongly basic conditions. This finding stays in contrast to the double proton abstraction observed for the isomeric [3,4-*c*] sulfolene pyridinone, which has the less acidic α-methylene group in *peri*-position of the carbonyl function.

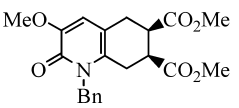
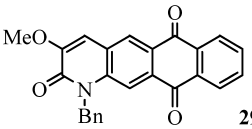
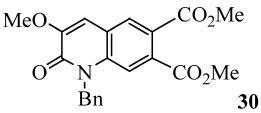
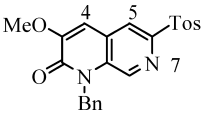
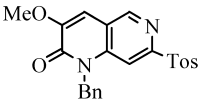
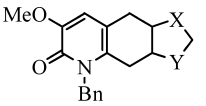
Ester precursor **37** could easily be deprotonated at the 7-position to produce a stable anion. However, further functionalisation of this unreactive species was unsuccessful even when using reactive electrophiles such as methyl chloroformate and benzyl bromide. Attempts to transform the ester into the corresponding amide compounds equally failed.

The sulfolene pyridinone also could be regioselectively brominated by irradiating a solution of **19** and NBS (1.1 equiv.) in CCl_4 for 1 h (500 W tungsten-lamp). This furnished 7-bromo derivative **39** in 45% yield. Apparently this low yield was due to decomposition of compounds **19** and/or **39** upon irradiation. When bromination was carried out under thermal conditions (CCl_4, NBS, benzoylperoxide, reflux) compound **39** was isolated in 67% yield.

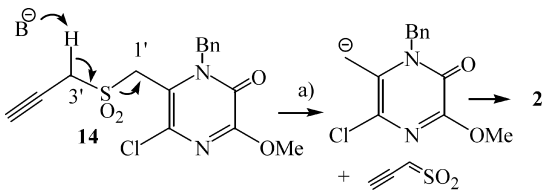
The substituted compounds were characterised by NMR-analysis, which confirmed that substitution indeed had occurred at position 7. Indeed, whereas the spectrum of **19** displayed a singlet signal for the benzylic protons, an AB quartet was observed for the substituted analogues, due to the *peri*-interaction of the 7-substituent and the benzyl group (Table 4). In the spectrum of the 1,7-dibenzyl compound **34**, proton H-7 was identified as a triplet (4.17 ppm, t, ^3J=5.5 Hz). A NOESY experiment further revealed a strong NOE correlation between H-7 and one of the benzylic protons on the pyridinone nitrogen atom. A weak NOE correlation also was observed between protons of the benzylic methylene groups at the 1- and 7-position.

Attempts to substitute one of the α-positions 1′ or 3′ in the side chain of monocyclic sulfone **14** were unsuccessful.

Table 2. Intermolecular Diels–Alder reactions with various dienophiles

Dienophile	Adduct
Dimethyl maleate	 **28** (77%)
1,4-Naphthoquinone	 **29** (70%)
Dimethyl acetylenedicarboxylate	 **30** (60%)
p-Toluenesulfonylcyanide	 **31** (40%)  **32** (27%)
Dihydrofuran	 50 % (crude) **33a** X = O, Y = CH_2 **33b** X = CH_2, Y = O

Various conditions using different bases and solvents invariably led to isolation of pyrazinone **2** in 30–45% yield. Presumably, the anion generated at position 3′ triggers an elimination reaction producing a sulfene and a stabilised 6-methyl carbanion, which eventually yields pyrazinone **2** upon aqueous workup of the reaction mixture (Scheme 5).



Scheme 5. Attempted substitution of sulfone **14**. *Reagents and conditions*: (a) (i) 1.1 equiv. BuLi, −78 °C, THF, (ii) 2 equiv. BnBr; (b) (i) 2.1 equiv. BuLi, −78 °C, THF, (ii) 2 equiv. BnBr; (c) (i) 1.1 equiv. NaH, −0 °C, DMF, (ii) 2 equiv. BnBr; (d) (i) 1.2 equiv. KO*t*Bu, 0 °C to room temperature, THF, (ii) 2 equiv. BnBr.

2.4. Intramolecular Diels–Alder reactions

Substitution of precursor **19** allowed to introduce various dienophilic side chains at the 7-position. The 7-substituted compounds **35**, **36**, and **38** now were submitted to thermolysis in order to generate the corresponding *o*-QDM intermediates. Upon intramolecular cycloaddition, these can produce polycyclic pyridinones. To this end a solution of the substituted precursor in *o*-DCB was heated at 150 °C for several hours. Table 5 shows the outcome of these experiments.

Table 3. Substitution of sulfolene pyridinone **19**

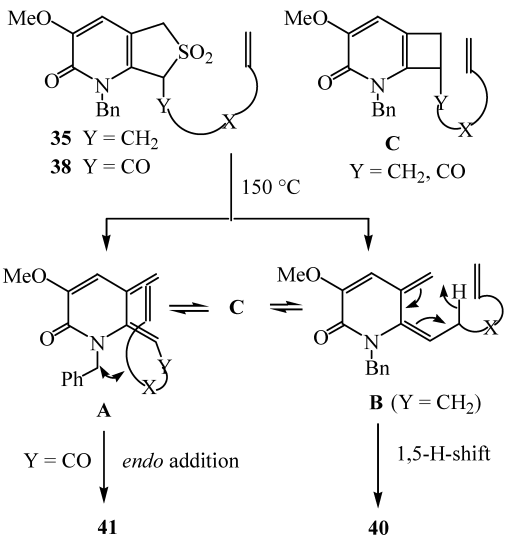
Electrophile RX	R	Product number (yield)
Benzylbromide	$CH_2C_6H_5$	**34** (60)
5-Bromopentene	$(CH_2)_3CH{=}CH_2$	**35** (57)
Allyl chloroformate	$CO_2CH_2CH{=}CH_2$	**36** (61)
Methyl chloroformate	CO_2CH_3	**37** (59)
N,*N*-Diallylcarbamoyl chloride	$CON(allyl)_2$	**38** (58)

Table 4. Selected NMR data

Compound number	H-benzyl (ppm)	^2J
19	5.23	/
34	4.33/5.70	16.0
35	4.95/5.45	15.7
36	4.96/5.88	15.9
37	4.99/5.41	15.7
38	4.37/5.68	15.8
39 (7-Br)	4.83/6.10	15.9

Thermolysis of compound **35** exclusively produced rearranged product **40**. Extrusion of SO_2 may result in generation of the *Z*- or *E*-*o*-QDM intermediate **A** or **B**, both of which experience a large steric repulsion with either the exocyclic methylene group or the *N*-benzyl substituent in *peri*-position (Scheme 6). *o*-QDM **B** now can undergo a 1,5-sigmatropic hydrogen shift to afford the rearranged product **40**. Furthermore, equilibration of **A** and **B** conceivably may proceed via cyclobutene intermediate **C**.

Thermolysis of **36** furnished a complex mixture of products, which were not further characterised. Finally, from the thermolysis of precursor **38** the *cis*-fused adduct **41** was isolated as a single product. Again both **A** and **B** type

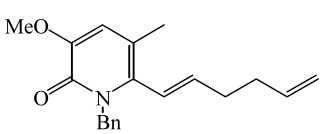
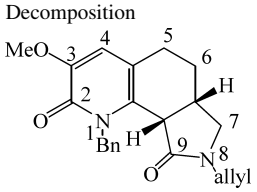


Scheme 6. Intramolecular cycloaddition/rearrangement.

intermediates (Y=CO) may be generated. However, in this case **B** cannot undergo a 1,5-H-shift since no H-atoms are available. Furthermore, cycloaddition involving type **B** intermediates (Y=CH_2, CO) is disfavoured as this requires a highly strained *exo* transition state. Hence, cycloaddition can proceed only starting from intermediate **A** (Y=CO): the more favourable *endo* transition state then leads to the formation of *cis*-fused adduct **41**.

The *cis*-fused structure of *endo*-adduct **41** was established by NMR-spectroscopy. Proton H-9a was identified as a doublet at 3.57 ppm showing coupling (^3J=6.3 Hz) with H-6a (δ 2.43). The presumed *cis*-disposition of the angular protons H-9a and H-6a was confirmed by their strong NOE correlation. A NOE also was observed between H-9a and one of the benzylic protons (δ 5.49). The signals at 2.94 ppm (d, 1H, ^2J=10 Hz) and 3.48 ppm (dd, ^2J=10 Hz, ^3J=6 Hz) were assigned to the geminal protons H-7, both of which display a NOE with H-6a. This implies the occurrence of half-chair **A**. By conformational modelling **A** was shown to be more stable (ca. 3.5 kcal/mol) than half-chair **B**, which displays a highly unfavourable axial 6-methylene group (Fig. 3).

Table 5. Intramolecular Diels–Alder reactions

Substituted precursor	Product number (yield, %)
35	 **40** (55)
36	Decomposition
38	 **41** (65)

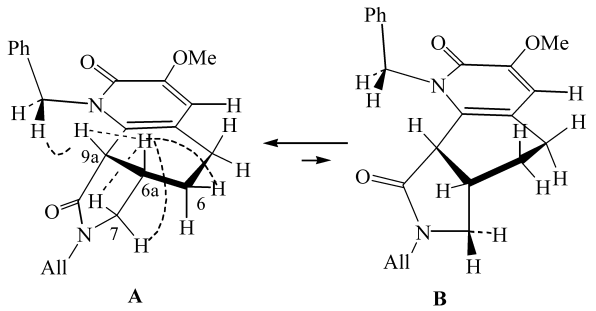


Figure 3. NOE correlations observed for adduct **41**.

