Reactions of Pyridine Analogues of Aza-*o*-xylylenes Generated from 1,3-Dihydroisothiazolo[4,3-*b*]pyridine 2,2-Dioxides (Pyridosultams) − Formation of 2:1 Adducts with *N*-Phenylmaleimide

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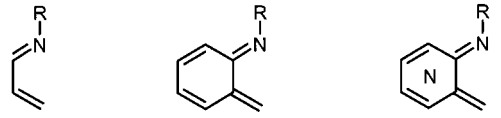
Pyridine analogues **16**–**20** of aza-*o*-xylylenes, generated from pyridosultams **11**–**15**, enter into Diels–Alder reactions with dienophiles to form 1,2,3,4-tetrahydronaphthyridines **23**–**28**, which then add another equivalent of a dienophile to form 2:1 adducts **29**–**36**. Intramolecular Diels–Alder reactions of aza-*o*-xylylenes **45** and **46**, generated from pyridosultams **43** and **44**, produced tricyclic pyrrolo- and pyridonaphthyridines **47** and **48**, which were used for the construction of the 10,14-diazasteroid frameworks **52** and **54**.

Introduction

[4+2] Cycloadditions of 1-aza-dienes **1** are a well-established method used for the construction of six-membered heterocyclic systems.[1] Some unusual representatives of 1-azadienes are aza-*o*-xylylenes **2** (also known as 6-methylenecyclohexa-2,4-dien-1-imines or *o*-quinonemethyleneimines[2,3]), which are potential building blocks for the construction of 1,2,3,4-tetrahydroquinoline derivatives.



1 **2** **3**

Aza-*o*-xylylenes **2** can be generated by electrocyclic ring-opening of benzoazetines,[4] by 1,4-elimination of water from 2-aminobenzyl alcohols either in the presence of Lewis acids[5,6] or under flash vacuum thermolysis (FVT) conditions,[7,8] by base-induced 1,4-elimination of HCl from 2-aminobenzyl chlorides[9,10] or of amines from 2-aminobenzylamine derivatives,[11,12] or by a [4+2] cycloreversion reaction proceeding with expulsion of CO_2 from 3,1-benzoxazin-2-ones.[13] We have developed a method for the generation of aza-*o*-xylylenes by thermal cheletropic extrusion of SO_2 from easily accessible 1-alkyl-1,3-dihydro[2,1]benzisothiazole 2,2-dioxides (benzosultams).[14−19]

o-Xylylenes[20,21] and their heteroanalogues[22,23] containing five- and six-membered heterocyclic rings are widely used in organic synthesis. Contrarily, the chemistry of heteroanalogues of aza-*o*-xylylenes **3** with a six-membered pyridine ring in place of the benzene moiety is practically unknown. There are only few reports dealing with the generation of such species. Storr et al. have described the intramolecular reaction of a pyridine analogue of aza-*o*-xylylene generated by 1,4-elimination of water from a 4-amino-3-(hydroxymethyl)pyridine derivative under FVT conditions.[8] 1,5-Elimination of hydrogen chloride from an imidochloride derived from 4-amino-3-methylpyridine under FVT conditions provided cumulated xylylene, which then electrocyclized to 2-phenyl-5-azaindole.[24] Strekowski applied a base-induced 1,4-elimination of hydrogen fluoride from 3-amino-4-(trifluoromethyl)quinoline to the generation of difluoroxylylene, which added ketone enolates to form phenanthridine derivatives.[25] Lewis acid catalysed 1,4-elimination of water from 3-amino-2-(1-hydroxyalkyl)-pyridines afforded diazaxylylenes, which then electrocyclized to form [1,5]naphthyridines.[6]

We have recently applied the thermal extrusion of SO_2 from 1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-dioxides (pyridosultams) to the generation of pyridine analogues of aza-*o*-xylylenes [2-methylenepyridine-3(*2H*)-imines, **16−20**].[26−28] We found that the diazaxylylenes generated from 1,3-dialkylpyrydosultams underwent sigmatropic [1,5] hydrogen shifts to afford 3-alkylamino-2-vinylpyridine derivatives in high yields.[27]

In one of our previous papers[26] we reported the formation of 2:1 addition products from *N*-phenylmaleimide (NPMI) and diazaxylylenes. For the structures of these products we tentatively proposed the pyridoazocine derivative **4**. Similar structures of condensed eight-membered derivatives **6** and **9** were proposed for 2:1 adducts of NPMI with quinoxalino-*o*-quinodimethanes[29] and pyrimidino-*o*-

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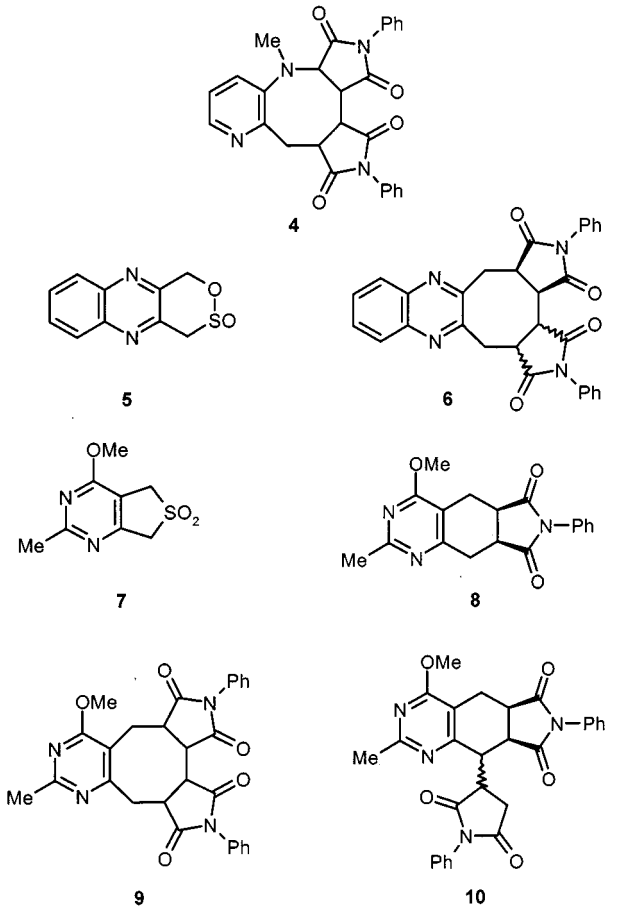
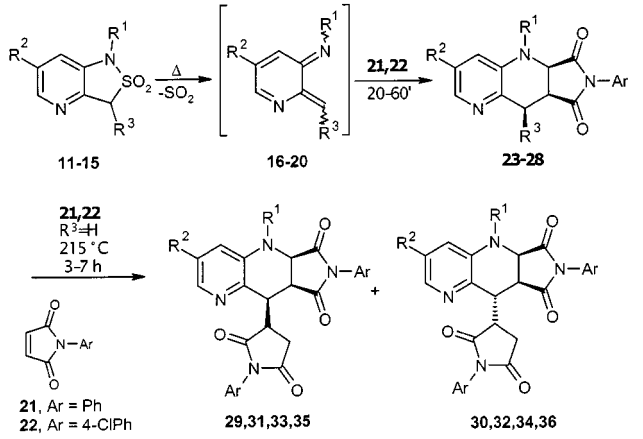
quinodimethanes[30,31] generated by thermal extrusion of sulfur dioxide from sultine **5** or condensed dihydrothiophene dioxide **7**, respectively.



In a review published in "Progress in Heterocyclic Chemistry",[32] Storr et al. disputed the previously assigned[30,31] eight-membered ring structure and suggested that the 2:1 adducts **10** were products of the Michael addition of NPMI to the initially formed [4+2] cycloaddition product **8**. However, no details for this assignment were given. The formation of an eight-membered compound **6** in the reaction between NPMI and quinoxalinoxylylene generated from the sultine **5** was called into question by Storr et al.,[32] but the authors confirmed their earlier results.[33] The structures **4** also assigned by us were also called into question by Storr, who suggested structures similar to **10** for these compounds. This prompted us to reinvestigate the assignment of the products obtained earlier.[26] We now give a full report on the results of our studies on the reactions of aza-*o*-xylylenes generated from pyridosultams.

