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1,3-Dihydro-2,2-dioxothieno[3,4-*c*]pyridines as precursors for pyridine *o*-quinodimethane systems

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Abstract—Various pyridine *o*-quinodimethane systems were generated via thermal extrusion of sulfur dioxide from 1,3-dihydro-2,2-dioxothieno[3,4-*c*]pyridine precursors and derivatives functionalised in the 1- or 3-position of the sulfolene ring moiety. Depending on the nature of the *peri*-substituents on the pyridine ring either the *E*- or *Z*-isomers are formed, which react further via inter- and intramolecular Diels–Alder reactions or via an 1,5-H shift, respectively. © 2001 Elsevier Science Ltd. All rights reserved.

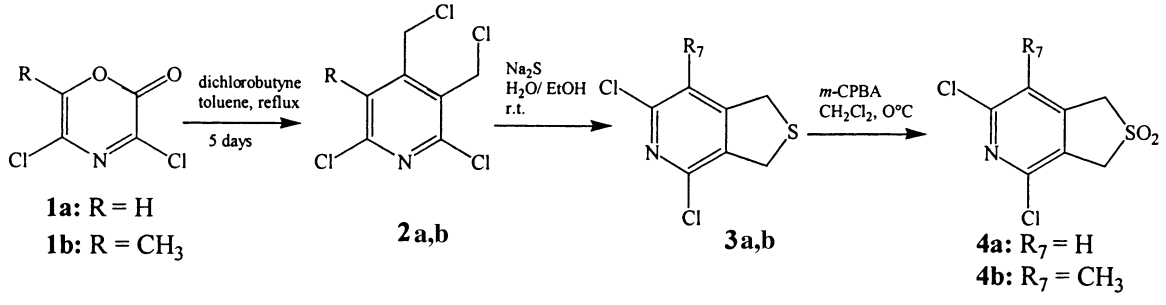
1. Introduction

In previous contributions we reported on the use of *o*-bis(chloromethyl)-pyridines as precursors of the corresponding pyridine *o*-quinodimethanes (*o*-QDM).[1] In spite of its good accessibility and straightforward conversion to pyridine *o*-QDM, a major drawback of this precursor type is the inability to functionalise the diene heads. In this respect, better prospects are being offered by sulfolene pyridines which, like benzosulfolenes and their heterocyclic analogues,[2] could more easily be manipulated and functionalised prior to thermolytic generation of the pyridine *o*-QDM system. Therefore we engaged in the synthesis of novel sulfolene pyridines bearing substituents appropriate for both inter- and intramolecular Diels–Alder reactions.

2. Results and discussion

2.1. Preparation and substitution of sulfolene pyridines

To our knowledge, only two articles refer to the preparation of sulfolene pyridines.[3] Application of this reported two-step conversion to the *o*-bis(chloromethyl)pyridines **2** described in our previous work, should provide access to the sulfolene pyridines **4**. Our sequence (Scheme 1) started with the cycloaddition of oxazinones **1** and 1,4-dichloro-2-butyne, proceeding with concomitant expulsion of carbon dioxide. In the next step compounds **2** were treated with sodium sulfide in a 1:1 mixture of ethanol and water to afford 1,3-dihydrothieno[3,4-*c*]pyridines **3**. In contrast with the easy breakdown observed for 1,3-dihydrothieno[3,4-*b*] pyridines,[3] these polysubstituted 1,3-dihydro-



Scheme 1. Synthesis of sulfolene pyridines **4a,b.**

Keywords: *ortho*-quinodimethane systems; Diels–alder reactions; pyridines.

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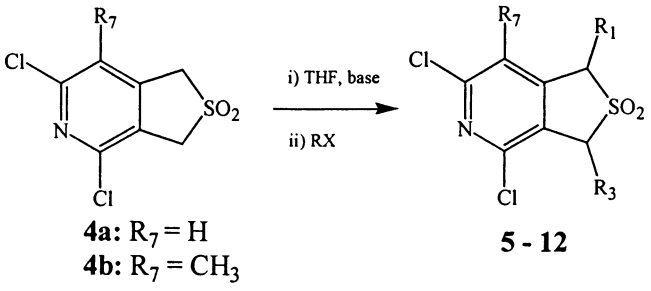


Scheme 2. Substitution of sulfolene pyridines.

thieno[3,4-*c*]pyridines could be isolated for spectral characterisation. Presumably the electron withdrawing chloro substituents and bulky methyl group counteract oxidative degradation of the cyclic thioethers **3**. Final conversion of **3** to the stable sulfolene pyridines **4** was effected by treatment with *m*-chloroperoxybenzoic acid. Optimisation of the three reaction steps gave the sulfolene pyridine **4a** in 78% and **4b** in 96% yield, respectively.

Similar to the conversions reported for some other heteroaromatic sulfolenes,[4] regioselective functionalisation also can be accomplished for sulfolene pyridines **4a** and **4b**. This proceeds (Scheme 2 and Table 1) via substitution of the mono- and dianions formed by successive deprotonation at the αpositions 1 and 3. In the first deprotonation step, the 1-anion is produced exclusively due to a better stabilisation by the pyridine N atom. Alternative reaction of **4a** and **4b** with 2 equivalents of a strong base, i.e. BuLi, leads to formation of the 1,3-dianion, which can then be converted to the 3-mono or 1,3-difunctionalised products. 1-Alkyl-substituted sulfolene pyridines were prepared by successive treatment of **4** with tetrabutylammoniumfluoride (TBAF) and alkyl halogenides. In an attempt to broaden the scope of this substitution reaction, the mono-anion generated with TBAF was treated with other electrophilic reagents, i.e. an acid chloride, ester, or ethyl chloroformate, but this failed to give the expected ketone or ester products. Substitution of the 3-position was achieved by treatment of **4** with 2 equivalents of BuLi, followed by dropwise addition of 1 equivalent of an electrophile. Addition of an excess electrophile to the dianion led to the 1,3-disubstituted product. We could also successfully introduce a 4-pentenyl group, useful for the study of intramolecular Diels–Alder reactions.

The alkylation experiments proceeding through formation of the 1-anion generated with TBAF, revealed a higher yield for alkylation of **4b** compared to **4a**. When using the less reactive 5-bromopentene as the electrophile, the 1-(4-pentenyl) substituted sulfolene **10** was isolated in 85% yield, whereas the 7-H analogue **12** was not detected. The desired conversion of **4a** to **12** could be accomplished, however, by using KH (1.1 equiv.) as a base and DMF as a solvent, thus increasing the nucleophilic character of the 1-anion.

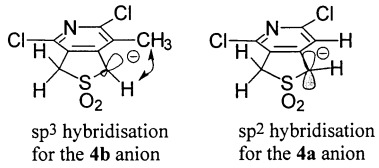


Figure 1.

The contrasting behaviour observed for compounds **4a** and **4b** with regard to 1-alkylation probably relates to the influence of the substituent in the *peri*-position of the anionic site (Fig. 1). In the case of **4a** the anion can adopt the planar configuration required for an efficient delocalisation of the negative charge, but this sp^2-hybridisation also implies a decreased nucleophilic character of the anion. On the other hand, a less planar structure probably applies to the anion derived from **4b** due to steric repulsion by the methyl group. This leads to a higher reactivity for the more localised sp^3-anion in spite of the steric interaction of the larger *peri*-substituent with the incoming electrophile.

2.2. Generation of pyridine-*o*-quinodimethanes and their Diels–Alder reactions

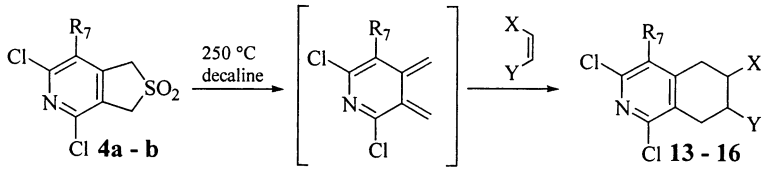
The sulfolene precursors **4**–**12** were converted to the corresponding pyridine *o*-QDM via thermal extrusion of sulfur dioxide. No extrusion reaction could be observed when heating sulfolene compounds **4** below 150°C. The thermolysis experiments were carried out by heating solutions of **4**–**12** in decaline at 250°C in the presence of various dienophiles, which served for in situ capture of the diene intermediates generated (Scheme 3 and Table 2).

Application of this procedure gave a higher yield than the reported iodide method,[1] except for the reaction with NPMA that is only slightly soluble in decaline. However, due to the much higher temperatures required to generate

Table 1.

