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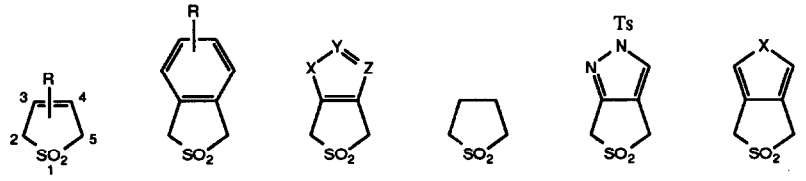
Generation and Chemical Reactions of Quinoxalino-*o*-quinodimethane

Ta-shue Chou* and Chung-Wen Ko

Institute of Chemistry, Academia Sinica, Taipei, Taiwan and
Department of Chemistry, National Taiwan University, Taipei, Taiwan, R.O.C.

Abstract: We have prepared the unsubstituted quinoxalino-3-sulfolene **7** *via* two convenient routes and discovered its unusual stability toward thermal extrusion of SO_2. The generation of the *o*-quinodimethane **14** from **7** was achieved at temperatures higher than 290 °C.

Substituted 3-sulfolenes **1** are excellent precursors for 1,3-butadienes.[1] Extrusion of SO_2 from 3-sulfolenes usually occurs at temperatures at 100-120 °C. Benzo-3-sulfolenes **2**[2] and many heteroaromatic-fused 3-sulfolenes **3**[3] also lose SO_2 upon thermolysis, usually at 160-200 °C, to yield the corresponding *o*-quinodimethanes. Higher temperatures are required for two reasons: (1) the aromaticity is destroyed during SO_2 extrusion; (2) there is partial single bond character between C_3-C_4 of these fused 3-sulfolenes due to resonance hybridization. Sulfolane **4** in which there is a pure single bond between C_3-C_4 is fragmented to ethylene and SO_2 at even higher temperatures (>500 °C).[4] Comparison of these temperatures reveals that, in a five-membered sulfone system, the more single bond character between C_3-C_4 is, the higher temperature would be required to extrude SO_2. In fact, thermolytic removal of SO_2 from fused 3-sulfolenes **5**[3f] and **6**[5], which have high degree of single bond character between C_3-C_4, have not been successful. Compounds **6** prefer to undergo Diels-Alder reactions on the heteroaromatic ring under thermal conditions.

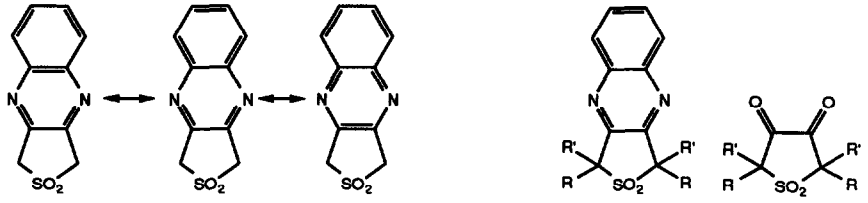


1 **2** **3** **4** **5** **6**

X= O, S, NR; Y= Z= CH
or X= O, NR; Y= N; Z= CH
or X= O, S; Y= CH; Z= N

X= O, NR

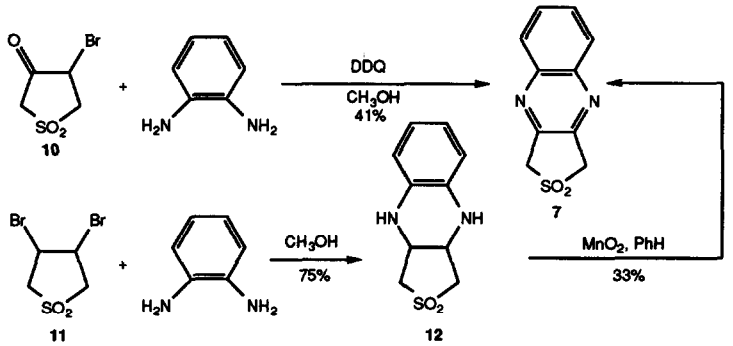
In continuation of our efforts in the study of heteroaromatic *o*-quinodimethanes,[6] we were interested in quinoxalino-3-sulfolene **7** because of its special structural feature. The real structure of **7** should be represented by the hybrid of the forms **7A**, **7B** and **7C**. Forms **7A** and **7B** should have more contribution to the real structure because they keep the more aromatic benzene ring, whereas **7C** does not. The bridging bond between the quinoxaline ring and the 3-sulfolene ring of **7** should have more single bond character than the bridging bond in compound **2**. We thus predicted that thermolytic removal of SO_2 from **7** should require high temperature.



