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Reactions of 1-Arylbuta-1,3-dienes Generated from 3-Allyl-1,3-dihydro-2,1-benzisothiazole 2,2-Dioxides

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Thermal (215°C) extrusion of sulfur dioxide from 3-allyl-1,3-dihydro-2,1-benzisothiazole 2,2-dioxides (3-allylbenzosultams) leads to aza-*ortho*-xylylenes, which by [1,5] sigmatropic hydrogen shift transform into 1-(2-aminophenyl)buta-1,3-dienes. In the presence of dienophiles, *N*-phenylmaleimide (NPMI) or dimethyl fumarate, these dienes enter Diels-Alder reaction and the formed adducts transform into 6a,7,8,10a-tetrahydro-5*H*-phenanthridin-6-one derivatives. Aza-*ortho*-xylylene **16** generated from 3,3-diallylbenzosultam **15** transforms into arylcyclohexadiene **19**, which finally adds NPMI to form bicyclo[2.2.2]octene derivative **20**.

Key words: Diels-Alder reaction, benzosultams, pericyclic reactions, sigmatropic hydrogen shift

6-Methylenecyclohexa-2,4-dien-1-imines, known as aza-*ortho*-xylylenes or *ortho*-quinone methylene imines, are potential building blocks for the construction of heterocyclic systems [1,2]. These reactive, non isolable, 1-azadienes can be generated by diverse procedures. We developed a method of generation of aza-*ortho*-xylylenes *via* thermal extrusion of sulfur dioxide from 1,3-dihydro-2,1-benzisothiazole 2,2-dioxides (benzosultams) [3,4]. Aza-*ortho*-xylylenes generated from 3-alkylbenzosultams undergo [1,5] sigmatropic hydrogen shift leading to 2-vinylaniline derivatives [5]. This approach was used for the synthesis of 2-arylbuta-1,3-dienes from 3,3-trimethylenebenzosultams [5] and their pyridine analogues [6]. The key step of this reaction was electrocyclic ring opening of cyclobutene ring formed *via* a [1,5] hydrogen shift in the intermediate aza-*ortho*-xylylene. These 2-arylbutadienes were then introduced into Diels-Alder reaction leading to 1-arylcyclohexenes.

In one of our previous papers [5] we reported that extrusion of SO_2 from 1,3-diallylbenzosultam **1** leads to 1-arylbuta-1,3-diene **3**, which then underwent intramolecular Diels-Alder reaction leading to phenanthridine derivative **4** in moderate yield (Scheme 1).

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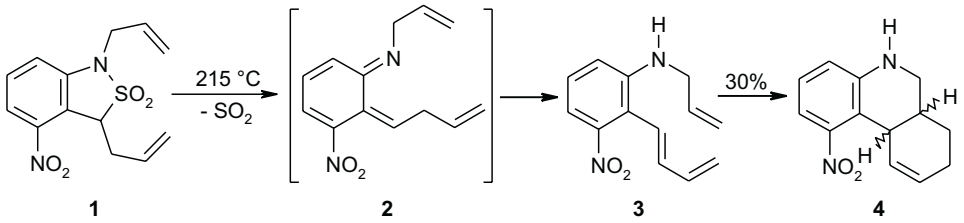
Scheme 1



1 2 3 4

RESULTS AND DISCUSSION

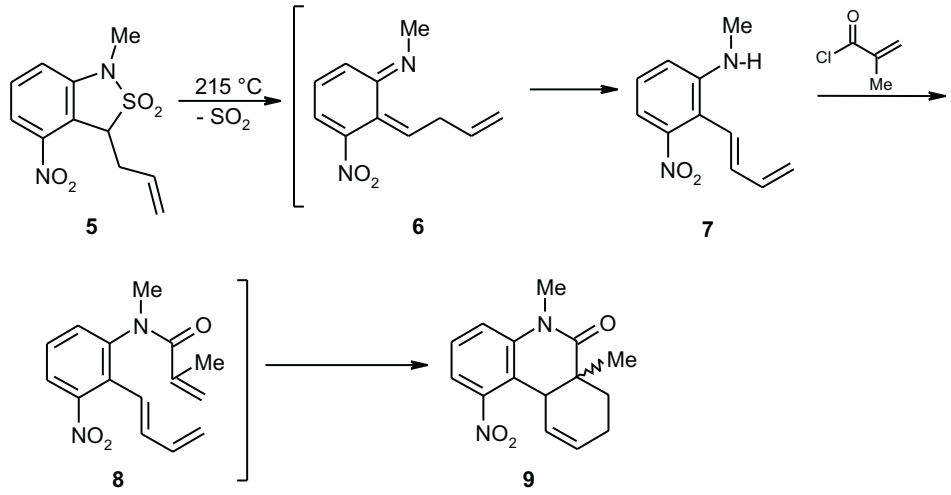
Now we report results of our studies on the synthesis of 1-(2-aminophenyl)butadienes and their intermolecular Diels-Alder reactions. The known methods of synthesis of 1-(2-aminophenyl)buta-1,3-dienes consist in the Meerwein reaction of 2-nitrophenyldiazonium chloride with buta-1,3-diene followed by elimination of HCl and reduction of the nitro group [7]. Such butadienes were also formed from azaxylylenes generated by dehydration of 2-aminophenyl vinyl carbinols [8].