3. Conclusion

In this work we established a route leading to various substituted [3,4-*b*] sulfolene pyridinones. Upon thermolysis these were converted into the corresponding pyridinone *o*-QDM intermediates, which in the presence of dienophiles allowed for intermolecular Diels–Alder reactions. However, no regioselectivity was observed for cycloadditions with non-symmetric dienophiles. When dienophilic side chains were introduced, intramolecular cycloaddition only succeeded if no competing rearrangement involving a 1,5-H-shift of the *o*-QDM intermediate was viable.

4. Experimental

Melting points were determined using a Reichert–Jung Thermovar apparatus and an Electrothermal IA 9000 digital melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 297 grating IR spectrophotometer and a Perkin–Elmer 1720 Fourier transform spectrometer. Mass spectra were run using a Hewlett–Packard MS-Engine 5989A apparatus for EI and CI spectra, and a Kratos MS50TC instrument for exact mass measurements performed in the EI mode at a resolution of 10,000. For the NMR spectra (δ, ppm) a Bruker Avance 300 and a Bruker AMX 400 spectrometer were used. All NMR spectra were taken up in $CDCl_3$ with TMS as an internal standard unless otherwise stated. Analytical and preparative thin layer chromatography was carried out using Merck silica gel 60 PF-224, for column chromatography 70–230 mesh silica gel 60 (E. M. Merck) was used as the stationary phase.

4.1. Synthesis of the precursors 19–21

The preparation and the analytical data of the pyrazinones **1**, **2** and **4** were reported previously.[8] The substituted pyrazinone **3** was prepared analogously using sodium ethanethiolate in THF.

4.1.1. 1-Benzyl-5-chloro-3-(ethylsulfanyl)-6-methyl-2(1*H*)-pyrazinone 3. Yield: 90%; yellow crystals; mp 82.5–83.3 °C (ethanol); IR (KBr/cm^{-1}): 3061, 2971, 1706, 1650, 1567; ^{1}H NMR: δ 1.38 (t, 3H, ^3J=7.4 Hz, CH_3), 2.34 (s, 3H, 6-CH_3), 3.08 (q, 2H, ^3J=7.4 Hz, CH_2), 5.30 (s, 2H, CH_2–N), 7.17 (d, 2H, J_o=6.7 Hz, H–Ph), 7.26–7.32 (m, 3H, H–Ph); ^{13}C NMR: δ 13.5 (CH_3), 16.2 (CH_3), 24.1 (CH_2), 48.6 (CH_2–N), 126.8 (C-6), 126.9 (CH), 128.4 (C-5), 128.9 (CH), 134.5 (C-*ipso*), 154.4 (C-3), 156.3 (C-2); MS [*m*/*z* (%)]: EI: 294 (26, $M^{+\cdot}$), 203 (7, $M^{+\cdot}-C_7H_7$), 91 (100,

$C_7H_7^+$); HRMS: calcd for $C_{14}H_{15}N_2OSCl$: 294.0594; found: 294.0591.

The experimental data of the bromomethyl substituted pyrazinones **5** and **7** were reported previously.[8] Compound **6** was prepared using the same procedure.

4.1.2. 1-Benzyl-6-bromomethyl-5-chloro-3-(ethylsulfanyl)-2(1*H*)-pyrazinone 6. Yield: 90%; yellow crystals; mp 73.2–75.1 °C (ethanol); IR (KBr/cm^{-1}): 3050, 2973, 1680, 1592; ^{1}H NMR: δ 1.39 (t, 3H, ^3J=7.4 Hz, CH_3), 3.10 (q, 2H, ^3J=7.4 Hz, CH_2), 4.41 (s, 3H, CH_2–Br), 5.47 (s broad, 2H, CH_2–N), 7.18 (d, 2H, J_o=6.8 Hz, H–Ph), 7.29–7.35 (m, 3H, H–Ph); ^{13}C NMR: δ 13.3 (CH_3), 24.4 (CH_2), 25.4 (CH_2) 47.7 (CH_2–N), 126.5 (C-6), 126.4 (CH), 128.0 (CH), 128.5 (C-5), 129.2 (CH), 134.9 (C-*ipso*), 153.8 (C-3), 161.1 (C-2); MS [*m*/*z* (%)]: EI: 371 (6, $M^{+\cdot}$), 293 (7, $M^{+\cdot}-Br$), 265 ($M^{+\cdot}-Br$, –CO), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{14}H_{14}N_2BrClOS$: 371.9699; found: 371.9720.

4.2. General procedure for the synthesis of thioesters 8–10

To a stirred solution of bromide **5**–**7** (0.1 mol) and thiolacetic acid (0.12 mol) in dry THF (500 mL) was added dropwise NEt_3 (0.3 mol) under an inert atmosphere. After completion of the reaction, water (500 mL) was added and the mixture was extracted with CH_2Cl_2 (3×200 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography (Silica gel, 5 EtOAc/95 CH_2Cl_2) to afford the following compounds.

4.2.1. *S* ^{1}-[(1-Benzyl-3-chloro-1,6-dihydro-5-methoxy-6-oxo-2-pyrazinyl)methyl]ethanethioate 8. Yield: 80%; pale yellow crystals; mp 134.5–136 °C (ethanol); IR (KBr/cm^{-1}): 2991, 1671, 1587; ^{1}H NMR: δ 2.36 (s, 3H, CH_3), 4.02 (s, 3H, OCH_3), 4.17 (s, 2H, CH_2S), 5.32 (s, 2H, CH_2–N), 7.21 (d, 2H, ^3J=7.0 Hz, H–Ph), 7.30–7.33 (m, 3H, H–Ph); ^{13}C NMR: δ 27.9 (CH_2), 30.2 (CH_3), 48.1 (CH_2–N), 55.3 (CH_3), 124.5 (C), 125.5 (C), 126.7 (CH), 128.1 (CH), 129.0 (CH), 135.0 (C-*ipso*), 151.3 (C), 154.6 (C), 193.9 (C); MS [*m*/*z* (%)]: EI: 338 (15, $M^{+\cdot}$), 295 (9, $M^{+\cdot}-C_2H_3O$), 263 (11, $M^{+\cdot}-C_2H_3OS$), 247 (15, $M^{+\cdot}-C_7H_7$), 205 (27, $M^{+\cdot}-C_7H_7$, $-C_2H_3O$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{15}H_{15}N_2O_3SCl$: 338.0492; found 338.0489. CHN analysis: calcd for $C_{15}H_{15}ClN_2O_3S$: C 53.18, H 4.46, N 8.27; found: C 53.41, H 4.18, N 8.10.

4.2.2. *S* ^{1}-{[1-Benzyl-3-chloro-1,6-dihydro-5-(ethylsulfanyl)-6-oxo-2-pyrazinyl}methyl]ethanethioate 9. Yield: 94%; yellow crystals; mp 102–102.5 °C (ethanol); IR (KBr/cm^{-1}): 2963, 1701, 1646, 1563; ^{1}H NMR: δ 1.39 (t, 3H, ^3J=7.2 Hz, CH_3), 2.37 (s, 3H, CH_3), 3.08 (q, 2H, ^3J=7.2 Hz, CH_2), 4.18 (s, 2H, 6-CH_2), 5.30 (s, 2H, CH_2–N), 7.20–7.34 (m, 5H, H–Ph); ^{13}C NMR: δ 13.3 (CH_3), 24.3 (CH_2), 27.9 (CH_2), 30.2 (CH_3), 48.2 (CH_2–N), 126.7 (C-6), 126.8 (CH), 128.1 (CH), 128.5 (C-5), 129.0 (CH), 134.9 (C-*ipso*), 154.1 (C-3), 159.3 (C-2), 193.8 (CO); MS [*m*/*z* (%)]: EI: 368 (15, $M^{+\cdot}$), 325 (4, $M^{+\cdot}-C_2H_3O$), 293 (14, $M^{+\cdot}-C_2H_3OS$), 277 (16, $M^{+\cdot}-C_7H_7^+$), 235 (32, $M^{+\cdot}-C_7H_7NCO$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{16}H_{17}N_2O_2S_2Cl$: 368.0420; found: 368.0416. CHN analysis: calcd for $C_{16}H_{17}ClN_2O_2S_2$: C 52.09, H 4.64, N 7.59; found: C 51.86, H 4.68, N 7.44.

4.2.3. *S* ^{1}-[(1-Benzyl-3-chloro-1,6-dihydro-5-phenyl-6-oxo-2-pyrazinyl)methyl]ethanethioate 10. Yield: 90%; yellow crystals; mp 146–147 °C (ethanol); IR (KBr/cm^{-1}): 3052, 2965, 1648, 1546; ^{1}H NMR: δ 2.38 (s, 3H, CH_3), 4.27 (s, 2H, CH_2), 5.42 (s, 2H, CH_2–N), 7.23–7.34 (m, 5H, H–Ph), 7.43–7.45 (m, 3H, H–Ph), 8.39–8.42 (m, 2H, H–Ph);^{13}C NMR: δ 28.2 (CH_2), 30.1 (CH_3), 48.5 (CH_2–N), 126.7 (C-5), 127.9 (CH), 128.0 (CH), 128.1 (C-6), 129.1 (CH), 129.3 (CH), 130.7 (CH), 132.8 (CH), 134.1 (C-*ipso*), 135.5 (C-*ipso*), 150.7 (C-3), 155.1 (C-2), 194.4 (CO); MS [*m*/*z* (%)]: EI: 384 (30, $M^{+\cdot}$), 341 (19, $M^{+\cdot}-C_2H_3O$), 309 (12, $M^{+\cdot}-C_2H_3OS$), 251 (39, $M^{+\cdot}-C_7H_7NCO$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{20}H_{17}N_2O_2SCl$: 384.0699, found: 384.0698; CHN analysis: calcd for $C_{20}H_{17}ClN_2O_2S$: C 62.41, H 4.45, N 7.28; found: C 62.10, H 4.45, N 7.28.