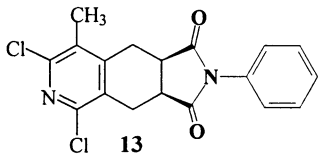
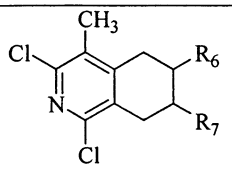
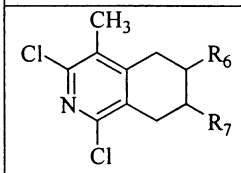
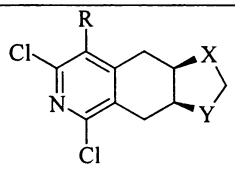
Sulfolene pyridine	RX (eq)	Base (eq)	No	Product	Yield (%)
4a	BnBr (2.0)	TBAF (1.5)	**5**	R^1=Bn; R^3=R^7=H	60
4b	BnBr (2.0)	TBAF (1.5)	**6**	R^1=Bn; R^3=H, R^7=Me	74
4b	BnBr (4.0)	BuLi (2.0)	**7**	R^1=R^3=Bn; R^7=Me	72
4b	BnBr (1.0)	BuLi (2.0)	**8**	R^1=H; R^3=Bn; R^7=Me	85
4b	EtI (1.2)	TBAF (1.2)	**9**	R^1=Et; R^3=H; R^7=Me	70
4b	BrPent[a] (1.2)	TBAF (1.2)	**10**	R^1=Pent; R^3=H; R^7=Me	85
4b	BrPent (1.2)	BuLi (2.0)	**11**	R^1=H; R^3=Pent; R^7=Me	55[b]
4a	BrPent (1.2)	TBAF (1.2)	**12**	R^1=Pent; R^3=R^7=H	0
4a	BrPent[c] (1.2)	KH (1.1)	**12**	R^1=Pent; R^3=R^7=H	62[b]

[a] BrPent: $BrCH_2CH_2CH_2CH{=}CH_2$
[b] lower yield due to competitive elimination reaction
[c] DMF used as solvent



Scheme 3. Generation of *o*-quinodimethanes and subsequent cycloaddition with NPMA, methyl acrylate, ethyl vinyl ether or dihydrofuran.

Table 2. Diels–Alder reactions of the unsubstituted *o*-quinodimethane system.

Adduct	Yield % (Ratio **a**:**b**)	Adduct	Yield % (Ratio **a**:**b**)
 **13**	31	 **15 a**: R_6= OEt, R_7 = H **15 b**: R_6 = H, R_7 = OEt	>95 (3:1)
 **14 a**: R_6= CO_2Me, R_7 = H **14 b**: R_6 = H, R_7 = CO_2Me	67 (2:3)	 **16 a**: X = O, Y = CH_2; R= CH_3 **16 b**: X =CH_2, Y = O ; R= CH_3 **17 a**: X = O, Y = CH_2; R= H **17 b**: X =CH_2, Y = O ; R= H	> 95 (4:1) **16 a – 16 b** > 72 (3:1) **17 a – 17 b**

the *o*-QDM intermediates, a lower regioselectivity was observed when using the thermolytic method in the reaction with electron rich dienophiles, i.e. dihydrofuran and ethyl vinyl ether.

Thermal extrusion of sulfur dioxide from 1- or 3-substituted sulfolene pyridines leads to terminally substituted dienes that can have either the *E*- or *Z*-configuration (Fig. 2). According to literature data regarding the electrocyclic ring opening of substituted benzocyclobutenes,[5] the distribution of *E*- and *Z*-isomers is determined not only by the thermodynamic preference of the diene, but also by the kinetic-electronic effect exerted by the substituents on the four-membered ring. During conrotatory opening of this ring, electron withdrawing groups (aldehydes, iminium) tend to rotate inward to give the *Z*-isomers, while electron donating alkyl groups prefer an outward rotation producing the *E*-isomers. By analogy with the latter preferred outward mode of rotation, one could expect a similar effect on the extrusion reaction of the alkyl substituted sulfolene pyridines, favouring the thermodynamically more stable *E*-isomers. However, such a preference is counteracted by a bulky methyl *peri*-substituent, which tends to favour the *Z*-isomer. The latter in turn can undergo a 1,5-H shift to the other diene head yielding the rearranged product.[6]

Thermolysis of the 1-benzylsulfolene **6** in the presence of NPMA afforded the *all-cis* ring-fused adduct **18** (17%) and the rearranged product **19** (57%). In a similar way NPMA adduct **20** (30%) and rearranged **21** (42%) were produced from the thermolysis of 1-ethylsulfolene **9**. The *all-cis* stereochemical disposition of adduct **18** was inferred from the coupling constant values observed in the ^{1}H NMR spectrum, as compared with the values found for the unsubstituted NMPA adduct **13**. To the latter compound a boat conformation was assigned on the basis of the coupling constant $J_{3a,9a}$ (=10 Hz) and the NOE observed between the 8-methyl group and the equatorial proton H-9eq.[1] A further NOE was found between H-9ax and the *cis*-disposed angular proton H-9a. These data correlate with an eclipsed situation for the *cis*-oriented protons H-3a and H-9a and an axial orientation for the maleimide ring. The spectrum of

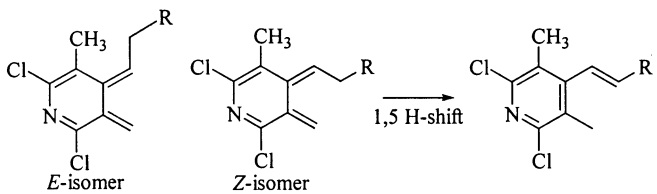


Figure 2. *E*- and *Z*-configurations—1,5-H shift for the *Z*-isomer.

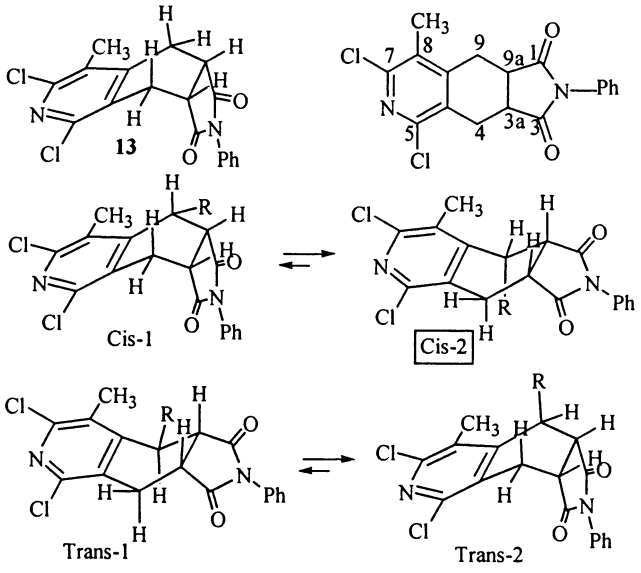


Figure 3. Diaxial boat conformer for the unsubstituted adduct **13** and the two pairs of boat conformers for the *cis*- and *trans*-isomers of the adduct **18**.

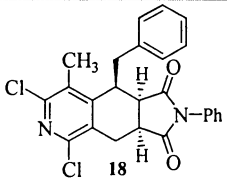
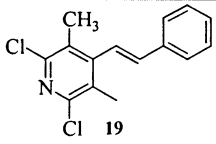
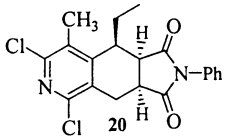
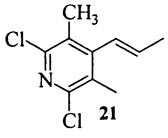
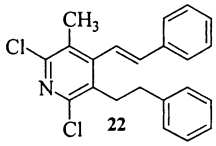
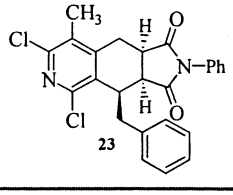
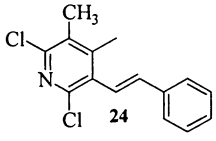
adduct **18** revealed a similar value for $J_{3a,9a}$ (=10 Hz) indicating an unchanged eclipsing situation for the protons located at the angular positions of a ring-fused boat conformer.

Fig. 3 displays the structures of the two pairs of boat conformers corresponding with the *cis* (*cis*-1 and *cis*-2) and *trans* isomers (*trans*-1 and *trans*-2) of adduct **18**. The value $J_{9,9a}$=6 Hz indicates that the conformer *trans*-1 with a diaxial orientation for H-9 and H-9a cannot be the main form. Indeed, an equatorial orientation for the bulky benzyl group as seen in forms *trans*-1 and *cis*-1 is highly unfavourable, due to the strong *peri*-interaction with the neighbouring methyl group (Johnson A strain[7]). Conformational calculations indicate an energy increase of about 8 kcal/mol when an axial benzyl at C-9 is interchanged with H-9eq. Therefore, on the basis of this *peri*-interaction both *trans*-1 and *cis*-1 can be excluded.

