Rearrangement of 3-Methoxy Substituted [2,1]Benzisoxazole- and Naphth[2,3-*c*]isoxazolequinones in Dimethyl Sulfoxide Solution

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The reactions of the 3-methoxy-isoxazole quinones **1** and **9** in a highly polar solution of dimethyl sulfoxide have been studied. Quinones of type **2, 4/11, 5/12, 6** and **7/13** have been isolated; nmr measurements give a detailed insight into the reaction mechanism.

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The preceding papers [1,2] described an improved method of synthesis of 3-methoxy substituted [2.1]benzisoxazole- and naphth[2,3-*c*]isoxazolequinones and also a preparative method of synthesis of sulfoximidoquinones and sulfimidoquinones with dimethyl sulfoxide and dimethyl sulfide, respectively. These new procedures arose out of the observed instability of **1** and **9** in dimethyl sulfoxide noted while recording their nmr spectra in this solvent.

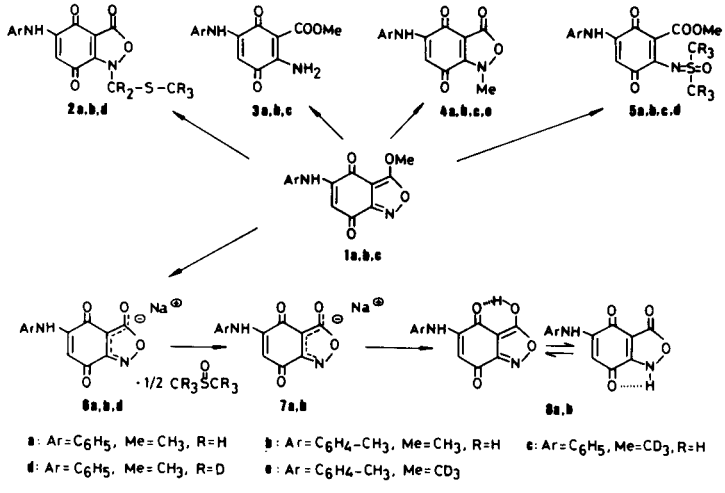
We report here experiments concerning the rearrangement reactions of 3-methoxyisoxazolequinones **1** and **9** in a highly polar solution of dimethyl sulfoxide. We have analysed the different reaction products and carried out experiments to establish the reaction pathways of the rearrangements. In the first part of this communication we describe the products isolated from the reactions of quinones **1** and **9** in dimethyl sulfoxide, following this are reported experiments concerning the reaction mechanism.

Analysis of the Reaction Products.

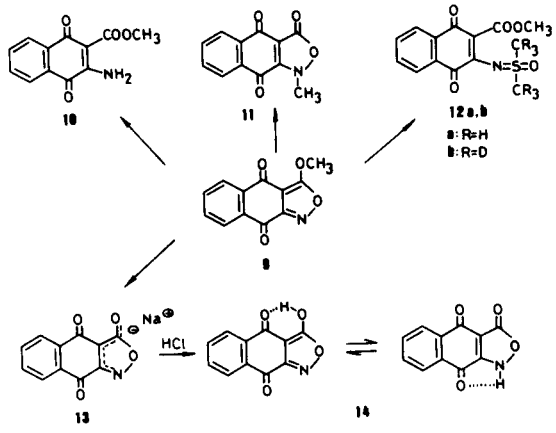
A suspension of **1a,b,c** in dimethyl sulfoxide was stirred at room temperature for three days. According to tlc the dark red violet solution did not contain starting material. For isolating the reaction products the reaction mixture was adsorbed on silica gel.

Chloroform soluble components were eluted with this solvent and afterwards separated by column chromatography on silica gel. Four products were isolated (Scheme 1): a) quinones of the types **2** and **3** in about 1% yield and b) the quinones **4** and **5** in 10% and 16% yield, respectively. The polar compounds were desorbed from the silica gel with acetone to give quinones **6** as main products (about 50%). Quinone **1a** and deuteriodimethyl sulfoxide reacted to give the deuterated products **2d, 5d** and **6d** besides the undeuterated quinones **3a** and **4a**. This result proved that dimethyl sulfoxide was indeed involved in the reaction; the result was important for establishing the structure of the new types of sulfur containing quinones.

The naphthisoxazolequinone **9** reacted with dimethyl sulfoxide in an analogous way to give **10, 11, 12** and **13** (Scheme 2). As will be demonstrated below, **1** and dimethyl sulfoxide form a dimethylmethoxysulfonium salt I (Scheme 3). So, the polar components, the complexes of the sodium salts with dimethyl sulfoxide **6a,b,d** and the sodium salts **7a,b** and **13** themselves might be formed by cation exchange of the salts of type I due to the high content of sodium ions (about 30%) of the silica gel used. As expected, the salts **6, 7** and **13** are transformed to the cor-



Scheme 1



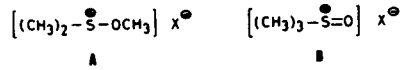
Scheme 2

responding 3-hydroxyisoxazolequinones **8a,b** and **14** by treatment with aqueous hydrochloric acid. They may also be formulated as the corresponding isoxazol-3(1*H*)-onequinones but we have not studied the problem of tautomerism in detail [3]. Structures **8a,b** and **14** were proved by catalytic reductive ring opening. On reoxidation of the intermediate hydroquinone well known 2-amino-3-carboxyquinones are formed. In addition, treatment of **8a,b** and **14** with diazomethane in ether gave mixtures of **1a,b/-4a,b** and **9/11**, respectively.