The reports on application of (2-aminophenyl)butadienes as dienes in intermolecular Diels-Alder are scarce. The only known examples deal with a condensation of phenylisocyanates with iminophosphoranes derived from (2-aminophenyl)buta-1,3-diene, which resulted in indolo[2,3-*b*]quinolines [9,10]. The corresponding 1-(2-nitrophenyl)buta-1,3-dienes were introduced into Diels-Alder reaction with acrylic and maleic acid derivatives and the formed adducts after reduction of the nitro group cyclized to phenanthridinones [7,11,12].

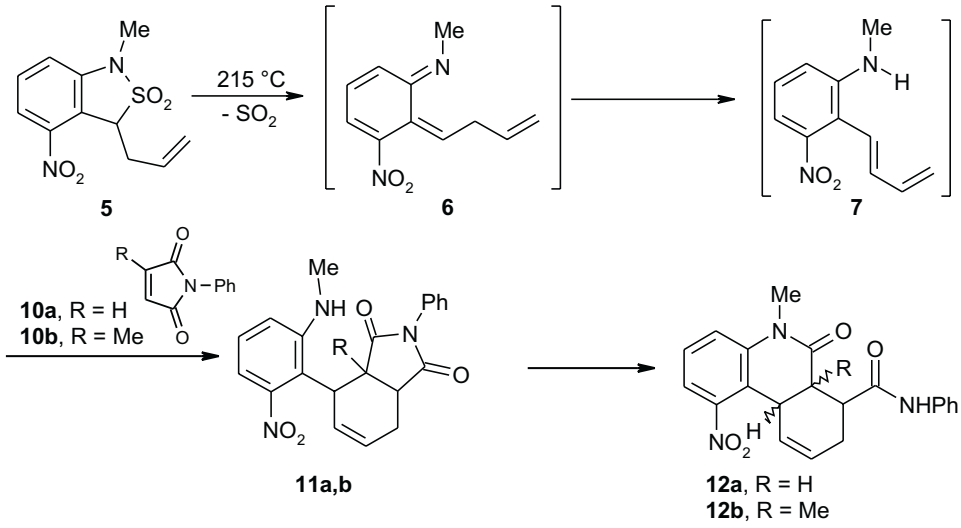
We have found that in boiling 1,2,4-trichlorobenzene (215°C) the extrusion of SO_2 from 3-allyl-4-nitrobenzosultam **5** proceeds smoothly but isolation of butadiene **7** proved impossible. The GC-MS analysis of the crude reaction mixture has revealed large amounts of the dimerization products besides of the expected diene **7**. The attempts to trap the intermediate amine with methacryloyl chloride were partly successful. In the presence of an excess of the chloride acylation of the aminobutadiene **7** occurred but the intramolecular [4+2] cycloaddition product **9** was formed in low yield (Scheme 2).