To distinguish between *cis*-2 and *trans*-2, the coupling constants $J_{3a,4ax}$ and $J_{3a,4eq}$ are of interest. These values (9, 10 Hz) indicate an axial orientation of the angular proton H-3a, in agreement with structure *cis*-2 (values of about 160° and 40° were calculated for the torsion angles H-3a, H-4ax and H-3a, H-4eq). An equatorial orientation of proton H-3a corresponding to structure *trans*-2 is precluded by spectral comparison with the unsubstituted adduct **13**. While **13** displays a conformational structure comparable to that of *trans*-2, its ^{1}H NMR spectrum revealed smaller coupling constant values ($J_{3a,4}$=4, 6 Hz). Hence, the conformational structure *cis*-2 was established for adduct **18**, although the fully axial form *trans*-2 was calculated to be more stable by about 2 kcal/mol. In the ^{1}H NMR spectra of the isomeric adduct **23**, similar coupling patterns and NOE correlations were observed, which confirmed the *all-cis* configuration and conformational structure assigned to adduct **18** (see left; Fig. 3).

Since the *endo*-mode of cycloaddition generally prevails for Diels–Alder reactions of NPMA, one may conclude that most probably the *all-cis* adducts are generated from the *E*-diene isomers; *endo*-addition of NPMA to the *Z*-isomer would give the *trans* adduct. As mentioned above, steric repulsion between the benzyl or ethyl group and the methyl *peri*-substituent in the *E*-diene isomers may result in preferential formation of the *Z*-isomers, which seem to be likely intermediates for the subsequent 1,5-H shift producing the

Table 3. Intermolecular Diels–Alder reactions of the substituted *o*-quinodimethane system.

Precursor	Adduct	Yield %	Rearranged Product	Yield %
6	 **18**	17	 **19**	57
9	 **20**	30	 **21**	42
7			 **22**	
8	 **23**	56	 **24**	10

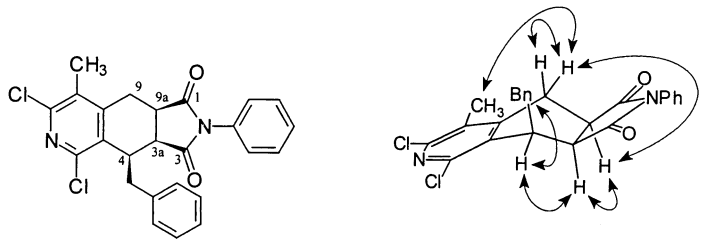


Figure 4. NOE correlations for adduct **23.**

rearranged products. Indeed, compound **19** was isolated as the only product following thermolysis of **6** in the presence of a less reactive dienophile, i.e. methyl acrylate.

From the reaction of the dibenzylated sulfolene **7** and NPMA only the rearranged compound **22** was isolated, probably via generation and further rearrangement of a comparable *Z*-isomer. The ^{1}H coupled ^{13}C-NMR-spectrum of **22** displayed a triplet for C-2 of the pyridine ring revealing a ^{3}J coupling with the CH_2 group in position 3. From this result it is clear that the larger methyl *peri*-substituent dictates which of the two possible *Z*-isomers is formed.

Thermolysis of the 3-benzylsulfone **8** with NPMA produced 56% of adduct **23** and only 10% rearranged **24** (Table 3). Structure analysis of **23** as discussed below established the *all-cis*-configuration of the adduct, consistent with *endo*-addition of the *E*-diene. Presumably, the altered product distribution for the 3-benzylsulfone as compared to the 1-benzyl isomer can be traced back to a higher contribution of the *E*-diene in the mixture of *o*-QDM intermediates. This in turn can be accounted for by a lower steric repulsion between the *peri*-substituent (Cl versus Me) and the terminal benzyl group in the *E*-diene.

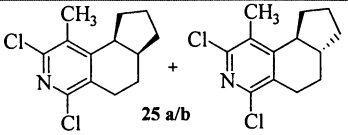
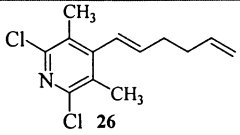
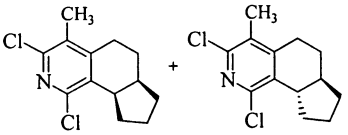
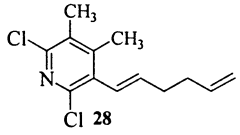
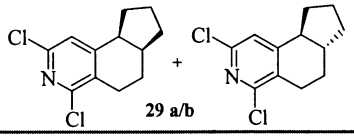
The configuration and conformational boat structure of **23** characterised by an axial benzyl group and equatorial maleimide ring were determined by an ^{1}H NMR analysis similar to that used for **18**, confirmed by NOEDIFF and NOESY measurements (Fig. 4). The structural assignments can be summarised as follows. A boat structure similar to that for adduct **18** was revealed by the value J_{3a-9a}=10 Hz and a NOE interaction between the 8-methyl group and H-9eq, which further allows to differentiate this proton from H-9ax. The *trans*-diaxial disposition of H-9ax and H-9a was inferred from the value J_{9ax-9a}=10 Hz and the absence of a NOE correlation. The *all-cis*-relationship for protons H-9eq, H-9a, H-3a, and H-4 was established by appropriate correlations in the NOESY-spectrum. Finally, the coupling constant J_{3a-4}=6.4 Hz observed for H-3a and H-4 is consistent with their axial–equatorial relationship as implied by the axial orientation of the benzyl group.

2.3. Intramolecular Diels–Alder reactions

Here we describe our results regarding the intramolecular Diels–Alder reactions of the isomeric 1- and 3-pentenyl sulfolene precursors **10** and **11**, and the 7-H analogue **12** without the 7-methyl *peri*-substituent (Table 4). The intramolecular Diels–Alder reaction can proceed, starting from the *E*- or *Z*-diene, through either the *endo*- or *exo*-addition mode. Hence both *cis*- and *trans*-fused cycloadducts can be expected, besides the rearranged products resulting from 1,5-H shift in the *Z*-dienes.

The reaction mixture produced by thermolysis of the 1-pentenyl derivate **10** was subjected to HPLC affording the *cis,trans*-adduct mixture **25a,b** (27%) and rearranged product **26** (34%). Thermolysis of sulfolene **11** likewise furnished a mixture of *cis,trans* adducts **27a,b** (50%) and rearranged product **28** (24%). From the thermolysis of the 7-H analogue **12**, only the *cis,trans* mixture **29a,b** was isolated (92%). This varying product distribution again demonstrates the important role of the *peri*-substituents located at either the 7- or 4-position in controlling the ratio of *E* and *Z*-isomers giving rise to addition and

Table 4. Intramolecular Diels–Alder reactions of 1- and 3-pentenyl sulfolenes **10**–**12**.

Precursor	Adduct	Yield %	Rearranged product	Yield %
10	 **25 a/b**	27	 **26**	34
11	 **27 a/b**	48	 **28**	24
12	 **29 a/b**	92		

rearrangement reactions, respectively. A similar result was described for the intramolecular cycloaddition of an analogous unsubstituted pyridine-*o*-quinodimethane, where only the adduct and no rearranged product was formed.[8] An 1,5-H shift was observed by Oppolzer et al. for the thermolysis reaction of an analogous benzosulfolene derivative, unsubstituted in the *peri*-position.[9]

Although the exact stereochemical structures of the *cis*- and *trans*-fused stereoisomers could not be assigned from the NMR-spectra of the product mixtures, these spectra indicated a 1:1 ratio for the unsubstituted cycloadducts **29a** and **29b**, and a 4:1 to 5:1 ratio for the substituted analogues **25a** and **25b** and their regioisomers **27a** and **27b**.

3. Conclusion

In this work we show that 1,3-dihydro-2,2-dioxothieno[3,4-*c*]pyridines (**4**) are easily accessible from the corresponding oxazinones and can be substituted regioselectively in the 1- and 3-position. Thermolytic extrusion of sulfur dioxide from the unsubstituted precursors **4a,b** produces the corresponding pyridine *o*-QDM intermediates that can be captured in situ by addition of various dienophiles. Similar results were obtained from the thermolysis of the 1- or 3-substituted sulfolene pyridines (**5**–**12**); however, besides the expected adduct, these experiments also gave a rearranged product evolving from a 1,5-H shift in the *Z*-diene intermediate. This rearrangement was observed with intermolecular as well as intramolecular Diels–Alder reactions and strongly depends on the nature of the substituent in the *peri*-position (methyl or hydrogen).

To avoid this side reaction, sulfolene pyridine precursors without substituents in the *peri*-position have to be developed to provide access to well defined target molecules.

4. Experimental

4.1. General methods

Infrared spectra were recorded on a Perkin–Elmer 297 grating IR spectrophotometer and a Perkin–Elmer 1720 Fourier transform spectrometer. ^{1}H NMR spectra and ^{13}C NMR spectra were recorded on a Bruker WM 300 or on a Bruker AMX 400 instrument. The ^{1}H and ^{13}C chemical shifts are reported in ppm relative to tetramethylsilane or the deuterated solvent as an internal reference. Mass spectra were run by using a Kratos MS50TC instrument and a DS90 data system. For TLC and column chromatography analytical plates (Alugram Sil G/UV$_{254}$) and 70–230 mesh silica gel 60 (E.M. Merck) were used, respectively. Melting points were determined using a Reichert–Jung Thermovar apparatus and an Electrothermal IA 9000 digital melting point apparatus and are uncorrected. HPLC was performed on a Waters Associates configuration coupled to a 410 differential refractometer. Microanalyses were performed by Janssen Pharmaceutica.

