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1,3-DIHYDRO-2,1-BENZISOTHIAZOLE 2,2-DIOXIDES (BENZOSULTAMS) IN ORGANIC SYNTHESIS

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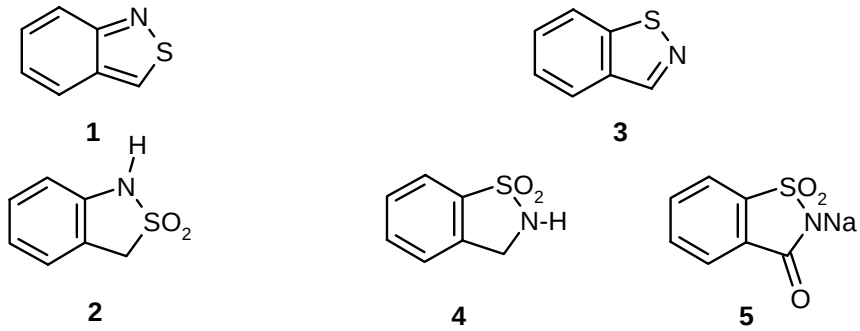
Abstract - Methods of synthesis of 1,3-dihydro-2,1-benzisothiazole 2,2-dioxides and their applications in the synthesis of heterocyclic compounds are reviewed.

1. INTRODUCTION

The chemistry of 2,1-benzisothiazole (**1**) has been a subject of numerous reviews.[1-4] Usually this chemistry is discussed together with chemistry of isomeric 1,2-benzisothiazoles (**3**), which the most prominent representative is 1,2-benzisothiazolin-3(2*H*)-one 1,1-dioxide (saccharin, **5**). These reviews practically omitted the chemistry of 1,3-dihydro-2,1-benzisothiazoles 2,2-dioxides (**2**) despite that such derivatives are also versatile starting materials for organic synthesis, particularly for the construction of heterocycles. Even in a recent review[5] devoted to benzosultams only the chemistry of 1,2-benzisothiazoline 1,1-dioxides (**4**) was presented, focusing particularly on their applications as chiral auxilliaries in stereocontrolled synthesis.

Figure 1.

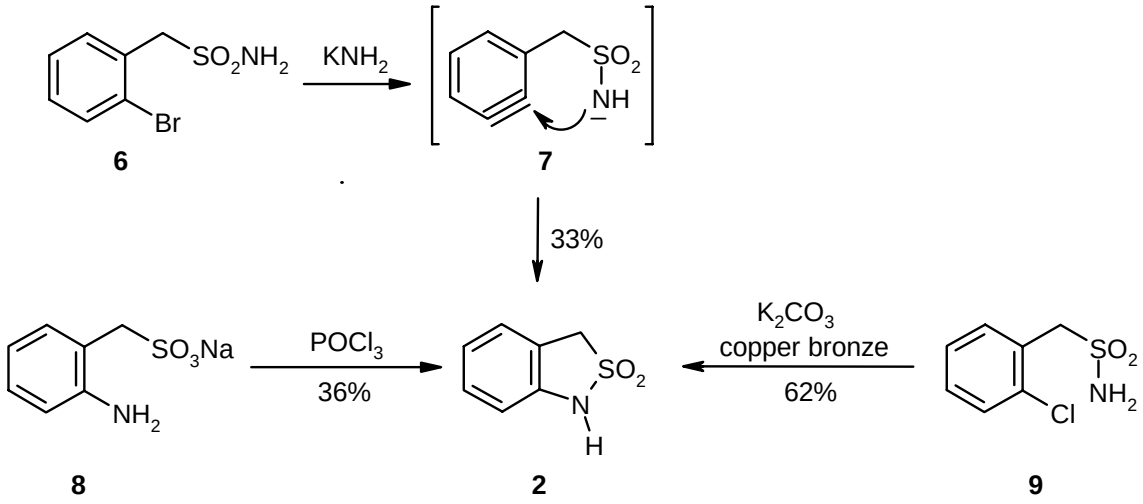


The aim of this review is to present the chemistry of the isomeric 1,3-dihydro-2,1-benzisothiazole 2,2-dioxides (**2**), particularly focusing on the methods of synthesis of this heterocyclic system and their synthetic applications.

2. SYNTHESIS OF BENZOSULTAMS

Numerous methods employing easily available starting materials have been developed for the synthesis of 1,3-dihydro-2,1-benzisothiazole 2,2-dioxides (we will name them benzosultams for brevity). Benzosultam (**2**) can be considered as the cyclic sulfonamide of 2-aminobenzylsulfonic acid, thus the simplest method of its synthesis consists in dehydration of free acid or better its sodium salt (**8**) with $POCl_3$ (36% yield).[6] Another method of synthesis of **2** consists in cyclization of 2-chlorophenylmethanesulfonamide (**9**) in the presence of K_2CO_3 and copper bronze in 62% yield (Scheme 1).[6]

Scheme 1.

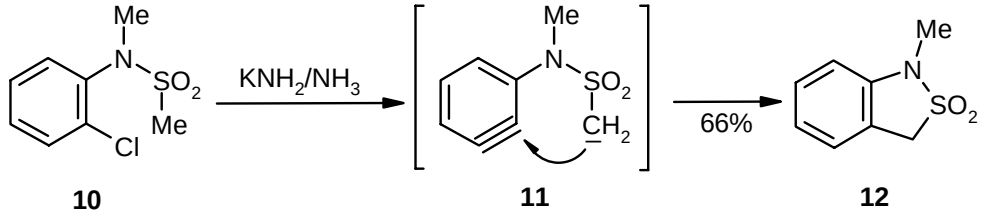


One of general methods of synthesis of *N*-alkylbenzosultams (**12**) deals with aryne-mediated intramolecular substitution in 2-chloro-*N*-methyl-*N*-methanesulfonylanilines (**10**) (Scheme 2).[7,8] In a similar process 2-bromophenylmethanesulfonamide (**6**) was transformed into the benzosultam (**2**) (Scheme 1).[9]

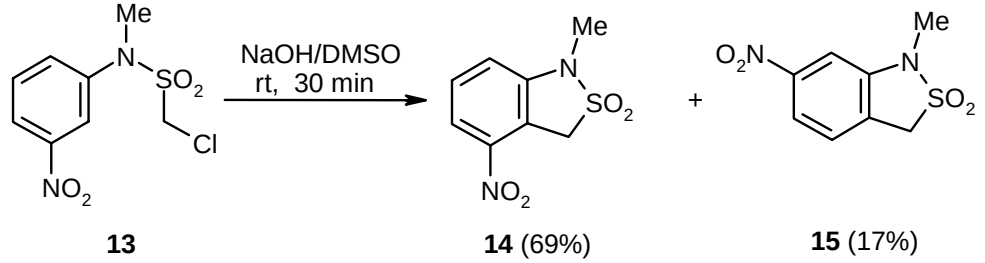
We developed methods of synthesis of benzosultams based on intramolecular reactions of carbanions with aromatic nitro compounds.[10-12] These reactions start from the formation of σ^H-adducts *ortho* or *para* to the nitro group. The σ^H-adduct transforms into a final product by various ways depending on the nature of the attacking carbanion and reaction conditions.

The reaction of carbanions bearing at the α-position a leaving group, known as vicarious nucleophilic substitution of hydrogen (VNS)[13-15] was used for the synthesis of nitro derivatives of benzosultams from *N*-alkyl-*N*-chloromethanesulfonyl-3-nitroanilines.[10,11] For example, the sulfonamide (**13**) in the presence of solid sodium hydroxide in dimethyl sulfoxide gives a mixture of 4- and 6-nitro-2,1-benzisothiazoline 2,2-dioxides (**14**) and (**15**) in good yield (Scheme 3).

Scheme 2.

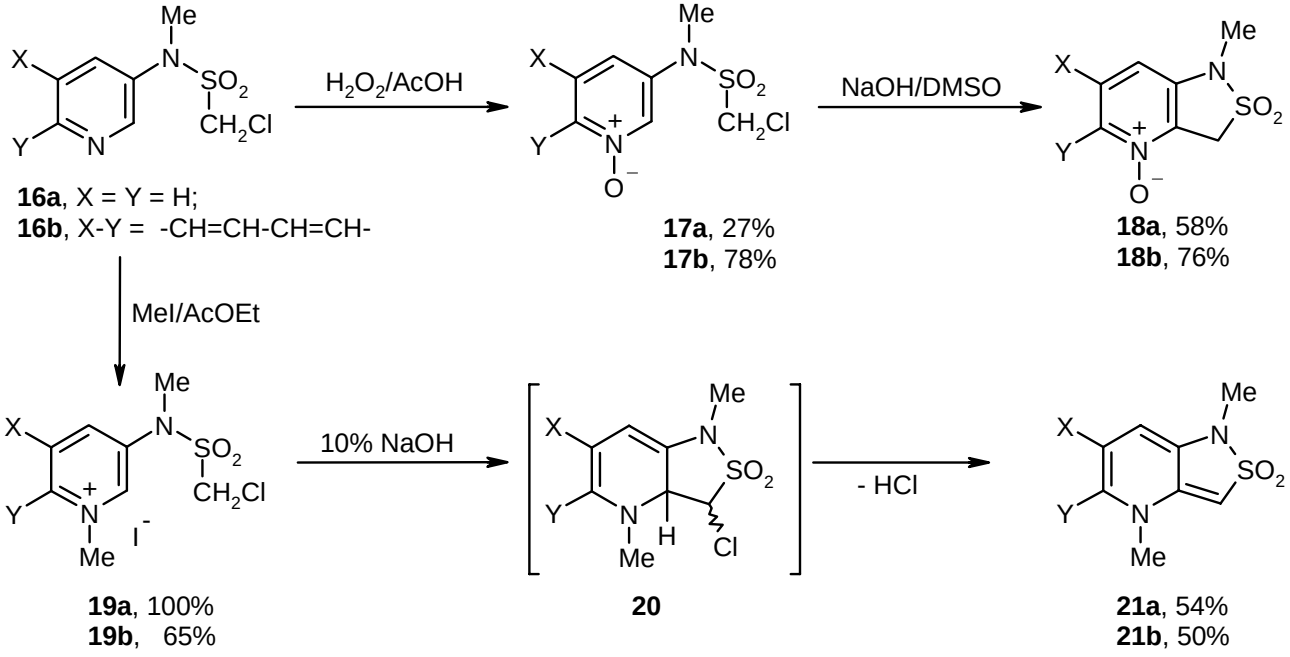


Scheme 3.