Reaction Mechanisms.

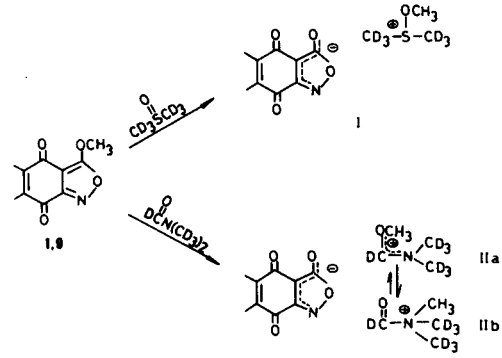
NMR Measurements in Dimethyl Sulfoxide.

Dimethyl sulfoxide can be methylated with methyl iodide and silver nitrate or perchlorate or fluoroborate in a kinetically controlled reaction to give the dimethylmethoxysulfonium salt **A** [4,5]. On the other hand using only methyl iodide and dimethyl sulfoxide the thermodynamically stable trimethylsulfoxonium salt **B** is obtained [6]. Both



salts show different nmr spectra in deuteriodimethyl sulfoxide solution. The resonance signal δ 3.86 in salt **B** (X = I^-) is exchangeable with deuterium oxide [4]. The nmr spectrum of our quinone **1a** in deuteriodimethyl sulfoxide solution showed a singlet at δ 4.4 ppm, which disappeared within three days with the simultaneous formation of a new signal at δ 4.0 ppm. The protons corresponding to this signal were slowly exchanged with deuterium oxide (still incomplete after four weeks), but a rapid exchange was observed with deuteriohydrochloric acid. On addition of hexadeuteriodimethylmethylsulfoxonium iodide (prepared according to [6]) a new signal at δ 3.86 ppm was observed. Its intensity increased within 1-2 days and a simultaneous decrease of the signal δ 4.0 ppm happened. On the other hand we have prepared hexadeuteriodimethylmethoxysulfonium *p*-toluenesulfonate from *p*-toluenesulfonic acid methyl ester and deuteriodimethylsulfoxide [4].

The nmr spectrum of this compound in deuteriodimethyl sulfoxide showed a singlet corresponding to the methoxy group at δ 4.00 ppm besides the signals at δ 2.32 and 7.3 ppm corresponding to the protons of the tosyl moiety. Addition of a solution of this salt in deuteriodimethylsulfoxide to the reaction mixture of **1** in dimethyl sulfoxide provided an increase of the signal at 4.0 ppm. From these results we assume that in the first reaction step of **1** with dimethyl sulfoxide, the sulfoxide was methylated to the dimethylmethoxy sulfonium salt I of type **A** (Scheme 3) which rearranges slowly. Addition of hexadeuteriodimethylmethylsulfoxonium iodide converts it quickly, to the more stable trimethyl sulfoxonium salt of type **B**. Analogous results were obtained in the naphtho series, using **9** as an example.



Scheme 3

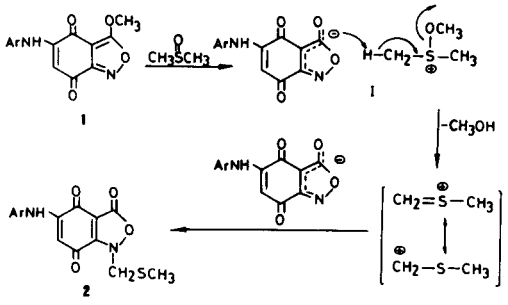
NMR Measurements in Dimethylformamide.

In the same way dimethylformamide was methylated by **1a**. A solution of **1a** in deuteriodimethylformamide showed the nmr signal of the methoxy group at δ 4.53; this signal disappeared within 2-3 days with an increase of a signal at δ 4.49, which was replaced during the reaction by a signal at δ 3.71. The sum of the intensity of all three signals was equivalent to three protons. In accordance with studies on the methylation of dimethylformamide [7,8,9] and combined with nmr measurements [10-14] we assume that primarily from **1a** (δ .453) the *N,N*-dimethyl[d_6]methoxymethylene[d_1]iminium salt IIa (δ 4.49) (Scheme 3) was formed in a kinetically controlled reaction, followed by rearrangement to the thermodynamically more stable *N,N,N*-trimethyl[d_6]-1-oxomethan[d_1]aminium salt IIb (δ 3.71).

5-Arylamino-1-methylthiomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinones **2**.