4.2. General procedure for the synthesis of thienopyridines (3)

To a solution of 5 g pyridine **2** in 200 mL ethanol under an inert atmosphere a solution of 30 g Na_2S in 500 mL ethanol/water (80/20) was added over a period of 20 h. After another 30 min of stirring 150 mL water was added. The reaction mixture was extracted with CH_2Cl_2 (3×150mL), the organic layer washed with brine, dried with $MgSO_4$ and the solvent was evaporated. The products were purified by column chromatography (silica gel, CH_2Cl_2) for spectral characterisation.

4.2.1. 4,6-Dichloro-1,3-dihydrothieno[3,4-*c*]pyridine (3a). Yield: 70%; yellow oil; ^{1}H NMR ($CDCl_3$/TMS): δ 7.3 (s, 1H, Pyr-H), 4.3 (s, 2H, CH_2), 4.1 (s, 2H, CH_2).

4.2.2. 4,6-Dichloro-7-methyl-1,3-dihydro-thieno[3,4-*c*]-pyridine (3b). Yield: 85%; m.p.: 142–144.5°C ($CHCl_3$/Hexane); ^{1}H NMR ($CDCl_3$/TMS): δ 4.24 (s, 2H, CH_2), 4.23 (s, 2H, CH_2), 2.30 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 154.2 (C-7a), 148.6 (C-6), 142.9 (C-4), 134.6 (C-3a), 127.7 (C-7), 38.2 (CH_2), 36.5 (CH_2), 16.0 (CH_3); MS [*m*/*z* (%)]: 219 (80) $M^{+\cdot}$; 218 (100) $M^{+\cdot}$ –H; 184 (52) $M^{+\cdot}$ –Cl; 148 (20) $M^{+\cdot}$ –HCl, –Cl; HRMS: calcd for $C_8H_7Cl_2NS$: 218.9676; found: 218.9687.

4.3. General procedures for the synthesis of 1,3-dihydro-2,2-dioxo-thieno[3,4-*c*]pyridines (4)

To a solution of 4.8 g of **3** in 50 mL CH_2Cl_2 at 0°C under an inert atmosphere, three equivalents *m*-chloroperoxybenzoic acid were slowly added. The reaction mixture was stirred for 6 h at room temperature. Subsequently a saturated $NaHCO_3$ solution (25mL) was added and stirring was continued for 2 h. The mixture was then extracted with CH_2Cl_2 (3×150 mL) and the organic phase was dried with $MgSO_4$ and evaporated. Chromatographic purification on silica gel using a step gradient CH_2Cl_2/ethyl acetate (100% CH_2Cl_2 to 85 CH_2Cl_2 / 15 ethyl acetate) gave the sulfolenepyridines **4**.

4.3.1. 4,6-Dichloro-1,3-dihydro-2,2-dioxothieno[3,4-*c*]-pyridine (4a). Yield: 78%;white powder; m.p.: 160.5–162.5°C ($CHCl_3$/Hexane); IR (KBr): 1320 cm^{-1}; 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): δ 7.30 (s, 1H, Pyr-H), 4.44 (s, 2H, CH_2), 4.38 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$): δ 150.5 (C-7a), 147.8 (C-6), 145.2 (C-4), 126.1 (C-7), 120.2 (C-3a), 57.3 (CH_2), 54.8 (CH_2); MS [*m*/*z* (%)]: 237 (5) $M^{+\cdot}$; 173 (100) $M^{+\cdot}$ –SO_2; 138 (38) $M^{+\cdot}$ –Cl, –SO_2; 102 (40) $M^{+\cdot}$ –Cl, –HCl, –SO_2; HRMS: calcd for $C_7H_5Cl_2NO_2S$: 236.9418; found: 236.9402.

4.3.2. 4,6-Dichloro-1,3-dihydro-7-methyl-2,2-dioxothieno-[3,4-*c*]pyridine (4b). Yield: 96%;white needle crystals; m.p.: 192–193°C ($CHCl_3$/Hexane); IR (KBr): 1310 cm^{-1}; 1135 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): δ4.41 (s, 2H, CH_2), 4.40 (s, 2H, CH_2), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ150.5 (C-6), 144.3 (C-7a), 144.1 (C-4), 128.5 (C-7), 125.8 (C-3a), 57.2 (CH_2), 55.9 (CH_2), 16.6 (CH_3); MS [*m*/*z* (%)]: 251 (14) $M^{+\cdot}$; 187 (100) $M^{+\cdot}$ –SO_2; 152 (26) $M^{+\cdot}$ –Cl, –SO_2; 116 (28) $M^{+\cdot}$ –Cl, –HCl, –SO_2; HRMS: calcd for: 250.9574; found: 250.9581; CHN analysis: calcd for

$C_8H_7Cl_2NO_2S$: C 38.07, H 2.68, N 5.53; found: C 38.11, H 2.80, N 5.56.

4.4. General procedure for alkylation in position 1

To a solution of 0.250 g of compound **4** in 15 mL THF under an inert atmosphere 1.5 equivalents of TBAF (1 M solution in THF) was added. After 10 min 2 equivalents electrophile were added and the reaction mixture was stirred for 6–12 h. After addition of a saturated $NaHCO_3$ solution (10mL) and extraction with CH_2Cl_2 (3×15mL), the organic phase was dried with $MgSO_4$ and the solvent was removed. Chromatographic purification (silica/$CHCl_3$ 90/ethyl acetate 10) yielded the products **5, 6, 9, 10**.

4.4.1. (±) 1-Benzyl-4,6-dichloro-1,3-dihydro-2,2-dioxothieno[3,4-*c*]pyridine (5). Yield: 60%; white powder; m.p.: 173–174°C ($CHCl_3$/Hexane); IR (KBr): 1315 cm^{-1} (w); 1125 cm^{-1} (m); ^1H NMR ($CDCl_3$/TMS): δ 7.35–7.25 (m, 3H, Ph–H), 7.20–7.15 (m, 2H, Ph–H), 6.69 (s, 1H, H-7), 4.48 (dd, ^3J=9 Hz, ^3J=6 Hz, 1H, H-1), 4.32 (d, ^2J=16 Hz, 1H, H-3), 4.19 (d, ^2J=16 Hz, 1H, H-3), 3.61 (dd, ^2J=14 Hz, ^3J=6 Hz, 1H, CH_2Ph), 3.02 (dd, ^2J=14 Hz, ^3J=9 Hz, 1H, CH_2Ph); ^{13}C NMR ($CDCl_3$): δ150.2 (C-6), 149.4 (C-7a), 147.6 (C-4), 134.1 (C-*ipso*), 129.3 (C-*o*), 129.1 (C-*m*), 128.0 (C-*p*), 125.1 (C-3a), 120.2 (C-7), 67.2 (C-1), 53.3 (C-3), 35.4 (CH_2) MS [*m/z* (%)]: 328 (1) MH^+; 262 (100) $M^{+\cdot}$ $-SO_2$, –H; 227 (31) $M^{+\cdot}$ $-SO_2$, –Cl; 226 (22) $M^{+\cdot}-SO_2$, –HCl; 91 (52) CH_2Ph^+; HRMS: calcd for $C_{14}H_{11}Cl_2NO_2S$: 326.9887; found: 326.9882.

4.4.2. (±)1-Benzyl-4,6-dichloro-1,3-dihydro-7-methyl-2,2-dioxothieno[3,4-*c*]pyridine (6). Yield: 74%; white crystals; m.p.: 150–151.5°C ($CHCl_3$/Hexane); IR (KBr): 1326 cm^{-1} (w); 1125 cm^{-1} (m); ^1H NMR ($CDCl_3$/TMS): δ7.27–7.22 (m, 3H, Ph–H), 7.01–6.97 (m, 2H, Ph–H), 4.48 (dd, ^3J=7 Hz, ^3J=6 Hz, 1H, H-1), 4.22 (d, ^2J=16 Hz, 1H, H-3), 3.84 (d, ^2J=16 Hz, 1H, H-3), 3.54 (dd, ^2J=14 Hz, ^3J=6 Hz, 1H, CH_2Ph), 3.13 (dd, ^2J=14 Hz, ^3J=7 Hz, 1H, CH_2Ph), 1.95 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ150.8 (C-6), 148.4 (C-7a), 144.4 (C-4), 133.8 (C-*ipso*), 129.7 (C-*o*), 129.4 (C-7), 128.8 (C-*m*), 127.9 (C-*p*), 125.7 (C-3a), 67.3 (C-1), 53.4 (C-3), 36.8 (CH_2), 16.2 (CH_3) MS [*m/z* (%)]: 342 (1) MH^+; 276 (100) $M^{+\cdot}$ $-SO_2$, –H; 241 (34) $M^{+\cdot}$ $-SO_2$, –Cl; 240 (21) $M^{+\cdot}-SO_2$, –HCl; 91 (65) CH_2Ph^+; HRMS: calcd for $C_{15}H_{13}Cl_2NO_2S$: 341.0044; found: 341.0038.