4.3. General procedure for the synthesis of thioethers 11–13

To a solution of thioesters **8**–**10** (0.05 mol) in methanol (250 mL) was added under an inert atmosphere 1.3 equiv. of sodium methoxide. After reaction at room temperature for 1 h, 3 equiv. of propargylic bromide were added. Subsequently, the reaction mixture was stirred at room temperature for another 2.5 h and neutralised with a dilute solution of HCl in MeOH. The solution was concentrated, the residue redissolved in CH_2Cl_2 (150 mL), and the CH_2Cl_2 solution washed with water (2×150 mL). The organic layer was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography (Silica gel, 70 Hexane/30 EtOAc) to afford thioether compounds **11**–**13**.

4.3.1. 1-Benzyl-5-chloro-3-methoxy-6-[(2-propynylsulfanyl)methyl]-2-(1*H*)-pyrazinone 11. Yield: 90%; yellow crystals; mp 147.5–149.0 °C (CH_2Cl_2/hexane); IR (KBr/cm^{-1}): 2993, 1668, 1583; ^{1}H NMR: δ 2.21 (t, 1H, ^4J=2.5 Hz, ≡CH), 3.36 (d, 2H, ^4J=2.5 Hz, CH_2), 3.87 (s, 2H, 6-CH_2), 4.03 (s, 3H, OCH_3), 5.55 (s, 2H, CH_2–N), 7.16 (d, 2H, ^3J=7.0 Hz, H–Ph), 7.26–7.32 (m, 3H, H–Ph); ^{13}C NMR: δ 20.8 (CH_2), 29.7 (CH_2), 47.5 (CH_2–N), 55.2 (CH_3), 71.6 (CH), 79.5 (C), 123.9 (C) 125.8 (CH), 126.4 (CH), 127.9 (CH), 135.2 (C-*ipso*), 151.4 (C), 154.4 (C); MS [*m*/*z* (%)]: EI: 334 (19, $M^{+\cdot}$), 299 (5, $M^{+\cdot}-Cl$), 264 (21, $M^{+\cdot}-C_3H_3S$), 243 (4, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{16}H_{15}N_2O_2SCl$: 334.0543, found: 334.0543; CHN analysis: calcd for $C_{16}H_{15}ClN_2O_2S$: C 57.40, H 5.52, N 8.37; found: C 57.33, H 5.38, N 8.27.

4.3.2. 1-Benzyl-5-chloro-3-(ethylsulfanyl)-6-[(2-propynylsulfanyl)methyl]-2(1*H*)-pyrazinone 12. Yield: 88%; unstable yellow oil; ^{1}H NMR: δ 1.38 (t, 3H, ^3J=7.2 Hz, CH_3), 2.21 (t, 1H, ^4J=2.6 Hz, ≡CH), 3.08 (q, 2H, ^3J=7.2 Hz, CH_2), 3.37 (d, 2H, ^4J=2.6 Hz, CH_2), 3.89 (s, 2H, 6-CH_2S), 5.52 (s, 2H, CH_2–N), 7.14 (d, 2H, J_o=6.9 Hz, H–Ph), 7.20–7.35 (m, 3H, H–Ph); ^{13}C NMR: δ 13.4 (CH_3), 19.9 (CH_2S), 24.4 (CH_2), 29.9 (CH_2-6), 47.6 (CH_2–N), 71.8 (CH), 79.5 (C), 126.6 (C-6), 126.7 (CH), 128.1 (CH), 128.5 (C-5), 129.1 (CH), 134.9 (C-*ipso*), 154.1 (C-3), 159.1 (C-2);

MS [*m*/*z* (%)]: CI: 365 (90, MH^+), 304 (65, MH^+-ClCN), 293 (100, $MH^+-C_3H_4S$), 91 (10, $C_7H_7^+$).

4.3.3. 1-Benzyl-5-chloro-3-phenyl-6-[(2-propynylsulfanyl)methyl]-2(1*H*)-pyrazinon 13. Yield: 70%; yellow crystals; mp 94–94.5 °C; IR (KBr/cm^{-1}): 3027, 2940, 1654, 1543; ^{1}H NMR: δ 2.19 (t, 1H, ^4J=2.5 Hz, ≡CH), 3.34 (d, 2H, ^4J=2.5 Hz, CH_2), 3.90 (s, 2H, CH_2S), 5.56 (s, 2H, CH_2–N), 7.15 (d, 2H, J_o=7.0 Hz, H–Ph), 7.25–7.29 (m, 3H, H–Ph), 7.39–7.41 (m, 3H, H–Ph), 8.40–7.42 (m, 2H, H–Ph); ^{13}C NMR: δ 19.9 (CH_2), 29.9 (CH_2), 47.8 (CH_2–N), 71.8 (CH), 79.2 (C), 126.3 (C-5), 127.1 (CH), 127.8 (CH), 127.9 (C-6), 128.8 (CH), 129.6 (CH), 130.5 (CH), 133.1 (CH), 134.6 (C-*ipso*), 134.8 (C-*ipso*), 150.2 (C-3), 154.9 (C-2); MS [*m*/*z* (%)]: EI: 380 (4, $M^{+\cdot}$), 341 (2, $M^{+\cdot}-C_3H_3$), 319 (29, $M^{+\cdot}-ClCN$), 247 (28, $M^{+\cdot}-C_7H_7NCO$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{21}H_{17}N_2OSCl$: 380.0750; found: 380.0749.

4.3.4. 1-Benzyl-5-chloro-3-methoxy-6-[(2-propynylsulfonyl)methyl]-2-(1*H*)-pyrazinon 14. To a solution of thienopyridinone **11** (2 g, 0.006 mol) in dry CH_2Cl_2 (100 mL) are added 3 mol equiv. of *m*-CPBA. The mixture is stirred for 3 h at room temperature. Then a saturated solution of $NaHCO_3$ (50 mL) is added, and stirring is continued for 1 h. The organic phase is separated and the aqueous phase is further extracted with CH_2Cl_2. The combined organic layers are washed with water and dried over $MgSO_4$ and the solvent evaporated. The residue is purified by column chromatography (alumina, 15 EtOAc/85 CH_2Cl_2).

Yield: 70%; white powder; mp 48.5 °C (decomposition); IR (KBr/cm^{-1}): 2947, 1964, 1684, 1339, 1128, 1576; ^{1}H NMR: δ 2.54 (t, 1H, ^4J=2.7 Hz, CH), 4.00 (d, 2H, ^4J=2.7 Hz, CH_2), 4.07 (s, 3H, OCH_3), 4.57 (s broad, 2H, CH_2), 5.62 (s broad, 2H, CH_2–N), 7.15 (d, 2H, H–Ph), 7.26–7.34 (m, 3H, H–Ph); ^{13}C NMR: δ 47.06 (CH_2), 48.5 (CH_2), 52.3 (CH_2), 55.6 (CH_3), 70.7 (C), 77.3 (CH), 118.4 (C-5), 126.6 (CH), 128.3 (CH), 129.3 (CH), 133.6 (C-6), 134.6 (C-*ipso*), 151.0 (C), 155.7 (C); MS [*m*/*z* (%)]: EI: 366 (7, $M^{+\cdot}$), 305 (2, $M^{+\cdot}-ClCN$), 263 (75 ($M^{+\cdot}-C_3H_3O_2S$), 233 (21, $M^{+\cdot}-C_7H_7NCO$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{16}H_{15}N_2O_4SCl$: 366.0441; found: 366.0436. CHN analysis: calcd for $C_{16}H_{15}ClN_2O_4S$: C 52.39, H 4.12, N 7.64; found: C 52.70, H 3.85, N 7.45.

4.4. General procedure for the synthesis of thienopyridinones 16–18

A solution of thioether **11**–**13** (0.04 mol) in dry toluene (300 mL) was refluxed under an inert atmosphere (6–48 h depending on the thioether). The solvent was evaporated and the residue was purified by column chromatography (silica gel, 15 EtOAc/85 CH_2Cl_2) to give cyclic sulfides **16**–**18**.

4.4.1. Benzyl-3-methoxy-5,7-dihydrothieno[3,4-*b*]pyridin-2(1*H*)-one 16. Yield: 74%; yellow crystals; mp 51–52 °C; IR (KBr/cm^{-1}): 3031, 2935, 1662, 1605; ^{1}H NMR: δ 3.83 (s, 3H, OCH_3), 4.05 (s broad, 4H, 2×CH_2), 5.27 (s, 2H, CH_2–N), 6.55 (s, 1H, CH), 7.18–7.29 (m, 5H, H–Ph); ^{13}C NMR: δ 35.6 (CH_2), 35.9 (CH_2), 48.9 (CH_2–N), 55.9 (CH_3), 109.6 (CH-4), 114.7 (C-7a), 126.9 (CH), 127.6 (CH), 128.7 (CH), 134.8 (C-4a), 135.9 (C-*ipso*), 148.4 (C-3), 158.0 (C-2); MS [*m*/*z* (%)]: EI: 273 (39, $M^{+\cdot}$), 182 (22, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{15}H_{15}NO_2S$: 273.0824; found: 273.0823.