7A 7B 7C 8 9

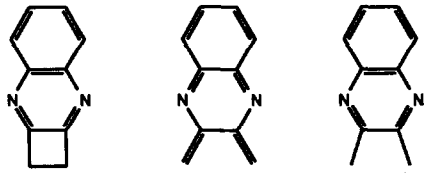
Compound **7** is so far unknown although several of its derivatives **8**, which contain at least two aromatic substituents at the α– and α'-positions of the sulfone group, have been studied.[7] These derivatives are successfully prepared by the condensation of substituted 3,4-sulfolanediones **9** with *o*-phenylenediamine. However, all of our efforts toward the preparation of the parent sulfolanedione[7] (**8**, R=R'=H) using above mentioned strategy were unsuccessful. We therefore prepared **7** *via* a procedure involving the reaction of α-bromoketone **10**[3d] and phenylenediamine in the presence of DDQ. Alternatively, **7** was prepared from 3,4-dibromosulfolane **11**[8] and phenylenediamine *via* the tetrahydro-quinoxaline derivative **12** (Scheme I).

Scheme I



10 7 11 12

The thermal stability of **7** was found to be remarkable. Heating a toluene solution of **9** at 230 °C in a sealed tube for 6 h with or without a dienophile present resulted in no reaction. Compound **7** started to decompose when the temperature was raised up to 290 °C. Thermolysis of a toluene solution of **7** with methyl acrylate at 290 °C in a sealed tube for 2 h gave a complex mixture which contained neither starting material nor cycloadduct. On the other hand, flash pyrolysis of **7** in benzene at 500 °C followed by addition of an excess of *N*-phenylmaleimide to the pyrolysate at -78 °C gave mainly polymerization product. Compound **13** was obtained in low yield (10%), but no Diels-Alder adduct was observed. The formation of **13** indicates that **14** should have been a transient intermediate. The ease of polymerization must be due to the high reactivity of **14**. The extrusion of SO_2 from compound **7** could proceed *via* either a concerted cheletropic reaction or a stepwise homolytic carbon-sulfur bond cleavage mechanism. At this stage, we are unable to differentiate these two possibilities.