4.4.3. (±)4,6-Dichloro-1-ethyl-1,3-dihydro-7-methyl-2,2-dioxothieno[3,4-*c*]pyridine (9). Yield: 70%;white crystals; m.p.: 142–145°C ($CHCl_3$/Hexane); IR (KBr): 1326 cm^{-1} (s); 1130 cm^{-1} (s); ^1H NMR ($CDCl_3$/TMS): δ4.36 (d, ^2J=16.5 Hz, 1H, H-3), 4.25 (d, ^2J=16.5 Hz, 1H, H-3), 4.22 (dd, ^3J=8 Hz, ^3J=4 Hz, 1H, H-1), 2.37 (s, 3H, CH_3), 2.14 (dq, ^3J=8 Hz, ^3J=8 Hz, 1H, H-1 $_{Et}$), 2.05 (dq, ^3J=4 Hz, ^3J=8 Hz, 1H, H-1 $_{Et}$), 1.10 (t, ^3J=8 Hz, 3H, H-2 $_{Et}$); ^{13}C NMR ($CDCl_3$): δ 150.9 (C-7a), 148.9 (C-6), 144.4 (C-4), 128.8 (C-7), 125.3 (C-3a), 67.7 (C-1), 54.1 (C-3), 24.1 (CH_2 $_{Et}$) 16.4 (CH_3), 10.7 (CH_3 $_{Et}$); MS [*m/z* (%)]:279 (8) $M^{+\cdot}$; 215 (66) $M^{+\cdot}$ $-SO_2$; 180 (100) $M^{+\cdot}$ –Cl, $-SO_2$; 144 (50) $M^{+\cdot}$ –Cl, –HCl, $-SO_2$; 115 (23) $M^{+\cdot}$ –Cl, –HCl, $-CH_2CH_3$, $-SO_2$; HRMS: calcd for $C_{10}H_{11}Cl_2NO_2S$: 278.9887; found: 278.9887.

4.4.4. (±) 4,6-Dichloro-1,3-dihydro-7-methyl-2,2-dioxo-1-(4-pentenyl)thieno[3,4-*c*]pyridine (10). Yield: 85%; white crystals; m.p.: 113.5–114.5°C ($CHCl_3$/Hexane); IR (KBr): 1637 cm^{-1} (m); 1313 cm^{-1} (m); 1137 cm^{-1} (m); ^1H NMR ($CDCl_3$/TMS): δ 5.74 (ddt, ^3J=16.5 Hz, ^3J=10.5 Hz, ^3J=6 Hz, 1H, H-4'), 5.03 (dd, ^3J=16.5 Hz, ^4J=2 Hz, 1H, H-5'), 5.01 (dd, ^3J=10.5 Hz, ^4J=2 Hz, 1H, H-5'), 4.35 (d, ^2J=17 Hz, 1H, H-3), 4.27 (d, ^2J=17 Hz, 1H, H-3), 4.25 (dd, ^3J=9 Hz, ^3J=4 Hz, 1H, H-1), 2.35 (s, 3H, CH_3), 2.20–2.05 (m, 3H, H-3', H-1'), 1.87 (m, 1H, H-1'), 1.63 (m, 2H, H-2'); ^{13}C NMR ($CDCl_3$): δ151.1 (C-6), 149.1 (C-7a), 144.5 (C-4), 136.9 (C-4'), 128.5 (C-7), 125.0 (C-3a), 115.9 (C-5'), 66.5 (C-1), 53.8 (C-3), 33.0 (C-1'), 30.2 (C-2'), 25.3 (C-3'), 16.4 (CH_3) MS [*m/z* (%)]: 320 (12) MH^+; 254 (16) MH^+ $-SO_2$, –2H; 251 (23) MH^+ $-C_5H_9$; 212 (100) MH^+ $-SO_2$, $-C_3H_7$; 201 (33) MH^+ $-SO_2$, $-C_4H_7$; HRMS: calcd for $C_{13}H_{15}Cl_2NO_2S$: 319.0200; found: 319.0195.

4.4.5. (±) 4,6-Dichloro-1,3-dihydro-2,2-dioxo-1-(4-pentenyl)thieno[3,4-*c*]pyridine (12). To a solution of 0.250 g of sulfolene pyridine **4a** in 15 mL DMF under an inert atmosphere 1.1 equivalents of KH was added. After 15 min, 2 equivalents 5-bromopentene were added and the reaction mixture was stirred for 24 h. After addition of a saturated $NaHCO_3$ solution (15 mL) and extraction with CH_2Cl_2 (3×10 mL), the organic layer was dried with $MgSO_4$ and the solvent was removed. Chromatographic purification (silica gel/CH_2Cl_2 90/ ethyl acetate 10) yielded compound **12**.

Yield: 62%;white crystals; m.p.: 84–85.5°C ($CHCl_3$/Hexane); IR (KBr): 1620 (m); 1320 cm^{-1} (m); 1130 cm^{-1} (m); ^1H NMR ($CDCl_3$/TMS): δ7.21 (s, 1H, Pyr-H), 5.75 (ddt, ^3J=17 Hz, ^3J=10 Hz, ^3J=6 Hz, 1H, H-4'), 5.01 (dd, ^3J=17 Hz, ^4J=2 Hz, 1H, H-5'), 5.01 (dd, ^3J=10 Hz, ^4J=2 Hz, 1H, H-5'), 4.28 (s, 2H, H-3), 4.23 (dd, ^3J=9 Hz, ^3J=4 Hz, 1H, H-1), 2.25–1.50 (m, 6H, H-3', H-2', H-1'); ^{13}C NMR ($CDCl_3$): δ 149.5, 149.3, 146.7, 136.1 (C-4'), 124.3, 118.7 (C-7), 115.1 (C-5'), 65.1 (C-1), 52.7 (C-3), 32.2 (C-1'), 27.3 (C-2'), 24.5 (C-3') MS [*m/z* (%)]: 305 (9) $M^{+\cdot}$; 240 (22) $M^{+\cdot}$ $-SO_2$, –H; 198 (100) $M^{+\cdot}-SO_2$, $-C_3H_7$; HRMS: calcd for $C_{12}H_{13}Cl_2NO_2S$: 305.0044; found: 305.0044.

4.5. General procedures for substitution in position 3

2.1 Equivalents butyllithium were added to a solution of 200 mg of sulfolene pyridine **4** in 10 mL dry THF under an inert atmosphere at −78°C. After stirring for 15 min 1.1 equivalent electrophile was added dropwise. To get disubstitution (compound **7**) 3 equivalents were added. Then the cooling bath was removed and stirring was continued for 4 h. After addition of 10 mL saturated NH_4Cl solution the mixture was extracted with CH_2Cl_2 (3×10 mL). The organic layer was dried with $MgSO_4$ and the solvent removed. Chromatographic purification (silica gel 90 $CHCl_3$\10 ethyl acetate) yielded the substituted products **7**, **8** and **11**.

4.5.1. (±) 1,3-Dibenzyl-4,6-dichloro-1,3-dihydro-2,2-dioxo-7-methylthieno[3,4-*c*]pyridine (7). Yield: 72%; white crystals; m.p.: 202–203.5°C ($CHCl_3$/Hexane); IR (KBr): 1315 cm^{-1} (m); 1110 cm^{-1} (m); ^1H NMR ($CDCl_3$/TMS): δ 7.35–7.25 (m, 7H, h-H), 7.08–6.95 (m, 3H, Ph–H),

4.59 (dd, ^3J=7 Hz, ^3J=3 Hz, 1H, H-3), 4.39 (t, ^3J=7 Hz, 1H, H-1), 3.39 (dd, ^2J=15 Hz, ^3J=7 Hz, 1H, H-1''), 3.26 (dd, ^2J=15 Hz, ^3J=3 Hz, 1H, H-1''), 3.14 (dd, ^2J=15 Hz, ^3J=7 Hz, 1H, H-1'), 2.38 (dd, ^2J=15 Hz, ^3J=7 Hz, 1H, H-1'), 1.88 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 151.2 (C-6), 148.2 (C-7a), 145.3 (C-4), 135.8 (C-*ipso*), 135.5 (C-*ipso*), 129.4, 130.0, 129.5, 129.1, 129.0, 128.7, 127.7 (C-*p*), 127.5 (C-*p*), 67.7 (C-1), 67.4 (C-3), 37.1 (C-1'), 35.2 (C-1''), 16.5 (CH_3); MS [*m*/*z* (%)]:431 (1) $M^{+\cdot}$; 366 (17) $M^{+\cdot}$ –H, –SO_2; 91 (100) $PhCH_2^{+\cdot}$; HRMS: calcd for $C_{22}H_{19}Cl_2NO_2S$: 431.0513; found: 431.0511.