Methylthiomethyl derivatives **2a,b** were formed from **1a,b** respectively in dimethyl sulfoxide solution in about 1% yield [15,16]. From **1c** and dimethyl sulfoxide **2a** was

obtained. According to the above mentioned nmr studies the salt I is the first product of the reaction of **1** and dimethyl sulfoxide (Scheme 4). The quinonoid anion of this salt might eliminate methanol from the corresponding cation to give a carbonium ion intermediate [15], a reaction which may be favoured in the polar solvent dimethylsulfoxide. The new cation and the quinonoid anion may stabilize themselves leading to the quinone **2**.



Scheme 4

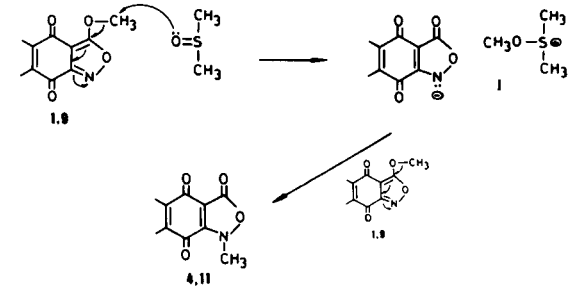
This mechanism is analogous to the Pummerer rearrangement [15], where an alkoxydialkylsulfonium salt rearranges on treatment with bases to give thioalkyl derivatives. Indeed, from the reaction of **1a** and deuteriodimethyl sulfoxide a perdeuteriomethylthiomethyl group was introduced to give the quinone **2d**.

N-Methylisoxazolonequinones **4**, **11**.

Quinones **4** and **11** are products of an intermolecular rearrangement of the methyl group of quinones **1** and **9** in dimethyl sulfoxide. This was proved by a cross experiment, where equimolar amounts of **1b** and **1c** were reacted with dimethyl sulfoxide. We got twelve different quinones which were separated by chromatography and identified by comparing their spectroscopic and chromatographic data:

$$\mathbf{1c} + \mathbf{1b} \xrightarrow{DMSO} \begin{matrix}\mathbf{2b,3b,4b,4e,5b,6b} \\ \mathbf{2a,3c,4a,4c,5c,6a}\end{matrix}$$

Formation of **4a** and **4e** assured the intermolecular rearrangement of the methyl groups. Formation of quinones **4** and in an analogous way **11** is easily understood by the assumption that the quinonoid anion of salt I is methylated by **1** (Scheme 5). One may imagine that the cation of salt I may function as methylating agent. But this possibility was excluded because the yield of **4** did not increase with time. If it were so, we should have isolated only *N*-methyl products and methoxydimethylsulfonium salts would not be detected. From the nmr spectra we saw that this was not the case. Quinones **4** and **11** are formed also in the reaction of **1** and **9** with dimethylformamide.



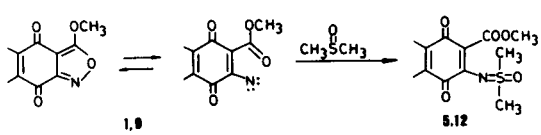
Scheme 5

Sulfoximidoquinones **5**, **12**.

Isoxazolequinones **1** and **9** may be regarded as vinylogous intramolecular stabilized carbonyl nitrenes. Stabilization seems possible by a coordinative binding of the singlet nitrene to the carbonyl oxygen of the methoxy carbonyl group in ortho position. Thereby a change of spin singlet → triplet nitrene seems to be more difficult [17-20].

Arylnitrenes may react as an electrophilic singlet nitrene or as a diradical triplet nitrene [17]; in both states they can be involved in intramolecular reactions. Intramolecular reactions of nitrenes with a carbonyl substituent or with an unsaturated side chain in ortho position respectively, lead to *N*-heterocyclic five ring systems [17,19,20]. On photolysis arylazides, with a carbonyl substituent in ortho position, are stabilized as 2,1-benzisoxazoles [21,22]. Also the reverse process is well known; several *N*-heterocyclic ring systems may be split with the formation of nitrene products [21,23-25].

On the other hand carbonylnitrenes react with sulfoxides to give sulfoximines in about 30% yield [22,26-29]. With sulfides acylsuflimides are obtained [29]. Vice versa sulfoximides and sulfimides yield nitrenes under thermal and photochemical reaction conditions [30]. By the same way **1** and **9** may react, by addition of the singlet nitrene to an unoccupied d-orbital of the sulfur atom to give **5** and **12** (Scheme 6). Following the same mechanism dialkylsulfides and isoxazolequinones **1** and **9** give sulfimidoquinones as reaction products [2].