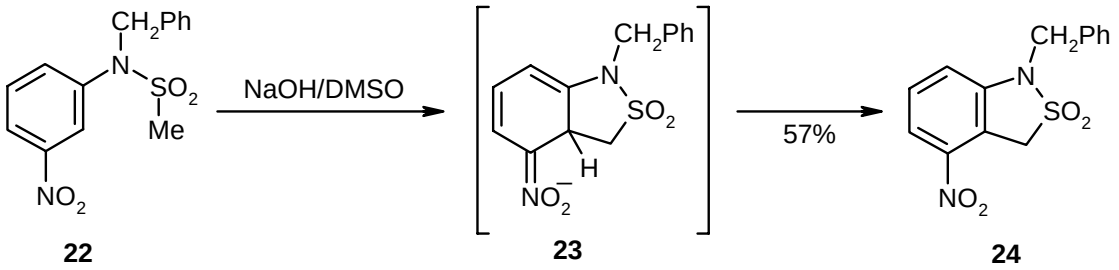
In analogous process pyridine and quinoline *N*-oxides (**17a**) and (**17b**) give isothiazolo[4,3-*b*]pyridine and quinoline 2,2-dioxides (**18a**) and (**18b**), respectively, as shown in the Scheme 4.[16] Similarly, strongly activated towards nucleophilic attack pyridinium and quinolinium salts (**19**) derived from the sulfonamides (**16a**) and (**16b**) undergo VNS of hydrogen in the presence of 10% aqueous NaOH and give 1,4-dihydroisothiazolo[4,3-*b*]pyridine 2,2-dioxide (**21a**) and its quinoline analogue (**21b**), respectively.[16]

Scheme 4.



Oxidative nucleophilic substitution of hydrogen (ONSH)[17-19] is another process leading to nitro substituted benzosultams.[12,20,21] In the intramolecular reaction carbanions generated from *N*-alkanesulfonyl-3-nitroanilines (**22**) add predominantly into the *ortho* position to the nitro group and the formed σ^H-adduct (**23**) is then oxidized to benzosultam (**24**) as exemplified in the Scheme 5.[12]

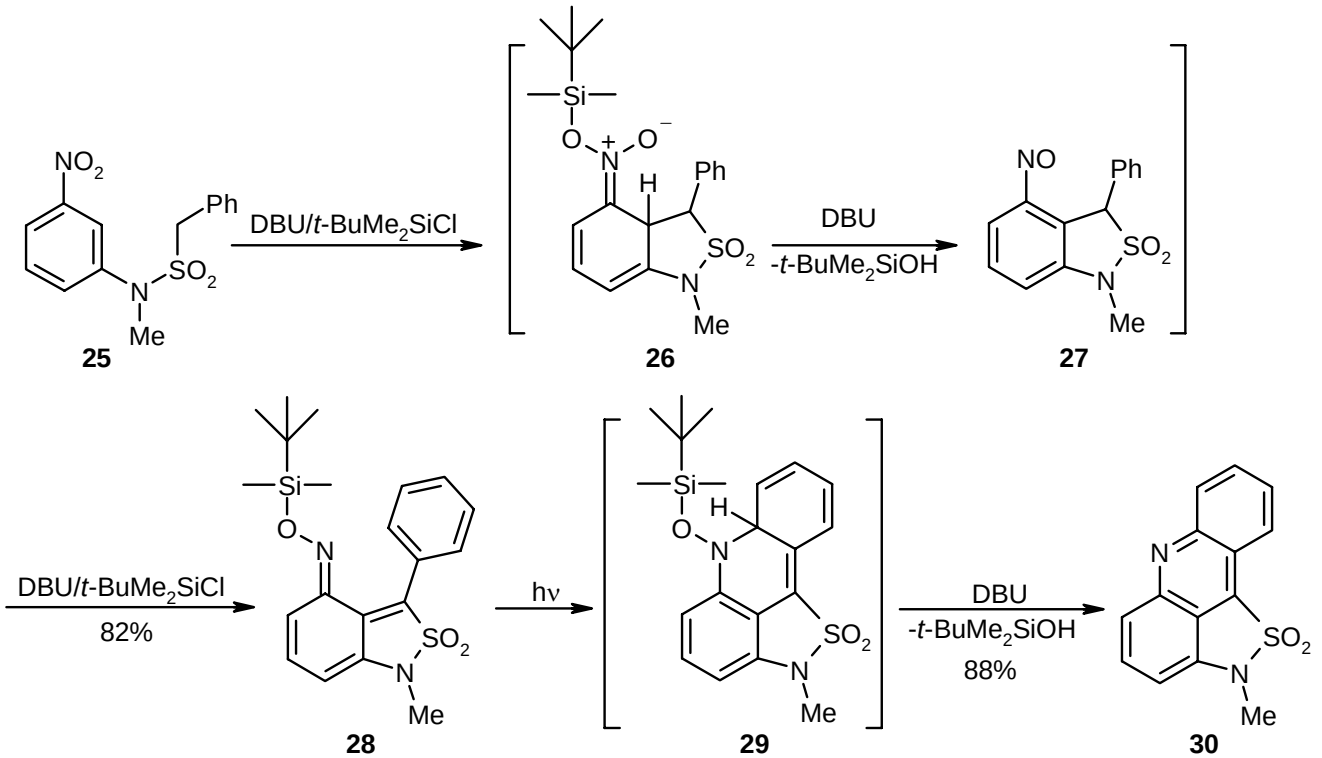
Scheme 5.



22 **23** **24**

In particular instances transformations of σ^H-adducts formed from carbanions and nitroarenes proceed with a reduction of the nitro to nitroso group. Such process is involved in the cyclization of benzyl-sulfonamide (**25**) in the presence of diazabicycloundecene (DBU) and *tert*-butyldimethylchlorosilane. The intermediate nitroso sultam (**27**) is silylated under reaction conditions to form 4-silyloxyimino-1,4-dihydro-2,1-benzisothiazole 2,2-dioxide (**28**).[22] The quinoidal compound (**28**) upon UV irradiation undergoes a photochemical 6π-electrocyclization to **29**, which by an elimination of trialkylsilanol gives dioxoisothiazolo[5,4,3-*kl*]acridine (**30**) (Scheme 6).[22]

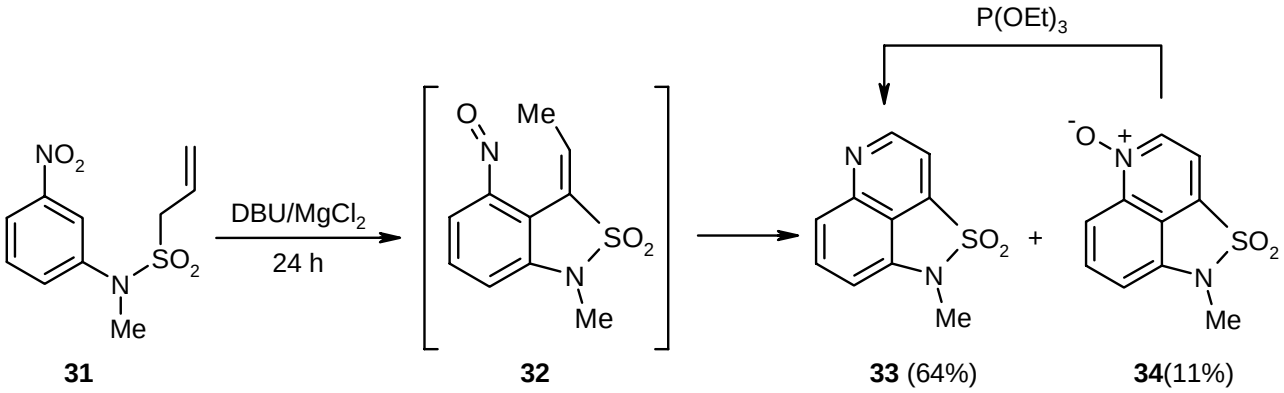
Scheme 6.



25 **26** **27** **28** **29** **30**

In a multistep transformation of *N*-allylsulfonylaniline (**31**) into 2,2-dioxoisothiazolo[5,4,3-*de*]quinoline (**33**) an initially formed σ^H-adduct transforms into a nonisolable nitroso compound (**32**), which then undergoes cyclization resulting in a formation of pyridine ring.[23] Some amounts of the formed *N*-oxide (**34**) can be then deoxygenated with triethyl phosphite.

Scheme 7.

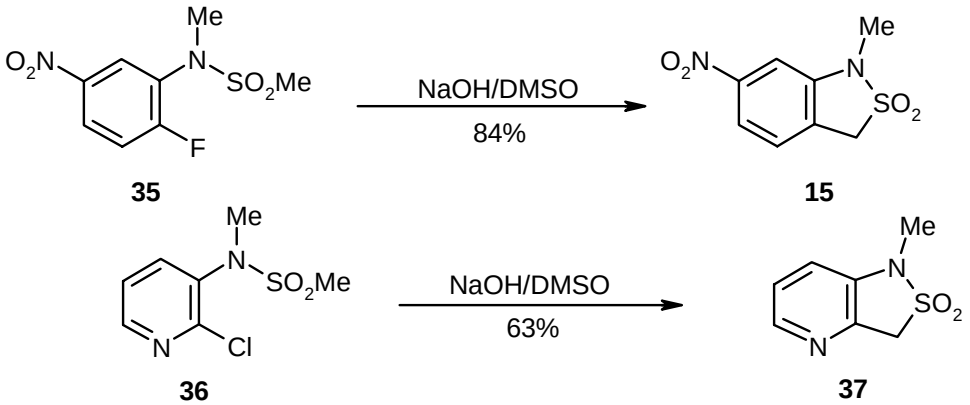


31 **32** **33** (64%) **34**(11%)

An intramolecular aromatic nucleophilic substitution (S_NAr) of fluorine in sulfonamide (**35**) leads to benzosultam (**15**).[12] In a similar process 2-chloro-3-methanesulfonylaminopyridine (**36**) cyclizes to isothiazolo[4,3-*b*]pyridine 2,2-dioxide (**37**) (Scheme 8).[24,25]

Small amounts (0.9-4.3%) of benzosultam (**2**) were detected among products formed during flash vacuum thermolysis (350-450 °C) of phenylmethanesulfonyl azide (**38**).[9] The generated sulfonylnitrene (**39**) inserted into C-H bond, but the formed benzosultam (**2**) instantaneously extruded SO_2 to give aza-*ortho*-xylylene (**40**) (Scheme 9). Employing injector of GC-MS system as a micropyrolytic oven we have found that at 350 - 400 °C decomposition of benzosultams in a gas phase actually proceeds to a large extent.[26]

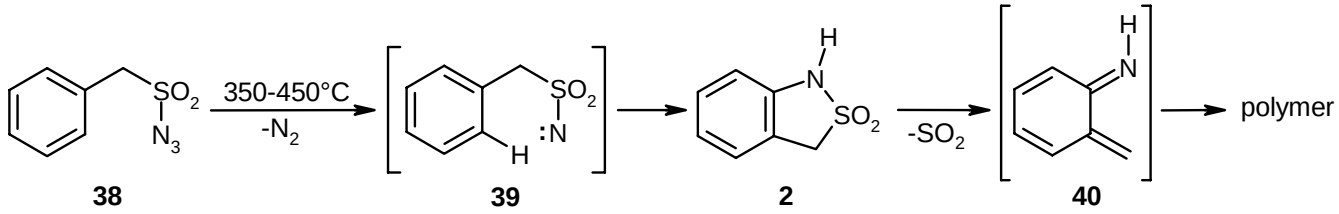
Scheme 8.