When the extrusion of SO_2 from benzosultam **5** was performed in the presence of two-fold excess of *N*-phenylmaleimide (**10a**, NPMI) the product, whose molecular mass corresponded to an addition of one molecule of NPMI to butadiene **8**, was formed. To this product we assigned the structure of tetrahydro-5*H*-phenanthridin-6-one **12a** (Scheme 3). The crucial proof of this structure was taken from the mass spectrum, which revealed a strong peak [M-92], corresponding to the loss of PhNH fragment. In ^{1}H NMR spectrum a broad signal at 9 ppm corresponding to an amide proton was observed. The product was formed in a domino reaction [13] consisted of

Scheme 2

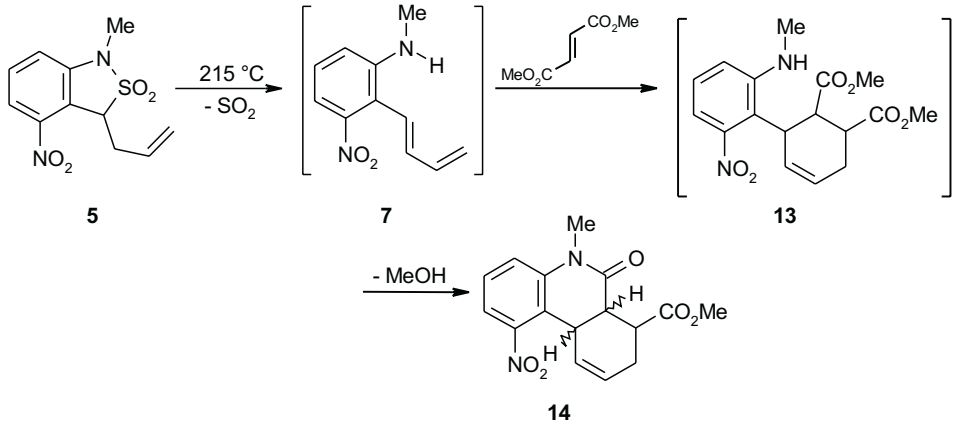


Scheme 3



a series of pericyclic processes: extrusion of SO_2, [1,5] sigmatropic hydrogen shift, [4+2] cycloaddition, and terminated by a ring closure of six-membered ring with simultaneous opening of imide, as shown in Scheme 3. Analogous reaction with citraconic imide **10b** led to the 6a-methyl substituted phenanthridinone **12b** in 36% yield. Diene **7** with dimethyl fumarate formed the ester **14** as shown in Scheme 4.

Scheme 4

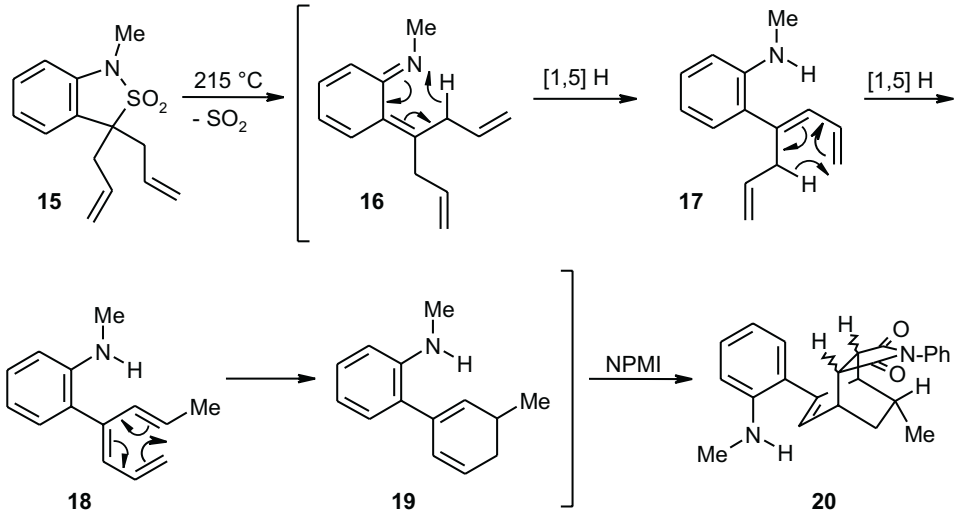


5 **7** **13** **14**

Our attempts to determine the relative configuration across C6a–C10a bond in compounds **9**, **12a**, **12b**, and **14** were unsuccessful. We were unable to obtain crystals suitable for X-ray analysis. Also from the NMR spectra these structures could not be established unambiguously. These reactions represent a new approach to the construction of tetrahydrophenanthridin-6-ones. This ring system is present in numerous natural compounds, it consists a fragment of dynemicin A [14] and corynoline alkaloids [15]. The known methods of synthesis of tetrahydro-5*H*-phenanthridin-6-ones consist of reductive cyclization of 1,2,3,4-tetrahydro-2′-nitrobiphenyl-2-carboxylic acid and its derivatives [7,11,12], palladium mediated cyclization of cyclohexenoyl-2-bromoaniline [14], or photocyclization of cyclohexenoylanilides [15-17].