Scheme 6

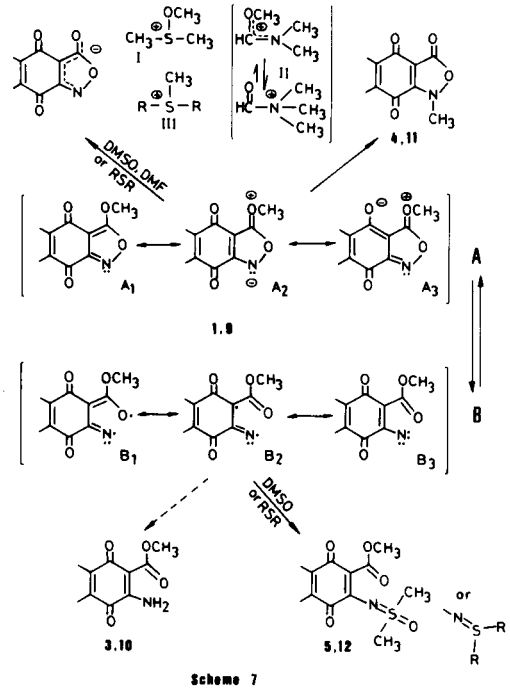
Aminoquinones **3**, **10**.

Aminoquinones **3** and **10** were isolated from the reaction of **1** and dimethylsulfoxide in about 1% yield. The reaction products **3** and **10** probably are impurities accompanying the starting materials **1** and **9**, because these

quinones were prepared from **3** and **10** by oxidative cyclisation using lead tetraacetate [1]. Because of low solubility of compounds **1** in organic solvents and the inability to purify them by chromatography they may contain small amounts of **3**; impurities of 0.5% or less cannot possibly be detected by tlc in this case. If indeed quinones **3** and **10** are reaction products, one has to think of a stabilization of a triplet nitrene by proton abstraction [17].

Reaction Mechanism - Conclusions.

The above described results demonstrate a twofold reactivity of isoxazolequinones **1** and **9**: a) the quinones function as methylating reagents. They methylate dimethyl sulfoxide to give methoxydimethylsulfonium salts I, and in an analogous manner salts II are obtained from dimethylformamide. Methylation of the anion of these salts by **1** and **9** leads to isoxazolonequinones **4** and **11**, while from dialkylsulfides trialkylsulfonium salts III are obtained [2]. This potential may demonstrate an important contribution of structures A_2 and A_3 to the resonance hybrid **A** (Scheme 7); b) Quinones **1** and **9** may react as singlet nitrenes **B**; they may add sulfoxides and sulfides to give sulfoximidoquinones **5** and **12** and sulfimidoquinones [2], respectively.



Scheme 7

One could think of an equilibrium **A** ⇋ **B** influenced by the polarity of the solvent. The methylating potential represented by form **A** may be prevailing in polar solvents like dimethyl sulfoxide; methylation products or their transformation products such as **6** and **13** (50-60% yield) and **4** and **11** (8-15% yield) are isolated in this case in much higher yield than nitrene products **5** and **12** (2-15%).

On the other hand the reaction of the same quinones **1** with dimethyl sulfoxide in an apolar solvent (chloroform) leads to a drastic decrease in yields of the methylation products **6** (0%) and **4** (2%), while nitrene products **5** originating from apolar form **B** are isolated in about 70% yield [2]. It is presumable that yields of methylation products in the naphtho series are higher than those obtained in analogous reactions in the benzo series and consequently yields of nitrene products are lower. This could signify a bigger importance of the polar form **A** in the equilibrium **A** ⇋ **B** in the naphtho series.

EXPERIMENTAL

For melting points, spectroscopic apparatus and analysis please see the preceding paper.

Reaction of 5-Arylamino-3-methoxy[2,1]benzisoxazole-4,7-quinones **1** with Dimethyl Sulfoxide: General Procedure.

A suspension of 1 mmole of **1** in 15 ml of dimethyl sulfoxide was stirred at room temperature in the dark under anhydrous conditions. Within 3 days the orange red colored suspension changed to a red brown solution. It was mixed and shaken with a suspension of 30 g of silica gel (Woelm, particle size >0.063 mm, desactivated with 10% of water) in chloroform. The mixture was filtered by suction and the silica gel residue was washed with chloroform until the eluent was colorless. The dark red organic extracts were washed with water, dried with magnesium sulfate and evaporated. Chromatography of the residue on silica gel with chloroform/acetone 10:1 as eluent gave 4 products: the corresponding 5-arylamino-1-methylthiomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone **2** from the first red zone; the corresponding 2-amino-5-arylamino-3-carbomethoxy-1,4-benzoquinone **3** are from the second red violet zone; the 5-arylamino-1-methyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone **4** from the third red band, and the corresponding 5-arylamino-3-carbomethoxy-2-dimethylsulfoximido-1,4-benzoquinone **5** from the dark violet main band. The initial silica gel after washing with chloroform was eluted with acetone. On concentration to about 15-20 ml and addition of a few drops of chloroform, red crystals separated after cooling and were dried at 60° in vacuum. The compound was identified as a 2:1 complex of the corresponding 5-arylamino-3-hydroxy[2,1]benzisoxazole-4,7-quinone sodium salt and dimethyl sulfoxide **6** which crystallized without dimethyl sulfoxide from acetone or acetonitrile to give **7**. The quinones **6** also lost the dimethyl sulfoxide on treatment with water.

