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REACTIONS OF DIAZOMETHANE WITH SULFONYL-ACTIVATED DOUBLE BONDS

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Abstract—The cyclo-addition reaction of diazomethane with α,β-unsaturated sulfones is described. Divinyl sulfone and phenyl vinyl sulfone give 1- or 2-pyrazolines depending on the reaction conditions. cis- and trans-1,2-Bis(methylsulfonyl)ethene form pyrazolines, which on reaction with either triethylamine or excess of diazomethane lead to substituted pyrazoles.

The addition of diazomethane to double bonds activated by electron-withdrawing substituents such as carbonyl, nitro and nitrile is a well-documented route to substituted pyrazolines.1 However, the addition of diazomethane to α,β-unsaturated sulfones is scarcely mentioned. Parham et al.2 reported the formation of two types of pyrazolines from α,β-unsaturated sulfones and diazomethane viz a normal addition product in which the C atom of the diazomethane is attached to the β-C of the vinyl sulfone and an abnormal product with the diazocarbon attached to the α-C of the unsaturated system. It is generally accepted1 that the initial reaction products of diazomethane with activated double bonds are 1-pyrazolines, which however, may undergo a facile prototropic rearrangement to the corresponding 2-pyrazolines during crystallization, by gently warming or by a trace of acid or base.1a Backer et al.3 reported that treatment of thiophene-1,1-dioxides with excess of diazomethane gave rise to addition of diazomethane to only one double bond of the thiophene-1,1-dioxides.

We investigated the reaction of divinyl sulfone (1)—an open chain analogue of the thiophene-1,1-dioxides—with diazomethane under similar conditions and we found that instead of one, both double bonds of 1 reacted smoothly.

Treatment of divinyl sulfone (1) with a basefree ethereal solution of diazomethane gave the 1-pyrazoline 2 as a mixture of the meso and dl form in yields up to 90%. In the presence of a trace of triethylamine the 2-pyrazoline 3 was obtained in 76% yield. Heating of 2 in acetonitrile in the presence of a little of triethylamine gave a quantitative rearrangement to 3 (Scheme 1).

The structure of 3 was established by a correct elemental analysis, a NH absorption at 3340 cm⁻¹ in the IR spectrum and an A₂B₂ pattern for the protons at C₄ and C₅ in the NMR spectrum. The structure of 2 (meso + dl) was evident from the elemental analysis, the NMR spectrum which showed four multiplets in the intensity ratio of 1:1:4:4 and the absence of a NH IR absorption. Careful crystallization of the reaction product 2 gave one of the isomers (either meso or dl) as a pure substance. Its NMR showed three multiplets in the intensity ratio of 1:2:2. Heating of this pure isomer gave a quantitative tautomerization to bis-2-pyrazoline 3.

Parham et al.2 studied the addition of diazomethane to sulfones of the type R¹—SO₂—CH=CHR². With R² being aryl, they found normal as well as abnormal addition products. With R² being H or alkyl, only normal addition took place. The position of the double bond with respect to the substituent in the isolated 2-pyrazolines was not established.2 Since we were able to isolate a 1-pyrazoline from the (normal) addition reaction of diazomethane to 1 and since we could adjudge the position of the double bond in the corresponding 2-pyrazoline 3, we decided to reinvestigate one of Parham’s sulfones. We found that the addition of diazomethane
to phenyl vinyl sulfone produced a 1-pyrazoline (4). However, when the reaction was carried out in the presence of a trace of base, we isolated just as Parham et al.2 did, a 2-pyrazoline (5), erroneously denoted as 6 by these authors.

Having studied so far the addition of diazomethane to a double bond linked with one sulfonyl group (phenyl vinyl sulfone) and a sulfone connected with two double bonds (divinyl sulfone, 1) the series was completed by investigating the behaviour of a double bond flanked by two sulfonyl functions, e.g. cis-1,2-bis (methylsulfonyl)-ethene (7)* (Scheme 2).

*When this work was carried out Meek and Fowler published their results on the reaction of diazomethane with cis-1,2-bis(p-tolylsulfonyl) ethene (compare 7). When the reaction was stopped as soon as the starting alkene was dissolved 3-p-tolylsulfonylpyrazole (compare 10) was isolated in 17% yield. Leaving overnight cis-1,2-bis(p-tolylsulfonyl) ethene with excess of diazomethane resulted in a mixture from which 1-methyl-5-methylsulfonylpyrazole (11) and the isomer with m.p. 77-78° to be 1-methyl-3-methylsulfonylpyrazole (12) – see Scheme 2. In order to gain more insight in the reaction of 7 with excess of diazomethane, it was treated with one equivalent of diazomethane solution was decolorized immediately and the adduct 9 precipitated nearly quantitatively and analytically pure. The IR† of 9 showed a NH absorption at 3370 cm⁻¹ and was identical to the IR spectrum of the product obtained by treatment of trans-1,2-bis(methylsulfonyl) ethene (13) with one equivalent of diazomethane. The reaction of 7 with one equivalent of diazomethane and one equivalent of triethylamine gave pyrazole 10 in 94% yield. The NMR spectrum of 10 showed two doublets for the ring protons, characteristic for 3-substituted pyrazoles.

The reaction sequence depicted in Scheme 2 is a likely explanation for the product formation from 7 in the presence of excess of diazomethane.

The alternative that sulfonic acid elimination from 8 takes place prior to the prototropic shift must be discarded because of the great ease by which the tautomerization to the 2-pyrazoline 9 takes place. Further evidence for the proposed mechanism is the nearly equal ratios of the quantities of 11 and 12 formed by the reaction of cis-1,2-bis(methylsulfonyl) ethene (7), trans-1,2-bis(methylsulfonyl)-

Scheme 2
ethene (13) and 3-methylsulfonylpyrazole (10) with diazomethane under identical conditions. As a third possibility can be envisaged N-methylation of the 2-pyrazoline 9 with subsequent elimination of sulfinic acid. In that case one would expect only 1-methyl-3-methylsulfonylpyrazole (12). However, pyrazole 12 was isolated in a much lower yield than its isomer 11.