4.4.2. 1-Benzyl-3-(ethylsulfanyl)-5,7-dihydrothieno[3,4-*b*]pyridin-2(1*H*)-one 17. Yield: 93%; yellow oil; IR (NaCl/cm^{-1}): 2966, 1650; ^{1}H NMR: δ 1.35 (t, 3H, ^3J=7.4 Hz, CH_3), 2.87 (q, 2H, ^3J=7.4 Hz, CH_2), 4.03 (d, 2H, ^2J=18.5 Hz, CH_2), 4.09 (d, 2H, ^2J=18.5 Hz, CH_2), 5.26 (s, 2H, CH_2–N), 7.04 (s, 1H, H-4), 7.19 (d, 2H, J_o=7.0 Hz), 7.24–7.29 (m, 3H, H–Ph); ^{13}C NMR: δ 13.3 (CH_3), 25.1 (CH_2), 35.6 (CH_2), 35.9 (CH_2), 49.1 (CH_2–N), 116.6 (CH-4), 127.0 (C-7a), 127.7 (CH), 128.8 (CH), 129.3 (CH), 129.5 (C-4a), 135.9 (C-*ipso*), 141.0 (C-3), 160.6 (C-2); MS [*m*/*z* (%)]: EI: 303 (52, $M^{+\cdot}$), 270 (39, $M^{+\cdot}-HS$), 242 (2, $M^{+\cdot}-C_2H_5S$), 212 (11, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{17}H_{17}NOS_2$: 303.0752; found: 303.0748.

4.4.3. 1-Benzyl-3-phenyl-5,7-dihydrothieno[3,4-*b*]pyridin-2(1*H*)-one 18. Yield: 65%; yellow crystals; mp 183–184 °C (ethanol); IR (KBr/cm^{-1}): 3029, 2919, 1650, 1597; ^{1}H NMR: δ 4.08 (d, 1H, ^2J=17.5 Hz, CH_2), 4.12 (d, 1H, ^2J=17.7 Hz, CH_2), 4.15 (2×d, 2H, ^2J=17.7 Hz, CH_2), 5.29 (s, 2H, CH_2–N), 7.20–7.40 (m, 9H, H–Ph+H-4), 7.65–7.70 (m, 2H, H–Ph); ^{13}C NMR: δ 35.6 (CH_2), 36.3 (CH_2), 49.1 (CH_2–N), 116.9 (C-7a), 126.9 (CH), 127.9 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.9 (CH), 129.8 (C-4a), 134.4 (C-4), 136.5 (C-*ipso*), 137.3 (C-*ipso*), 145.2 (C-3), 162.2 (C-2); MS [*m*/*z* (%)]: CI: 320 (100, MH^+). HRMS: calcd for $C_{20}H_{17}NOS$: 319.1031; found: 319.1029.

4.5. General procedure for the oxidation of cyclic sulfides 16–18

To a solution of thienopyridinone **16**–**18** (0.02 mol) in dry CH_2Cl_2 (150 mL) was added *m*-CPBA (0.06 mol). The mixture was stirred for 18 h at room temperature. Then a saturated solution of $NaHCO_3$ (50 mL) was added, and stirring was continued for 4 h. The organic phase was separated and the aqueous phase further extracted with CH_2Cl_2. The combined organic layers were washed with water and dried over $MgSO_4$ and the solvent evaporated. The residue was purified by column chromatography (Silica gel, 15 EtOAc/85 CH_2Cl_2) to afford sulfones **19**–**21**.

4.5.1. 1-Benzyl-3-methoxy-5,7-dihydro-6,6-dioxothieno[3,4-*b*]pyridin-2(1*H*)-one 19. Yield: 80%; white crystals; mp 148 °C (decomposition); IR (KBr/cm^{-1}): 2986, 1652, 1601, 1321, 1134; ^{1}H NMR: δ 3.57 (s, 3H, OCH_3), 4.13 (s, 2H, CH_2), 4.22 (s, 2H, CH_2), 5.23 (s, 2H, CH_2–N), 6.58 (s, 1H, H-4), 7.17 (d, 2H, ^3J=7.0 Hz, H–Ph), 7.26–7.35 (m, 3H, H–Ph); ^{13}C NMR: δ 49.4 (CH_2–N), 55.5 (CH_3), 56.2 (CH_2), 56.8 (CH_2), 107.4 (C-7a), 108.7 (CH-4), 129.2 (C-4a), 126.9 (CH), 127.1 (CH), 128.2 (CH), 134.9 (C-*ipso*), 150.8 (C-3), 157.9 (C-2); MS [*m*/*z* (%)]: EI: 305 (19, $M^{+\cdot}$), 241 (26,$M^{+\cdot}-SO_2$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{15}H_{15}NO_4S$: 305.0722; found: 305.0718.

When compound **14** was heated in toluene at reflux temperature for 2 h the yield of **19** was 64%.

4.5.2. 1-Benzyl-3-(ethylsulfonyl)-5,7-dihydro-6,6-dioxothieno [3,4-*b*]pyridin-2(1*H*)-one 20. Yield: 50%; white

crystals; mp 152.5–153 °C (decomposition); IR (KBr/cm^{-1}): 2974, 1652, 1536, 1304, 1120; ^{1}H NMR: δ 1.29 (t, 3H, ^3J=7.4 Hz, CH_3), 3.54 (q, 2H, ^3J=7.4 Hz, CH_2), 4.26 (s, 2H, CH_2), 4.29 (s, 2H, CH_2), 5.25 (s, 2H, CH_2–N), 7.17 (dd, 2H, J_o=7.9 Hz, J_m=2.1 Hz, H–Ph), 7.33–7.40 (m, 3H, H–Ph), 8.12 (s, 1H, H-4); ^{13}C NMR: δ 6.9 (CH_3), 47.3 (CH_2–N), 49.4 (CH_2), 55.7 (CH_2), 55.8 (CH_2), 108.3 (CH-4), 127.0 (CH), 128.8 (CH), 129.5 (CH), 129.8 (C-4a), 133.6 (C-*ipso*), 140.3 (C-7a), 145.2 (C-3), 157.6 (C-2); MS [*m*/*z* (%)]: EI: 367 (25, $M^{+\cdot}$), 303 (11, $M^{+\cdot}-SO_2$), 211 (18, $M^{+\cdot}-SO_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{16}H_{17}NO_5S_2$: 367.0548; found: 367.0549.

4.5.3. 1-Benzyl-3-phenyl-5,7-dihydro-6,6-dioxothieno[3,4-*b*]pyridin-2(1*H*)-one 21. Yield: 57%; white crystals; mp 160 °C (decomposition); IR (KBr/cm^{-1}): 3029, 2958, 1647, 1596; ^{1}H NMR: δ 4.23 (s, 2H, CH_2), 4.27 (s, 2H, CH_2), 5.27 (s broad, 2H, CH_2–N), 7.21–7.42 (m, 9H, H–Ph+H-4), 7.65–7.09 (m, 2H, H–Ph); ^{13}C NMR: δ 49.8 (CH_2–N), 56.3 (CH_2), 56.9 (CH_2), 109.0 (C-7a), 126.9 (CH), 128.3 (CH), 128.5 (CH), 128.6 (CH), 129.2 (CH), 133.8 (C-4), 134.3 (C-4a), 135.4 (C-4a), 136.2 (C-*ipso*), 136.8 (C-*ipso*); MS [*m*/*z* (%)]: EI: 351 (24, $M^{+\cdot}$), 287 (78, $M^{+\cdot}-SO_2$), 91 (100, $C_7H_7^+$).

4.6. Intermolecular Diels–Alder reactions of sulfolene pyridinones 19–21

General procedure. A solution of 0.2 g sulfolene pyridinones **19**–**21** and 5 equiv. of a dienophile in 10 mL *o*-dichlorobenzene is brought into a glass tube and the solution is subjected to three consecutive freeze–pump–thaw cycles. The tube is sealed off and is then heated in an oven at 160 °C for 12 h. After cooling, the tube is opened, and the solvent is removed by Kugelrohr distillation. The products are purified by column chromatography (silica gel, CH_2Cl_2/EtOAc: 95/5 to 85/15) to give the following adducts.

4.6.1. ((5a*R* *,8a*S* *)-1-Benzyl-3-methoxy-7-phenyl-5,5a,8a,9-tetrahydro-1*H*-pyrrolo[3,4-*g*]quinoline-2,6,8(7*H*)-trione 22. Yield: 70%; yellow crystals; mp 197 °C (ethanol); IR (KBr/cm^{-1}): 3061, 2933, 1710, 1651, 1599; ^{1}H NMR: 2.51 (dd, 1H, ^2J=15.6 Hz, $^3J_{ax-eq}$=5.0 Hz, H-5_{ax}), 2.71 (dd, 1H, ^2J=14.0 Hz, $^3J_{ax-eq}$=4.5 Hz, H-9_{ax}), 3.06 (dd, 1H, ^2J=14.0 Hz, $^3J_{eq-eq}$=2.0 Hz, H-9_{eq}), 3.34–3.36 (m, 2H, H-5a+H-8a), 3.42 (dd, 1H, ^2J=15.6 Hz, $^3J_{eq-eq}$=2.2 Hz, H-5_{eq}), 5.06 (d, 1H, ^2J=16.0 Hz, CH_2–N), 5.86 (d, 1H, ^2J=16.0 Hz, CH_2–N), 6.51 (s, 1H, H-4), 6.98 (dd, 2H, J_o=8.0 Hz, J_m=1.0 Hz, H–Ph), 7.17 (d, 2H, J_o=7.3 Hz, H–Ph), 7.25–7.42 (m, 6H, H–Ph); ^{13}C NMR: δ 25.9 (CH_2-5), 28.6 (CH_2-9), 39.5 (CH), 39.8 (CH), 47.2 (CH_2–N), 55.9 (CH_3), 111.5 (C-9a), 113.6 (CH-4), 126.2 (CH), 126.7 (CH), 127.5 (CH), 128.8 (CH), 129.2 (CH), 131.4 (C-4a), 132.2 (C-*ipso*), 136.5 (C-*ipso*), 148.8 (C-3), 158.5 (C-2), 177.4 (C), 177.9 (C); MS [*m*/*z* (%)]: EI: 414 (72, $M^{+\cdot}$), 323 (15, $M^{+\cdot}-C_7H_7$), 176 (75, $M^{+\cdot}-C_7H_7$,$-C_8H_5NO_2$; HRMS: calcd for $C_{25}H_{22}N_2O_4$: 414.1580; found: 414.1584.