Reaction of 5-Anilino-3-methoxy[2,1]benzisoxazole-4,7-quinone (**1a**) with Dimethyl Sulfoxide.

The reaction of 890 mg (3.3 mmoles) of **1a** and 45 ml of dimethyl sulfoxide gave the following products:

5-Anilinomethylthiomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**2a**).

Four mg of 72a (0.5%) was obtained as red crystals from ethanol/hexane, mp 165-166°; ir (potassium bromide): 3278 cm^{-1} (NH), 1786 (C=O), 1661 (C=O), 1565, 1535, 1512; uv (ethanol): λ 247 nm (log ε 4.13), 275 sh (3.88), 368 (4.16), 505 (3.54); nmr (deuteriochloroform): δ 2.33 (s, S-CH_3, 3H), 5.56 (s, N-CH_2-S, 2H), 6.13 (s, quinone-H, 1H), 7.15-7.60 (m, aromatic, 5H), 8.15 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 316 (M^+, 7), 298 (M-18, 18), 269 (M-S CH_3, 12), 144 (12), 61 (100); ms: (high resolution) calcd. for $C_{15}H_{12}N_2O_4S$: 316.05177. Found: 316.05175.

2-Amino-5-anilino-3-carbomethoxy-1,4-benzoquinone (**3a**).

About 1 mg of **3a** was obtained as a red powder [31], mp 263° dec (lit [31] mp 263° dec); ir (potassium bromide): 3350 cm^{-1} (NH), 3200 (NH), 1656 (C=O), 1565, 1500; nmr (deuteriodimethyl sulfoxide): δ 3.75 (s, $COOCH_3$, 3H), 5.79 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 8.88, 9.45, 9.58 (broad, exchangeable by deuterium oxide, NH, 3H); ms: 272

(M⁺, 100), 241 (M-OCH_3, 13), 213 (M-$COOCH_3$, 12), 144 (87).

Anal. Calcd. for $C_{14}H_{12}N_4O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.74; H, 4.57; N, 10.20.

5-Anilino-1-methyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**4a**).

Compound **4a** was obtained in 12% yield (108 mg) as dark red crystals from benzene, mp 212° dec (lit [2] mp 212°).

5-Anilino-3-carbomethoxy-2-dimethylsulfoximido-1,4-benzoquinone (**5a**).

Compound **5a** was obtained in 16% yield (189 mg) as black violet crystals from ethyl acetate, mp 200° (lit [2] mp 199-200°).

5-Anilino-3-hydroxy[2,1]benzisoxazole-4,7-quinone, Sodium Salt/Dimethyl Sulfoxide Complex (2:1) (**6a**).

Compound **6a** was obtained in 46% yield (480 mg) as red crystals, dec 220°; ir (potassium bromide): 3270 cm^{-1} (NH), 1719, 1703, 1632, 1587, 1560, 1532, 1509; uv (ethanol): λ 243 nm sh (log ε 4.18), 256 (4.33), 272 sh (4.08), 370 (4.26), 456 sh (3.32); nmr (deuteriodimethylformamide): δ 2.58 (s, $(CH_3)_2SO$, 3H), 5.85 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 8.87 (broad, exchangeable by deuterium oxide, NH, 1H).

Anal. Calcd. for $C_{13}H_7N_2O_4Na \cdot \frac{1}{2}(C_2H_6SO)$: C, 53.00; H, 3.18; N, 8.82; O, 22.69; S, 5.05. Found: C, 52.80; H, 3.24; N, 8.82; O, 22.91; S, 5.06.

5-Anilino-3-hydroxy[2,1]benzisoxazole-4,7-quinone, Sodium Salt (**7a**).

Orange crystals of **7a** were obtained from acetone, mp 237° dec; ir (potassium bromide): 3198 cm^{-1} (NH), 1704, 1686, 1630, 1562, 1508; uv (ethanol): λ 245 nm sh (log ε 4.11), 256 (4.16), 272 sh (4.03), 371 (4.20), 456 sh (3.37); nmr (deuteriodimethylformamide): δ 5.86 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 8.85 (broad, exchangeable by deuterium oxide, NH, 1H).

Anal. Calcd. for $C_{13}H_7N_2O_4Na$: C, 56.13; H, 2.54; N, 10.06. Found: C, 56.32; H, 2.72; N, 10.03.

Reaction of 3-Methoxy-5-*p*-toluidino[2,1]benzisoxazole-4,7-quinone (**1b**) and Dimethyl Sulfoxide.

From 300 mg (1.06 mmoles) of **1b** and 15 ml of dimethyl sulfoxide the following products were isolated:

5-*p*-Toluidino-1-methylthiomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**2b**).

Two mg (0.5%) of **2b** was obtained as a red powder; nmr (deuteriochloroform): δ 2.33 (s, SCH_3, 3H), 2.39 (s, Ar-CH_3, 3H), 5.56 (s, N-CH_2-S, 2H), 6.08 (s, quinone-H, 1H), 7.0-7.3 (m, aromatic, 4H), 8.12 (broad, exchangeable by deuterium oxide, NH, 1H); ms: (high resolution) calcd. for $C_{16}H_{14}N_2O_4S$: 330.06742; found: 330.06740.