Results and Discussion

The previously unknown 1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-dioxides (pyridosultams) **11**−**15** were synthesised from readily available 3-amino-2-chloropyridines and alkanesulfonyl chlorides.[27] When equimolar amounts of pyridosultam **11** and *N*-phenylmaleimide (**21**) were heated in boiling 1,2,4-trichlorobenzene (215 °C), the extrusion of SO_2 proceeded readily. After 30 min, the starting sultam **11** had completely disappeared, but the expected 8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (**23**) had been formed only in low yield. An analogous procedure with a threefold excess of *N*-phenylmaleimide gave the expected 1,5-naphthyridine **23** in 54% yield, but the two additional products **29** and **30** were also isolated. The molecular masses of the products **29** and **30** each corresponded to a reaction between 2 equiv. of NPMI and 1 equiv. of xylylene **16**. We observed that the yield of **29** and **30** increased with the reaction time. Extension of the reaction time to 4.5 h resulted in the complete disappearance of the 1:1 adduct **23**, and the products **29** and **30** were formed in a 1:1 ratio in 71% total yield. The compounds **29** and **30** were two diastereomeric Michael addition products of the formed pyrrolo[3,4-*b*]-1,5-naphthyridine **23** to maleimide **21**, this reaction proceeding by deprotonation at the α-position of the initially formed 1:1 adduct. Pyridosultams **12** and **13** reacted analogously, forming 1:1 adducts **24**−**26** or 2:1 adducts **31**−**36**, depending on the reaction conditions (Scheme 1).



Substrate	Xylylene	R^1	R^2	R^3	Maleimide	Conditions	Products (yield %)	
11	**16**	Me	H	H	**21**	215 °C, 30'	**23** (54)	**29**+**30** (18)
11	**16**	Me	H	H	**21**	215 °C, 4.5 h	**23** (0)	**29**+**30** (71)
11	**16**	Me	H	H	**22**	215 °C, 20'	**24** (36)	**31**+**32** (18)
11	**16**	Me	H	H	**22**	215 °C, 7 h	**24** (0)	**31**+**32** (55)
12	**17**	Pr	H	H	**21**	215 °C, 40'	**25** (71)	**33**+**34** (tr)
12	**17**	Pr	H	H	**21**	215 °C, 3.5 h	**25** (0)	**33**+**34** (84)
13	**18**	Me	Cl	H	**21**	215 °C, 20'	**26** (67)	**35**+**36** (tr)
14	**19**	Me	H	Ph	**21**	110 °C, 1 h	**27** (23)	
15	**20**	Pr	H	Ph	**21**	110 °C, 1 h	**28** (16)	

Scheme 1

We initially assigned the eight-membered ring structure **4** to the 2:1 adducts and proposed a plausible mechanism for its formation, involving a thermal retro-Michael reaction followed by the tandem Michael addition of another equivalent of NPMI.[26] Since the structure **4** was later questioned,[32] we reinvestigated our earlier assignment of the structures of the 2:1 adducts. Unfortunately, we were unable

to obtain the products **29−34** in crystal forms suitable for X-ray analysis. Thus, our assignment is based on analysis of the NMR spectra. We employed 2D NMR "long-range" correlation ^{1}H-^{13}C NMR techniques for the 2:1 adduct **29** (the less polar isomer of the adduct pair **29** and **30**). The data from this experiment were consistent with formula **29** and not with the eight-membered structure **4**. Figure 1 presents long correlation signals *H*−C−C and *H*−C−C−C observed for the 9a-carbon atom (marked with an asterisk).

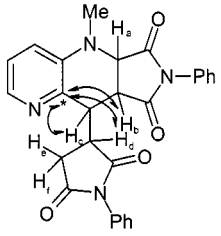


Figure 1. "Long range correlations" of the pyridine 9a-carbon atom (marked with an asterisk)

In the HETCORR 2D ^{1}H-^{13}C NMR spectrum optimised for long-range correlation we observed strong correlation of this carbon atom to the hydrogen atoms H_b, H_c and H_d, and no correlation to H_e or H_f. On this basis we reassigned the formula of this 2:1 adduct as **29**.

To prove this assignment we synthesised 3,3-dideuteriopyridosultam **11d$_2$** and obtained the corresponding adducts **29d** and **30d** on treatment with *N*-phenylmaleimide. The ^{1}H NMR spectrum of the less polar adduct **29d** was simpler than that obtained for **29**. We observed almost complete disappearance of the signal of hydrogen atom H_c and partial disappearance of the signals of H_e and H_f. This observation was consistent with the Michael addition mechanism shown in Scheme 2.

If the formed 2:1 adduct had contained an eight-membered ring, as in compound **37**, the hydrogen atom H_c would not have been replaced by deuterium and only the signals of hydrogen atoms H_e and H_f would have disappeared.

As expected, the other aza-*o*-xylylene pyridine analogues **17** and **18**, generated from 1-alkylpyridosultams **12** and **13**, entered into [4+2] cycloaddition reactions with *N*-arylmaleimides, with 1,5-naphthyridine derivatives **24−26** being obtained in good yields (Scheme 3). In the case of the 3-phenylpyridosultams **14** and **15**, the extrusion of SO_2 occurred at lower temperature (refluxing toluene, 110 °C) and the aza-*o*-xylylenes **19** and **20** entered into the Diels−Alder reaction with *N*-phenylmaleimide to form the 1:1 adducts, but in low yield. No further reactions between the 1:1 adducts **27** and **28** and excess **21** were observed. On the basis of their ^{1}H NMR spectra, we assigned *cis*-*cis* configurations to compounds **27** and **28**. Such an assignment is also in agreement with an energetically favourable *endo* transition state during the [4+2] cycloaddition.

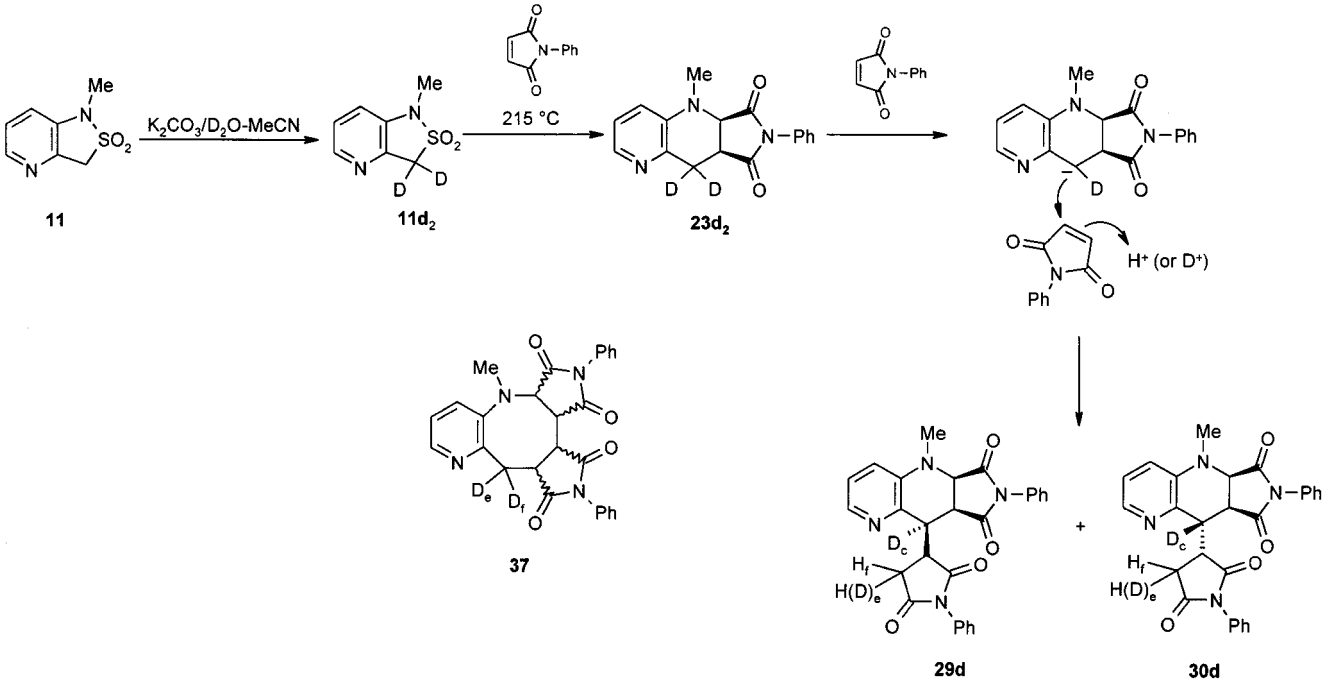
In the reaction between dimethyl fumarate and *N*-methyl-aza-*o*-xylylene **16**, generated from pyridosultam **11**, the 1:1 cycloadduct **38** was formed in moderate yield (Scheme 3). GC/MS analysis of the crude reaction mixture also revealed the presence of products arising from dimerization of aza-*o*-xylylene **16**. No products of further Michael reaction were detected after extended heating of the 1:1 adduct **38** with an excess of dimethyl fumarate. The extended heating resulted only in a decrease in the yield of product **38**.