Extrusion of SO_2 from 3,3-diallylbenzosultam **15** in the presence of NPMI led to a product, whose molecular mass corresponded to an addition of NPMI to aza-*ortho*-xylylene. One could expect the formation of 10a-allyl-5-methyl-6a,7,8,10a-5*H*-tetrahydrophenanthridin-6-one. However, the ^{1}H NMR spectrum has revealed the presence of only one vinyl proton at 6.5 ppm, what excluded participation of the diene **17** or triene **18** in a Diels-Alder reaction. The characteristic feature of the proton spectrum is the presence of a doublet at 0.91 ppm (J = 6.6 Hz). In the ^{13}C NMR spectrum signals corresponding to only twelve carbon atoms (ten aromatic and two olefinic) in the down-field region were present. On the basis of ^{1}H and ^{13}C NMR spectra we proposed for this product the tricyclic structure **20**, but we were unable to determine the configuration of the product. Taking into account the steric hindrance, caused by the aminophenyl substituent, we can suppose that formation of an *exo* adduct should prevail. The plausible way of formation of the product **20** is shown in Scheme 5. Extrusion of SO_2 from the sultam **15** gives diallyl xylylene **16**, which then undergoes a sigmatropic [1,5] hydrogen shift to allyl butadiene **17**. Another [1,5] hydrogen shift

Scheme 5



in the allyl butadiene **17** leads to 4-arylhepta-1,3,5-triene **18**, which electrocyclizes into methylcyclohexadiene derivative **19**. The final step is a [4+2] cycloaddition reaction of NPMI to diene **19**.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained with Varian Mercury 400 BB (400 or 100 MHz, respectively) instruments in $CDCl_3$ with TMS as internal standard. Coupling constants *J* are given in Hz. IR were obtained with Perkin Elmer 2000 FT IR instrument. Mass spectra (electron impact, 70 eV) were obtained on AMD 604 (AMD Intectra GmbH, Germany) instrument. HRMS were measured in the presence of perfluorokerosene as the reference compound. Column chromatography was performed using silica gel 240–400 mesh (Merck).

3-Allyl-1-methyl-1,3-dihydro-2,1-benzisothiazole 2,2-dioxide (5). A solution of 1-methyl-4-nitrobenzosultam [18] (1.14 g, 5 mmol), allyl bromide (0.7 g, 5.5 mmol) and tetrabutylammonium bromide (50 mg) in acetonitrile (15 ml) was stirred with solid potassium carbonate (5 g) at room temperature until the starting benzosultam disappeared (*ca*. 4 h, TLC control). Then the solid was separated and acetonitrile was evaporated. The residue was dissolved in methylene chloride and washed with diluted hydrochloric acid. The organic solution was dried over magnesium sulfate. After evaporation of the solvent the product was recrystallized from ethanol. Yield 91%. M.p. 125–127°C. ^{1}H NMR: δ = 2.70–2.79 (m, 1H), 2.88–2.97 (m, 1H), 3.20 (s, 3H), 5.00–5.10 (m, 3H), 5.72–5.82 (m, 1H), 7.04 (d, *J* = 8.0, 1H), 7.54 (dd, *J* = 8.1, 8.0, 1H), 7.86 (d, *J* = 8.1, 1H). ^{13}C NMR: δ = 26.6, 34.4, 60.0, 114.5, 117.7, 118.4, 119.9, 120.6, 130.3, 130.9, 131.1. MS (EI 70 eV, m/z, %): 268 (M^+, 100), 251 (3), 227 (32), 212 (24), 203 (11), 187 (20), 174 (15), 160 (16), 159 (16), 158 (18), 157 (30), 156 (17). HRMS for $C_{11}H_{12}N_2O_4S$ calcd. 268.0518, found 268.0526.