2-Amino-3-carbomethoxy-5-*p*-toluidino-1,4-benzoquinone (**3b**).

About 1 mg of **3b** was obtained as red powder, mp 242° dec (lit [1] mp 242-243° dec).

1-Methyl-5-*p*-toluidino[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**4b**).

Compound **4b** was obtained in 10% yield (30 mg) as dark red needles from acetone, mp 217-219° (lit [2] mp 217-219°).

2-Dimethylsulfoximido-3-carbomethoxy-5-*p*-toluidino-1,4-benzoquinone (**5b**).

Compound **5b** was obtained in 16% yield (63 mg) as black violet crystals from ethyl acetate, mp 224° (lit [2] mp 224-225°).

3-Hydroxy-5-*p*-toluidino[2,1]benzisoxazole-4,7-quinone, Sodium Salt/Dimethylsulfoxide Complex (**6b**).

Compound **6b** was obtained in 41% yield (142 mg) as red crystals, mp 215° dec; correct analysis was not available because of a non-stochiometric content of dimethyl sulfoxide.

3-Hydroxy-5-*p*-toluidino[2,1]benzisoxazole-4,7-quinone Sodium Salt (**7b**).

Orange crystals of **7b** were obtained from acetone, mp 238-240° dec; ir (potassium bromide): 3200 cm^{-1} (NH), 1705, 1690, 1629, 1579, 1555, 1512; uv (ethanol): λ 245 nm sh (4.07), 257 (4.12), 272 sh (3.98), 372 (4.11), 455 (3.39); nmr (deuteriodimethylformamide): δ 2.33 (s, Ar-CH_3, 3H), 5.79 (s, quinone-H, 1H), 7.29 (s, aromatic, 4H), 8.8 (broad, exchangeable by deuterium oxide, NH, 1H).

Anal. Calcd. for $C_{14}H_9N_2O_4Na$: C, 57.54; H, 3.10; N, 9.59. Found: C, 57.28; H, 3.21; N, 9.50.

Reaction of 5-Anilino-3-deuteriomethoxy[2,1]benzisoxazole-4,7-quinone (**1c**) and Dimethyl Sulfoxide.

From the reaction of 300 mg (1.1 mmoles) of **1c** and 15 ml of dimethyl sulfoxide the following products were isolated: a) 2 mg (0.5%) of **2a**; b) about 1 mg of 2-amino-5-anilino-3-deuteriomethoxy-1,4-benzoquinone (**3c**), mp 260° (lit [1] mp 261°); c) 43 mg (14%) of 5-anilino-1-deuteriomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**4c**) as dark red crystals from benzene, mp 210-212° dec; ir (potassium bromide): 3200 cm^{-1} (NH), 1785, 1774 (C=O), 1656, 1619, 1589, 1550; uv (ethanol): λ 247 nm (log ε 4.11), 273 sh (3.88), 361 (4.15), 492 (3.45); nmr (deuteriochloroform): δ 6.13 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 8.19 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 273 (M⁺, 40), 144 (100); d) 5-anilino-3-deuteriocarbomethoxy-2-dimethylsulfoximido-1,4-benzoquinone (**5c**) 61 mg (16%) as dark violet crystals from ethylacetate, mp 200-201°; ir (potassium bromide): 3244 cm^{-1} (NH), 1924, 1708, 1631, 1607, 1588, 1514; uv (ethanol): λ 249 nm (log ε 4.15), 359 (4.27), 530 (3.20); nmr (deuteriochloroform): δ 3.39 (s, $SOCH_3$, 6H), 6.02 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H); 7.78 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 351 (M⁺, 16), 317 (M-OCD_3, 6), 144 (100); e) 144 mg (41%) of **6a** as red crystals.

Reaction of 5-Anilino-3-methoxy[2,1]benzisoxazole-4,7-quinone (**1a**) and Deuteriodimethyl Sulfoxide.