In an additional experiment we generated aza-*o*-xylylene **16** from the pyridosultam **11** in the absence of a dienophile. This reaction gave a complex mixture of products in which dimers were detected by GC-MS. To lessen the possibility of xylylene side reactions, particularly of [1,5] sigmatropic hydrogen shifts giving Schiff bases,[16] we generated the xylylene from 1-propylpyridosultam **12**. In this case the dimer was isolated in 25% yield (Scheme 4). The ^{1}H NMR spectrum of this product showed in the aliphatic region only one singlet other than the signals corresponding to the propyl group, and in the aromatic region only one set of signals corresponding to three pyridine protons. On the basis of this spectrum for the isolated dimer we assigned the structure as the azocine **40**.

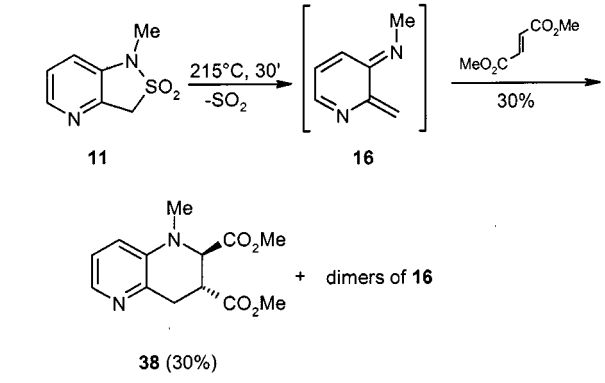
To the best of our knowledge, this is the first example of a [4+4] cycloaddition reaction of aza-*o*-xylylenes. The aza-*o*-xylylene dimers so far described have exclusively been [4+2] cycloadducts.[34,35] On the other hand, the formation of a [4+4] cycloadduct from *o*-xylylene generated at higher temperatures by cheletropic extrusion of SO_2 from 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide is a known process.[36]

In one of our previous papers[26] we described the intramolecular [4+2] cycloaddition reaction of aza-*o*-xylylene generated from 1-(1-pent-4-enyl)pyridosultam **43** to afford 5,6,6a,7,8,9-hexahydropyrrolo[1,2-*a*][1,5]naphthyridine (**47**). Analogous treatment of xylylene **46**, generated from 1-(1-hex-5-enyl)pyridosultam **44**, afforded 6,6a,7,8,9,10-hexahydro-5*H*-pyrido[1,2-*a*][1,5]naphthyridine (**48**) (Scheme 5).

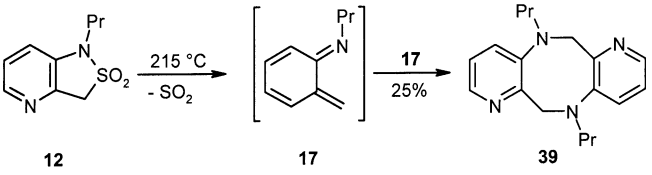
We applied the tricyclic compound **47** and its homologue **48** to the synthesis of the 10,14-diazasteroid framework. Numerous methods directed towards the synthesis of steroid analogues bearing nitrogen atoms in various skeleton positions have been developed. In partial syntheses, the *all-C* natural or synthetic steroids have been transformed into their nitrogen analogues.[37] In recent years various methodologies for the total synthesis of azasteroid skeletons have been developed. For example, 13-azaandrosta-1,4-diene-3,17-dione was obtained by an acyliminium ion initiated tandem cyclization,[38] 8,13-diazagonane derivatives were obtained by condensation of 1-(1,2,3,4-tetrahydroisoquinolyl)acetates with butyrolactims,[39] 13-azasteroids and their 4,13-diaza analogues were obtained from thermal intramolecular cycloaddition of nitrones to acetylenes,[40] 9-aza-estra-1,3,5(10)-trien-17-one was obtained through the intramolecular Diels−Alder reaction of aza-*o*-xylylene generated from a (2-aminobenzyl)ammonium salt,[35] and 3,4-cyclopentano-1,2,3,4-tetrahydronaphthyridine, a 7-aza-steroid skeleton, was formed in an intramolecular Diels−Alder reaction undergone by the aza-*o*-xylylene generated by thermal extrusion of SO_2 from 3-(1-pent-4-enyl)-1,3-dihydrothieno[3,4-*b*]isoquinoline 2,2-dioxide.[41]



Scheme 2. tr = traces

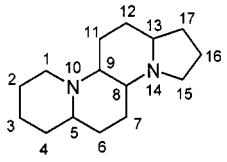


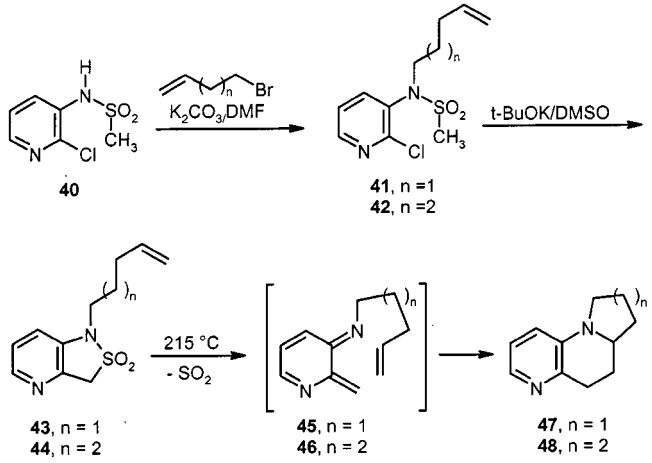
Scheme 3



Scheme 4

In diazasteroids, 136 positional isomers with nitrogen atoms replacing the carbon atoms in the steroid framework are possible. To the best of our knowledge the diazasteroid skeleton bearing nitrogen atoms in positions 10 and 14 has not yet been synthesized.