4.6.2. (5a*R* *,8a*S* *)-1-Benzyl-3-(ethylsulfonyl)-7-phenyl-5,5a,8a,9-tetrahydro-1*H*-pyrrolo[3,4-*g*]quinoline-2,6,8(1*H*,7*H*)-trione 23. Yield: 60%; yellow crystals, mp 124–125 °C (CH_2Cl_2/hexane); IR (KBr/cm^{-1}): 2974, 1652, 1536, 1304, 1120; ^{1}H NMR: δ 1.22 (t, 3H, ^3J=7.4 Hz, CH_3), 2.66 (dd, 1H, ^2J=15.9 Hz, ^3J=5.5 Hz, H-9ax), 2.75 (dd, 1H, ^2J=15.5 Hz, ^3J=6.2 Hz, H-5ax), 3.11 (dd, 1H, ^2J=15.5 Hz, ^3J=2.4 Hz, H-5eq), 3.39 (m, 3H, H-9eq+H-5a+H-8a), 3.50 (q, 2H, ^3J=7.4 Hz, CH_2), 5.10 (d, 1H, ^2J=15.7 Hz, CH_2–N), 5.86 (d, 1H, ^2J=15.7 Hz, CH_2–N), 6.98 (d, 2H, J_o=8 Hz, H–Ph), 7.10 (d, 2H, J_o=8 Hz, H–Ph), 7.20–7.40 (m, 6H, H–Ph), 8.06 (s, 1H, H-4); ^{13}C NMR: δ 7.0 (CH_3), 27.7 (C-9), 28.4 (C-5), 39.4 (CH), 39.5 (CH), 47.0 CH_2–N), 47.4 (CH_2–SO_2), 112.6 (C), 125.7, 126.4, 127.0 (C), 128.4, 129.3, 129.6, 131.6 (C), 135.7 (C-*ipso*), 143.7 (CH), 151.6 (C-3), 158.7 (C-2), 177.2 (CO), 177.4 (CO); MS [*m*/*z* (%)]: EI: 476 (24, $M^{+\cdot}$), 385 (3, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{26}H_{24}N_2O_5$: 476.1406; found: 476.1412.

4.6.3. (5a*R* *,8a*S* *)-1-Benzyl-3,7-diphenyl-5,5a,8a,9-tetrahydro-1*H*-pyrrolo[3,4-*g*]quinoline-2,6,8(1*H*,7*H*)-trione 24. Yield: 87%; pale yellow crystals, mp 98–98.5 °C; IR (KBr/cm^{-1}): 3032, 2953, 1711, 1643, 1595; ^{1}H NMR: δ 2.65 (dd, 1H, ^2J=14.0 Hz, ^3J=3.8 Hz, H-9ax), 2.75 (dd, 1H, ^2J=15.0 Hz, ^3J=3.9 Hz, H-5ax), 3.12 (dd, 1H, ^2J=15.0 Hz, ^3J=1.7 Hz, H-5eq), 3.37 (m, 2H, H-5a+H-8a), 3.49 (dd, 1H, ^2J=14.0 Hz, ^3J=1.6 Hz, H-9eq), 5.11 (d, 1H, ^2J=15.6 Hz, CH_2–N), 5.89 (d, 1H, ^2J=15.6 Hz, CH_2–N), 7.03 (d, 2H, J_o=7.0 Hz, H–Ph), 7.21–7.42 (m, 12H, H–Ph+H-4), 7.71 (d, 2H, J_o=7.1 Hz, H–Ph); ^{13}C NMR: δ 27.1 (CH_2), 28.6 (CH_2), 39.8 (CH), 39.9 (CH), 47.8 (CH_2–N), 113.1 (C-9a), 126.1 (CH), 126.7 (CH), 127.5 (CH), 127.8 (CH), 128.1 (CH), 128.6 (CH), 128.8 (CH), 128.9 (CH), 129.1 (CH), 130.2 (C-*ipso*), 131.9 (C-4a), 137.0 (C-*ipso*), 137.1 (C-*ipso*), 138.6 (C-4), 142.3 (C-3), 162.3 (C-2), 177.7 (C-8), 178.2 (C-6); MS [*m*/*z* (%)]: EI: 460 (57, $M^{+\cdot}$), 369 (7, $M^{+\cdot}-C_7H_7$), 383 (2, $M^{+\cdot}-C_6H_5$), 222 (57, $M^{+\cdot}-C_7H_7$,$-C_6H_5NC_2O_2$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{30}H_{24}N_2O_3$: 460.1787; found: 460.1788.

4.6.4. Methyl 1-benzyl-3-methoxy-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-7-carboxylate 25a and methyl 1-benzyl-3-methoxy-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-6-carboxylate 25b. Yield: 70%; yellow oil; ^{1}H NMR (C_6D_6): δ 1.34–1.44 (m, 0.5H, H–CH_2), 1.47–1.53 (m, 0.5H, H–CH_2), 1.59–1.64 (m, 0.5H, H–CH_2), 1.66–1.72 (m, 0.5H, H–CH_2), 1.85–1.93 (m, 0.5H, H–CH_2), 2.05–2.20 (m, 2.5H, H-7 **a**+H-6 **b**+3×H–CH_2), 2.32 (dd, 0.5H, ^2J=16 Hz, ^3J=5.2 Hz, H-5eq **b**), 2.42 (dd, 0.5H, ^2J=17 Hz, ^3J=5.6 Hz, H-8eq **a**), 2.54 (dd, 0.5H, ^2J=16 Hz, ^3J=8 Hz, H-5ax **b**), 2.58 (dd, 0.5H, ^2J=17 Hz, ^3J=9 Hz, H-8ax **a**), 3.24 (s, 1.5H, OCH_3 **a**), 3.34 (s, 1.5H, OCH_3 **b**), 3.42 (s, 3H, OCH_3 **a**+**b**), 4.99–5.30 (m breed, 2H, CH_2N **a**+**b**), 5.96 (s, 0.53H, H-4 **b**), 5.99 (s, 0.47H, H-4 **a**), 6.96–7.16 (m, 5H, H–Ph **a**+**b**).

($CDCl_3$): δ 1.74–1.82 (m, 1H, H–CH_2), 2.06–2.11 (m, 1H, H–CH_2), 2.53–2.82 (m, 5H, 2×H–CH_2+H–CH), 5.10–5.50 (m, 2H, CH_2N), 6.40 (s, 0.53H, H-4), 6.42 (s, 0.47H, H-4), 7.11–7.28 (m, 5H, H–Ph); ^{13}C NMR: δ 24.4 (CH_2), 24.6 (CH_2), 25.1 (CH_2), 26.7 (CH_2), 27.7 (CH_2), 29.8 (CH_2), 38.2 (CH), 38.9 (CH), 46.5 (CH_2N), 51.6 (OCH_3), 51.7 (OCH_3), 55.5 (OCH_3), 110.9 (C), 111.9 (C), 114.3 (CH), 114.4 (CH), 126.2 (CH-arom), 126.3 (CH-arom), 126.9 (CH-arom), 128.4 (CH-arom), 131.3, 132.4, 136.4 (C-*ipso*), 147.5 (C-3), 158.3 (C-2), 174.3 (CO), 174.5 (CO); MS [*m*/*z*

(%)]: EI: 327 (40, $M^{+\cdot}$), 295 (20, $M^{+\cdot}-MeOH$), 236 (45, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{19}H_{21}NO_4$: 327.1471; found: 327.1480.

4.6.5. Methyl 1-benzyl-3-(ethylsulfonyl)-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-7-carboxylate 26a and methyl 1-benzyl-3-(ethylsulfonyl)-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-6-carboxylate 26b. Yield: 94%; yellow oil; IR (NaCl/cm^{-1}): 3032, 2951, 1737, 1659, 1593; ^1H NMR: δ 1.28 (t, 3H, ^3J=8.7 Hz, CH_3–Et), 1.77–1.86 (m, 1H, H–CH_2), 2.03–2.16 (m, 1H, H–CH_2), 2.66–3.00 (m, 5H, 2×CH_2+H–CH), 3.54 (q, 2H, ^3J=8.7 Hz, CH_2–Et), 3.67 (s, 1.3H, OCH_3), 3.69 (s, 1.7H, OCH_3), 5.12–5.23 (m, 2H, CH_2N), 7.10–7.91 (m, 5H, H–Ph), 8.00 (s, 0.45H, H-4 b), 8.10 (s, 0.55H, H-4 a); MS [*m*/*z* (%)]: EI: 389 (28, $M^{+\cdot}$), 330 (22, $M^{+\cdot}-CO_2Me$), 298 (7, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{20}H_{23}NO_5S$: 389.1297; found: 389.1296.