35 **15**

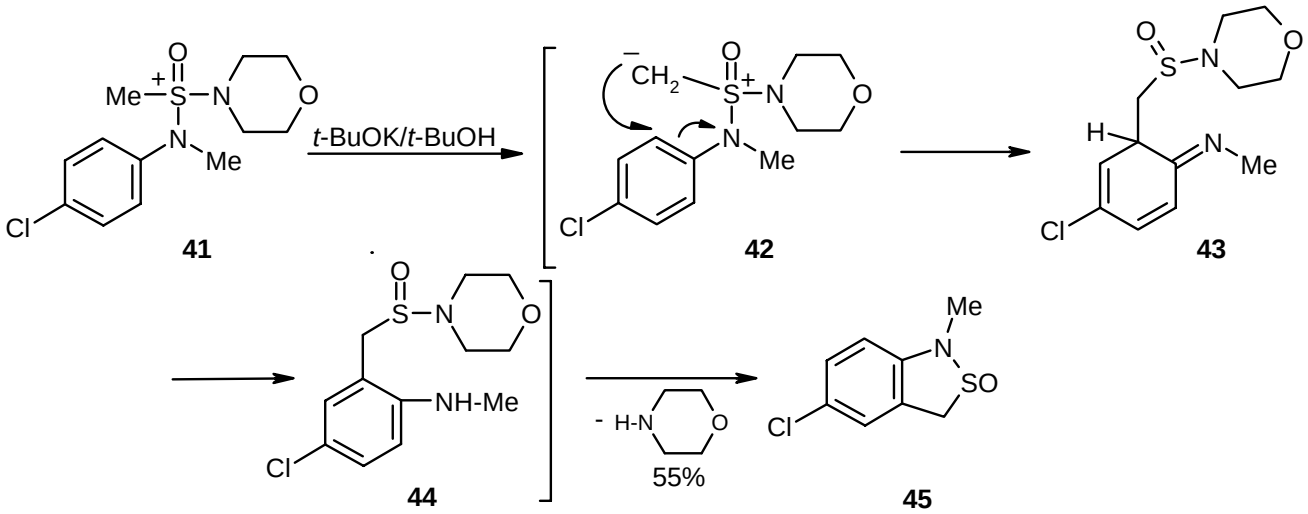
36 **37**

Scheme 9.



It is worth of mention that mono *S*-oxides of 1,3-dihydro-2,1-benzisothiazoline (**45**) are much less abundant than the corresponding dioxides. The only known method of synthesis of these compounds employs a base-induced rearrangement of diaminosulfoxonium ylides (**42**) generated from sulfoxylimines (**42**),[27-29] as shown in the Scheme 10.

Scheme 10.



3. TRANSFORMATIONS OF BENZOSULTAMS

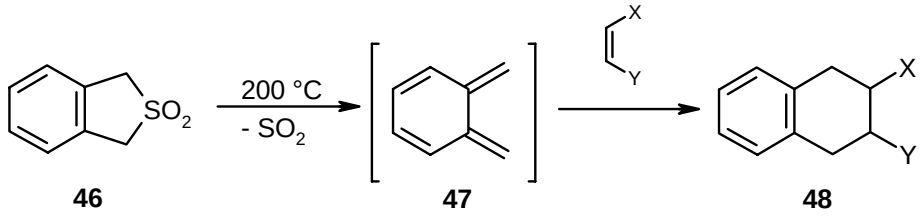
Benzosultams are relatively strong C-H acids, thus can be easily functionalized in the position 3 by alkylation (Scheme 11),[25,30,31] nitroarylation (Scheme 33),[21,32] Knoevenagel condensation with aldehydes,[23,30,33] Michael addition[30] or chlorination with hexachloroethane.[34] These reactions will be further presented together with transformations of the formed 3-substituted benzosultams. The substituents into benzene ring of benzosultams can be introduced by classic transformations, such as nitration,[6,35] halogenation,[35] or acylation.[35]

3.1. Thermal extrusion of sulfur dioxide from benzosultams.

The most important reaction involving benzosultams is cheletropic extrusion of sulfur dioxide leading to 6-methylenecyclohexa-2,4-dien-1-imines, known also as quinone methylene imines or aza-*ortho*-

xylylenes. The last name will be used thorough this review. Benzosultams can be considered as aza-analogues of 1,3-dihydrobenzo[*c*]thiophene 2,2-dioxide (**46**), which on heating undergoes thermal cheletropic extrusion of SO_2 to generate *ortho*-xylylene (**47**).[36] This reactive buta-1,3-diene enters into Diels-Alder reaction with dienophiles resulting in 1,2,3,4-tetrahydronaphthalene derivatives (**48**).[37,38]

Scheme 11.

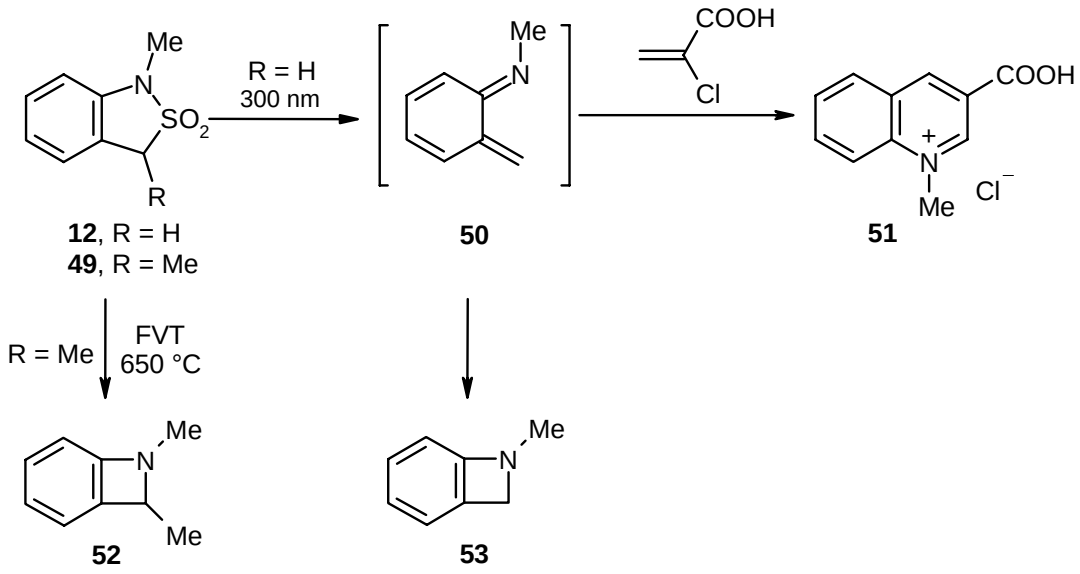


46 **47** **48**

Heteroanalogues of dihydrobenzo[*c*]thiophene 2,2-dioxide bearing five- and six-membered heterocycles instead of the benzene ring react similarly and have found numerous applications to the synthesis of condensed heterocycles.[39-44]

The structural similarity of **46** to benzosultam (**2**) prompted us to employ benzosultams as precursors of aza-*ortho*-xylylenes.[45] According to Lancaster and Smith[46] intermediate aza-*ortho*-xylylene (**50**) generated *via* photolytic (300 nm) extrusion of SO_2 from 1-methyl-2,1-benzisothiazoline 2,2-dioxide (**12**) transforms into 1-methylbenzoazetine (**53**). In the presence of dienophile the azaxylylene (**50**) was trapped by 3-chloroacrylic acid to form quinolinium salt (**51**). It was also claimed that flash vacuum thermolysis (FVT) of 1,3-dimethylbenzosultam (**49**) at 650 °C leads to 1,2-dimethylbenzoazetine (**52**) (Scheme 12).

Scheme 12.



12, R = H
49, R = Me

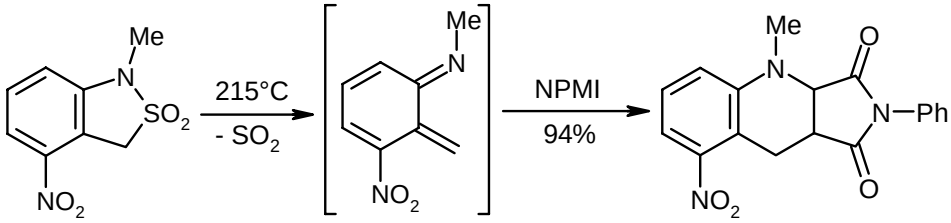
50 **51**

52 **53**

This result seems erroneous since benzoazetines easily undergo thermal ring opening at much lower temperature (80-100 °C).[47,48] We studied the thermal extrusion of SO_2 from benzosultams (**2**) and (**12**) using ultraviolet photoelectron spectroscopy combined with FVT and have found that at high temperatures no benzoazetine was formed, thus a valence isomerization of aza-*ortho*-xylylene (**50**) into benzoazetine (**53**) seems to be doubtful.[49]

We developed an efficient method of generation of aza-*ortho*-xylylenes *via* thermal extrusion of sulfur dioxide from benzosultams.[45,50] Thus nitrobenzosultam (**14**) in boiling 1,2-dichlorobenzene (180 °C) or 1,2,4-trichlorobenzene (215 °C) forms aza-*ortho*-xylylene (**54**) which can be trapped with dienophile, *e.g.* *N*-phenylmaleimide (NPMI), to from 1,2,3,4-tetrahydroquinoline derivative (**55**) in high yield (Scheme 13).

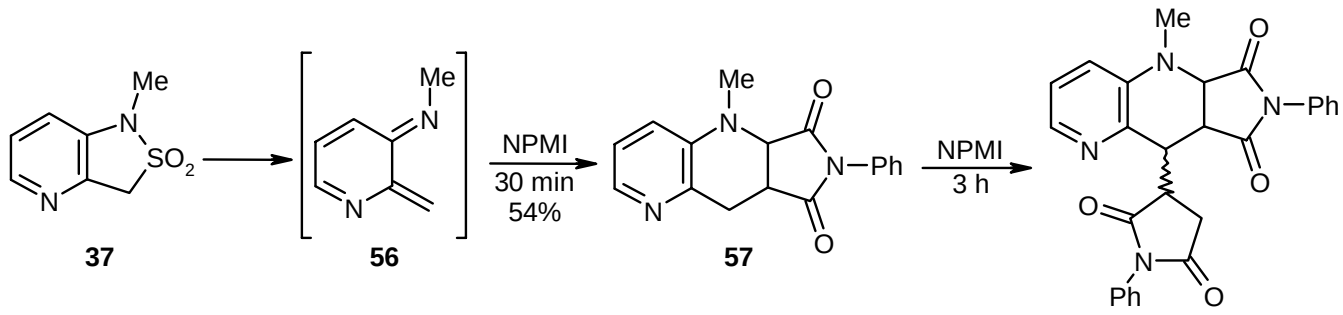
Scheme 13.



14 **54** **55**

Extrusion of SO_2 from pyridosultam (**37**) generates diazaxylylene (**56**) which enters into Diels-Alder reaction with NPMI leading to tetrahydro[1,5]naphthyridine derivative (**57**) (30 min, 54% yield).[24] The formed adduct (**57**) can add another molecule of NPMI giving finally a mixture of two products (**58**) (total yield 84%, 1:1 ratio) consisting of two molecules of NPMI and one molecule of diazaxylylene (**56**) (Scheme 14).[51]

Scheme 14.