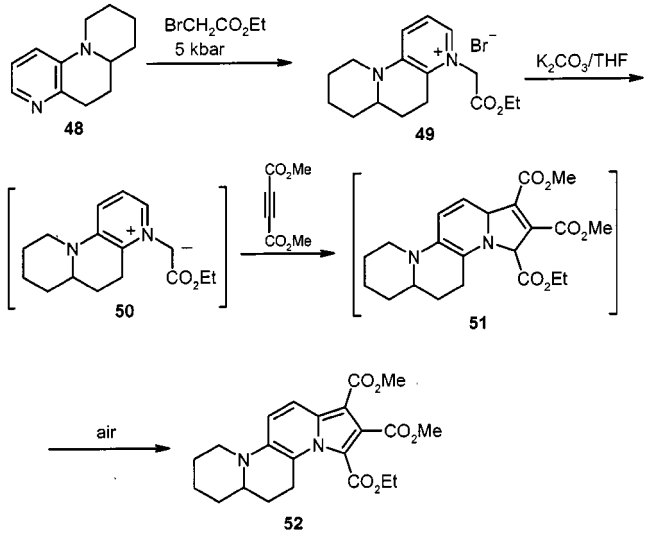


Scheme 5

In our approach, the obtained tricyclic compounds **48** and **47** were employed as a steroid system ABC ring, to which the five-membered D ring was attached by simple transformations.

Compound **48** was quaternized with ethyl bromoacetate. Since this process was sluggish under standard conditions in refluxing ethyl acetate or toluene, and contamination of the formed pyridinium salt with tarry products occurred after prolonged heating, we employed a high-pressure technique for this quaternization. Thus, quaternization was complete at 5 kbar in 24 h and the desired salt **49** was formed in quantitative yield. It is worth mentioning that no quaternization of N-9b occurred under the employed conditions. The pyridinium salt **49** was then subjected to treatment with potassium carbonate in the presence of a catalytic amount of dicyclohexyl-18-crown-6, and the formed

ylide **50** reacted with dimethyl acetylenedicarboxylate. Under the reaction conditions, the initially formed [3+2] cycloadduct was oxidized and the indolizine was produced in moderate yield. The synthetic pathway is outlined in

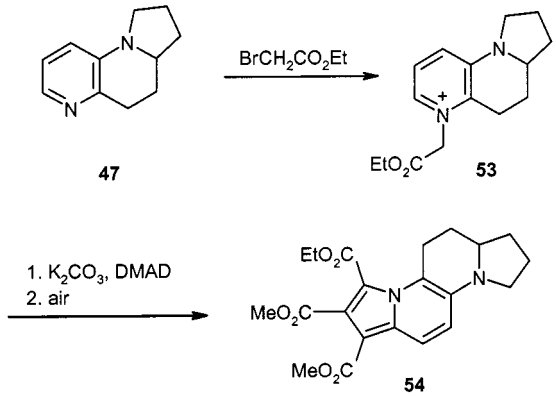


Scheme 6

Scheme 6. Under anaerobic conditions, the reaction did not give the intermediate **51** and only compound **52** was isolated. Probably oxidation of compound **51** occurred during the workup of the reaction mixture. We attempted to use other base/solvent systems, such as diazabicycloundecene (DBU) or diazabicyclononene (DBN) in acetonitrile and sodium hydride in DMF or DMSO, also varying the temperature of the reaction, but no improvement in the yield of product **52** was achieved.

Attempts to induce the ylide **50** to react with dimethyl maleate and fumarate were unsuccessful and no cycloaddition products were formed.

The 5,6,6a,7,8,9-hexahydropyrrolo[1,2-*a*][1,5]naphthyridine derivative **47**[26] was transformed into the A-norgonane derivative **54** in an analogous reaction sequence as shown in Scheme 7.



Scheme 7

Experimental Section

Melting points are uncorrected. ^{1}H and ^{13}C NMR and spectra were obtained with Bruker AMX (500 MHz), Varian Mercury 400 BB (400 MHz) and Varian Gemini (200 MHz) instruments in $CDCl_3$ with TMS as internal standard. Coupling constants *J* are given in Hz. Mass spectra (electron impact, 70 eV) were obtained with AMD 604 (AMD Intectra GmbH, Germany) instrument. HRMS were measured in the presence of perfluorokerosene as the reference compound. Column chromatography was performed with 240−400 mesh silica gel (Merck). Pyridosultams **11**−**16** were obtained according to the procedure described earlier.[27] High-pressure quaternization of compound **48** was performed in a piston-type apparatus designed and constructed in the Institute of Physical Chemistry (Warsaw). For a general description see ref.[42]

3,3-Dideuterio-1-methyl-1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-Dioxide (11d$_2$): Solid anhydrous K_2CO_3 (1 g) was added to a stirred solution of *N*-methylpyridosultam **11** (100 mg, 0.27 mmol) in acetonitrile (2 mL) and D_2O (0.5 mL). Stirring was continued for 15 min. The solid was separated and washed with acetonitrile, and the solvent was evaporated. The operation was repeated three times. Yield quantitative. Deuterium content 95% (according to MS).

General Procedure for Cycloaddition Reactions: A solution of pyridosultam (0.5 mmol) and dienophile (1.5 mmol) in 1,2,4-trichlorobenzene (10 mL) was heated under reflux for a period of time as given in the Table (with dimethyl fumarate 30 min). The reaction mixture was then subjected to column chromatography on silica gel. The solvent was eluted with hexane/ethyl acetate (10:1), and the products were separated with hexane/ethyl acetate (2:1). The following compounds were obtained.

***cis*-5-Methyl-7-phenyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (23):** M.p. 156−158 °C. ^{1}H NMR (200 MHz): δ = 3.21 (dd, *J* = 14.8, *J* = 6.8, 1 H), 3.24 (s, 3 H), 3.33 (dd, *J* = 14.8, *J* = 4.9, 1 H), 3.71 (ddd, *J* = 9.2, *J* = 6.8, *J* = 4.9, 1 H), 4.30 (d, *J* = 9.2, 1 H), 7.02−7.20 (m, 3 H), 7.15 (dd, *J* = 8.1, *J* = 4.7, 1 H), 7.30−7.45 (m, 3 H), 8.04 (dd, *J* = 4.7, *J* = 1.5, 1 H). ^{13}C NMR (100 MHz): δ = 30.4, 37.2, 42.7, 60.5, 119.4, 123.2, 126.2, 128.8, 129.1, 131.1, 140.1, 141.6, 145.5, 174.0, 175.8. IR (KBr): ṽ = 2928, 2855, 1717, 1712, 1582, 1501, 1456, 1387 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 293 (85) [M$^+$], 200 (7), 172 (21), 146 (36), 145 (100), 129 (4), 120 (8). HRMS for $C_{17}H_{15}N_3O_2$ calcd. 293.1164, found 293.1162.

***cis*-7-(4-Chlorophenyl)-5-methyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (24):** M.p. 186−188 °C. ^{1}H NMR (200 MHz): δ = 3.30 (s, 3 H), 3.37 (d, *J* = 5.6, 2 H), 3.68−3.88 (m, 1 H); 4.38 (d, *J* = 9.1, 1 H), 7.08−7.15 (m, 2 H), 7.15−7.27 (m, 2 H), 7.37−7.46 (m, 2 H), 8.09 (dd, *J* = 4.9, *J* = 1.4, 1 H). ^{13}C NMR (100 MHz): δ = 30.3, 37.2, 42.8, 60.5, 119.4, 123.2, 127.4, 129.3, 129.5, 134.6, 140.4, 141.5, 145.5, 173.7, 175.6. IR (KBr): ṽ = 3061, 1784, 1714, 1759, 1494, 1455, 1383, 1277, 1213, 1181, 1091 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 327 (77) [M$^+$], 206 (10), 180 (37), 179 (100), 154 (10). HRMS for $C_{17}H_{14}ClN_3O_2$ calcd. 327.0775, found 327.0761.