4.6.6. Methyl 1-benzyl-3-phenyl-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-7-carboxylate 27a and methyl 1-benzyl-3-phenyl-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-6-carboxylate 27b. Yield: 85%; light yellow oil; IR (NaCl/cm^{-1}): 3029, 2950, 1735, 1650, 1599; ^1H NMR ($CDCl_3$): δ 7.76–1.85 (m, 1H, H–CH_2), 2.07–2.13 (m, 1H, H–CH_2), 2.61–2.91 (m, 5H, 2×CH_2+H–CH), 5.30–5.52 (m broad, 2H, CH_2N), 7.15–7.22 (m, 3H, H–Ph), 7.26–7.30 (4H, H–Ph+H-4), 7.35–7.37 (m, 2H, H–Ph), 7.71–7.73 (m, 2H, H–Ph); (C_6D_6): δ 1.33–1.40 (m, 0.5H, H–CH_2), 1.43–1.50 (m, 0.5H, H–CH_2), 1.57–1.61 (m, 0.5H, H–CH_2), 1.64–1.69 (m, 0.5H, H–CH_2), 1.88–1.97 (m, 0.5H, H–CH_2), 2.02–2.25 (m, 2.5 H, 2×CH_2+H–CH), 2.36 (dd, 0.5H, ^2J=17.5 Hz, ^3J=5.6 Hz, H-8 **a**), 2.36 (dd, 0.5H, ^2J=15.9 Hz, ^3J=5.1 Hz, H-5 **b**), 2.52 (dd, 0.5H, ^2J=15.9 Hz, ^3J=9.8 Hz, H-5 **b**), 2.63 (dd, 0.5H, ^2J=17.5 Hz, ^3J=8.8 Hz, H-8 **a**), 3.24 (s, 1.4H, OCH_3 **a**), 3.34 (s, 1.6H, OCH_3 **b**), 5.00–5.50 (m broad, 2H, CH_2N **a**+**b**), 6.97 (s, 0.43H, H-4 **a**), 6.99 (s, 0.57H, H-4 **b**), 7.04–7.10 (m, 4H, H–Ph), 7.16–7.20 (m, 2H, H–Ph), 7.29–7.33 (m, 2H, H–Ph), 8.00–8.02 (m, 2H, H–Ph); ^{13}C NMR: δ 24.6 (CH_2), 24.7 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 28.7 (CH_2), 29.6 (CH_2), 38.3 (CH), 38.9 (CH), 46.9 (CH_2N), 51.8 (OCH_3), 51.9 (OCH_3), 112.5 (C), 113.4 (C), 126.3 (CH-arom), 126.4 (CH-arom), 127.1 (CH-arom), 127.4 (CH-arom), 127.9 (CH-arom), 128.5 (CH-arom), 128.7 (CH-arom), 136.5 (C-*ipso*), 136.6 (C-*ipso*), 136.9, 139.2, 139.3, 140.7, 141.6, 161.8 (C-2), 174.3 (CO), 174.6 (CO); MS [*m*/*z* (%)]: EI: 373 (100, $M^{+\cdot}$), 314 (56, $M^{+\cdot}-CO_2Me$), 282 ($M^{+\cdot}-C_7H_7$), 222 ($M^{+\cdot}-C_7H_7$, $-CO_2Me$), 91 (60, $C_7H_7^+$); HRMS: calcd for $C_{24}H_{23}NO_3$: 373.1678; found: 373.1681.

4.6.7. Dimethyl (6*R,7*S**) 1-benzyl-3-methoxy-5,6,7,8-tetrahydro-2-oxo-1*H*-quinoline-6,7-dicarboxylate 28.** Yield: 77%; white crystals; mp 152–153 °C; IR (KBr/cm^{-1}): 3029, 2949, 1743, 1655, 1598; ^1H NMR: δ 1.75–2.91 (m, 2H), 2.90–3.10 (m, 4H), 3.55 (s, 3H, OCH_3), 3.59 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 5.24 (d, 1H, ^2J=20.1 Hz, CH_2–N), 5.41 (d, 1H, ^2J=20.1 Hz, CH_2–N), 6.37 (s, 1H, H-4), 7.09 (d, 2H, J_o=8.0 Hz, H–Ph), 7.15–7.22 (m, 3H, H–Ph); ^{13}C NMR: δ 26.5 (CH_2), 28.1 (CH_2), 39.2 (CH), 39.7 (CH), 46.7 (CH_2–N), 52.0 (CH_3), 52.1 (CH_3), 55.7 (CH_3), 110.9 (C-8a), 114.1 (CH-4), 126.5 (CH), 127.2 (CH), 128.6 (CH), 131.4 (C-4a), 136.9 (C-*ipso*), 148.4 (C-3), 158.9 (C-2), 172.6 (C), 172.9 (C); MS [*m*/*z* (%)]: EI: 385 (71, $M^{+\cdot}$), 354 (8, $M^{+\cdot}-OCH_3$), 326 (41, $M^{+\cdot}-C_2H_3O_2$), 294 (19, $M^{+\cdot}-C_7H_7$), 266 ($M^{+\cdot}-C_2H_3O_2$, $-C_2H_3O_2$), 234 (20, $M^{+\cdot}-C_2H_3O_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{21}H_{23}NO_6$: 385.1525; found: 385.1525.

4.6.8. 1-Benzylnaphto[2,3-*g*]quinoline-2,6,11(1*H*)-trione 29. Yield: 80%; yellow oil; ^1H NMR: δ 4.07 (s, 3H, CH_3), 5.70 (s, 2H, CH_2–N), 7.06 (s, 1H, H-4), 7.24–7.38 (m, 6H, H-arom), 7.76–7.79 (m, 2H, H-arom), 8.22 (s, 1H, CH), 8.25–8.30 (m, 2H, H-arom), 8.40 (s, 1H, CH); ^{13}C NMR: δ 46.9 (CH_2–N), 56.4 (CH_3), 109.9, 113.5, 125.4, 127.1, 127.3, 127.8, 127.9, 128.9, 131.7, 133.7, 133.8, 134.1, 134.2, 135.5 (C-*ipso*), 138.3, 150.7 (C-3), 158.2 (C-2), 182.0 (CO), 182.3 (CO); MS [*m*/*z* (%)]: EI: 395 (28, $M^{+\cdot}$), 304 (7, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{25}H_{17}NO_4$: 395.1158, found: 395.1153.

4.6.9. Dimethyl 1-benzyl-3-methoxy-2-oxo-1*H*-quinoline-6,7-dicarboxylate 30. Yield: 77%; yellow oil; IR (KBr/cm^{-1}): 2952, 1793, 1657, 1622; ^1H NMR: δ 3.56 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 5.17 (d, 1H, ^2J=20 Hz, CH_2–N), 5.63 (d, 1H, ^2J=20 Hz, CH_2–N), 6.51 (s, 1H, H-4), 7.24–7.30 (m, 6H, H-8+H–Ph), 7.47 (s, 1H, H-5); ^{13}C NMR: δ 47.6 (CH_2–N), 52.7 (CH_3), 52.9 (CH_3), 56.5 (CH_3), 113.2 (CH), 116.4 (CH-4), 127.3, 127.4, 127.9, 128.9, 129.2, 130.1, 136.8 (C-*ipso*), 151.2 (C-3), 158.0 (C-2), 163.0, 166.5 (CO), 171.4 (CO); MS [*m*/*z* (%)]: EI: 383 (29, $M^{+\cdot}$), 324 (21, $M^{+\cdot}-C_2H_3O_2$), 292 (19, $M^{+\cdot}-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: Calcd for $C_{21}H_{21}NO_6$: 383.1369, Found: 383.1368.

4.6.10. 1-Benzyl-3-methoxy-6-[(4-methylfenyl)sulfonyl][1,7]naphthyridin-2(1*H*)-one 31. Yield: 40%; yellow crystals; mp 237–238 °C; IR (KBr/cm^{-1}): 3067, 2930, 1660, 1319, 1158; ^1H NMR: δ 2.39 (s, 3H, CH_3), 4.03 (s, 3H, OCH_3), 5.58 (s, 2H, CH_2–N), 6.97 (s, 1H, H-4), 7.18–7.30 (m, 7H, H–Ph), 7.90 (d, 2H, J_o=8.3 Hz, H–Ph), 8.30 (s, 1H, H-5), 8.63 (s, 1H, H-8); ^{13}C NMR: δ 21.6 (CH_3), 46.6 (CH_2), 56.6 (CH_3), 107.9 (CH), 119.4 (CH), 126.8 (CH), 127.3 (C), 128.0 (C), 128.8 (CH), 129.1 (CH), 129.8 (CH), 132.0 (C), 134.8 (C), 136.1 (C), 137.4 (CH), 144.7 (C), 151.9 (C), 152.9 (C); MS [*m*/*z* (%)]: EI: 420 (2, $M^{+\cdot}$), 355 (83, $M^{+\cdot}-SO_2$, –H), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{23}H_{20}N_2O_4S$: 420.1144, found: 420.1139; CHN analysis: calcd for $C_{23}H_{20}N_2O_4S$: C 65.70, H 4.79, N 6.66; found: C 65.36, H 4.94, N 6.33.

4.6.11. 1-Benzyl-3-methoxy-7-[(4-methylphenyl)sulfonyl][1,6]naphthyridin-2(1*H*)-one 32. Yield: 27%; pale yellow crystals; mp 218–220 °C; IR (KBr/cm^{-1}): 3058, 2927, 1668, 1316, 1158; ^1H NMR: δ 2.38 (s, 3H, CH_3), 3.99 (s, 3H, OCH_3), 5.62 (s, 2H, CH_2–N), 6.92 (s, 1H, H-4), 7.23–7.33 (m, 7H, H–Ph), 7.76 (d, 2H, J_o=8.3 Hz, H–Ph), 8.10 (s, 1H, H-8), 8.70 (s, 1H, H-5); ^{13}C NMR: δ 21.6 (CH_3), 46.6 (CH_2–N), 56.5 (OCH_3), 106.7 (CH), 108.2 (CH), 118.9 (C), 127.3 (CH), 128.0 (CH), 128.8 (CH), 129.1 (CH), 129.8 (CH), 134.7 (C), 135.9 (C), 140.3 (C), 144.8 (C), 149.2 (C), 151.2 (C), 156.1 (C), 158.0 (C); MS [*m*/*z* (%)]: EI: 420 (6, $M^{+\cdot}$), 356 (43, $M^{+\cdot}-SO_2$), 265 (9, $M^{+\cdot}-SO_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{23}H_{20}N_2O_4S$: 420.1144, found: 420.1147.