In strong contrast to the stability of pyrazoline 9 are unsuccessful attempts described recently by Witiak and Sinha to isolate or detect intermediate 1- or 2-pyrazolines in the reaction of cis- and trans-β-chloroacrylates with diazomethane.

**EXPERIMENTAL**

M.ps are uncorrected. Microanalyses were performed by the analytical department of our laboratory under supervision of Mr. W. M. Hazenberg. NMR spectra were determined on a Varian A-60 spectrometer, using TMS as internal standard. IR spectra were taken on an Unicam SP 200.

**Di(1-pyrazolin-3-yl)sulfone (2).** To a soln of 820 mg (6.9 mmole) of 1 in 50 ml ether was added at 0° 24 ml 0.4 M ethereal CH₂N₂. After 18 hr at 0°, 2 was filtered off and washed with ether, yield, 800 mg (58%). Two crystallizations from CH₃Cl₂-ether-pentane gave 600 mg of an equimolar mixture of both diastereomers 2. NMR (CDCl₃): δ 6-44 (m, 1 H on Cα), δ 5-93 (m, 1 H on Cα), δ 4-80 (m, 4 H on Cβ) and δ 8-13 (m, 4 H on Cα); IR: no NH absorption. (Found: C, 35-69; H, 5-06; N, 27-72; S, 15-87. Calc. for C₁₃H₁₄N₂O₂S: C, 35-63; H, 4-98; N, 27-71; S, 15-85%). After 4 crystallizations one diastereomer 2 was obtained pure; NMR (CDCl₃): δ 5-93 (m, 1 H on Cα), δ 4-80 (m, 2 H on Cα) and δ 2-13 (m, 2 H on Cα); IR: no NH absorption, m.p. 99-103°. (Found: C, 35-45; H, 4-99; N, 27-79; S, 15-83%). Analytically pure 2 (one diastereomer) heated for 15 min in MeCN in the presence of Et₃N gave a complete rearrangement to 3 as was evident from the NMR spectrum.

**Di(2-pyrazolin-3-yl)sulfone (3).** To a soln of 1773 mg (15-0 mmole) of 1 in 150 ml ether was added at 0° 60 ml of 1 M CH₃N₂ in ether and 200 mg NaOH. After 18 hr at -5° the mixture was filtered giving 2300 mg (76%) of 3. Two crystallizations from CH₃Cl₂-ether-pentane afforded analytically pure product, m.p. 101-5-103-5° (dec). (Found: C, 35-78; H, 5-14; N, 27-58; S, 15-88. Calc. for C₁₃H₁₄N₂O₂S: C, 35-63; H, 4-98; N, 27-71; S, 15-85%). NMR (CDCl₃): δ 6-48 (s, 0-8 H, N-H) and δ 3-40 (A₂B₂ pattern, 2 H on Cα and 2 H on Cβ); IR: 3330 cm⁻¹ (NH). 3-Phenylsulfonyl-1-pyrazoline (4). To 840 mg (5 mmole) phenyl vinyl sulfone in 20 ml dry ether was added at 0° 35 ml 0-4 M ethereal CH₂N₂. After 48 hr at -20° 790 mg (75%) of 4 was filtered off. Two crystallizations from CH₃Cl₂-ether-pentane afforded analytically pure 4, m.p. 79-82° (dec). (Found: C, 51-15; H, 4-90; N, 13-06; S, 15-20. Calc. for C₁₄H₁₂N₂O₂S: C, 51-41; H, 4-79; N, 13-35; S, 15-25%). NMR (CDCl₃): δ 7-75 (m, 5 H), δ 5-75 (m, 1 H on Cα), δ 4-57 (m, 2 H on Cα) and δ 2-05 (m, 2 H on Cβ); IR: no NH absorption. 3-Phenylsulfonyl-2-pyrazoline (5). To 840 mg (5 mmole) phenyl vinyl sulfone in 20 ml dry ether was added at 0° 20 ml 0-4 M ethereal CH₂N₂ and 30 mg Et₃N. After 48 hr at -20° 885 mg (85%) of 5 was isolated by filtration. After 3 crystallizations from EtOH-pentane 5 was obtained analytically pure, m.p. 95-5-97°. (Found: C, 51-44; H, 4-90; N, 13-04; S, 15-24. Calc. for C₁₄H₁₂N₂O₂S: C, 51-41; H, 4-79; N, 13-33; S, 15-25%). NMR (CDCl₃): δ 7-75 (m, 5 H), δ 6-30 (broad s, NH) and δ 3-30 (A₂B₂ pattern, 4 H); IR: 3380 cm⁻¹ (NH). The reaction of cis- resp. trans-1,2-bis(methylsulfonyl)ethene and 10 with CH₂N₂ under identical conditions. To 92 mg of 7 in 5 ml CH₃Cl₂ was added at 0° 15 ml of 0-4 M CH₂N₂ in ether. After standing for 1 week at 5° volatile components were removed on a vacuum evaporator, giving a nearly colourless oil. The NMR spectrum showed 11 and 12 to be present in the ratio of 3:4:1, and in addition some minor impurities. The same procedure was applied to 13. The ratio of 11 and 12 was found to be...
4:7:1. When 35 mg of 10 in 5 ml CH₂Cl₂ was treated with 15 ml 0·45 M CH₃N₂ the ratio of 11 and 12 amounted to 4:5:1.

REFERENCES

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