3,3-Diallyl-1-methyl-1,3-dihydro-2,1-benzisothiazole 2,2-dioxide (15). To a stirred solution of 1-methylbenzosultam [19] (0.36 g, 2 mmol) and allyl bromide (0.65 g, 5 mmol) in dimethylsulfoxide (5 ml) powdered sodium hydroxide (1.0 g) was added in one portion. The reaction mixture was stirred for 30 min and then poured into cold 5% hydrochloric acid (100 ml). The product was extracted with methylene chloride and dried over magnesium sulfate. After evaporation of the solvent the product was purified by column chromatography (silica gel, cyclohexane - ethyl acetate 2:1). Yield 58%. Oil. ^{1}H NMR: δ = 2.73 (dd, *J* = 14.3, 7.1, 2H), 2.85 (dd, *J* = 14.3, 7.1, 2H), 3.12 (s, 1H), 5.18 (dd, *J* = 17.0, 2.0, 2H), 5.23 (dd, *J* = 10.3, 2.0, 2H), 5.82 (dddd, *J* = 17.2, 10.3, 7.5, 7.1, 2H), 6.73 (d, *J* = 8.2, 1H), 7.01 (dd, *J* = 7.9, 7.6, 1H), 7.10 (dd, *J* = 7.9, 1.5, 1H), 7.31 (ddd, *J* = 8.2, 7.6, 1.5, 1H). MS (EI 70 eV, m/z, %): 263 (M^+, 8), 222 (5), 198 (18), 184 (30), 170 (12), 158 (100), 143 (55), 130 (35), 118 (30), 116 (28).

Cycloaddition Reactions (General Procedure). Benzosultam (1 mmol) and dienophile (2 mmol or 5 mmol in the case of reaction with methacryloyl chloride) were refluxed in 1,2,4-trichlorobenzene (5 ml) until the starting material disappeared (2–4 h, TLC control). The reaction mixture was then subjected to a column chromatography on silica gel. Solvent was separated with cyclohexane and then the product was eluted with cyclohexane-ethyl acetate (4:1). The following compounds were obtained:

5,6a-Dimethyl-1-nitro-6a,7,8,10a-tetrahydro-5*H*-phenanthridin-6-one (9). Yield 16%. M.p. 210°C. ^{1}H NMR: δ = 1.01 (s, 3H), 1.50 (ddd, *J* = 17.5, 11.3, 6.8, 1H), 2.10 (br d, *J* = 17.5, 1H), 2.27–2.40 (m, 1H), 2.43 (dddd, *J* = 13.0, 6.8, 1.1, 1.1, 1H), 3.37 (s, 1H), 5.48 (dddd, *J* = 10.1, 1.8, 1.8, 1.8, 1H), 5.83 (dddd, 10.1, 4.7, 2.2, 2.2, 1H), 7.20 (dd, *J* = 8.2, 1.0, 1H), 7.40 (dd, *J* = 8.2, 8.2, 1H), 7.59 (dd, *J* = 8.2, 1.0, 1H). ^{13}C NMR: δ = 22.9, 24.3, 30.4, 31.0, 39.5, 41.0, 118.39, 118.46, 122.7, 124.6, 128.0, 129.9, 140.9, 150.1, 172.9. IR (KBr) ν: 2964, 2924, 1680, 1605, 1530, 1473, 1460, 1357, 1272, 1137, 1118, 1054, 1005. MS (EI 70 eV, m/z, %): 272 (M^+, 78), 255 (100), 238 (46), 228 (13), 224 (38), 212 (82), 201 (70), 197 (29), 184 (32), 173 (88), 167 (35), 115 (48). HRMS for $C_{15}H_{16}N_2O_3$ calcd. 272.1161, found 272.1169.

5-Methyl-1-nitro-7-phenylaminocarbonyl-6a,7,8,10a-tetrahydro-5*H*-phenanthridin-6-one (12a)

22.2, 30.75, 31.8, 33.1, 33.7, 43.95, 44.04, 45.5, 110.0, 116.9, 123.9, 126.4, 127.6, 128.5, 128.6, 128.7, 129.0, 131.7, 140.4, 145.7, 177.87,177.91. IR (KBr) ν: 3428, 2953, 3925, 1710, 1597, 1503, 1380, 1314, 1184. MS (EI 70 eV, m/z, %): 372 (M^+, 100), 357 (3), 330 (7), 199 (17), 198 (77), 171 (79), 157 (13), 144 (9), 130 (24). HRMS for $C_{24}H_{24}N_2O_2$ calcd. 372.1838, found 372.1841.

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