4.7. Substitution of sulfolene pyridinone 19 in position 7

General procedure A. To a solution of 0.2 g (0.65 mmol) of the precursor **19** in dry THF (25 mL) under argon atmosphere was added slowly 1.3 equiv. of tetrabutylammonium fluoride. After stirring at room temperature for 1 h, 2 equiv. of electrophile were added. The reaction mixture was stirred for 12 h at room temperature; then a solution of NH_4Cl (25 mL) was added, the mixture was stirred further at room temperature for 1 h and extracted with CH_2Cl_2 (3×10 mL). The combined organic phases were dried ($MgSO_4$) and evaporated to give a residue that was purified by column chromatography (alumina, 15 EtOAc/85 CH_2Cl_2).

General procedure B. To a cooled (0 °C) suspension of 1.1 equiv. of NaH in DMF (10 mL) was added under a nitrogen atmosphere a solution of 0.2 g (0.65 mmol) sulfolene pyridinone **19**. Stirring was continued at 0 °C for 1 h, after which time 2 equiv. of an electrophile was added. The reaction mixture was allowed to slowly warm to room temperature. After work up by adding 20 mL of saturated NH_4Cl solution and extraction with CH_2Cl_2 (3×15 mL), the combined organic layers were dried over $MgSO_4$. The solvent was evaporated and the residue was purified by column chromatography (alumina, 15 EtOAc/85 CH_2Cl_2).

4.7.1. 1,7-Dibenzyl-5,7-dihydro-3-methoxy-6,6-dioxothieno [3,4-*b*]pyridin-2(1*H*)-one 34. Yield: 60% (procedure B); 40% (procedure A); oil; IR (NaCl/cm^{-1}): 3055, 2976, 1607, 1325, 1124; ^{1}H NMR: δ 3.21 (dd, 1H, ^2J=14.7 Hz, ^3J=5.5 Hz, CH_2–Ph), 3.39 (dd, 1H, ^2J=14.7 Hz, ^3J=5.5 Hz, CH_2–Ph), 3.58 (d, 1H, ^2J=15.0 Hz, H-5), 3.82 (s, 3H, OCH_3); 3.87 (d, 1H, ^2J=15.0 Hz, H-5), 4.17 (t, 1H, ^3J=5.5 Hz, H-7), 4.33 (d, 1H, ^2J=16.0 Hz, CH_2–N), 5.70 (d, 1H, ^2J=16.0 Hz, CH_2–N), 6.38 (s, 1H, H-4), 7.03–7.07 (m, 4H, H–Ph), 7.24–7.29 (m, 6H, H–Ph); ^{13}C NMR: δ 36.9 (CH_2-5), 48.3 (CH_2–N), 54.8 (CH_2–Bn), 56.2 (CH_3), 64.9 (CH-7), 108.8 (C-7a), 108.9 (CH-4), 126.4 (CH), 127.8 (CH), 128.6 (CH), 128.8 (CH), 129.1 (CH), 129.7 (CH), 132.1 (C-4a), 134.1 (C-*ipso*), 135.1 (C-*ipso*), 150.6 (C-3), 157.9 (C-2); MS [*m*/*z* (%)]: EI: 395 (42, $M^{+\cdot}$), 331 (60, $M^{+\cdot}-SO_2$), 304 (12, $M^{+\cdot}-C_7H_7$), 240 (35, $M^{+\cdot}-SO_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{22}H_{21}NO_4S$: 395.1112, found: 395.1120.

4.7.2. 1-Benzyl-5,7-dihydro-3-methoxy-7-(4-pentenyl)-6,6-dioxothieno[3,4-*b*]pyridin-2(1*H*)-one 35. Yield: 57% (method B), 25% (method A); yellow crystals; mp 54.6–55.8 °C (CH_2Cl_2/hexane); IR (KBr/cm^{-1}): 3064, 2925, 1658, 1607, 1315, 1125; ^{1}H NMR: δ 1.33–1.51 (m, 2H, CH_2-3′), 1.69–1.92 (m, 4H, CH_2-1′+CH_2-2′), 3.79 (s, 3H, OCH_3), 3.91 (dd, 1H, ^3J=7.7, 3.2 Hz, H-7), 4.03 (d, 1H, ^2J=15.4 Hz, H-5), 4.10 (d, 1H, ^2J=15.4 Hz, H-5), 4.89 (dt, 1H, $^3J_{trans}$=16.9 Hz, ^4J=1.3 Hz, H-5′), 4.92 (d broad, 1H, $^3J_{cis}$=9.0 Hz, H-5′), 4.96 (d, 1H, ^2J=15.8 Hz, CH_2–N), 5.45 (d, 1H, ^2J=15.8 Hz, CH_2–N), 5.60 (ddt, 1H, $^3J_{trans}$=16.9 Hz, $^3J_{cis}$=9.0 Hz, ^3J=7.0 Hz, H-4′), 6.48 (s, 1H, H-4), 7.58 (dd, 2H, J_o=6.4 Hz, J_m=1.8 Hz, H–Ph), 7.22–7.27 (m, 3H, H–Ph); ^{13}C NMR: δ 25.3 (CH_2), 30.5 (CH_2), 33.4 (CH_2), 48.6 (CH_2–N), 55.7 (CH_2-5), 56.6 (CH_3), 64.7 (CH-7), 108.1 (C-7a), 109.4 (CH-4), 116.0 (CH_2-5′), 126.0 (CH), 127.9 (CH), 129.0 (CH), 132.5 (C-4a), 135.5 (C-*ipso*), 137.5 (CH-4′), 150.9 (C-3), 158.5 (C-2); MS [*m*/*z* (%)]: EI: 373 (24, $M^{+\cdot}$), 309 (25, $M^{+\cdot}-SO_2$), 254 (38, $M^{+\cdot}-SO_2$, $-C_4H_7$), 218 (37, $M^{+\cdot}-SO_2$, $-C_4H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{20}H_{23}NO_4S$: 373.1348, found: 373.1350.

4.7.3. Allyl 1-benzyl-5,7-dihydro-3-methoxy-2,6,6-trioxo-1*H*-thieno[3,4-*b*]pyridine-7-carboxylate 36. Yield: 61% (method B); yellow oil; ^{1}H NMR: δ 3.88 (s, 3H, OCH_3), 4.17 (d, 1H, ^2J=14.8 Hz, H-5), 4.39 (d, 1H, ^2J=14.8 Hz, H-5), 4.46 (dt, 2H, ^3J=6.0 Hz, ^4J=1.3 Hz, H-3′), 4.87 (s, 1H, H-7), 4.96 (d, 1H, ^2J=15.9 Hz, CH_2–N), 5.27 (dd, 1H, $^3J_{cis}$=10.4 Hz, ^4J=1.3 Hz, H-5′), 5.32 (dd, 1H, $^3J_{trans}$=17.2 Hz, ^4J=1.3 Hz, H-5′), 5.44 (d, 1H, ^2J=15.9 Hz, CH_2–N), 5.80 (ddt, 1H, $^3J_{trans}$=17.2 Hz, $^3J_{cis}$=10.4 Hz, ^3J=6.0 Hz, H-4′), 6.56 (s, 1H, H-4), 7.12 (d, 2H, J_o=6.0 Hz, H–Ph), 7.28–7.30 (m, 3H, H–Ph); ^{13}C NMR: δ 48.8 (CH_2–N), 56.1 (OCH_3), 56.2 (CH_2-5), 67.6 (CH_2-3′), 69.1 (CH-7), 108.5 (CH-4), 110.3 (C-7a), 120.0 (CH_2-5′), 126.6 (CH), 127.4 (C-4a), 128.1 (CH), 128.9 (CH), 130.3 (CH-4′), 134.4 (C-*ipso*), 151.4 (C-3), 157.6 (C-2), 162.5 (C-1′); MS [*m*/*z* (%)]: EI: 389 (20, $M^{+\cdot}$), 325 (6, $M^{+\cdot}-SO_2$), 284 (14, $M^{+\cdot}-SO_2$, $-C_3H_5$), 240 (19, $M^{+\cdot}-SO_2$, $-C_4H_5O_2$), 234 (2, $M^{+\cdot}-SO_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{19}H_{19}NO_6S$: 389.0933, found: 389.0939.

4.7.4. Methyl 1-benzyl–5,7-dihydro-3-methoxy-2,6,6-trioxo-1*H*-thieno[3,4-*b*]pyridine-7-carboxylate 37. Yield: 59% (method B); yellow oil; IR (NaCl/cm^{-1}): 3055, 2926, 1750, 1655, 1319, 1110; ^{1}H NMR: δ 3.62 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 4.15 (d, 1H, ^2J=14.8 Hz, H-5), 4.40 (d, 1H, ^2J=14.8 Hz, H-5), 4.86 (s, 1H, H-7), 4.99 (d, 1H, ^2J=15.7 Hz, CH_2–N), 5.41 (d, 1H, ^2J=15.7 Hz, CH_2–N), 6.55 (s, 1H, H-4), 7.12 (dd, 2H, J_o=6.8 Hz, J_m=1.5 Hz, H–Ph), 7.26–7.30 (m, 3H, H–Ph); ^{13}C NMR: δ 48.9 (CH_2–N), 54.0 (OCH_3), 56.2 (CH_2-5), 56.3 (OCH_3), 69.2 (CH-7), 108.5 (CH-4), 110.3 (C-7a), 126.7 (CH), 127.5 (C-4a), 128.2 (CH), 129.0 (CH), 134.4 (C-*ipso*), 151.6 (C), 157.9 (C-2), 163.4 (C); MS [*m*/*z* (%)]: EI: 363 (22, $M^{+\cdot}$), 299 (14, $M^{+\cdot}-SO_2$), 240 (17, $M^{+\cdot}-SO_2$, $-C_7H_7$), 91 (100, $C_7H_7^+$); HRMS: calcd for $C_{17}H_{17}NO_6S$: 363.0777, found: 363.0778.