***cis*-7-Phenyl-5-propyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (25):** M.p. 123−125 °C. ^{1}H NMR (200 MHz): δ = 1.01 (t, *J* = 7.3, 3 H), 1.74 (hex, *J* = 7.3, 2 H), 3.18 (dd, *J* = 14.7, *J* = 6.9, 1 H), 3.32 (dd, *J* = 14.7, *J* = 4.5, 1 H), 3.44−3.64 (m, 2 H), 3.70 (ddd, *J* = 9.3, *J* = 6.9, *J* = 4.5, 1 H), 4.42 (d, *J* = 9.3, 1 H), 6.99−7.17 (m, 3 H), 7.31−7.47 (m, 4

H), 8.03 (dd, J = 1.8, J = 4.5, 1 H). ^{13}C NMR (100 MHz): δ = 11.4, 19.6, 30.4, 42.8, 51.0, 58.9, 120.2, 123.0, 126.2, 128.7, 129.1, 131.1, 139.8, 140.7, 146.0, 174.3, 175.9. IR (KBr): $\tilde{\nu}$ (cm^{-1}) = 2926, 1777, 1714, 1598, 1545, 1499, 1448, 1385, 1176. MS (EI 70 eV): *m*/*z* (%) = 321 (58) [M$^+$], 292 (100), 276 (8), 173 (320), 149 (16), 145 (29), 131 (37), 119 (25), 92 (15), 77 (22). HRMS for $C_{19}H_{19}N_3O_2$ calcd. 321.1477, found 321.1480.

***cis*-3-Chloro-5-methyl-7-phenyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (26):** M.p. 165−167 °C. ^{1}H NMR (200 MHz): δ = 3.10 (dd, J = 15.0, J = 6.8, 1 H), 3.28 (dd, J = 15.0, J = 5.1, 1 H), 3.67 (ddd, J = 9.1, J = 6.8, J = 5.1, 1 H), 4.31 (d, J = 9.1, 1 H), 7.03 (d, J = 2.0, 1 H), 7.08−7.15 (m, 2 H), 7.34−7.48 (m, 3 H), 7.99 (d, J = 2.0, 1 H). MS (EI 70 eV): *m*/*z* (%) = 327 (93) [M$^+$], 206 (10), 180 (37), 179 (100), 154 (10). HRMS for $C_{17}H_{14}ClN_3O_2$ calcd. 327.0775, found 327.0778.

5-Methyl-7,9-diphenyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (27): M.p. 221−223 °C. ^{1}H NMR (200 MHz): δ = 3.38 (s, 3 H), 3.70 (dd, J = 8.8, J = 6.9, 1 H), 4.40 (d, J = 8.8, 1 H), 4.85 (d, J = 6.9, 1 H), 6.41−6.47 (m, 2 H), 7.15−7.35 (m, 10 H), 8.02 (dd, J = 3.6, J = 2.3, 1 H). ^{13}C NMR: δ = 37.4, 44.2, 47.8, 59.4, 117.9, 123.6, 126.3, 127.9, 128.7, 128.9, 129.4, 130.7, 136.7, 139.1, 141.1, 144.7, 173.5, 175.1. IR ($CHCl_3$): $\tilde{\nu}$ = 2924, 1721, 1598, 1580, 1496, 1479, 1456, 1386, 1340, 1270, 1211, 1178, 1162, 1091 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 369 (100) [M$^+$], 315 (5), 304 (10), 290 (18), 288 (17), 285 (20), 249 (18), 222 (23), 207 (30), 195 (80), 145 (55). HRMS for $C_{23}H_{19}N_3O_2$ calcd. 369.1477, found. 369.1484.

7,9-Diphenyl-5-propyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-dione (28): M.p. 172−175 °C (from ethyl acetate). ^{1}H NMR (200 MHz): δ = 3.38 (s, 3 H), 3.70 (dd, J = 8.8, J = 6.9, 1 H), 4.40 (d, J = 8.8, 1 H), 4.85 (d, J = 6.9, 1 H), 6.41−6.47 (m, 2 H), 7.15−7.35 (m, 10 H), 8.02 (dd, J = 3.6, J = 2.3, 1 H). ^{13}C NMR (100 MHz): δ = 11.2, 18.0, 43.9, 47.5, 51.6, 58.0, 118.1, 123.5, 126.3, 127.9, 128.7, 128.9, 129.3, 130.7, 136.9, 139.6, 144.1, 173.6, 175.1. IR ($CHCl_3$): $\tilde{\nu}$ = 2967, 1718, 1599, 1501, 1458, 1388, 1149 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 397 (96) [M$^+$], 368 (100), 276 (13), 235 (13), 223 (19), 221 (27), 220 (40), 207 (18), 205 (21), 195 (34), 173 (27), 167 (15), 131 (25). HRMS for $C_{25}H_{23}N_3O_2$ calcd. 397.1790, found 397.1793.

9-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-5-methyl-7-phenyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-diones 29 and 30 (1:1 Ratio). − Less Polar Isomer: M.p. 144−147 °C (from ethyl acetate). ^{1}H NMR (500 MHz): δ = 3.14 (dd, J = 17.8, J = 8.9, 1 H), 3.17 (dd, J = 17.8, J = 6.5, 1 H), 3.27 (s, 3 H), 3.43 (dd, J = 11.1, J = 2.2, 1 H), 3.90 (dd, J = 11.1, J = 8.7, 1 H), 4.219 (ddd, J = 8.9, J = 6.5, J = 2.2, 1 H), 4.225 (d, J = 8.7, 1 H), 7.13 (dd, J = 8.3, J = 1.3, 1 H), 7.20 (ddd, J = 8.3, J = 4.7, J = 0.8, 1 H), 7.27−7.30 (m, 1 H), 7.33−7.39 (m, 2 H), 7.41−7.52 (m, 7 H), 8.00 (dd, J = 4.7, J = 1.3, 1 H). ^{13}C NMR (125 MHz): δ = 34.0, 36.8, 38.1, 41.3, 42.7, 60.3, 118.2, 123.4, 118.2, 123.4, 126.4, 126.7, 128.4, 128.9, 129.0, 129.2, 131.1, 132.5, 138.5, 141.9, 142.8, 174.4, 174.8, 176.0, 178.8. IR (KBr): $\tilde{\nu}$ = 3018, 1777, 1713, 1581, 1500, 1456, 1388, 1325, 1188, 867, 753, 694 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 466 (100) [M$^+$], 346 (60), 345 (53), 291 (23), 290 (22), 145 (53). HRMS for $C_{27}H_{22}N_4O_4$ calcd. 466.1641, found 466.1652. − **Less Polar Isomer d_2:** ^{1}H NMR (200 MHz): δ = 3.11−3.19 (m, ca. 1.5 H − H_E and H_F), 3.27 (s, 3 H), 3.42 (dd, J = 11.1, J = 2.6, about 0.4 H − H_C), 3.86−3.95 (m, 1 H), 4.16−4.25 (m, 2 H), 7.08−7.22 (m, 2 H), 7.28−7.56 (m, 9 H), 7.97 (dd, J = 4.4, J = 1.7, 1 H). − **More Polar Isomer:** M.p. 150−153 °C. ^{1}H NMR (500 MHz): δ = 2.83 (dd, J = 17.8, J = 5.4, 1 H), 3.00 (dd, J = 17.7, J = 9.1, 1 H), 3.31 (s, 3 H), 3.33 (dd, J = 10.4, J = 8.7, 1 H), 3.76 (ddd, J = 9.1, J = 5.4, J = 5.0, 1 H), 3.79 (dd, J = 10.4, J = 5.0, 1 H), 4.33 (d, J = 8.7, 1 H), 7.12 (dd, J = 8.3, J = 1.4, 1 H), 7.17 (ddd, J = 8.2, J = 4.7, J = 0.5, 1 H), 7.29−7.34 (m, 2 H), 7.38−7.45 (m, 4 H), 7.48−7.3 (m, 4 H), 7.97 (dd, J = 4.7, J = 1.3, 1 H). ^{13}C NMR (100 MHz): δ = 34.0, 36.9, 38.1, 41.3, 42.6, 60.3, 118.2, 123.5, 126.4, 126.7, 128.4, 128.9, 129.0, 129.2, 131.1, 132.4, 138.5, 141.9, 142.7, 174.5, 174.8, 176.1, 178.8. IR (KBr): $\tilde{\nu}$ = 3065, 2926, 1777, 1710, 1597, 1580, 1500, 1455, 1388, 1289, 1184, 910, 879, 797, 735 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 186 (69) [M$^+$], 121 (100), 107 (18), 81 (20). HRMS for $C_{27}H_{22}N_4O_4$ calcd. 466.1641, found 466.1655.