4.5.2. (±) 3-Benzyl-4,6-dichloro-1,3-dihydro-2,2-dioxo-7-methylthieno[3,4-*c*]pyridine (8). Yield: 85%; white powder; m.p.: 192–193.5°C ($CHCl_3$/hexane); IR (KBr): 1310 cm^{-1} (s),; 1115 cm^{-1} (s); ^{1}H NMR ($CDCl_3$/TMS): δ7.20–7.12 (m, 5H, Ph–H), 4.61 (dd, ^3J=5 Hz, ^3J=3 Hz, 1H, H-3), 4.04 (d, ^2J=16.5 Hz, 1H, H-1), 3.51 (dd, ^3J=3 Hz, ^3J=5 Hz, 2H, CH_2Ph), 3.48 (d, ^2J=16.5 Hz, 1H, H-1), 2.16 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 150.3, 144.7, 144.5, 134.1, 130.1, 129.8 (C-7), 128.4, 128.4 (C-3a), 127.6, 66.5 (C-3), 55.3 (C-1), 34.7 (CH_2Ph), 16.4 (CH_3); MS [*m*/*z* (%)]: 341 (20) $M^{+\cdot}$; 276 (77) $M^{+\cdot}$ –H, –SO_2; 241 (36) $M^{+\cdot}$ –HCl, –SO_2; 91 (100) $PhCH_2^{+\cdot}$; HRMS: calcd for $C_{15}H_{13}Cl_2NO_2S$: 341.0044; found: 341.0061.

4.5.3. (±) 4,6-Dichloro-1,3-dihydro-7-methyl-2,2-dioxo-3-(4-pentenyl)thieno[3,4-*c*]pyridine (11). Yield: 55%; white crystals; m.p.: 71.5–72.5°C ($CHCl_3$/Hexane); IR (KBr): 1640cm^{-1} (m); 1330cm^{-1} (s); 1127cm^{-1} (s), ^{1}H NMR ($CDCl_3$/TMS): δ5.77 (ddt, ^3J=16.5 Hz, ^3J=10 Hz, ^3J=6.5 Hz, 1H, H-4'), 5.03 (dd, ^3J=16.5 Hz, ^2J=1.5 Hz, 1H, H-5'), 4.98 (dd, ^3J=10 Hz, ^2J=1.5 Hz, 1H, H-5'), 4.32 (s, 2H, H-1), 4.28 (dd, ^3J=9 Hz, ^3J=4 Hz, 1H, H-3), 2.35 (s, 3H, CH_3), 2.20–1.90 (m, 4H, CH_2-1', CH_2-3'), 1.63 (dt, ^2J=7 Hz, 2H, H-2'); ^{13}C NMR ($CDCl_3$): δ 149.9 (C-6), 144.2 (C-4), 143.2 (C-7a), 137.1 (C-4'), 130.4 (C-3a), 128.5 (C-7), 115.4 (C-5'), 65.3 (C-3), 55.1 (C-1), 33.0 (C-1'), 29.5 (C-2'), 25.2 (C-3'), 16.5 (CH_3); MS [*m*/*z* (%)]: 319 (2) $M^{+\cdot}$; 250 (15) $M^{+\cdot}$ –C_5H_9; 214 (72) $M^{+\cdot}$–SO_2, –C_3H_5; 212 (100) $M^{+\cdot}$ –SO_2, –C_3H_7; 200 (52) $M^{+\cdot}$ –SO_2, –C_4H_7; 187 (15) $M^{+\cdot}$ –SO_2, –C_5H_9; HRMS: calcd for $C_{13}H_{15}Cl_2NO_2S$: 319.0200; found: 319.0202.

4.6. General procedure for intermolecular Diels–Alder reactions

A mixture of 200 mg sulfolene pyridine **4a**, 3 equivalents dienophile and 5 mL decaline was subjected to three freeze–pump–thaw cycles. The glass tube was sealed and heated at 250°C for 14 h. The reaction mixture was then subjected to a Kugelrohr distillation to remove the decaline. The residue was chromatographed on silica gel using chloroform as eluent; the regioisomers and the rearrangement product were separated by HPLC. Experimental data of **13**–**16** are described in the previous article.[1]

4.6.1. *cis* (±)-5,7-Dichloro-2,3,3a,4,9,9a-hexahydrofuro-[2,3-*g*]isoquinoline (17a). Yield: 54%;yellow oil; ^{1}H NMR (C_6D_6): δ 6.55 (s, 1H, H-8); 3.79 (dt, ^3J=8,5 Hz, ^3J=4.5 Hz, 1H, H-9a); 3.39 (td, ^3J=^2J=8.5 Hz, ^3J=3.5 Hz, 1H, H-2); 3.13 (td, ^3J=^2J=8.5 Hz, ^3J=6 Hz, 1H, H-2); 2.39 (dd, ^2J=15.5 Hz, ^3J=4.5 Hz, 1H, H-9eq); 2.35 (dd, ^2J=15.5 Hz, ^3J=5.5 Hz, 1H, H-4eq); 2.21 (dd, ^2J=15.5 Hz, ^3J=7 Hz, 1H, H-4ax); 2.10 (dd, ^2J=15.5 Hz, ^3J=4.5 Hz, 1H, H-9ax); 1.98 (tdd, ^3J=^3J=8,5 Hz, ^3J=7 Hz, ^3J=5.5 Hz, 1H, H-3a); 1.57 (dddd, ^2J=12 Hz, ^3J=8,5 Hz, ^3J=7 Hz, ^3J=3.5 Hz, 1H, H-3); 0.93 (dddd, ^2J=12 Hz, ^3J=8.5 Hz, ^3J=7 Hz, ^3J=6 Hz, 1H, H-3); ^{1}H NMR ($CDCl_3$/TMS): δ 7.11 (s, 1H, H-8); 4.32 (dt, ^3J=8 Hz, ^3J=4.5 Hz, 1H, H-9a); 3.74 (td, ^3J=^2J=8 Hz, ^3J=3 Hz, 1H, H-2); 3.51 (td, ^3J=9 Hz, ^3J=6 Hz, 1H, H-2); 2.91 (dd, ^2J=15.5 Hz, ^3J=4 Hz, 1H, H-9eq); 2.79 (dd, ^2J=15.5 Hz, ^3J=4.5 Hz, 1H, H-9ax); 2.70 (m, 2H; H-4ax, H-3a); 2.18 (m, 1H, H-3); 1.38 (m, 1H, H-3); ^{13}C NMR ($CDCl_3$): δ 151.8, 148.2, 147.3, 130.6 (C-4a), 122.9 (C-8), 76.0 (C-9a), 66.7 (C-2), 36.4, 34.3, 32.9, 28.3 MS [*m*/*z* (%)]:243 (83) $M^{+\cdot}$; 225 (97) $M^{+\cdot}$ –H_2O; 212 (48) $M^{+\cdot}$ –CH_2OH; 199 (52) $M^{+\cdot}$–Cl, –C_3H_6; 173 (100) $M^{+\cdot}$ –C_4H_6O; HRMS: calcd for $C_{11}H_{11}Cl_2NO$: 243.0217; found: 243.0227.

4.6.2. *cis* (±)-6,8-Dichloro-2,3,3a,4,9,9a-hexahydrofuro-[3,2-*g*]isoquinoline (17b). Yield: 18%;yellow oil; ^{1}H NMR ($CDCl_3$/TMS): δ 7.08 (s, 1H, H-5); 4.31 (dt, ^3J=8.5 Hz, ^3J=^3J=5 Hz, 1H, H-9a); 3.78 (dd, ^3J=9 Hz, ^3J=4 Hz, 1H, H-2); 3.56 (dd, ^3J=9 Hz, ^3J=6 Hz, 1H, H-2); 3.08 (dd, ^2J=16 Hz, ^3J=5 Hz, 1H, H-9eq); 2.89 (dd, ^2J=16 Hz, ^3J=5 Hz, 1H, H-9ax); 2.83–2.50 (m, 3H, H-4ax, H-4eq, H-3a); 2.14 (m, 1H, H-3); 1.43 (m, 1H, H-3); ^{13}C NMR ($CDCl_3$): δ 152.6, 149.1, 147.3, 129.7, 122.4, 76.4, 66.7, 36.2, 33.0, 32.8, 30.0 MS [*m*/*z* (%)]:243 (70) $M^{+\cdot}$; 225 (88) $M^{+\cdot}$ –H_2O; 173 (92) $M^{+\cdot}$ –C_4H_6O; 71 (100); HRMS: calcd for $C_{11}H_{11}Cl_2NO$: 243.0217; found: 243.0210.