From the reaction of 200 mg (0.74 mmole) of **1a** and 10 ml of deuteriodimethyl sulfoxide the following products were obtained: a) about 1 mg (0.5%) of 5-anilino-1-deuteriomethylthiodeuteriomethyl[2,1]benzisoxazol-3(1*H*)-one-4,7-quinone (**2d**) as red crystals, mp 165°; ms: 321 (M⁺, 6), 271 (M-SCD_3, 14), 66 (100); b) about 1 mg (0.5%) of **3a**; c) 27 mg (13%) of **4a**; d) 40 mg (15%) of 5-anilino-3-carbomethoxy-2-deuteriodimethylsulfoximido-1,4-benzoquinone (**5d**) as dark violet crystals from ethyl acetate, mp 200°; ir (potassium bromide): 3244 cm^{-1} 1709, 1630, 1609, 1587, 1579, 1510; uv (ethanol): λ 250 nm (log ε 4.17), 359 (4.30), 531 (3.19); nmr (deuteriochloroform): δ 3.89 (s, $COOCH_3$, 3H), 6.02 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 7.8 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 354 (M⁺, 36), 323 (M-OCH_3, 13), 144 (100); *Anal.* Calcd. for $C_{16}H_{10}D_6N_2O_5S$: C, 54.22; H + D, 6.25; N, 7.90. Found: C, 54.41; H + D, 6.09; N, 7.84; e) 95 mg (40%) of 5-anilino-3-hydroxy[2,1]benzisoxazole-4,7-quinone, sodium salt/deuteriodimethyl sulfoxide complex (2:1) (**6d**) as red crystals, dec 220°; ir (potassium bromide): 3270 (NH), 1719, 1703, 1632, 1587, 1560, 1532, 1509; uv (ethanol): λ 243 nm sh (4.18), 256 (4.24), 271 sh (4.11), 370 (4.26), 456 (3.40); nmr (deuteriodimethylformamide): δ 5.85 (s, quinone-H, 1H), 7.1-7.6 (m, aromatic, 5H), 8.86 (broad, exchangeable by deuterium oxide).

Anal. Calcd. for $C_{13}H_7N_2O_4Na \cdot \frac{1}{2}C_2D_6SO$: C, 52.50; H + D, 4.09; N, 8.75. Found: C, 52.30; H + D, 3.87; N, 8.89.

Reaction of 3-Methoxynaphth[2,3-*c*]isoxazole-4,9-quinone (**9**) and Dimethyl Sulfoxide.

From the reaction of 775 mg (3.38 mmoles) of **9** and 25 ml of dimethylsulfoxide and work up according to the general procedure described above for the benzo series the following substances were isolated: a) 13 mg (2%) of 2-amino-3-carbomethoxy-1,4-naphthoquinone **10**, mp 145° (lit [1] mp 145-146°); b) 59 mg (8%) of 1-methylnaphth[2,3-*c*]isoxazol-3(1*H*)-one-4,9-quinone (**11**) as yellow crystals from chloroform/*n*-hexane, mp 194-195° dec; ir (potassium bromide): 1768 cm^{-1}, 1690, 1647, 1560; uv (ethanol): λ 230 nm (log ε 4.29), 270 (4.11), 303 (3.87), 413 (3.41); nmr (deuteriochloroform): δ 4.12 (s, N-CH_3, 3H), 7.6-8.0 (m, aromatic C_6, C_7, 2H), 8.1-8.4 (m, aromatic, C_5, C_8, 2H); ms: 229 (M⁺, 83), 212 (100); *Anal.* Calcd. for $C_{12}H_7NO_4$: C, 62.89; H, 3.08; N, 6.11; Found: C, 62.72; H, 3.13; N, 6.11; c) 17 mg (2%) of 3-carbomethoxy-2-dimethylsulfoximido-1,4-naphthoquinone (**12a**) as yellow crystals from ethanol/*n*-hexane, mp

176-177° (lit [2] 177-178°); d) 485 mg (60%) of 3-hydroxynaphth[2,3-*c*]-isoxazol-4,9-quinone, sodium salt (**13**) as yellow crystals from acetone, mp > 360°, dec, beginning at 250-270° (lit [2] mp > 360°). In this case a stochiometric complex with dimethyl sulfoxide was not obtained.

Reaction of **9** with Deuteriodimethyl Sulfoxide.

According to the general procedure 200 mg (0.87 mmole) of **9** and 6 ml of deuteriodimethyl sulfoxide gave a) 3 mg (1%) of **10**, mp 146° (lit [1] mp 145-146°; b) 12 mg (6%) of **11**; c) 5 mg (2%) of 3-carbomethoxy-2-deuteriodimethylsulfoximido-1,4-naphthoquinone (**12b**) as yellow crystals from ethanol/*n*-hexane, mp 176°; ir (potassium bromide): 1730 cm^{-1}, 1675, 1635; nmr (deuteriochloroform): δ 3.92 (s, $COOCH_3$, 3H), 7.5-8.3 (m, aromatic, 4H); ms: 313 (M^+, 24), 84 (100); *Anal.* Calcd. for $C_{14}H_7D_6NO_5S$: C, 53.66; H, 6.11; N, 4.47; Found: C, 53.84; H, 6.34; N, 4.31; and c) 121 mg (58%) of **13**.

Reaction of 5-Anilino-3-methoxy[2,1]benzisoxazole-4,7-quinone (**1a**) with Dimethylformamide.

Following the general procedure described above for the reactions of **1** with dimethyl sulfoxide, starting from 210 mg (0.78 mmole) of **1a** and 10 ml of dimethylformamide within 4-5 days the following products were obtained: a) 8 mg (4%) of **4a**, mp 212° (lit [2] mp 212°); b) 109 mg (50%) of **7a**.