7-(4-Chlorophenyl)-9-[1-(4-chlorophenyl)-2,5-dioxopyrrolidin-3-yl]-5-methyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridine-6,8(5a*H*,7*H*)-diones 31 and **32** were formed in 55% yield (inseparable mixture,1:1 ratio according to HPLC). MS (EI 70 eV): *m*/*z* (%) = 534 (99) [M$^+$], 380 (96), 379 (100), 353 (20), 326 (30), 145 (61).

9-(2,5-Dioxo-1-phenylpyrrolidin-3-yl)-7-phenyl-5-propyl-8a,9-dihydro-5*H*-pyrrolo[3,4-*b*]-1,5-naphthyridin-6,8(5a*H*,7*H*)-diones 33 and 34 (1:1 Ratio). − Less Polar Isomer: M.p. 175−177 °C. ^{1}H NMR (500 MHz): δ = 0.98 (t, J = 7.4, 3 H), 1.68−1.80 (m, 2 H), 3.14 (dd, J = 17.9, J = 7.0, 1 H), 3.17 (dd, J = 17.9, J = 8.7, 1 H), 3.36 (dd, J = 11.3, J = 2.4, 1 H), 3.57−3.73 (m, 2 H), 3.80 (dd, J = 11.3, J = 8.5, 1 H), 4.21 (ddd, J = 8.7, J = 7.0, J = 2.4, 1 H), 4.45 (d, J = 8.5, 1 H), 7.05 (dd, J = 8.3, J = 1.2, 1 H), 7.16 (dd, J = 8.3, J = 4.7, 1 H), 7.27−7.30 (m, 2 H), 7.33−7.39 (m, 4 H), 7.41−7.52 (m, 4 H), 7.94 (dd, J = 4.7, J = 1.3, 1 H). MS (EI 70 eV): *m*/*z* (%) = 494 (100) [M$^+$], 465 (27), 374 (50), 373 (63), 344 (17), 320 (31), 292 (22), 276 (14), 173 (48), 131 (61). HRMS for $C_{29}H_{26}N_4O_4$ calcd. 494.1954, found 494.1949. − **More Polar Isomer:** M.p. 208−210 °C. ^{1}H NMR (500 MHz): δ = 1.01 (t, J = 7.4, 3 H), 1.67−1.86 (m, 2 H), 2.81 (dd, J = 17.8, J = 5.4, 1 H), 2.98 (dd, J = 17.8, J = 9.2, 1 H), 3.31 (dd, J = 10.3, J = 8.5, 1 H), 3.58−3.70 (m, 2 H), 3.71 (dd, J = 10.3, J = 5.0, 1 H), 3.76 (ddd, J = 9.2, J = 5.4, J = 5.0, 1 H), 4.50 (d, J = 8.5, 1 H), 7.05 (dd, J = 8.4, J = 1.3, 1 H), 7.14 (dd, J = 8.4, J = 4.7, 1 H), 7.23−7.30 (m, 2 H), 7.38−7.43 (m, 4 H), 7.46−7.52 (m, 4 H), 7.93 (dd, J = 4.7, J = 1.3, 1 H). MS (EI 70 eV): *m*/*z* (%) = 494 (100) [M$^+$], 465 (27), 374 (60), 373 (54), 320 (27), 292 (18), 276 (14), 173 (39), 131 (45). HRMS for $C_{29}H_{26}N_4O_4$ calcd. 494.1954, found 494.1954.

Dimethyl *trans*-1-Methyl-1,2,3,4-tetrahydro-1,5-naphthyridine-2,3-dicarboxylate (38): Yield 30%. Oil. ^{1}H NMR (200 MHz): δ = 3.00 (s, 3 H), 3.01 (dd, J = 17.8, J = 6.8, 1 H), 3.49 (ddd, J = 17.8, J = 2.0, J = 1.8 H, 1 H), 3.54 (ddd, J = 6.8, J = 2.0, J = 2.6, 1 H), 3.69 (s, 3 H), 3.74 (s, 3 H), 3.76 (s, 3 H), 4.51 (dd, J = 2.6, J = 1.8, 1 H), 6.92 (br. d, J = 8.5, 1 H), 7.10 (dd, J = 8.5, J = 5.0, 1 H), 7.91 (dd, J = 5.0, J = 1.3, 1 H). ^{13}C NMR (100 MHz): δ = 28.9, 39.5, 52.4, 52.5, 52.6, 61.4, 117.0, 122.4, 136.8, 139.9, 140.4, 171.8, 172.1. IR ($CHCl_3$): $\tilde{\nu}$ = 3110, 2957, 1739, 1679, 1558, 1486, 1438, 1144. MS (EI 70 eV): *m*/*z* (%) = 264 (18) [M$^+$], 205 (100), 146 (18), 145 (46) cm^{-1}. HRMS for $C_{13}H_{16}N_2O_4$ calcd. 264.1110, found 264.1128.

5,11-Dipropyl-1,5,7,11-tetraazadibenzo[*a*,*e*]cycloocta-1,5-diene (39): 1-Propylpyridosultam **12** (212 mg, 1 mmol) in 1,2,4-trichlorobenzene (5 mL) was heated under reflux until the starting material had disappeared (30 min). The reaction mixture was subjected to column chromatography. Trichlorobenzene was eluted with hexane/ethyl acetate (10:1), and the product was then isolated with hexane/ethyl acetate (2:1). Yield 37 mg (25%). Oil. ^{1}H NMR (500 MHz): δ = 0.69 (t, J = 7.4, 6 H), 1.45 (tq, J = 7.4, 4 H), 3.12 (t, J = 7.4,

4 H), 4.59 (s, 4 H), 7.09 (dd, J = 8.2, J = 4.5, 1 H), 7.14 (dd, J = 8.2, J = 1.1, 1 H), 7.97 (dd, J = 4.5, J = 1.1, 1 H). ^{13}C NMR (100 MHz): δ = 11.1, 20.4, 53.4, 58.8, 121.9, 122.5, 138.0, 145.8, 146.8. IR (neat): ṽ = 2961, 2928, 1674, 1578, 1465, 1426, 1345, 1293, 1255, 1220, 1174, 1111 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 296 (40) [M$^+$], 295 (18), 268 (19), 267 (100), 253 (20), 223 (15), 201 (14), 161 (42), 149 (22), 119 (50). HRMS for $C_{18}H_{24}N_4$ calcd. 296.2001, found 296.2007.

Alkylation of Sulfonamide 40: A solution of *N*-(2-chloro-3-pyridyl)-alkanesulfonamide (5 mmol), 5-bromopent-1-ene or 6-bromohex-1-ene (6 mmol), and tetrabutylammonium bromide (0.32 g, 0.001 mol) in DMF (20 mL) was stirred with K_2CO_3 (10 g) in room temperature. The progress of the reaction was monitored by TLC. When the starting sulfonamide had disappeared the reaction mixture was poured into a solution of Na_2SO_4. The product was extracted with ethyl acetate and dried with $MgSO_4$. After evaporation of the solvent, the crude product was used in the next step without further purification. The following compounds were obtained.