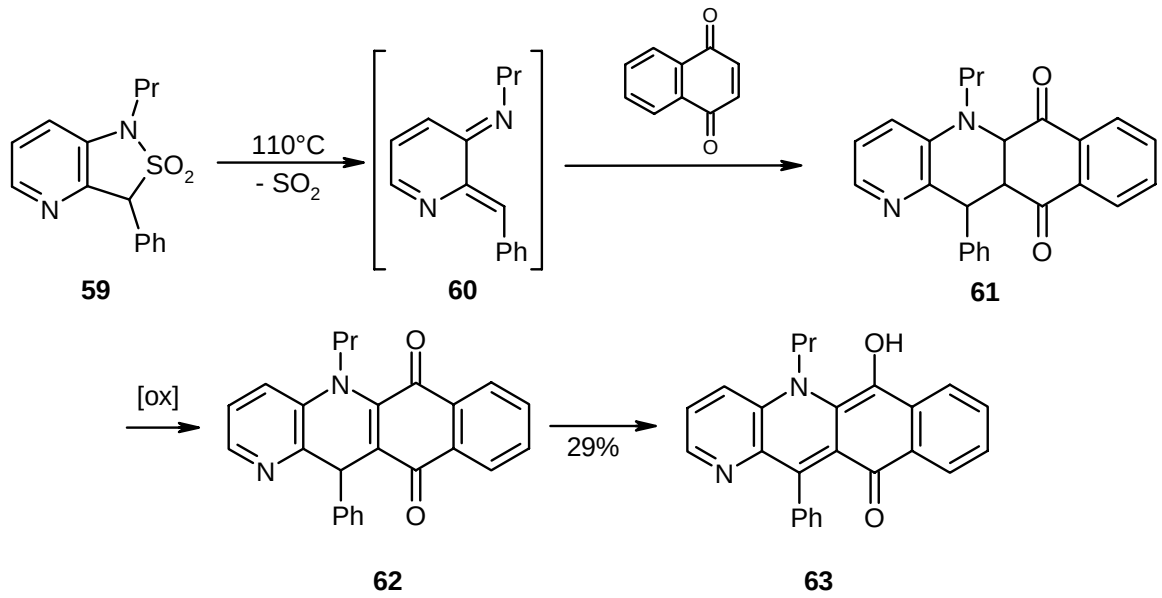


37 **56** **57**

58 (84%, two isomers)

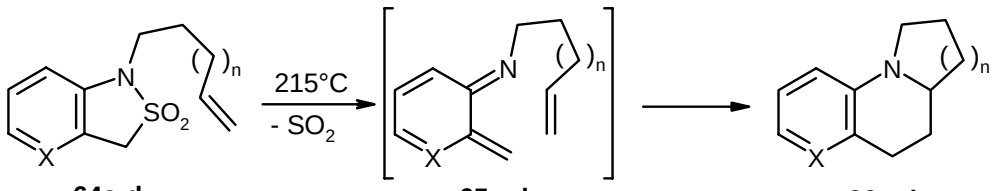
Tetracyclic derivative (**63**) was formed from 1,4-naphthoquinone and diazaxylylene (**60**) generated from 3-phenylpyridosultam (**59**).[48] The intermediate [4+2] adduct (**61**) was oxidized by an excess of the used quinone to **62**, which finally isomerized to **63** (Scheme 15).

Scheme 15.



Aza-*ortho*-xylylenes (**65a-d**) generated from benzosultams (**64a,b**)[50] and pyridosultams (**64c,d**)[24,51] bearing *N*-alkenyl substituents with terminal double bond enter into intramolecular [4+2] cycloaddition (Scheme 16). Thus 1-(1-pent-4-enyl)benzosultam (**65a**) and the homologous 1-(1-hex-5-enyl) derivative (**65b**) were transformed into hexahydropyrrolo[1,2-*a*]quinoline (**66a**) and hexahydrobenzo[*c*]quinolizine (**66b**), respectively. In analogous reactions diazaxylylenes (**65c,d**) generated from pyridosultams (**64c**) and (**64d**) lead to condensed [1,5]naphthyridines (**66c**) and (**66d**).[51]

Scheme 16.

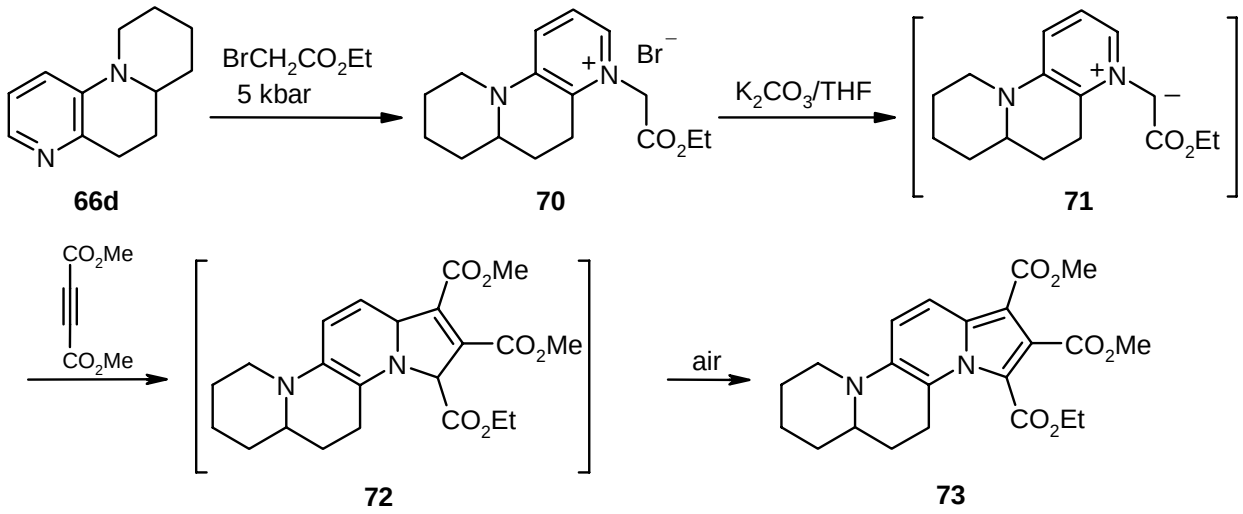


64a-d **65a-d** **66a-d**

		n	Yield (%)
a	C-NO_2	1	82
b	C-NO_2	2	51
c	N	1	68
d	N	2	83

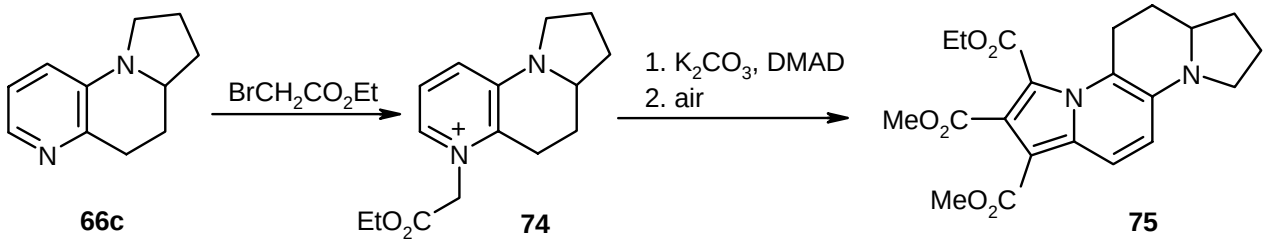
We applied the naphthyridines (**66c**) and (**66d**) to the synthesis of a novel 10,14-diazasteroid framework. In our approach, the tricyclic compounds (**66**) were employed as an ABC fragment of steroidal system to which, by simple transformations, the five-membered D ring has been attached. Quaternization of compound (**66d**) with ethyl bromoacetate gave the pyridinium salt (**70**). Deprotonation of the salt (**70**) (K_2CO_3/dicyclohexyl-18-crown-6) formed ylide (**71**) which entered [3+2] dipolar cycloaddition with dimethyl acetylenedicarboxylate. Under the reaction conditions the initially arising cycloadduct (**72**) was oxidized giving 10,14-diazagonatetraene derivative (**73**), containing indolizine and quinolizine fragments (Scheme 17).

Scheme 17.



In analogous reaction sequence the 1,2,3,3a,4,5-hexahydropyrrolo[1,2-*a*][1,5]napthyridine (**66c**) was transformed into A-norgonane derivative (**75**), containing two indolizine units (Scheme 18).[24]

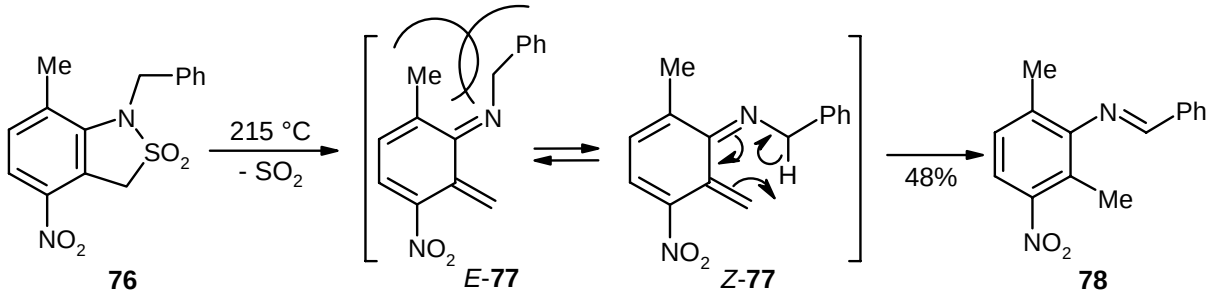
Scheme 18.



Benzosultams substituted in the position 7 with bulky substituents (methyl or methoxy group, or chlorine atom) form aza-o*rtho*-xylylenes which do not enter into Diels-Alder reaction, but instead undergo [1,5] sigmatropic hydrogen shift leading to Schiff bases.[50] This is due to steric interactions of substituents

which force the substituent at nitrogen to attain *Z*-configuration enabling hydrogen shift (Scheme 19). When the steric repulsion is diminished, as in the case of xylylene generated from 7-fluorobenzosultam, the reaction with *N*-phenylmaleimide gives both products arising from [4+2] cycloaddition and [1,5] hydrogen shift.[50] The [1,5] hydrogen shift leading to imines is also a dominating process in aza-*ortho*-xylylenes generated from 4-, 5-, and 6-substituted benzosultams in absence of a dienophile.[50]

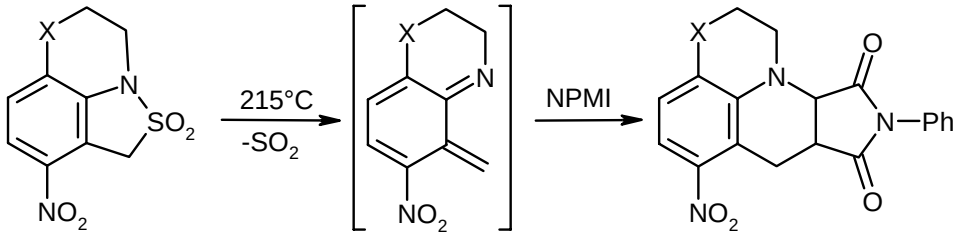
Scheme 19.



76 *E*-**77** *Z*-**77** **78**

Tricyclic sultams (**79a**) and (**79b**) are precursors of aza-*ortho*-xylylenes (**80**) with fixed *E*-configuration which enter readily the [4+2] cycloaddition to form the products (**81**) in high yields (Scheme 20).[50] The compound (**81a**) contains a fragment of julolidine tricyclic system.

Scheme 20.