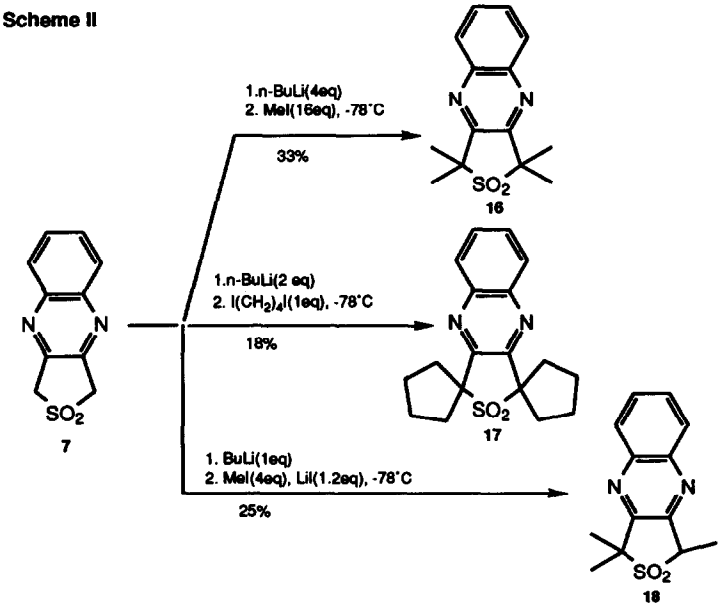


13 14 15

Thermolysis of **7** at 290 °C in the presence of PhSH gave 2,3-dimethylquinoxaline **15** in 47% yield. No 1,4-adduct nor cyclobutene **13** was observed. Similar results were obtained when thermolysis of **7** was performed in the presence of norbornene (15%) or norbornadiene (66%). Compound **15** should be derived from the *o*-quinodimethane **14** or the cyclobutene **13** by a hydrogen abstraction process. Indeed, compound **15** was obtained when **13** was heated in toluene at 290 °C. To examine the hydrogen source for the formation of **15**, **7** was thermolyzed as a solution in d_8-toluene at 290 °C in a sealed tube. The product **15** thus obtained (10%) was totally free of deuterium. This suggests that the solvent toluene does not act as the hydrogen source. Other than PhSH, and norbornadiene, Bu_3SnH was found to be a good hydrogen source so that thermolysis of **7** in the presence of Bu_3SnH (2 equiv) gave **15** in better yield (50%).

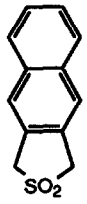
Similar to other fused 3-sulfolenes, compound **7** underwent smooth deprotonation/alkylation reactions[1] in relatively lower yields. Tetraalkylated and trimethylated derivative **16**, **17** and **18** were obtained when **7** was treated with excess of *n*-BuLi and alkyl iodide. When MeI was used in insufficient amount, the mono- and dimethylated products were obtained as evidenced by NMR analysis but could not be separated. The dissatisfactory results of these methylation reactions might be due to *N*-substitution and salt formation.[9]

Scheme II



In summary, we have prepared for the first time the unsubstituted quinoxalino-3-sulfolene **7**. Its structural feature where the bridging bond has partial single bond character causes the thermal extrusion of SO_2 to be difficult so that temperatures higher than 290 °C are required. This observation is consistent with

the report that extrusion of SO_2 from naphthaleno-3-sulfolene **19**[10] takes place at 300 °C. The formation of **13** and **15** from the thermolysis of **7** indicates the transient intermediacy of the so far unknown quinoxalino-*o*-quinodimethane **14**.



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Experimental Section

Preparation of Quinoxalino-3-sulfolene 7.

method A A mixture of 4-bromo-3-sulfolanone **10** (0.41 g, 1.92 mmol), *o*-phenylenediamine (2.06 g, 19.0 mmol), and dichlorodicyanoquinone (DDQ, 1.54 g, 6.81 mmol) in anhydrous MeOH (30 ml) was heated under reflux for 8 hr. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (aluminum oxide, hexane/EtOAc, 2:1) to give **7**; yield: 0.17 g (41%).

method B A mixture of 3,4-dibromosulfolane **11** (10.99 g, 39.5 mmol) and *o*-phenylenediamine (42.61 g, 395 mmol) in anhydrous MeOH (100 ml) was stirred at room temperature for 32 hr. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure. The crude product was washed with CH_2Cl_2 (3 x 40 ml) to remove the excess of phenylenediamine and was then recrystallized (EtOAc/hexane) to give **12** (6.65 g, 75%). Compound **12** was heated with MnO_2 (20 eq) in benzene under reflux for 3 days. The solvent was removed under reduced pressure and the product was purified by column chromatography (aluminum oxide, hexane/EtOAc, 2:1) to give **7**; yield: 2.16 g (33%).