***N*-(2-Chloro-3-pyridyl)-*N*-(1-pent-4-enyl)methanesulfonamide (41):** Yield 92%. Oil. The product was used in the next step without purification. ^{1}H NMR (200 MHz): δ = 1.5−1.7 (m, 2 H), 2.0−2.2 (m, 2 H), 3.05 (s, 3 H), 3.6−3.8 (m, 2 H), 4.93−5.05 (m, 2 H), 5.74 (ddt, J = 16.7, J = 10.5, J = 6.4, 1 H), 7.35 (dd, J = 7.8, J = 4.7, 1 H), 7.82 (dd, J = 7.8, J = 1.9, 1 H), 8.41 (dd, J = 4.7, J = 1.9, 1 H). MS (EI 70 eV, *m*/*z*,%): 274 (0.6) [M$^+$], 245 (5), 239 (8), 232 (19), 219 (41), 195 (13), 141 (100), 112 (11), 78 (14), 41 (14).

***N*-(2-Chloro-3-pyridyl)-*N*-(1-hex-5-enyl)methanesulfonamide (42):** Yield 93%. Oil. The product was used in the next step without purification. ^{1}H NMR (200 MHz): δ = 1.25−1.60 (m, 4 H), 2.03 (td, J = 6.9, J = 6.7, 2 H), 3.05 (s, 3 H), 3.6−3.8 (m, 2 H), 4.89−5.02 (m, 2 H), 5.73 (ddt, J = 17.1, J = 10.2, J = 6.7, 1 H), 7.35 (dd, J = 7.8, J = 4.7, 1 H), 7.82 (dd, J = 7.8, J = 1.8, 1 H), 8.41 (dd, J = 4.7, J = 1.8, 1 H). MS (EI 70 eV): *m*/*z* (%) = 288 (3) [M$^+$], 245 (40), 219 (23), 141 (100), 112 (12), 81 (20), 41 (29).

Procedure for the Synthesis of Pyridosultams 43 and 44: Potassium *tert*-butoxide (2.24 g, 20 mmol) was added to a stirred solution of *N*-(2-chloro-3-pyridyl)-*N*-methylalkanesulfonamide (**41** or **42**, 5 mmol) in DMSO (10 mL). The reaction mixture was stirred for 40 min at room temperature and then poured into the solution of NH_4Cl and saturated with solid Na_2SO_4. The product was extracted with ethyl acetate and dried with $MgSO_4$. After evaporation of the solvent the product was purified by column chromatography. The following compounds were obtained.

1-(1-Pent-4-enyl)-1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-Dioxide (43): Yield 86%. Oil. ^{1}H NMR (200 MHz): δ = 1.94 (quint, J = 7.5, 2 H), 2.20−2.33 (m, 2 H), 3.67 (dd, J = 7.5, J = 7.5, 2 H), 4.55 (s, 3 H), 5.07− 5.20 (m, 2 H), 5.88 (dddd, J = 16.8, J = 10.3, J = 6.5, J = 6.5, 1 H), 7.07 (dd, J = 8.1, J = 1.0, 1 H), 7.32 (dd, J = 8.1, J = 5.1, 1 H), 8.21 (dd, J = 5.1, J = 1.0, 1 H). MS (EI 70 eV): *m*/*z* (%) = 238 (23) [M$^+$], 196 (12), 183 (60), 173 (16), 145 (12), 131 (12), 120 (23), 119 (100), 106 (15), 92 (43), 78 (12), 65 (25), 41 (30), 39 (23). HRMS for $C_{11}H_{14}N_2O_2S$ calcd. 238.0776, found 238.0768.

1-(1-Hex-5-enyl)-1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-Dioxide (44): Yield 81%. Oil. ^{1}H NMR (200 MHz): δ = 1.52−1.73 (m, 2 H), 1.75−1.91 (m, 2 H), 2.05−2.23 (m, 2 H), 3.60 (t, J = 7.2, 2 H), 4.46 (s, 2 H), 4.95−5.1 (m, 2 H), 5.80 (ddt, J = 17.0, J = 10.2, J = 6.7, 1 H), 6.99 (dd, J = 8.1, J = 1.2, 1 H), 7.24 (dd, J = 8.1, J = 5.0, 1 H), 8.16 (dd, J = 5.0, J = 1.3, 1 H). IR ($CHCl_3$): ṽ = 2938, 1641, 1591, 1435, 1336, 1145, 996, 919 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 252 (34) [M$^+$], 187 (15), 183 (48), 170 (51), 159 (17), 145 (18), 131 (12), 119 (100), 106 (27), 92 (38), 83 (17), 82 (23), 65 (16), 55 (13). HRMS for $C_{12}H_{16}N_2O_2S$ calcd. 252.0933, found 252.0930.

Thermal Extrusion of SO_2 from Pyridosultams 43 and 44: Pyridosultam **43** or **44** (1 mmol) was heated under reflux in trichlorobenzene (10 mL) for 30 min. The reaction mixture was then subjected to column chromatography. Trichlorobenzene was eluted with hexane/ethyl acetate (10:1) and then the product with hexane/ethyl acetate (1:1). The following compounds were obtained.

5,6,6a,7,8,9-Hexahydropyrrolo[1,2-*a*][1,5]naphthyridine (47): Yield 68%. Oil (volatile under reduced pressure). ^{1}H NMR (500 MHz): δ = 1.45−1.55 (m, 2 H), 1.98 (dddd, J = 16.0, J = 12.4, J = 9.1, J = 6.9, 1 H), 2.07−2.20 (m, 2 H), 2.23 (dq, J = 13.2, J = 3.5, 1 H), 2.91−3.01 (m, 2 H), 3.17 (td, J = 9.2, J = 7.5, 1 H), 3.27 (td, J = 9.0, J = 2.1, 1 H), 3.45 (tdd, J = 10.7, J = 5.1, J = 3.1, 1 H), 6.58 (dd, J = 8.1, J = 1.2, 1 H), 6.95 (dd, J = 8.1, J = 4.7, 1 H), 7.75 (dd, J = 4.7, J = 1.2, 1 H). ^{13}C NMR (50 MHz): δ = 24.7, 26.4, 29.6, 33.4, 47.1, 58.4, 117.8, 123.5, 131.9, 141.8, 142.0. MS (EI 70 eV): *m*/*z* (%) = 174 (72) [M$^+$], 173 (100), 145 (28), 131 (18), 119 (24). HRMS for $C_{11}H_{14}N_2$ calcd. 174.1157, found 174.1156.

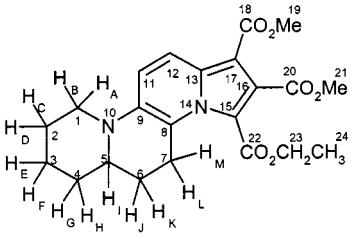
6,6a,7,8,9,10-Hexahydro-5*H*-pyrido[1,2-*a*][1,5]naphthyridine (48): Yield 83%. Oil (product volatile under reduced pressure). ^{1}H NMR (500 MHz): δ = 1.35−1.48 (m, 2 H), 1.52−1.64 (m, 1 H), 1.70−1.90 (m, 4 H), 2.03 (dddd, J = 9.2, J = 7.8, J = 5.8, J = 4.4, 1 H), 2.64 (td, J = 12.4, J = 2.8, 1 H), 2.86−3.01 (m, 3 H), 3.82 (br. d, J = 12.4, 1 H), 6.97 (dd, J = 8.4, J = 4.6, 1 H), 7.03 (dd, J = 8.4, J = 1.2, 1 H), 7.86 (dd, J = 4.6, J = 1.2, 1 H). ^{13}C NMR (100 MHz): δ = 24.1, 25.4, 29.4, 30.0, 32.8, 47.5, 56.2, 119.0, 121.8, 137.3, 143.1, 145.4. IR (neat): ṽ = 3051, 2934, 2853, 1678, 1576, 1452, 1317, 1239, 1144, 1122 cm^{-1}. MS (EI 70 eV): *m*/*z* (%) = 188 (100) [M$^+$], 187 (94), 173 (22), 159 (17), 147 (18), 145 (17), 132 (37), 131 (31). HRMS for $C_{12}H_{16}N_2$ calcd. 188.1313, found 188.1314. $C_{12}H_{16}N_2$ (188.3): calcd. C 76.56, H 8.57, N 14.88; found C 76.45, H 8.51, N 14.80.