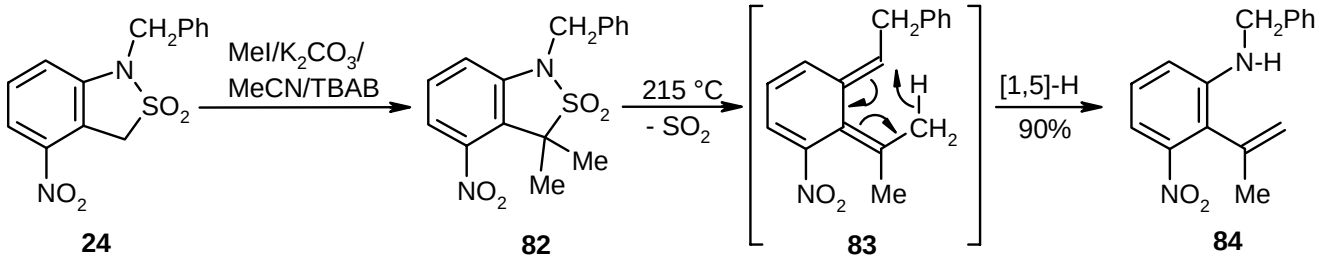


79a,b **80a,b** **81a,** X = CH_2, 69%
81b, X = O, 82%

3.2. Transformations of 3-alkylbenzosultams.

No [4+2] cycloaddition occurs with aza-*ortho*-xylylenes generated from 3-alkylbenzosultams (**82**). The only observed process is a [1,5] sigmatropic hydrogen shift leading to 2-vinylaniline derivatives (**85**) as exemplified in the Scheme 21.[25,31,52]

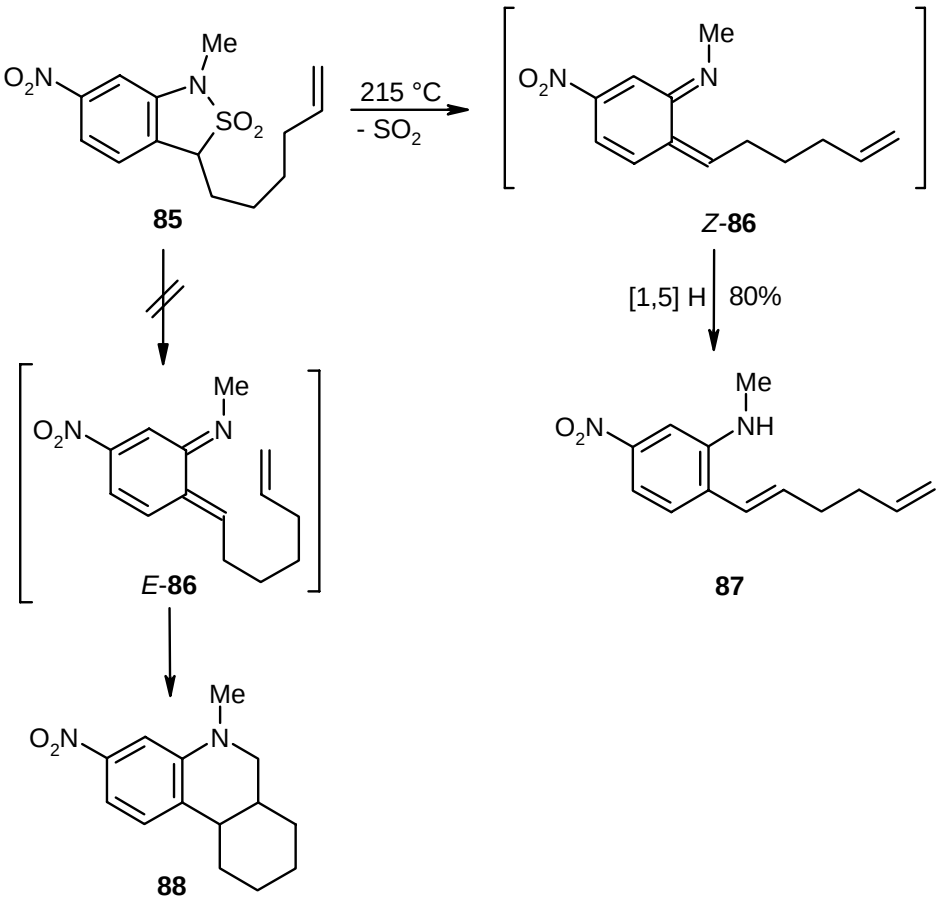
Scheme 21.



24 **82** **83** **84**

The [1,5] sigmatropic hydrogen shift occurs even with aza-*ortho*-xylylenes generated from benzosultams substituted in the position 3 with alkyl chain bearing double bond suitable for intramolecular Diels-Alder reaction.[50,53] For example, aza-*ortho*-xylylene (**86**) generated from 3-(1-hex-5-enyl)benzosultam (**85**) yields only the aniline derivative (**87**) instead of the tricyclic compound (**88**) (Scheme 22).[31]

Scheme 22.

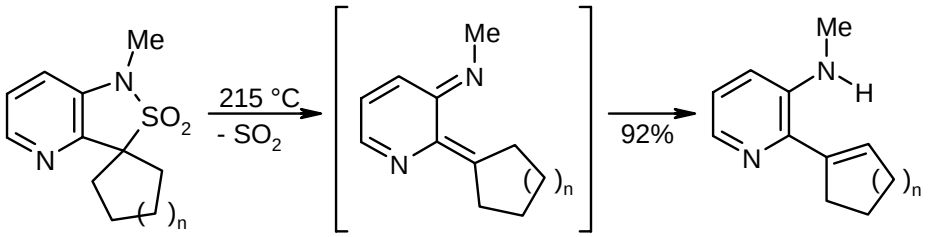


85 ***Z*-86** ***E*-86** **87** **88**

This [1,5] hydrogen shift was employed for the synthesis of variety of aryl- and heteroaryl cycloalkenes. 3-Amino-2-(cyclopenten-1-yl)pyridine (**91a**) is formed in good yield as a result of [1,5] hydrogen shift in

diazaxylylene (**90a**) generated from 3,3-tetramethylenepyridosultam (**89a**) (Scheme 23).[25] Analogous pyridylcyclohexene (**91a**) and cycloheptene derivative (**91b**) are also available from the corresponding 3,3-hexa- and 3,3-heptamethylenepyridosultams (**89b**) and (**89c**), respectively.[25]

Scheme 23.



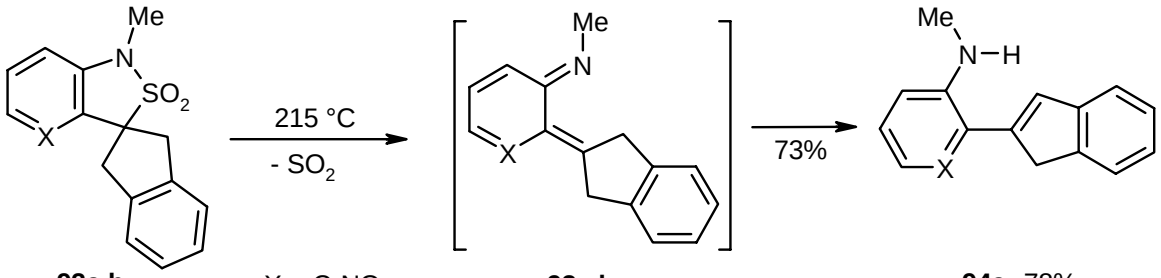
89a, n=1
89b, n=2
89c, n=3

90a-c

91a, n=1, 86%
91b, n=2, 93%
91c, n=3, 92%

Similarly, indano-2-spiro-3-benzosultam (**106a**) (X = C-NO_2) is readily transformed *via* **93a** into 2-arylindenes (**94a**) in high yield (Scheme 24).[52] The pyridine analogue (**92b**) gives corresponding 2-(2-pyridyl)indene (**94b**).[25]

Scheme 24.



92a,b

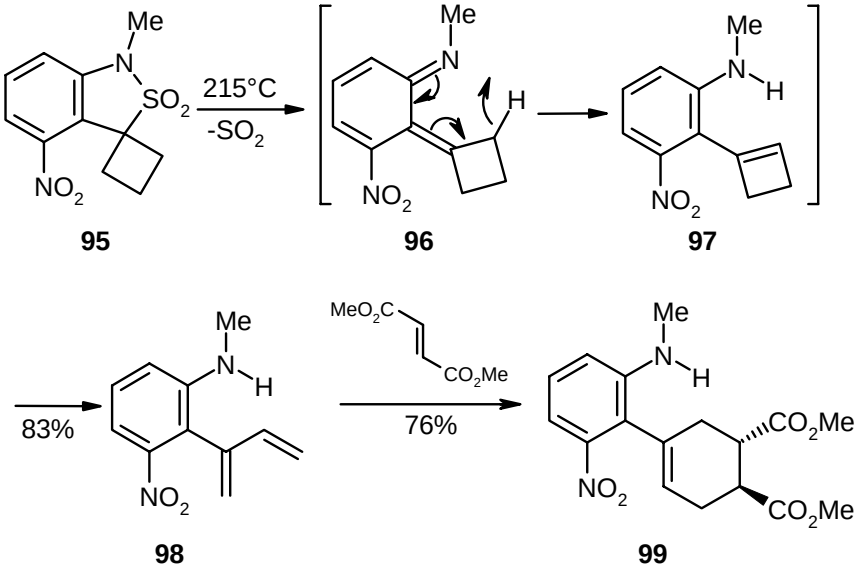
a, X = C-NO_2
b, X = N

93a,b

94a, 78%
94b, 90%

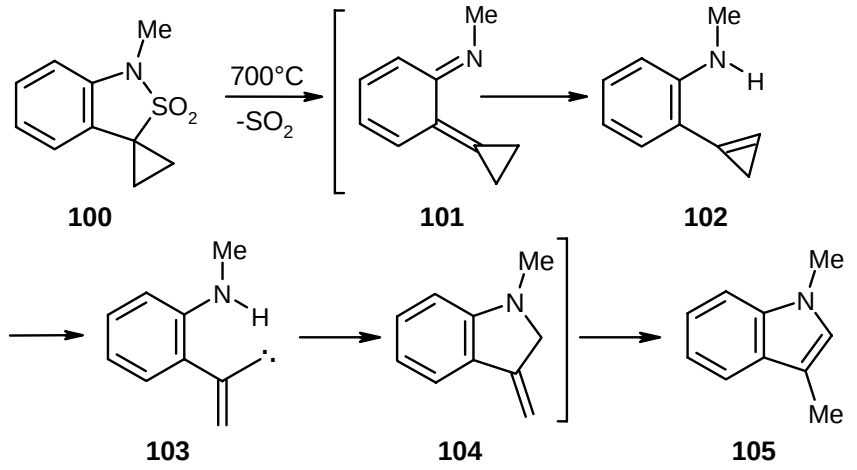
A *domino reaction*[54] consisting of a series of pericyclic transformations is initiated by thermal extrusion of SO_2 from 4-nitro-3,3-trimethylenebenzosultam (**95**).[31] The [1,5] hydrogen shift in azaxylylene (**96**) leads to thermally unstable cyclobutene derivative (**97**) which then undergoes electrocyclic opening of the four-membered ring to isolable 2-arylbuta-1,3-diene (**98**). When this reaction is run in the presence of dienophile (*e.g.* dimethyl maleate) the butadiene (**98**) enters Diels-Alder reaction to form 1-aryl-cyclohexene derivative (**99**) in good yield (Scheme 25).[31] Other 3,3-trimethylenebenzosultams[31] and the pyridine analogue[25] react analogously.