1,3-Dihydrothieno[3,4-*b*]- 1,2,3,4-tetrahydroquinoxaline 2,2-Dioxide 12: light brown solid: mp 203-205 °C; IR (KBr) 3340, 3332, 3246, 2883, 1284, 1122, 1092, 1034 cm^{-1}; ^1H NMR δ 3.26 (dd, 2H, J=13.2, 5.2 Hz), 3.36 (dd, 2H, J=13.2, 5.4 Hz), 3.73-4.02 (m, 2H), 4.24 (t, 2H, J=4.7 Hz), 6.56-6.63 (m, 2H), 6.66-6.73 (m, 2H); MS *m/z* 224 (M^+), 159, 145 (100%), 132, 119, 104, 92, 77, 65; Anal. Calcd. for $C_{10}H_{12}N_2O_2S$: C, 53.55; H, 5.39; N, 12.49. Found: C, 53.53; H, 5.57; N, 12.01.

Quinoxalino-3-sulfolene 7: pale yellow solid: mp 228-230 °C; IR (KBr) 3060, 2992, 2930, 1307, 1222, 1116, 1107 cm^{-1}; ^1H NMR δ 4.73 (s, 4H), 7.87-7.83 (m, 2H), 8.09-8.12 (m, 2H); MS *m/z* 220 (M^+), 156 (100%), 129, 103, 89, 76; Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.54; H, 3.66; N, 12.73. Found: C, 54.63; H, 3.69; N, 12.41.

Quinoxalino-[2,3,*c*]-cyclobutene 13 A solution of the quinoxalino-3-sulfolene **7** (0.062 g, 0.28 mmol) in dry toluene (8 ml) was pyrolyzed at 500 °C in a vertical hot tube. The pyrolysate was concentrated and purified by HPLC (Hexane/EtOAc, 2:1) to give **13** as a white crystal; yield: 0.0076 g (17%). mp 90-91 °C; IR (KBr) 2935, 1505, 1401, 1352, 1286, 1131, 1097 cm^{-1}; ^1H NMR δ 3.58 (s, 4H), 7.65-7.69 (m, 2H), 8.04-8.08 (m, 2H); MS *m/z* 156 (M^+, 100%), 129, 103, 76.

2,3-Dimethylquinoxaline 15 A solution of quinoxalino-3-sulfolene **7** (0.023 g, 0.1mmol), PhSH (0.2 ml, 2 mmol) in dry toluene (5 ml) in a sealed tube was heated at 290 °C for 1 hr. The crude mixture was

concentrated under reduced pressure and purified by HPLC [Merck Hibar LiChrosorb Si (7μ), Hexane/EtOAc, 2:1] to give compound **15** as a white crystal; yield: 0.0074 g (47%). ^{1}H NMR δ 2.74 (s, 6H), 7.64-7.68 (m, 2H), 7.96-8.00 (m, 2H). The ^{1}H NMR data are identical with those of an authentic sample from Aldrich chemicals.

Alternatively, a solution of the compound **7** (0.032 g, 0.14 mmol), norbornadiene (0.16 ml, 1.48 mmol) in dry toluene (5 ml) in a sealed tube was heated at 290 °C for 3.5 hr. The crude mixture was concentrated under reduced pressure and purified by HPLC (Hexane/EtOAc, 2:1) to give **15**; yield: 0.015 g (66%).

Alternatively, a solution of the compound **7** (0.049 g, 0.22 mmol), Bu_3SnH (0.6 ml, 2.23 mmol) in dry benzene (3 ml) in a sealed tube was heated at 290 °C for 1 hr. The crude mixture was concentrated under reduced pressure and purified by HPLC (Hexane/EtOAc, 2:1) to give **15**; yield: 0.017 g (49%).