4.7.5. *N*,*N*-Diallyl-1-benzyl-5,7-dihydro-3-methoxy-2,6,6-trioxo-1*H*-thieno[3,4-*b*]pyridine-7-carboxamide 38. Yield: 58% (method B); yellow oil; IR (NaCl/cm^{-1}): 3070, 2936, 1660, 1609, 1329, 1129; ^{1}H NMR: δ 3.71 (m, 2H, 2×CH_2–allyl), 3.78 (s, 3H, OCH_3), 3.89 (dd, 1H, ^3J=6 Hz, ^2J=17 Hz, CH_2–allyl), 4.09 (d, 1H, ^2J=14.6 Hz, CH_2-5), 4.13 (dd, 1H, ^3J=6 Hz, ^2J=15.1 Hz, CH_2–allyl), 4.35 (d, 1H, ^2J=14.6 Hz, CH_2-5), 4.38 (d, 1H, ^2J=16.5 Hz, CH_2–N), 4.98 (d+m, 2H, ^2J=16.5 Hz, CH_2–N+H–C=), 5.03 (s, 1H, H-7), 5.14 (dd, 1H, ^3J=6 Hz, ^4J=1.3 Hz, =CH_2), 5.19 (dd, 1H, ^3J=13 Hz, ^4J=1.3 Hz, =CH_2), 5.54 (m, 2H, =CH_2), 5.68 (m, H, H–C=), 6.50 (s, 1H, H-4), 6.94 (d, 2H, J_o=8.5 Hz, H–Ph), 7.20–7.25 (m, 3H, H–Ph); ^{13}C NMR: 48.7 (CH_2), 49.2 (CH_2), 50.3 (CH_2), 56.2 (CH_2), 56.5 (OCH_3), 66.8 (CH), 108.7 (CH), 110.0 (C), 118.7 (CH_2), 119.2 (CH_2), 125.6 (C-arom), 127.8 (C-arom), 128.9 (C-arom), 131.4 (CH), 131.6 (CH), 134.4 (C-*ipso*), 151.1 (C-3), 157.6 (C-2), 161.6 (C-1′); MS [*m*/*z* (%)]: EI: 428 (10, $M^{+\cdot}$), 364 (100, $M^{+\cdot}-SO_2$), 273 (36, $M^{+\cdot}-SO_2$, $-C_7H_7$), 190 (74, $M^{+\cdot}-SO_2$, $-C_7H_7$, $-C_6H_{11}$), 91 (76, $C_7H_7^+$); HRMS: calcd for $C_{22}H_{24}N_2O_5S$: 428.1406, found: 428.1412.

4.7.6. 1-Benzyl-7-bromo-5,7-dihydro-3-methoxy-6,6-dioxothieno[3,4-*b*]pyridin-2(1*H*)-one 39. (A) A solution

of 0.1 g (0.32 mmol) 2(1*H*)-pyrazinone **19** and 1.1 equiv. NBS in CCl_4 was irradiated with a 500 W tungsten-lamp for 1 h, then the solvent was evaporated. The residue was chromatographed (silica gel, 85 CH_2Cl_2/15 EtOAc) to yield 45% of compound **39**.

(B) A solution of **19** and NBS (1.1 equiv.) and a catalytic amount of benzoylperoxide in CCl_4 was refluxed for 3 h to afford compound **39**, in 67% yield, after chromatographic purification.

Yellow oil; ^{1}H NMR: δ 3.87 (s, 3H, CH_3), 4.08 (d, 1H, J=16 Hz, H-5), 4.29 (d, 1H, J=16 Hz, H-5), 4.83 (d, 1H, ^2J=15.7 Hz, CH_2–N), 5.09 (s, 1H, H-7), 6.10 (d, 1H, ^2J=15.7 Hz, CH_2–N), 6.67 (s, 1H, H-4), 7.05–7.12 (m, 2H, H–Ph), 7.13–7.35 (m, 3H, H–Ph); ^{13}C NMR: δ 50.0 (CH_2–N), 55.0 (OCH_3), 57.5 (CH_2-5), 70.1 (CH-7), 110.1 (CH-4), 113.3 (C-7a), 126.7 (CH), 128.0 (C), 128.2 (CH), 129.0 (CH), 134.4 (C-*ipso*), 152.8 (C), 160.1 (C), 164.1 (C); MS [*m*/*z* (%)]: EI: 305 (61, $M^{+\cdot}-Br$), 241 (20, $M^{+\cdot}-Br,-SO_2$), 91 (100, $C_7H_7^+$).

4.8. Intramolecular Diels–Alder reactions

4.8.1. 1-Benzyl-6-[(1*E*)-1,5-hexadienyl]-3-methoxy-5-methyl-2(1*H*)-pyridinone 40. Yield: 55%; yellow oil; IR (NaCl/cm^{-1}): 3004, 2933, 1650, 1605; ^{1}H NMR: δ 2.09 (s, 3H, CH_3), 2.16 (t broad, 2H, ^3J=6.7 Hz, CH_2), 2.24 (t, 2H, ^3J=6.6 Hz, CH_2), 3.83 (s, 3H, OCH_3), 4.90 (d, 1H, ^3J=9.0 Hz, H-6′), 5.01 (d, 1H, ^3J=16.5 Hz, H-6′), 5.34 (s broad, 2H, CH_2–N), 5.65–5.72 (m, 2H, H-2′+H-5′), 5.92 (d, 1H, $^3J_{trans}$=16.1 Hz, H-1′), 6.54 (s, 1H, H-4), 7.12–7.26 (m, 5H, H–Ph); ^{13}C NMR: δ 19.0 (CH_3), 32.0 (CH_2), 32.7 (CH_2), 48.4 (CH_2–N), 55.6 (OCH_3), 111.9 (C-5), 115.3 (CH_2-6′), 116.1 (CH-4), 122.0 (CH), 126.9 (CH), 128.2 (CH), 128.5 (CH), 134.6 (C-4), 136.9 (C-*ipso*), 137.3 (CH), 139.7 (CH), 147.8 (C-3), 157.7 (C-2); MS [*m*/*z* (%)]: EI: 309 (100, $M^{+\cdot}$), 294 (15, $M^{+\cdot}-CH_3$), 254 (82, $M^{+\cdot}-C_4H_7$), 218 (42, $M^{+\cdot}-C_7H_7$), 190 (12, $M^{+\cdot}-C_7H_7$, –CO), 91 (84, $C_7H_7^+$); HRMS: calcd for $C_{20}H_{23}NO_2$: 309.1729, found: 309.1733.

4.8.2. (6a*S,9a*S**)-8-Allyl-1-benzyl-3-methoxy-5,6,6a,7,8,9a-hexahydro-1*H*-pyrrolol[3,4-*b*]quinoline-2,9-dione 41.** Yield: 65%; dark yellow oil; IR (NaCl/cm^{-1}): 2934, 1683, 1609; ^{1}H NMR: δ 1.66 (ddd, ^3J=13, 9.1, 6 Hz, H-6ax), 1.79 (ddd, 1H, ^3J=13, 8, 4 Hz, H-6eq), 2.43 (m, 1H, H-6a), 2.50–2.64 (m, 2H, H-5), 2.94 (d, 1H, ^2J=10 Hz, H-7), 3.48 (dd, 1H, ^2J=10 Hz, ^3J=6 Hz, H-7), 3.57 (d, 1H, ^3J=6.2 Hz, H-9a), 3.81 (m, 1H, H-8′), 3.83 (s, 3H, OCH_3), 3.97 (dd, 1H, ^2J=15 Hz, ^3J=6 Hz, H-8′), 5.18 (dd 1H, $^{trans}J$=19 Hz, ^4J=1.3 Hz, H-8‴), 5.21 (d, 1H, ^{cis}J=9 Hz, H-8‴), 5.47 (d, 1H, ^2J=16.8 Hz, CH_2–N), 5.71 (ddt, 1H, $^{trans}J$=19 Hz, ^{cis}J=9 Hz, ^3J=6 Hz, H-8″), 6.21 (d, 1H, ^2J=16.8 Hz, CH_2–N), 6.40 (s, 1H, H-4), 7.05 (d, 2H, J_o=8.8 Hz, H–Ph), 7.17–7.28 (m, 3H, H–Ph); ^{13}C NMR: δ 24.9 (C-6), 26.5 (C-5), 32.1 (C-6a), 43.2 (C-9a), 45.6 (C-8′), 46.8 (CH_2–N), 50.4 (C-7), 55.6 (OCH_3), 113.9 (C), 114.0 (C-4), 118.7 (C-8‴), 126.0 (C–Ph_{ortho}), 126.8 (C–Ph_{para}), 128.6 (C–Ph_{meta}), 128.8 (C), 131.8 (C-8″), 137.4 (C-*ipso*), 148.6 (C-3), 158.5 (C-2), 171.0 (C-9); MS [*m*/*z* (%)]: EI: 364 (91, $M^{+\cdot}$), 323 (4, $M^{+\cdot}-C_3H_5$), 273 (39, $M^{+\cdot}-C_7H_7$), 190 (100, $M^{+\cdot}-C_7H_7$, $-CONC_3H_5$), 91 (92, $C_7H_7^+$); HRMS: calcd for $C_{22}H_{24}N_2O_3$: 364.1787, found: 364.1788.

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