4.6.3. (±)-9-Benzyl-5,7-dichloro-8-methyl-2-phenyl-3a,4,9,9a-tetrahydro-1*H*-pyrrolo[3,4-*g*]isoquinoline-1,3(2*H*)-dione (18). Yield: 17%; yellow crystals; m.p.: 243–246°C ($CHCl_3$/Hexane); IR (KBr): 1714 cm^{-1}; ^{1}H NMR ($CDCl_3$/TMS): δ 7.58–7.45 (m, 6H, Ph–H), 7.18–7.12 (m, 2H, Ph–H), 6.75 (dd, ^3J=9 Hz, ^4J=2 Hz, 2H, Ph–H), 4.10 (ddd, ^3J=12 Hz, ^3J=6 Hz, ^3J=3 Hz, 1H, H-9), 3.90 (dd, ^2J=17 Hz, ^3J=9 Hz, 1H, H-4eq), 3.40 (dt, ^3J=10 Hz, ^3J=9 Hz, 1H, H-3a), 3.30 (dd, ^3J=10 Hz, ^3J=6 Hz, 1H, H-9a), 3.05 (dd, ^2J=12 Hz, ^3J=3 Hz, 1H, H_{Bn}), 3.00 (dd, ^2J=17 Hz, ^3J=9 Hz, 1H, H-4ax), 2.55 (t, ^3J=^3J=12 Hz, 1H, H_{Bn}), 1.50 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 177.6 (C=O), 176.3 (C=O), 151.2, 148.8, 146.4, 137.0, 131.5, 129.8, 129.3 (C-8), 129.1, 129.0, 128.6, 128.0 (C-4), 127.3, 126.3, 43.8, 40.6, 38.1, 35.4, 24.0 (C-1'), 14.8 (CH_3); MS [*m*/*z* (%)]: 450 (34) $M^{+\cdot}$; 415 (4) $M^{+\cdot}$ –Cl; 276 (6) $M^{+\cdot}$ –H_2, –$(CO)_2$NPh; 175 (20) $M^{+\cdot}$ –CH_2Ph, –H$(CO)_2$NPh, –HCl; 91 (100) $PhCH_2^+$; HRMS: calcd for $C_{25}H_{20}Cl_2N_2O_2$: 450.0901; found: 450.0901.

4.6.4. 2,6-Dichloro-4-(2-phenylethenyl)-3,5-dimethylpyridine (19). Yield**:** 57%;white crystals; m.p.: 169–170°C ($CHCl_3$/Hexane); IR (KBr): 1639 cm^{-1} (w); ^{1}H NMR ($CDCl_3$/TMS): δ7.50–7.39 (m, 5H, Ph–H), 6.96 (d, ^3J=18 Hz, 1H, H-2'), 6.58 (d, ^3J=18 Hz, 1H, H-1'), 2.35 (s, 6H, CH_3) ^{13}C NMR ($CDCl_3$): δ 150.3 (C-4), 147.8 (C-2, -6), 137.3 (C-2'), 135.7 (C-*ipso*), 129.1 (C-3, -5), 128.8 (C-*o*, C-*m*), 126.6 (C-*p*) 123.8 (C-1'), 17.2 (CH_3) MS [*m*/*z* (%)]: 277 (100) $M^{+\cdot}$; 262 (30) $M^{+\cdot}$ –CH_3; 242 (20) $M^{+\cdot}$ –Cl; 226 (75) $M^{+\cdot}$ –HCl, –CH_3; 164 (77) $M^{+\cdot}$ –Ph, –HCl.

4.6.5. (±)-5,7-Dichloro-9-ethyl-3a,4,9,9a-tetrahydro-2-phenyl-8-methyl-1*H*-pyrrolo[3,4-*g*]isoquinoline-1,3(2*H*)-dione (20). Yield: 30%;yellow powder; m.p.: 256–258°C ($CHCl_3$/Hexane); IR (KBr): 1709 cm^{-1} (s); ^1H NMR ($CDCl_3$/TMS): δ 7.55–7.48 (m, 3H, Ph–H), 7.32–7.28 (m, 2H, Ph–H), 3.85 (dd+m, ^2J=17 Hz, ^3J=9.5 Hz, 2H, H-9, H-4eq), 3.37 (q, ^3J=9.5 Hz, ^3J=9.5 Hz 1H, H-3a), 3.20 (dd, ^3J=9.5 Hz, ^3J=6 Hz, 1H, H-9a), 2.90 (dd, ^2J=17 Hz, ^3J=9.5 Hz, 1H, H-4ax), 2.45 (s, 3H, CH_3), 1.80 (m, 1H, CH_{2Et}), 1.40 (m, 1H, CH_{2Et}), 0.78 (t, ^3J=7 Hz, 3H, CH_{3Et}); ^{13}C NMR ($CDCl_3$): δ 178.0, 176.4, 152.4, 149.2, 146.9, 131.7, 129.8, 129.4, 129.0, 128.2, 126.4, 44.0, 39.4, 38.0, 23.8, 22.1, 16.2 (CH_3), 12.1 (CH_{2Et}); MS [*m*/*z* (%)]: 388 (20) $M^{+\cdot}$; 353 (77) $M^{+\cdot}$ –Cl; 240 (77) $M^{+\cdot}$ –H$(CO)_2$NPh; 200 (92) $M^{+\cdot}$ –CH_3, –$(CHCO)_2$NPh; 91 (98) $PhN^{+\cdot}$; 77 (100) $Ph^{+\cdot}$ HRMS: calcd for $C_{20}H_{18}Cl_2N_2O_2$: 388.0745; found: 388.0763.

4.6.6. 2,6-Dichloro-3,5-dimethyl-4-(1-propenyl)pyridine (21). Yield: 42%; white crystals; m.p.: 73.5–74°C ($CHCl_3$/Hexane); IR (KBr): 1648 cm^{-1} (w); ^1H NMR ($CDCl_3$/TMS): δ 6.25 (dq, ^3J=16 Hz, ^4J=2 Hz, 1H, H-1') 5.74 (dq, ^3J=16 Hz, ^3J=6 Hz, 1H, H-2') 2.25 (s, 6H, CH_3) 1.95 (dd, ^3J=6 Hz, ^4J=2 Hz, 3H, H-3'); ^{13}C NMR ($CDCl_3$): δ 150.8, 147.5 (C-2, C-6), 134.4, 129.0 (C-3, C-5), 126.5, 18.7 (CH_3), 17.1 (CH_3); MS [*m*/*z* (%)]: 215 (13) $M^{+\cdot}$; 180 (23) $M^{+\cdot}$ –Cl; 165 (10) M^+ –CH_3, –Cl; 77 (45) Ph^+; 43 (100) $C_3H_7^+$; HRMS: calcd for $C_{10}H_{11}NCl_2$: 215.0268; found: 215.0267.

4.6.7. 2,6-Dichloro-4-(2-phenylethenyl)-3-(2-phenylethyl)-5-methylpyridine (22). Yellow oil; IR (KBr): 1642 cm^{-1} (w); ^1H NMR ($CDCl_3$/TMS): δ 7.45–7.36 (m, 6H, Ph–H), 7.22–7.18 (m, 2H, Ph–H), 7.06–6.94 (m, 2H, Ph–H), 6.67 (d, ^3J=15 Hz, 1H, H-1'), 6.48 (d, ^3J=15 Hz, 1H, H-2'), 3.06 (t, ^3J=8 Hz, 2H, H-1''), 2.88 (t, ^3J=8 Hz, 2H, H-2''), 2.34 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 150.8 (C-4), 148.2 (C-6), 147.4 (C-2), 140.8, 136.8 (HC=), 135.7, 132.5, 129.5, 128.8, 128.7, 128.5, 126.6, 126.2, 123.5, 34.7, 32.7, 17.4(CH_3) MS [*m*/*z* (%)]: 367 (42) M^+; 276 (65) $M^{+\cdot}$ –CH_2Ph; 241 (54) $M^{+\cdot}$ –CH_2Ph, –Cl; 178 (20) $M^{+\cdot}$ –Cl, –2 Ph; 91 (100) $PhCH_2^+$.