1,1,3,3-Tetramethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline 2,2-Dioxide 16 To a solution of the quinoxalino-3-sulfolene **7** (0.13 g, 0.60 mmol) and HMPA (1.7 ml, 9.8 mmol) in THF (8 ml) at -78 °C was slowly added *n*-BuLi (1.7 ml, 2.4 mmol) with stirring and the stirring was continued at -78 °C for 5 min. Methyl iodide (0.6 ml, 9.6 mmol) was added and the reaction mixture was then stirred at -78 °C for 1 hr. Saturated NH_4Cl (5 ml) was added and the layers separated. The aqueous layer was extracted with EtOAc (3 x 20 ml) and the combined organic layers were dried ($MgSO_4$) , concentrated and purified by HPLC (Hexane/EtOAc, 2:1) to give **16** as a white crystal; yield: 0.06 g (33%). mp 190-192 °C; IR (KBr) 2979, 2933, 1353, 1298, 1158, 1093 cm^{-1}; ^{1}H NMR δ 1.84 (s, 12H), 7.78-7.82 (m, 2H), 8.09-8.13 (m, 2H); MS *m/z* 276 (M^+), 212, 197 (100%), 182, 169, 130, 103, 84, 77; Anal. Calcd. for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14. Found: C, 60.67; H, 5.98; N, 9.90.

1,1,3,3-Bis(tetramethylene)-1,3-dihydrothieno[3,4-b]quinoxaline 2,2-Dioxide 17 To a solution of the quinoxalino-3-sulfolene **7** (0.066 g, 0.30 mmol) and HMPA (0.42 ml, 2.4 mmol) in THF (5 ml) at -78 °C was slowly added *n*-BuLi (0.43 ml, 0.6 mmol) with stirring and the stirring was continued at -78 °C for 5 min. Diiodobutane (0.04 ml, 0.3 mmol) was added and the reaction mixture was then stirred at -78 °C for 1 hr. Saturated NH_4Cl (5 ml) was added and the layers separated. The aqueous layer was extracted with EtOAc (3 x 20 ml) and the combined organic layers were dried ($MgSO_4$), concentrated and purified by HPLC (Hexane/EtOAc, 2:1) to give **17** as a white crystal; yield: 0.018 g (18%). mp 134-136 °C; IR (KBr) 2966, 2872, 1293, 1206, 1113 cm^{-1}; ^{1}H NMR δ 2.00-2.13 (m, 8H), 2.23-2.32 (m, 4H), 2.74-2.83 (m, 4H), 7.74-7.78 (m, 2H), 8.05-8.09 (m, 2H); MS *m/z* 328 (M^+), 287, 276, 262, 212, 197 (100%), 183, 169, 130, 103, 91, 77; Anal. Calcd. for $C_{18}H_{20}N_2O_2S$: C, 65.83; H, 6.14; N, 8.54. Found: C, 65.52; H, 5.95; N, 8.15.

1,1,3-Trimethyl-1,3-dihydrothieno[3,4-*b*]quinoxaline 2,2-Dioxide 18 To a solution of the quinoxalino-3-sulfolene **7** (0.066 g, 0.25 mmol), LiI (0.04 g, 0.30 mmol) and HMPA (0.15 ml, 0.86 mmol) in THF (5 ml) at -78 °C was slowly added n-BuLi (0.17 ml, 0.24 mmol) with stirring and the stirring was continued at -78 °C for 5 min. Methyl iodide (0.06 ml, 0.96 mmol) was added and the reaction mixture was then stirred at -78 °C for 1 hr. Saturated NH_4Cl (5 ml) was added and the layers separated. The aqueous layer was extracted with with EtOAc (3 x 20 ml) and the combined organic layers were dried ($MgSO_4$), concentrated and purified by HPLC (Hexane/EtOAc, 2:1) to give **18** as a white crystal; yield: 0.016 g (25%). mp 157-159 °C; IR (KBr) 2982, 2912, 1358, 1303, 1158, 1108, 1092 cm^{-1}; ^{1}H NMR δ 1.78 (s, 3H), 1.86 (s, 3H), 1.91 (d, 3H, J=7.0 Hz), 4.54 (q, 1H, J=7.0 Hz), 7.79-7.82 (m, 2H), 8.09-8.13 (m, 2H); MS *m/z* 262 (M^+), 198 (100%), 183, 169, 157, 143, 130, 103, 84, 77; Anal. Calcd. for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.69. Found: C, 59.42; H, 5.43; N, 10.32.

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