Scheme 25.



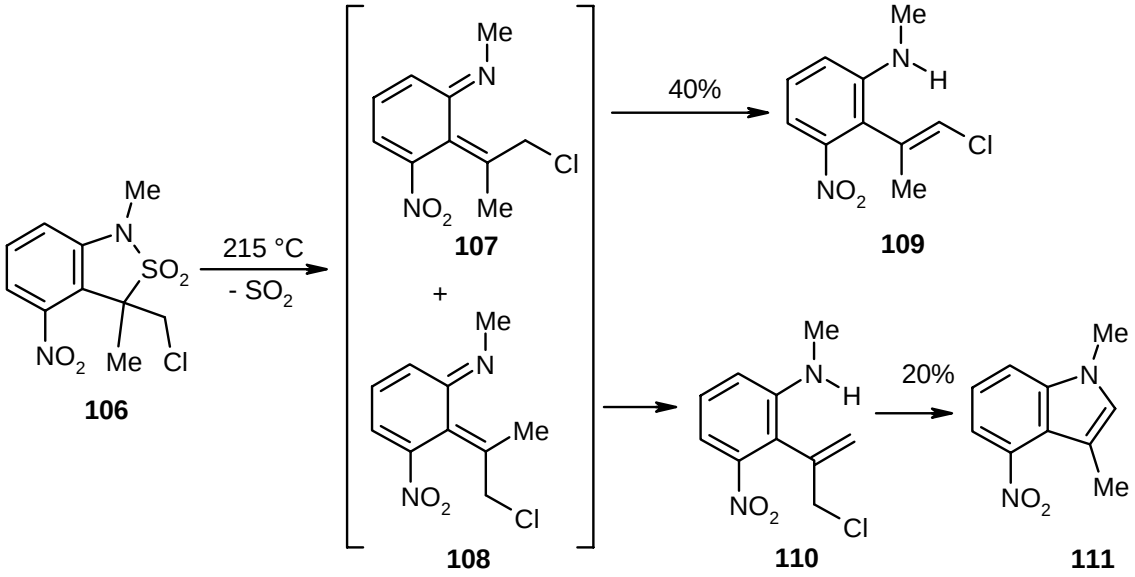
Under standard conditions in refluxing 1,2,4-trichlorobenzene (215 °C) no extrusion of SO_2 from the cyclopropanespirobenzosultam (**100**) occurs.[25] The xylylene would be a potential precursor of arylcyclopropene (**102**). Employing pyrolytic oven attached to the GC-MS system we have found that extrusion of SO_2 from **100** begins at about 400 °C and is complete at 700 °C giving a complex mixture of products in which 1,3-dimethylindole (**105**) predominates.[25,55] A plausible way of formation of the indole (**105**) is shown in the Scheme 26. The extrusion of SO_2 is followed by a [1,5] hydrogen shift and opening of cyclopropene ring (**102**) to vinylcarbene (**103**), which then inserts into N-H bond to form **104**. Final isomerisation leads to **105**.[55]

Scheme 26.



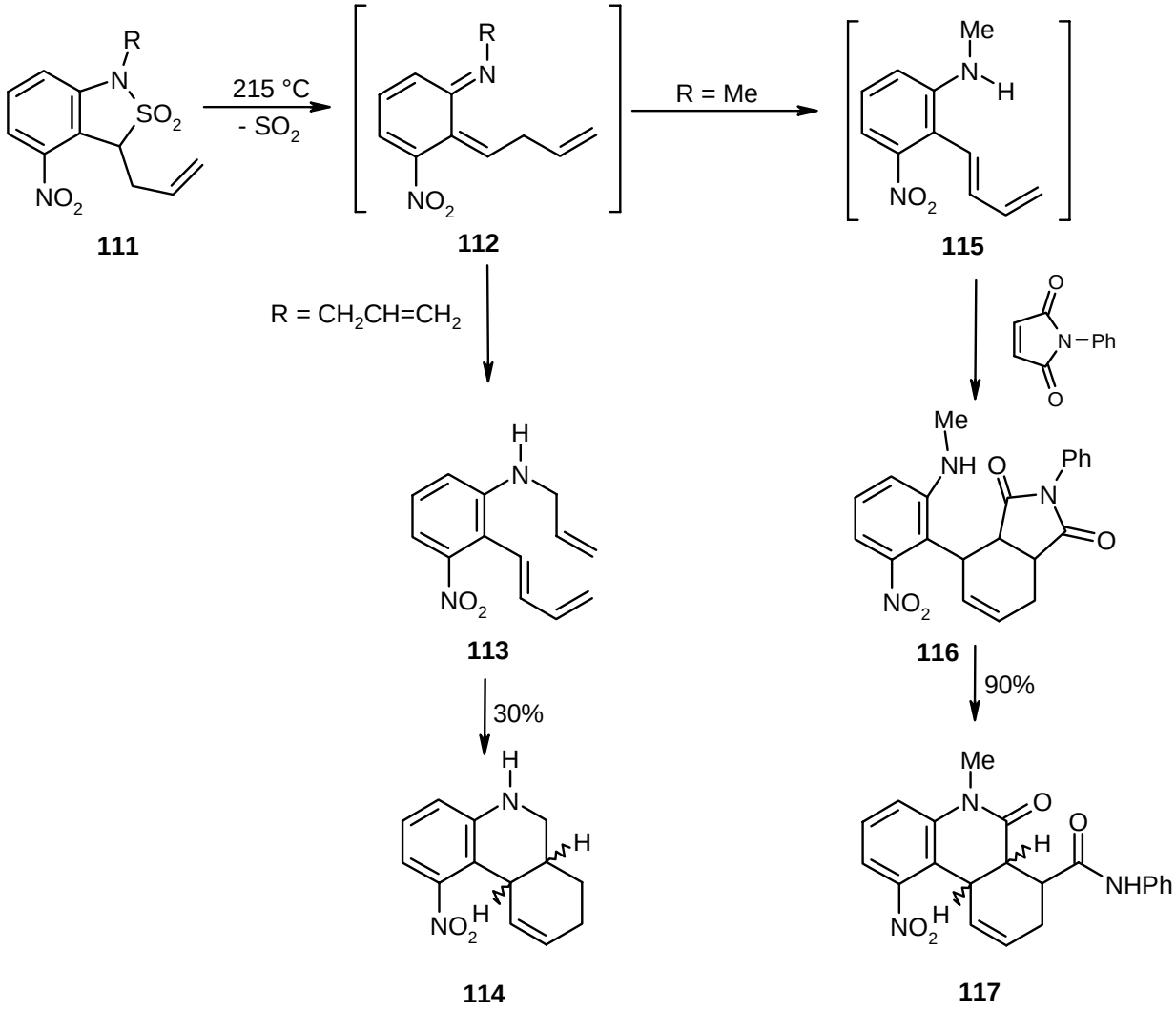
Two isomeric aza-*ortho*-xylylenes (**107**) and (**108**) generated by extrusion of SO_2 from 3-chloromethyl-3-methylbenzosultam (**106**) transform through [1,5]-hydrogen shift into vinyl and allyl derivatives (**109**) and (**110**), respectively. Under reaction conditions the allyl derivative (**110**) cyclizes to 4-nitro-1,3-dimethylindole (**111**) as shown in the Scheme 27.[31]

Scheme 27.

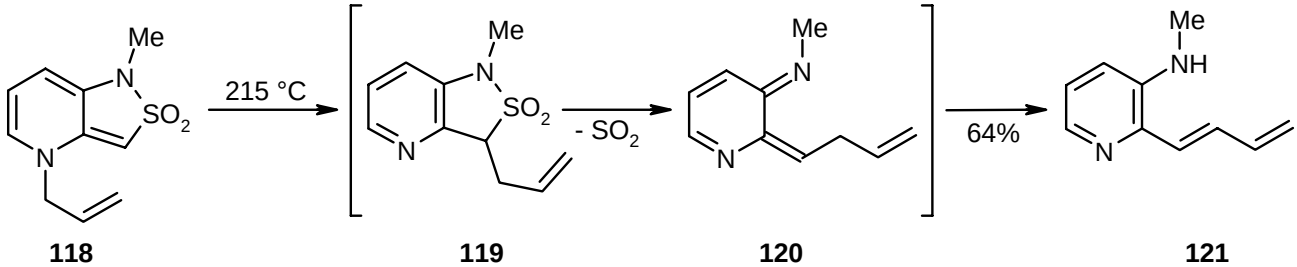


A series of pericyclic processes including cheletropic extrusion of SO_2, [1,5] sigmatropic hydrogen shift, and [4+2] cycloaddition are involved in thermally initiated transformation of 1-allyl-4-nitrobenzosultams (**111**). The 1-methyl-3-allyl derivative (**111**, R = Me) transforms into 1-arylbuta-1,3-diene (**115**) which can be isolated but in low yield due to a partial dimerization.[34] In the presence of dienophile, for example *N*-phenylmaleimide, the diene (**115**) enters Diels-Alder reaction and the reaction is terminated by intramolecular attack of amino group resulting in phenanthrolinone (**117**). 1,3-Diallyl derivative (**111**, R = allyl) transforms into non isolable diene (**113**) which undergoes intramolecular [4+2] cycloaddition resulting in the condensed heterocycle - 1-nitro-5,6,6a,7,8,10a-hexahydrophenanthridine (**114**) (Scheme 28).[31] Isothiazolo[4,3-*b*]pyridine 2,2-dioxides do not undergo thermal extrusion of SO_2. The only exception is 4-allyl derivative (**118**) which transfroms into pyridylbuta-1,3-diene (**121**).[16] Compound (**118**) when heated at 215 °C slowly rearranges to 3-allylpyridosultam (**119**), which then eliminates SO_2 and the formed xylylene (**120**) after the [1,5] sigmatropic hydrogen shift gives **121**.(Scheme 29).

Scheme 28.



Scheme 29.

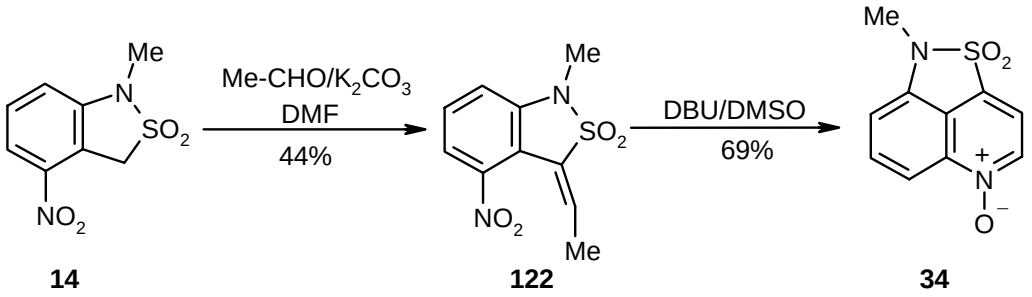


3.3. Transformations of 3-alkenylbenzosultams.

Condensation of benzosultams with aldehydes results in direct replacement of both hydrogen atoms in the position 3 with methylene group.[23,33] Thus, reaction of nitrobenzosultam (**14**) with acetaldehyde in the presence of potassium carbonate provides the ethylidene derivative (**122**). When the obtained product was subjected to a stronger base, such as diazabicycloundecene (DBU), further deprotonation occured and the

formed ambident carbanion attacked the adjacent nitro group giving finally the tricyclic sultam (**34**) as shown in the Scheme 30.[23]

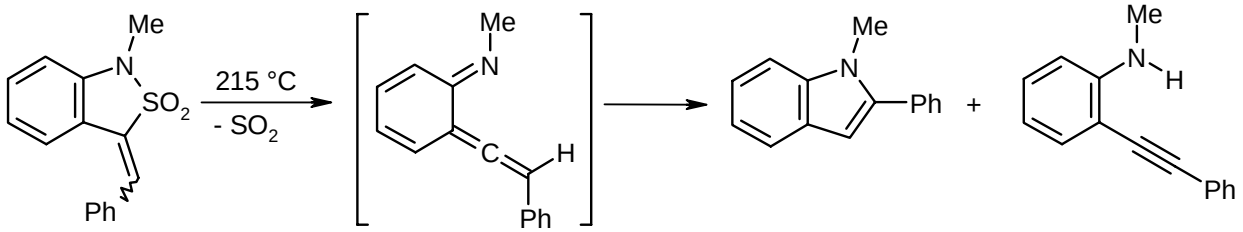
Scheme 30.