4.6.8. (±)-4-Benzyl-5,7-dichloro-2-phenyl-3a,4,9,9a-tetrahydro-8-methyl-1*H*-pyrrolo[3,4-*g*]isoquinoline-1,3(2*H*)-dione (23). Yield: 56%; yellow crystals; m.p.: 151–152°C ($CHCl_3$/Hexane); IR (KBr): 1705 cm^{-1} (s); ^1H NMR ($CDCl_3$/TMS): δ 7.42–7.38 (m, 4H, Ph–H), 7.19–7.13 (m, 4H, Ph–H), 6.75 (dd, ^2J=9 Hz, ^4J=2 Hz, 2H, Ph), 4.25 (ddd, ^3J=13 Hz, ^3J=6 Hz, ^3J=4 Hz, 1H, H-4), 3.57 (dd, ^3J=17 Hz, ^3J=8.5 Hz, 1H, H-9), 3.23 (dd, ^3J=10 Hz, ^3J=8.5 Hz, 1H, H-3a), 3.16 (td, ^3J=^3J=10 Hz, ^3J=8.5 Hz, 1H, H-9a), 3.03 (dd, ^2J=13 Hz, ^3J=4 Hz, 1H, H-1'), 2.78 (dd, ^2J=17 Hz, ^3J=10 Hz, 1H, H-9), 2.53 (dd, ^2J=^3J= 13 Hz, 1H, H-1'), 2.37 (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$): δ177.7 (C=O), 176.0 (C=O), 148.6, 148.0, 147.0, 136.7, 131.5, 131.3, 129.2, 129.2 129.1, 128.9, 128.2, 126.9, 126.2, 43.1 (C-9a), 39.0 (C-9), 38.3 (C-3a), 35.1 (C-1'), 24.8 (C-4), 15.6 (CH_3) MS [*m*/*z* (%)]: 450 (8) $M^{+\cdot}$; 212 (18) $M^{+\cdot}$ –H, –$(CHCO)_2$NPh, –CH_2Ph; 91 (100) $PhCH_2^+$; HRMS: calcd for $C_{25}H_{20}Cl_2N_2O_2$: 450.0901; found: 450.0900.

4.6.9. 2,6-Dichloro-3-(2-phenylethenyl)-3,4-dimethylpyridine (24). Yield: 10%;white crystals; m.p.: 95–96°C ($CHCl_3$/Hexane); IR (KBr): 1637 cm^{-1} (w); ^1H NMR ($CDCl_3$/TMS): δ 7.55–7.20 (m, 5H, Ph), 6.98 (d, ^3J=17 Hz, 1H, H-2'), 6.71 (d, ^3J=17 Hz, 1H, H-1'), 2.41 (s, 3H, CH_3), 2.36 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 149.2, 148.0, 146.3, 137.3, 136.3, 131.6, 130.3, 128.7, 128.5, 126.6, 122.5, 18.8 (CH_3), 16.3 (CH_3); MS [*m*/*z* (%)]: 277 (65) $M^{+\cdot}$;242 (100) $M^{+\cdot}$ –Cl; 206 (24) $M^{+\cdot}$ –HCl, –Cl; HRMS: calcd for $C_{15}H_{13}Cl_2N$: 277.0425; found: 277.0430.

4.7. General procedure for intramolecular Diels–Alder reactions

A mixture of 250 mg substituted sulfolene pyridine **10**,**11** or **12** and 5 mL decaline was subjected to three freeze–pump–thaw cycles, the glass tube was sealed and heated for 24 h at 250°C. The decaline was removed with a Kugelrohr distillation. Chromatographic purification (silica gel CH_2Cl_2) gave a mixture of the adduct and rearrangement product, which were separated by HPLC.

4.7.1. (±)-2,4-Dichloro-6,6a,7,8,9,9a-hexahydro-1-methyl-5*H*-cyclopent[*f*]isoquinoline (25a and 25b). Yield: 27%; white powder; ^1H NMR ($CDCl_3$/TMS): δ 3.09 (q, ^3J=8 Hz, 1H, H-9a); 2.93 (dd, ^3J=16 Hz, ^3J=16 Hz, 3.9H); 2.85–2.38 (m, 13.6H); 2.37 (s, 9.1H); 2.33 (s, 2.3H); 2.30–2.08 (m, 6.2H); 2.00–1.20 (m, 31.3H); ^{13}C NMR ($CDCl_3$): δ 154.0, 147.7, 147.6, 131.2, 129.8, 48.1, 44.9, 41.9, 37.4, 31.7, 31.4, 29.8, 29.7, 29.4, 26.4, 22.5, 26.0, 24.8, 22.7, 18.3 (CH_3), 15.6 (CH_3); MS [*m*/*z* (%)]: 255 (76) $M^{+\cdot}$; 220 (44) $M^{+\cdot}$ –Cl; 212 (40) $M^{+\cdot}$ –$(CH_2)_2$–CH_3; 199 (14) $M^{+\cdot}$–CH_3, –C_3H_5; 179 (61) $M^{+\cdot}$ –Cl, –CH_2=CH–CH_2; 41 (100) CH_2=$CHCH_2^+$; HRMS: calcd for $C_{13}H_{15}Cl_2N$: 255.0581; found 255.0589.

4.7.2. 2,6-Dichloro-4-(1,5-hexadienyl)-3,5-dimethylpyridine (26). Yield: 34%;yellow oil; ^1H NMR ($CDCl_3$/TMS): δ 6.26 (d,^3J=16 Hz, 1H, H-1'); 5.85 (ddt, ^3J=17 Hz, ^3J=10 Hz, ^3J=6 Hz, 1H, H-5'); 5.71 (dt, ^3J=16 Hz, ^3J=7 Hz, 1H, H-2'); 5.10 (dd, ^3J=17 Hz, ^4J=2 Hz, 1H, H-6'); 5.02 (dd, ^3J=10 Hz, ^4J=2 Hz; 1H, H-6'); 2.40–2.36 (m, 2H, H-3'); 2.30–2.23 (m, 2H, H-4'); 2.28 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ 150.7 (C-4), 147.5 (C-2, C-6), 138.7, 137.4, 129.0 (C-3, C-5), 125.8 (C-2'), 115.5 (C-6'), 32.9, 32.4, 17.1 (2×CH_3); MS [*m*/*z* (%)] 256 (100) MH^+; HRMS: calcd for $C_{13}H_{15}Cl_2N$: 255.0581; found 255.0598.

4.7.3. (±)-2,4-Dichloro-6,6a,7,8,9,9a-hexahydro-5*H*-cyclopent[*g*]isoquinoline (27a and 27b). Yield: 48%;yellow oil; ^1H NMR ($CDCl_3$/TMS): δ 3.20–1.20 (m, 24H), 2.27 (s, 3H, CH_3); 2.25 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ 151.7, 150.2, 146.9, 146.7, 134.5, 129.3, 45.8, 44.6, 40.6, 36.8, 31.8, 31.2, 30.0, 29.8, 27.6, 26.5, 25.0, 22.9, 22.5, 15.7 (CH_3), 15.4 (CH_3); MS [*m*/*z* (%)]: 255 (51) $M^{+\cdot}$; 220 (50) $M^{+\cdot}$ –Cl; 212 (40) $M^{+\cdot}$ –$(CH_2)_2$–CH_3; 199 (10) $M^{+\cdot}$–CH_3, –C_3H_5; 179 (48) $M^{+\cdot}$ –Cl, –CH_2=CH–CH_2; 41 (100) CH_2=$CHCH_2^+$.

4.7.4. 2,6-Dichloro-3-(1,5-hexadienyl)-4,5-dimethylpyridine (28). Yield: 24%;yellow oil; ^1H NMR ($CDCl_3$/TMS): δ 6.26 (dd, ^3J=16 Hz, ^4J=1 Hz, 1H, H-1'); 5.91 (dt, ^3J=16 Hz, ^3J=6 Hz, 1H, H-2'); 5.83 (ddt, ^3J=17 Hz, ^3J=10 Hz, ^3J=6 Hz, 1H, H-5'); 5.08 (dt, ^3J=17 Hz,

^4J=2 Hz, 1H, H-6'); 5.02 (dt, ^3J=10 Hz, ^4J=2 Hz, 1H; H-6'); 2.45–2.25 (m, 4H, H-3', H-4'); 2.32 (s, 6H, CH_3); ^{13}C NMR ($CDCl_3$): δ 149.1, 147.5, 146.1, 138.9, 137.6, 131.9, 130.0, 124.1, 115.3, 36.1, 33.1, 32.6, 18.6 (CH_3), 16.3 (CH_3).

4.7.5. (±)-2,4-Dichloro-6,6a,7,8,9,9a-hexahydro-5*H*-cyclopent[*f*]isoquinoline (29a and 29b). Yield: 93%; colorless oil; ^1H NMR ($CDCl_3$/TMS): δ 6.97 (s, 1H, H-1); 6.95 (s, 1H, H-1); 3.00–1.05 (m, 24H); ^{13}C NMR ($CDCl_3$): δ 155.9, 149.5, 146.4, 146.3, 130.2, 130.0, 123.0, 120.3, 47.3, 42.4, 42.3, 36.2, 33.9, 31.6, 30.1, 27.5, 27.0, 25.7, 25.3, 23.7, 22.5; CHN analysis: calcd for $C_{12}H_{13}Cl_2N$: C 59.52, H 5.41, N 5.78; found: C 59.44, H 5.10, N 5.66; MS [*m*/*z* (%)]: 241 (100) $M^{+\cdot}$; 206 (97) $M^{+\cdot}$ –Cl; 198 (40) $M^{+\cdot}$ $-C_3H_7$; 164 (52) $M^{+\cdot}$–Cl, $-C_3H_6$; HRMS: calcd for $C_{12}H_{13}Cl_2N$: 241.0425; found 241.0436.

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