Reaction of 3-Methoxynaphth[2,3-*c*]isoxazole-4,9-quinones (**9**) with Dimethylformamide.

By the same method, from 100 mg (0.44 mmole) of **9** and 5 ml of dimethylformamide were obtained: a) 2 mg (2%) of **11** and b) 48 mg (46%) of **13**.

5-Anilino-3-hydroxy[2,1]benzisoxazole-4,7-quinone (**8a**).

To a stirred solution of 250 mg of 0.79 mmole of **7a**, in 60 ml of water, 1.5 ml of 12 *N* hydrochloric acid was slowly added at room temperature. After 1 hour the brown red crystalline precipitate was collected, washed with a small amount of water and dried. The quinone, mp 199-202° dec, 146 mg (70%) contained half a molecule of water. Recrystallization from dimethylformamide-ether, followed by drying at 80° in high vacuum, gave dark brown crystals, mp 184-185° dec; ir (potassium bromide): 3120 cm^{-1} (NH), 3200-2000, 1700, 1615, 1584, 1548; uv (ethanol): λ 244 nm sh (4.14), 258 (4.20), 271 sh (4.06), 372 (4.24), 456 sh (3.38); nmr (deuteriodimethylformamide): δ 5.72 (s, exchangeable by deuterium oxide, quinone-H, 1H), 7.0 (broad, exchangeable by deuterium oxide, NH, 1H), 7.7-7.1 (m, aromatic, 5H), 9.2 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 258 (M + 2, 22), 256 (M^+, 3), 212 (M-44, 100), 144 (94).

Anal. Calcd. for $C_{13}H_8N_2O_4 \cdot \frac{1}{2}H_2O$: C, 58.87; H, 3.42; N, 10.56. Found: C, 59.12; H, 3.17; N, 10.49.

Anal. Calcd. for $C_{13}H_8N_2O_4$: C, 60.94; H, 3.15; N, 10.93. Found: C, 60.83; H, 3.16; N, 10.93.

Reaction of a solution of **8a** in methanol with diazomethane in ether gave a 1:3 mixture of **1a** and **4a**. Hydrogenation of **8a**, followed by air reoxidation of the intermediate hydroquinone gave (84% yield) of 2-amino-5-anilino-3-carboxy-1,4-benzoquinone, mp 245° [32].

3-Hydroxy-5-*p*-toluidino[2,1]benzisoxazole-4,7-quinone (**8b**).

By the same procedure as above, starting from **7b**, **8b** was obtained in 76% yield, giving on recrystallization from dimethylformamide-ether brown crystals, mp 185° dec; ir (potassium bromide): 3070 cm^{-1} (NH), 3200-2000, 1770, 1745, 1645, 1606, 1585, 1550, 1530; uv (ethanol): λ 245 nm sh (log ε 4.11), 256 (4.16), 271 sh (4.02), 372 (4.12), 453 sh (3.40); nmr (deuteriodimethylformamide): δ 2.34 (s, CH_3-Ar, 3H), 5.84 (s, exchangeable by deuterium oxide, quinone-H, 1H), 7.3 (broad, exchangeable by deuterium oxide, NH, 1H), 7.31 (s, aromatic, 4H), 9.1 (broad, exchangeable by deuterium oxide, NH, 1H); ms: 272 (M + 2, 38), 226 (M-44, 100), 158 (80).

Anal. Calcd. for $C_{14}H_{10}N_2O_4$: C, 62.22; H, 3.73; N, 10.37. Found: C, 61.98; H, 3.92; N, 10.18.

3-Hydroxynaphth[2,3-c]isoxazole-4,9-quinone (**14**).

To a solution of 150 mg (0.63 mmole) of **12** in 40 ml of water, 3 ml of 12 *N* hydrochloric acid was added. Within a few days 102 mg (72%) of yellow needles separated and were filtered by suction. The product, mp 202-203° dec, contained half a molecule of water. Recrystallization from dimethylformamide/ether and drying at 80° under high vacuum gave yellow crystals, mp 178-180° dec; ir (potassium bromide): 3200-2000 cm^{-1}, 1735, 1690, 1582, 1543, 1527; uv (ethanol): λ 235 nm (log ε 4.34), 287 (4.15), 430 (3.49); nmr (deuteriodimethylformamide): δ 7.3 (broad, exchangeable by deuterium oxide, NH, 1H), 7.5-8.3 (m, aromatic, 4H); m s: 217 (M + 2, 5), 215 (M^+, 67), 173 (M-42, 12), 104 (66).

Anal. Calcd. for $C_{11}H_5NO_4 \cdot \frac{1}{2}H_2O$: C, 58.94; H, 2.70; N, 6.25; O, 32.12. Found: C, 58.73; H, 2.74; N, 6.29; O, 31.84.

Anal. Calcd. for $C_{11}H_5NO_4$: C, 61.40; H, 2.35; N, 6.51. Found: C, 61.26; H, 2.44; N, 6.71.

Reaction of a solution of **14** in methanol with diazomethane in ether gave a mixture of **9** and **11**.

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