14 **122** **34**

3-Arylmethylenebenzosultams, obtained from benzosultams and aromatic aldehydes, slowly undergo extrusion of SO_2. Cumulated xylylene (**124**) generated from 3-benzylidenebenzosultam (**123**) transforms into 1-methyl-2-phenylindole (**125**) and diarylacetylene (**126**).[33] Formation of indole (**125**) involves 6π-electrocyclization of the xylylene (**124**) followed by a [1,2] hydrogen shift. Diarylacetylene (**126**) arises from [1,5] hydrogen shift in the xylylene (**124**).

Scheme 31.

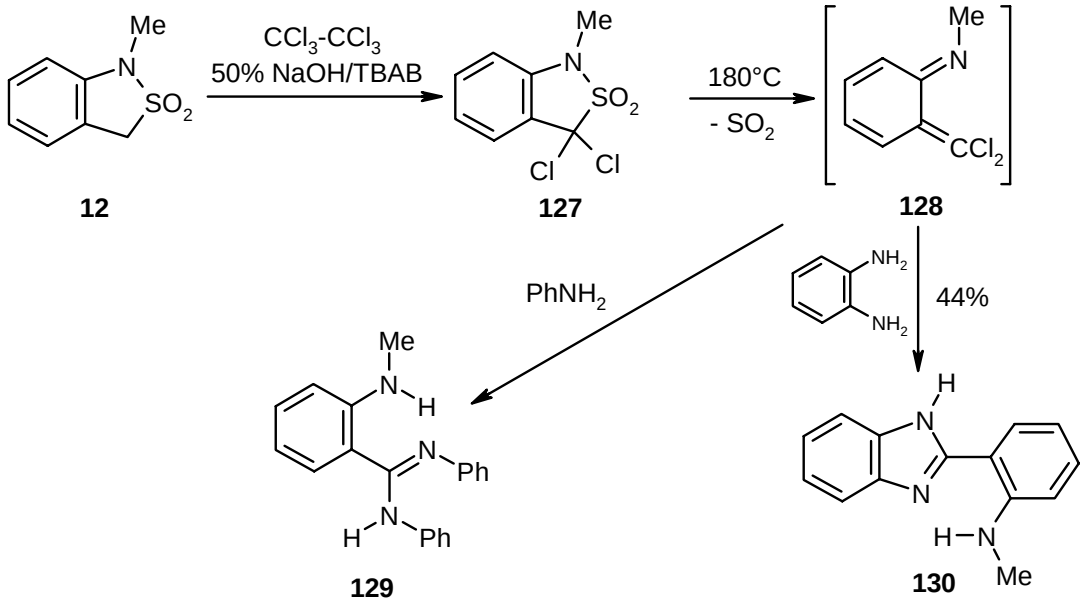


123 **124** **125** (40%) **126** (16%)

3.4. Transformations of 3,3-dichlorobenzosultams.

Chlorination of benzo- and pyridosultams with hexachloroethane under phase-transfer catalysis conditions in the presence concentrated 50% aqueous sodium hydroxide and tetraalkylammonium salt provides 3,3-dichloro derivatives.[34] Extrusion of SO_2 from such benzosultams proceeds readily but generated dichloroxylylenes do not enter into [4+2] cycloaddition reactions.[56] In the presence of nucleophiles Michael addition followed by an elimination of HCl occurs resulting in replacement of the both chlorine atoms. An addition of aniline or 1,2-diaminobenzene, for example, to a xylylene (**128**) generated from the dichlorosultam (**127**), produces amidine (**129**) or 2-(2-methylaminophenyl)benzimidazole (**130**), respectively. (Scheme 32).

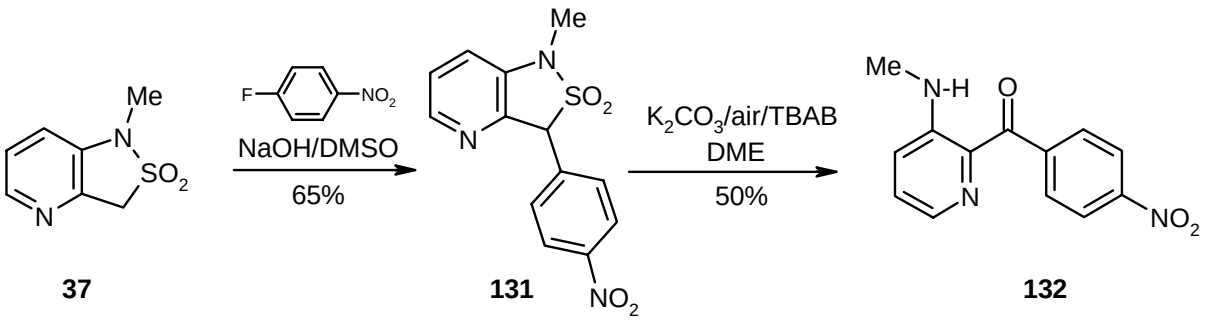
Scheme 32.



3.5. Oxidation of benzosultams

Carbanions of sulfones in the presence of air readily undergo autooxidation to carbonyl compounds.[21] This is also observed in the case of tertiary carbanions of benzo- and pyridosultams. 3-Methyl-1,3-dihydroisothiazolo[4,3-*b*]pyridine 2,2-dioxide is oxidized in the presence of NaOH in DMSO to 1-[3-methylamino]-2-pyridyl]ethanone.[25] 3-(4-Nitrophenyl)pyridosultam (**131**) in the presence of potassium carbonate and catalytic amount of tetrabutylammonium bromide in dimethoxyethane is oxidized to 4-nitrobenzoylpyridine (**132**) (Scheme 33).[21]

Scheme 33.

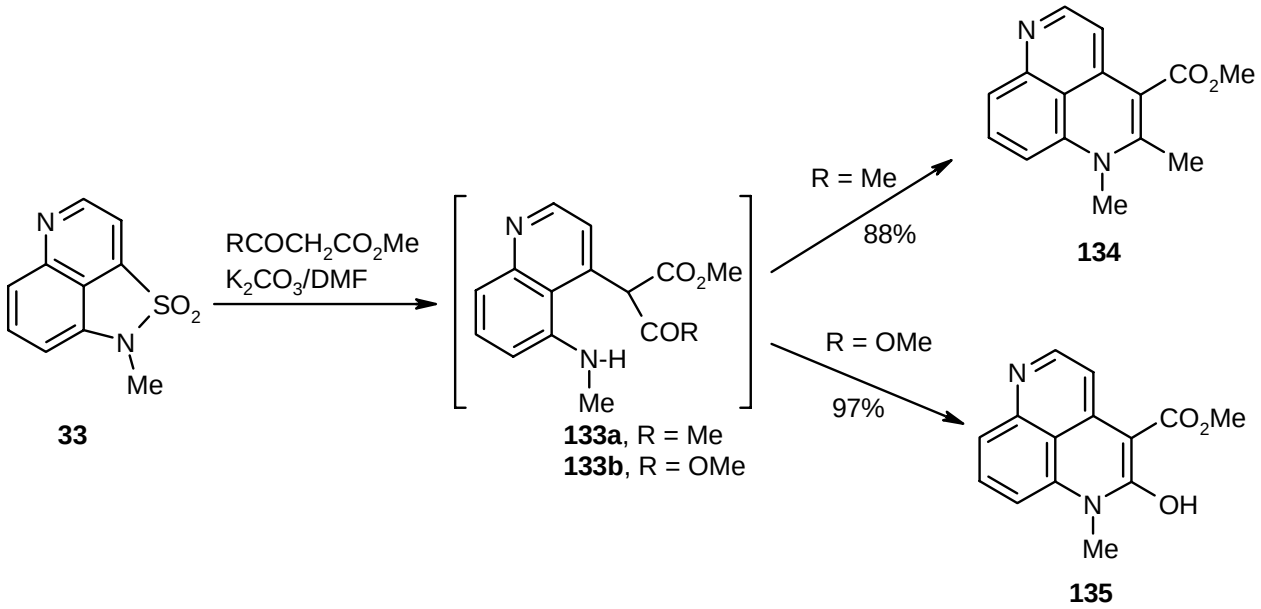


3.6. Substitution of sulfonyl group in condensed benzosultams.

The sulfonyl group in the tricyclic sulfonamide (**33**) can be easily substituted by nucleophiles. The sultam (**33**) treated with methyl acetoacetate in the presence of base gives 1*H*-benzo[*i*,*j*][1,5]naphthyridine (**134**)

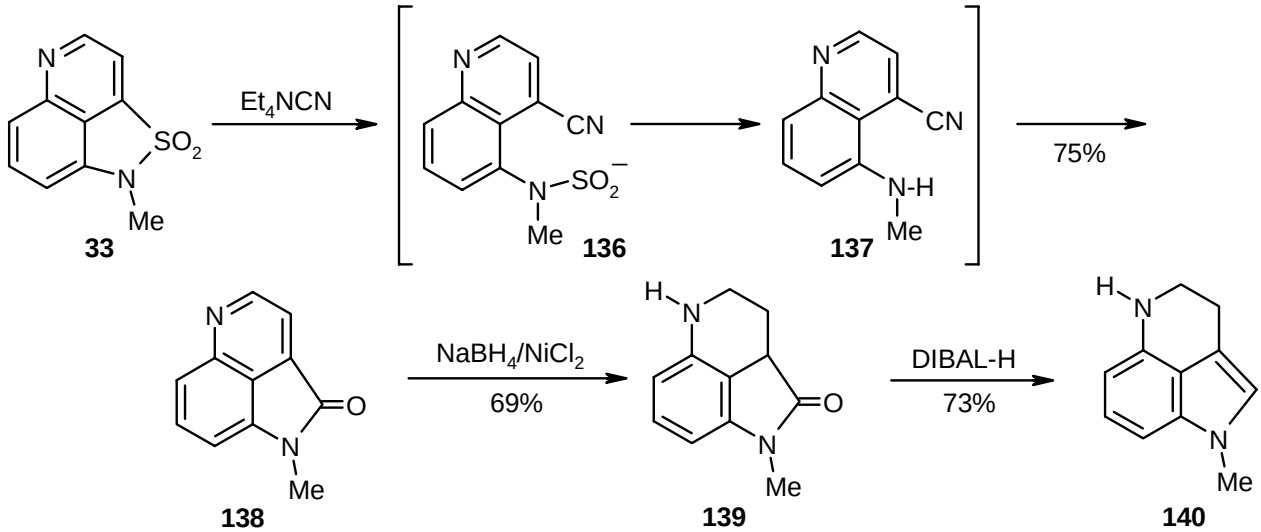
in high yield (Scheme 34). Analogous reaction of **33** with dimethyl malonate furnishes the hydroxy derivative (**135**).[57]

Scheme 34.