4-Ethoxycarbonylmethyl-6,6a,7,8,9,10-Hexahydro-5*H*-pyrido[1,2-*a*]-[1,5]naphthyridin-4-ium Bromide (49): The amine **48** (2 mmol) and ethyl bromoacetate (2.5 mmol) were dissolved in a mixture of benzene (1 mL), toluene (5.6 mL), and methanol (0.5 mL) and placed in a high pressure instrument (5 kbar) at room temperature for 24 h. The precipitate was filtered and washed with ether. Yield 100%. ^{1}H NMR (200 MHz, [D$_6$]DMSO): $\delta_{solv.}$= 2.55, 1.29 (t, J = 7.1, 3 H), 1.40−1.65 (m, 3 H), 1.70−1.90 (m. 4 H), 2.00−2.30 (m, 1 H), 2.70−3.10 (m, 3 H), 3.15−3.30 (m, 1 H), 4.00−4.20 (m, 1 H), 4.29 (q, J = 7.1, 2 H), 5.66 (s, 2 H), 7.77 (dd, J = 9.0, J = 5.9, 1H), 8.05 (d, J = 9.0, 1 H), 8.21 (d, J = 5.9, 1 H).

4-Ethoxycarbonylmethyl-5,6,6a,7,8,9-hexahydropyrrolo[1,2-*a*][1,5]-naphthyridin-4-ium Bromide (53): Ethyl bromoacetate (200 mg, 1.1 mmol) was added to pyrrolonaphthyridine **47** (170 mg, 1 mmol) dissolved in benzene (3 mL). The reaction mixture was left for 4 d at room temperature. The solid was separated and washed with ether. Yield 72%. ^{1}H NMR (200 MHz, [D$_6$]DMSO): δ_{solv} = 2.55, 1.29 (t, J = 7.1, 3 H), 1.31−1.73 (m, 2 H), 1.92−2.56 (m, 4 H), 2.92 (ddd, J = 18.6, J = 13.0, J = 5.7, 1 H), 3.10−3.59 (m, 4 H), 4.29 (q, J = 7.1, 2 H), 5.58 (d, J = 17.7, 1 H), 5.70 (d, J = 17.7, 1 H), 7.50 (d, J = 8.6, 1 H), 7.75 (dd, J = 8.6, J = 6.0, 1 H), 8.08 (d, J = 6.0, 1 H). IR (KBr): ṽ = 2944, 1747, 1585, 1505, 1450, 1400, 1332, 1230, 1178 cm^{-1}.

Addition of Ylides to Dimethyl Acetylenedicarboxylate: Dimethyl acetylenedicarboxylate (0.42 g, 2.8 mmol) was added to a solution of salt **49** or **53** (0.3 mmol) and dicyclohexyl-18-crown-6 (10 mg) in

THF (10 mL), precooled to −20 °C. Solid K_2CO_3 (2 g) was then added. The reaction mixture was stirred at this temperature for 10 min and then allowed to come to room temp. over 20 min. The solvent was then evaporated and the residue was subjected to column chromatography on silica gel (hexane/ethyl acetate 1:1). The following compounds were obtained.



15-Ethoxycarbonyl-16,17-bis(methoxycarbonyl)-10,14-diazagona-8(9),11,13(17),15-tetraene (52): Yield 18%. M.p. 174−175 °C (from ethyl acetate). ^{1}H NMR (500 MHz): δ = 1.36 (t, *J* = 7.1, 3 H, 24-CH_3), 1.40−1.49 (m, 2 H, H_E, H_H), 1.61−1.70 (m, 2 H, H_K, H_D), 1.73−1.83 (m, 2 H, H_G, H_C), 1.84−1.90 (m, 1 H, H_F), 1.95 [dddd, *J*(H_K) = 13.1, *J*(H_M) = 6.0, *J*(H_L) = 3.3, *J*(H_I) = 2.2, 1 H, H_J], 2.30 [ddd, *J*(H_M) = 17.5, *J*(H_K) = 4.7, *J*(H_J) = 3.3, 1 H, H_L], 2.74 [ddd, *J*(H_A) = 12.4, *J*(H_C or H_D) = 12.4, *J*(H_C or H_D) = 2.5, 1 H, H_B], 2.87 [dddd, *J*(H_K) = 10.4, *J*(H_H) = 10.4, *J*(H_g) = 2.2, *J*(H_J) = 2.2, 1 H, H_I], 3.27 [ddd, *J*(H_L) = 17.5, *J*(H_K) = 11.6, *J*(H_J) = 6.0, 1 H, H_M], 3.87 (s, 3 H), 3.88−3.94 (m, 1 H), 3.96 (s, 3 H), 4.32 (qd, *J* = 7.1, *J* = 1, 2 H, C-23), 7.28 (d, *J* = 9.8, 1 H), 8.14 (d, *J* = 9.8, 1 H). ^{13}C NMR (125 MHz): δ = 14.1 (C-24), 24.3 (C-3), 26.1 (C-2), 27.9 (C-7), 28.6 (C-6), 32.0 (C-4), 50.7 (C-1), 51.4, 52.5 (C-19, C-21), 56.9 (C-5), 61.2 (C-23), 117.6, 120.6 (C-11, C-12), 102.1, 114.1, 123.6 130.7, 134.4, 138.1 (C-8, C-9, C-13, C-15, C-16, C-17), 159.7, 163.5, 166.6 (C-18, C-20, C-22). IR (KBr): ṽ = 2928, 2855, 1738, 1712, 1580, 1501, 1456, 1386, 1221, 1184, 1097 cm^{-1}. MS (EI 70 eV): *m/z* (%) = 414 (100) [M$^+$], 383 (28), 382 (60), 369 (12), 368(14), 353(10), 310 (33), 309 (46), 224 (30). IR ($CHCl_3$): ṽ = 2954, 1737, 1699, 1502, 1458, 1376, 1185, 1099, 1021 cm^{-1}. HRMS for $C_{22}H_{26}N_2O_6$ calcd. 414.1791, found 414.1803. $C_{22}H_{26}N_2O_6$(414.5): calcd. C 63.77%, H 6.32%, N 6.76; found C 63.54%, H 6.32%, N 6.58%.

3-Ethoxycarbonyl-1,2-bis(methoxycarbonyl)-10,14-diaza-A-norgona-1(2),3,6,8(9)-tetraene (54): Yield 22%. Oil. ^{1}H NMR (200 MHz): δ = 1.39 (t, *J* = 7.1, 3 H), 1.2−1.4 (m, 1 H), 1.72−1.54 (m, 1 H), 1.95−2.4 (m, 4 H), 3.44−3.16 (m, 2 H), 3.7−3.56 (m, 3 H), 3.91(s, 3 H), 4.00 (s, 3 H), 4.35, 4.34 (dq, *J* = 7.1, *J* = 0.9, 2 H), 7.08 (d, *J* = 9.5, 1 H), 8.21 (d, *J* = 9.5, 1 H). ^{13}C NMR (50 MHz): 14.7, 24.8, 26.4, 28.9, 32.9, 49.9, 52.0, 53.2, 57.4, 61.6, 118.4, 118.5, 160.1, 164.0, 167.3, 170.3, 181.8, 183.8. IR ($CHCl_3$): ṽ = 2955, 1730, 1592, 1509, 1438, 1274, 1157 cm^{-1}. MS (EI 70 eV): *m/z* (%) = 400 (99) [M$^+$], 369 (38), 368 (100), 354 (20), 339 (50), 296(68), 295 (92), 268 (28), 267 (23), 238 (23), 210 (60), 132 (11). HRMS for $C_{21}H_{24}N_2O_6$ calcd. 400.1634, found 400.1650.

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