Quinoxalino-fused sulfinides and their application in Diels–Alder reactions

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The synthesis of 7,8-disubstituted quinoxalino[2,3-d]-[1,2,3]oxathiine 2-oxides 7a–c, precursors for quinoxalino-o-quinodimethanes 3a–c, and their application in the Diels–Alder reactions are reported.

The chemistry of heterocyclic o-quinodimethanes has attracted a great deal of attention recently. Various methods for generating these highly reactive dienes have been developed. Quinoxalines are important naturally occurring heterocycles among them, cheletropic elimination of SO2 from heteroaromatic-fused 3-sulfolene has drawn the most attention. Various methods for generating these highly reactive dienes have been developed. Finding an easy, high-yield method for generating quinoxalino-o-quinodimethanes is of particular interest.

Although Chou et al. reported generating quinoxalino-o-quinodimethanes 3a using SO2 extrusion of the quinoxalino-fused sulfolene 4, all their attempts to isolate the Diels–Alder adducts failed. Recently we described the generation of nonclassical heteroaromatic o-quinodimethanes 5 by thermal extrusion of SO2 from corresponding sulfinides 6. A significant advantage of using sulfinides is that their thermolysis occurs at a much lower temperature than that of corresponding sulfolenes. We report here our work on the synthesis of quinoxalino-fused sulfinides 7a–c and their applications in Diels–Alder reactions with alkenes and alkynes.

Previously unknown sulfinides 7a–c were synthesized in two steps with good yields as shown in Scheme 1. Reaction of the appropriate o-diamino-substituted benzene 8 with 1,4-dibromomobutane-2,3-dione 9 gave the known 2,3-bis(bromomethyl)quinoxaline 10a. and 6,7-dichloroquinoxaline 10b,c. The desired quinoxalino-fused sulfinides 7a–c and by-products 11 were obtained by the use of Rongalite® (sodium formaldehyde sulfoxylate) with the corresponding dibromides 10a–c. Although the yields of sulfinides 7a–c were only ca. 30%, fortunately the by-product 11 can be converted back to dibromide 10 via N-bromosuccinimide bromination, which makes the syntheses of the sulfinides more efficient.

The Diels–Alder reactions of quinoxalino-fused sulfinides 7a–c with several dienophiles are presented in Scheme 2. When heated in toluene (200 °C, sealed tube) in the presence of 3 equiv. of diethyl fumarate (EF) or dimethyl fumarate (MF), the sulfinides 7a–c all underwent extrusion of SO2 and the resulting quinoxalino-o-quinodimethanes 3a–c were intercepted as the 1:1 adducts (12 and 13) in 69–89% yield. The reactions with dimethyl acetylenedicarboxylate (DMAD) went similarly to 1:1 adducts and after loss of H2 gave 14a–c in 35–94% yield.

In the absence of a dienophile, sulfinide 7a underwent thermal extrusion of SO2 and the cyclobuta[1,2-b]quinoxaline 15a almost quantitatively. In contrast, 15a was reported to be isolated only in low yield (10%) when the corresponding sulfolene 4 was flash pyrolysed at 500 °C followed by addition of excess N-phenylmaleimide (NPM). Thermolysis of 7a in the presence of methanol or cyclohexa-1,4-diene, on the other hand, gave 2,3-dimethylquinoxaline 11a in 89–99% yield.

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estingly, Diels–Alder adducts (such as 12–14a) were also formed in excellent yield when the cyclobutene 15a was heated in the presence of dienophiles at 200 °C, indicating that cyclobutene 15a is also a good precursor of o-quinodimethane 3a.

The reaction of 7a–c with excess NPM at 200 °C gave a pair of new adducts 16 and 17 in 47–68% yields (Scheme 3). These 2:1 adducts showed similar spectral characteristics, consistent with the cis and trans cyclooctaquinoxalines 16 and 17. When only 1 equiv. of NPM was used, the yield of 1:1 adduct 18b was optimized to 72% and the 2:1 adducts (16 and 17) were present in only trace amounts. Similar observation of these 2:1 adducts was reported when sulfolene was heated with sodium iodide in the presence of NPM, even though this method is generally assumed to give a synthetic equivalent of o-quinodimethane. 10

Thus our results, obtained by pyrolysing 7,8-disubstituted quinoxalino-fused sulfoxides 7a–c strongly support the formation of quinoxalino-o-quinodimethanes 3a–c, which differ from the products formed when sulfolene 4 is pyrolysed, or when 10a and sodium iodide react. The easily synthesized sultines 7a–c reacted under milder conditions (200 °C) than the corresponding sulfoxide 4 (≥290 °C) is required) and their reaction products were different in many cases. When generated in the presence of a dienophile, sulfoxides 7a–c provided elegant synthons for the formation of [4 + 2] cycloadducts. If no trapping agents were used, the sulfoxides gave cyclobutyl[1,2-b]quinoloxine 15 almost quantitatively, which again is a good precursor of o-quinodimethanes 3. Further work to study the mechanism by laser flash photolysis is in progress.

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References