The reaction of **33** with cyanide anion leads to pyrrolo[4,3,2-*de*]quinolin-2(1*H*)-one (**138**). This product subjected to two consecutive reductions with $NaBH_4$-$NiCl_2$ and DIBAL-H transforms into 1,3,4,5-tetrahydropyrrolo[4,3,2-*de*]quinoline (**140**), an important fragment of marine alkaloids.[22]

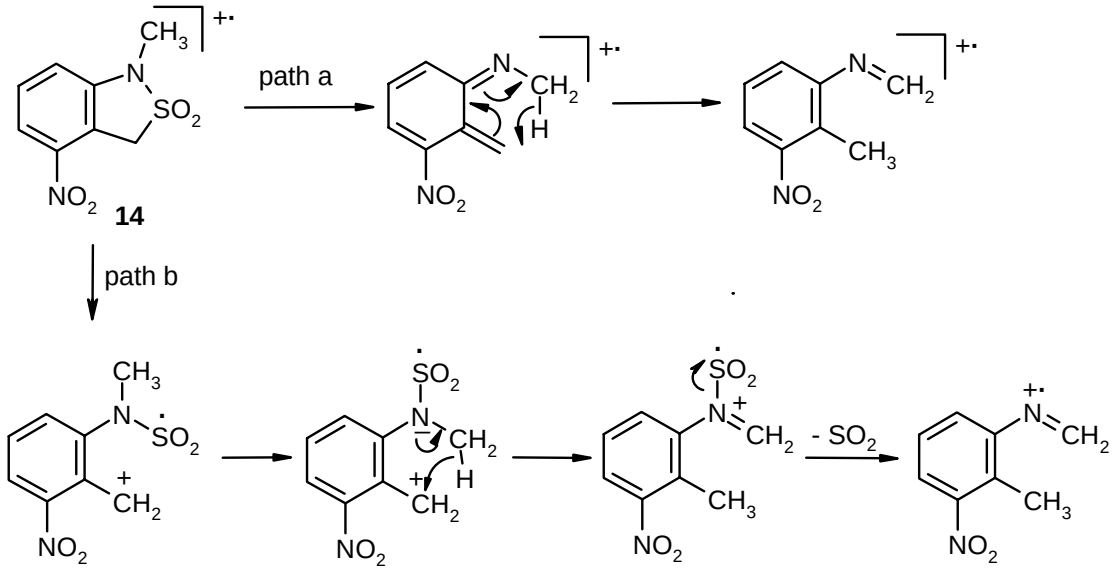
Scheme 35.



4. MASS SPECTROMETRY OF BENZOSULTAMS

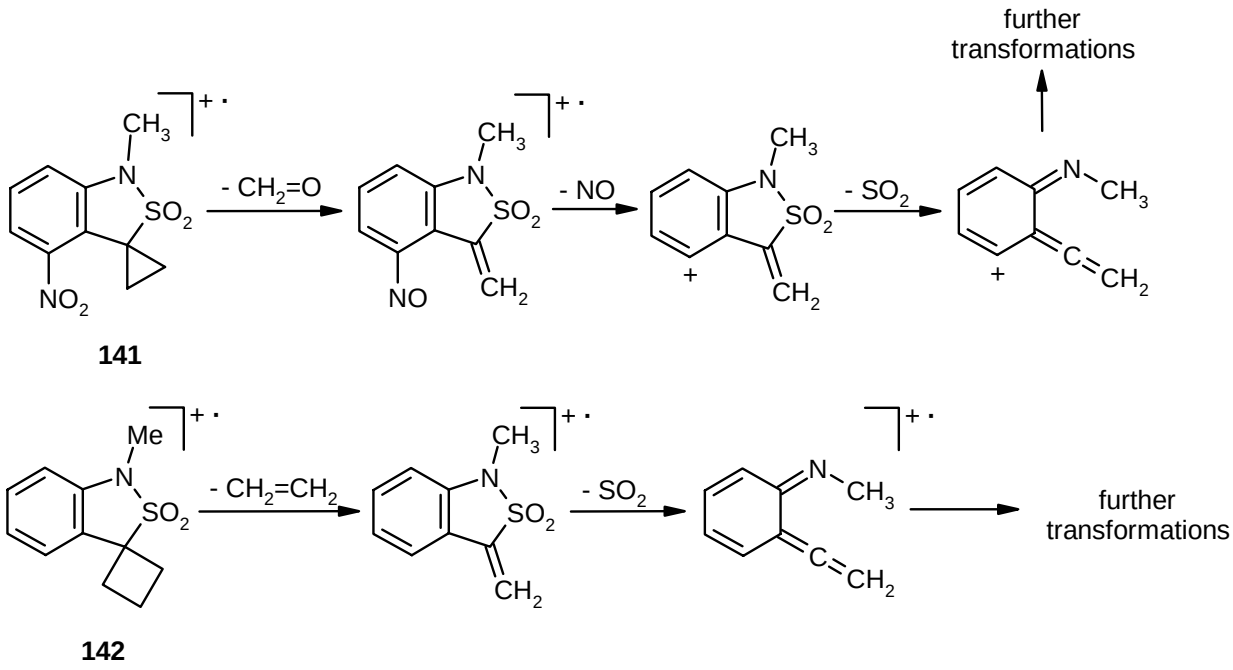
As was shown in former parts of this review the most important process involving benzosultams is an extrusion of sulfur dioxide leading to aza-*ortho*-xylylenes. We investigated mass spectra of benzosultams and have found that, usually, a loss of SO_2 from molecular ion resulting in the formation of [M-64] ion is a predominant process.[45,50,55,58,59] We proposed[59] two mechanisms of elimination of SO_2 from molecular ions of benzosultams: a) concerted mechanism with simultaneous break of sulfur-nitrogen and carbon-sulfur bonds resulting in direct formation of azaxylylene, and b) stepwise mechanism in which the carbon-sulfur bond is broken first, and [1,5] hydrogen shift precedes elimination of SO_2 (Scheme 36).

Scheme 36.



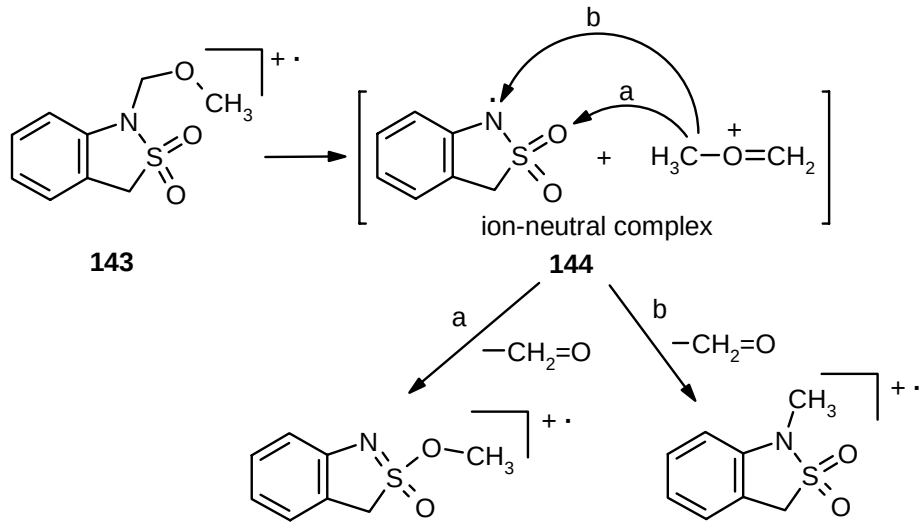
Some exceptions from these general rules have been found. The molecular ion of cyclopropanespiro-benzosultam (**100**) shows much more complex fragmentation patterns,[55] formation of [M-64] ion proceeds to a minor extent, probably due to a perturbation of hybridization of C-3, disabling the extrusion process. In the 4-nitro-3-cyclopropanespirobenzosultam (**140**) the initial fragmentation involves interaction of methylene and nitro groups and results in elimination of formaldehyde. In cyclobutane-spirobenzosultams, *e.g.* **142** the [2+2] cycloreversion resulting in elimination of ethylene precedes the elimination of SO_2 as shown in the Scheme 37.[55]

Scheme 37.



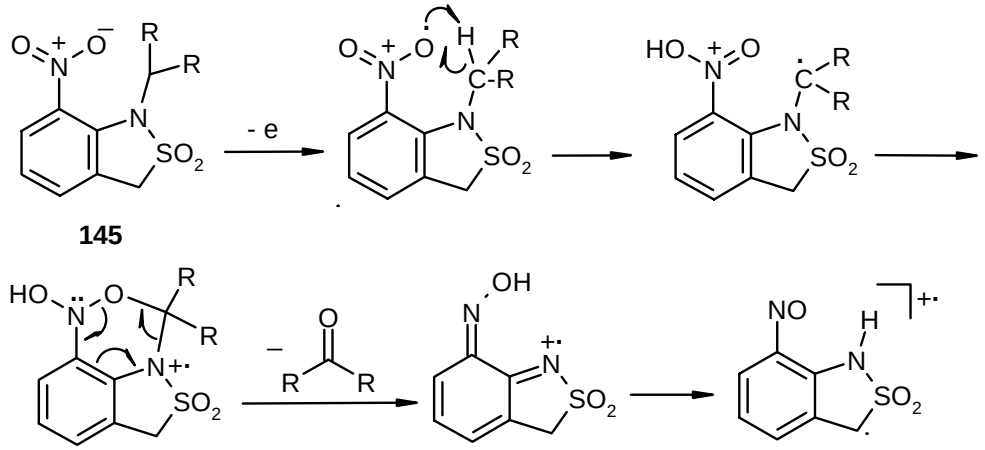
In *N*-methoxymethylbenzosultams (**143**) a novel rearrangement resulting in elimination of formaldehyde was observed. For this process we proposed a mechanism involving a presence of an ion-neutral complex (**144**)[60] as exemplified in the Scheme 38.

Scheme 38.



In 1-alkyl-7-nitrobenzosultams (**145**) primary fragmentations involve interaction of *N*-alkyl and nitro group resulting in an elimination of carbonyl compounds.[61] The proposed mechanism is shown in the Scheme 39.

Scheme 39.



5. CONCLUSIONS

Benzosultams are currently easily available compounds. The chemistry of benzosultams develops into two directions. The first leads to the construction of new sulfur containing condensed heterocycle. The second deals with a thermal extrusion of SO_2 from benzosultams under practically neutral conditions and enables generation of aza-*ortho*-xylylenes. These reactive 1-aza-dienes are valuable intermediates for the synthesis of complex molecules, particularly condensed heterocyclic compounds.

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