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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 tautomeration 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 sulphone 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.

\[
\begin{array}{ccc}
 \text{PhSO}_2 & \text{PhSO}_2 & \text{HN} \\
 \text{N} & \text{N} & \text{N}
\end{array}
\]

Having studied so far the addition of diazo-methane to a double bond linked with one sulfonyl group (phenyl vinyl sulphone) and a sulphone connected with two double bonds (divinyl sulphone, 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-3(5)-p-tolylsulfonylpyrazole (compare 11 and 12) could be isolated in 57% yield. Product formation is rationalized by Meek and Fowler assuming sulfmate elimination from the intermediate 1-pyrazoline (compare 8). (J. S. Meek and J. S. Fowler, J. Org. Chem. 33, 985 (1968)).

+A good NMR spectrum of 9 could not be obtained; 9 was only sparingly soluble in chloroform and carbon tetrachloride, reacted with acetone and decomposed in polar solvents like dimethyl sulfoxide, water and trifluoroacetic acid.

The reaction of 7 with excess of diazomethane afforded two isomeric 1-methyl-methylsulfonylpyrazoles (m.p. 66°-5°-67.5°, 67% and m.p. 77°-78°, 18%). The NMR spectra of these isomers differed only slightly (Experimental). The chemical shifts and coupling constants were compared with the literature data for the isomer identification of pyrazoles. On basis hereof the compound with m.p. 66°-5°-67.5° was shown to be 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. The added 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 sulfinic acid elimination from 8 takes place prior to the prototropic shift must be discarded because of the great ease by which the tautomeration 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)-

\[
\begin{array}{ccc}
 \text{MeSO}_2 & \text{SO}_2\text{Me} & \text{CH}_2\text{N}_2 \\
 \text{7} & \text{8} & \text{9}
\end{array}
\]

\[
\begin{array}{ccc}
 \text{HN} & \text{SO}_2\text{Me} & \text{Me} \\
 \text{10} & \text{11} & \text{12}
\end{array}
\]
ethene (13) and 3-methylsulfonylpyrazole (10) with diazomethane under identical conditions. As a third possibility can be envisaged N-methylation of the 2-pyrazolines 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 pyrazole 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 CH₂Cl₂. Immediate decolorization of the first part of the CH₂Cl₂ soln and formation of a white ppt indicated a fast reaction. After 18 hr at 0°, 2 was filtered off and washed with ether, yield, 800 mg (58%). Two crystallizations from CH₂Cl₂-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 Cα) and δ 8-2-13 (m, 4 H on Cα); IR: no NH absorption. (Found: C, 35-78; H, 5-14; N, 4-91; S, 25-52. Calc. for C₁₀H₁₀N₂O₂S: C, 31-70; H, 4-91; N, 4-91; S, 25-52%). IR: no NH absorption. Compound 12 was also obtained analytically pure by 2 crystallizations from ether, m.p. 66-5-67-5° (Found: C, 37-34; H, 4-86; S, 15-02%). NMR (CDCl₃): δ 7-51 (d, 1 H, J 2.5 c/s, 1 H, J 2.5 c/s, δ 4-16 (s, 3 H, N-Me) and δ 3-17 (s, 3 H, S0₂Me); IR: no NH absorption. Compound 12 was also obtained analytically pure by 2 crystallizations from ether, m.p. 66-5-67-5° (Found: C, 37-34; H, 4-86; S, 15-02%). NMR (CDCl₃): δ 7-48 (d, 1 H, J 2-5 c/s, δ 6-75 (d, 1 H, J 2-5 c/s, δ 4-00 (s, 3 H, N-Me) and δ 3-17 (s, 3 H, S0₂Me); IR: no NH absorption.

**2,3-Di(methylsulfonyl)-2-pyrazoline** (9). To 736 mg (4 mmole) of 7 in 20 ml CH₂Cl₂ and 20 ml ether was added at 0° 6 ml 0-5 M CH₃N₂ in ether. After cooling to -30° 810 mg (90%) of 9 could be filtered off. Washing with CH₂Cl₂ ether and pentane gave analytically pure product, m.p. 101-5-103-5°. (Found: C, 37-48; H, 5-03; N, 17-49; S, 20-02%). Calc. for C₁₀H₁₀N₂O₂S: C, 37-48; H, 5-03; N, 17-49; S, 20-02%. Conversion of 4 into 5. 420 mg of 4 and 3 mg of Et₃N in 50 ml ether were kept at 5° for 4 hr. After cooling to -20° filtration of the mixture gave 320 mg of 5 identified by IR (NH absorption at 3380 cm⁻¹ and m.p. (94-97°). 1-Methyl-5-methylsulfonylpyrazole (11) and 1-methyl-3-methylsulfonylpyrazole (12). To 920 mg (5 mmole) of 7 in 10 ml CH₂Cl₂ and 30 ml dioxane was added 100 ml 0-5 M etheral CH₃N₂. After standing for 1 week at 5° the CH₃N₂ had disappeared. Solvents were removed under diminished pressure. The resulting oil was chromatographed over Al₂O₃ (activity II-III, neutral, benzene-ether), yield, 540 mg (67%) of 11, and 147 mg (18%) of 12. Pyrazole 11 was obtained analytically pure by 2 crystallizations from ether, m.p. 66-5-67-5° (Found: C, 37-93; H, 5-08; N, 17-44; S, 20-13). Calc. for C₁₀H₁₀N₂O₂S: C, 37-84; H, 5-03; N, 17-49; S, 20-02%. NMR (CDCl₃): δ 7-51 (d, 1 H, J 2 c/s), δ 6-85 (d, 1 H, J 2 c/s), δ 4-16 (s, 3 H, N-Me) and δ 3-17 (s, 3 H, S0₂Me); IR: no NH absorption. Compound 12 was also obtained analytically pure by 2 crystallizations from ether, m.p. 77-78° (Found: C, 37-34; H, 4-86; S, 15-02%). NMR (CDCl₃): δ 7-48 (d, 1 H, J 2-5 c/s, δ 6-75 (d, 1 H, J 2-5 c/s, δ 4-00 (s, 3 H, N-Me) and δ 3-17 (s, 3 H, S0₂Me); IR: no NH absorption (3370 cm⁻¹). An attempt to obtain 9 analytically pure by crystallization from acetone (5x) failed since 9 reacted with acetone. The elemental analysis of the new product (m.p. 131-5-135°, dec), was in agreement with a structure of a compound formed by condensation of 2 mole of 9 with 1 mole of acetone. (Found: C, 32-15; H, 4-98; N, 11-29; S, 25-52. Calc. for C₁₀H₈N₄O₂S: C, 31-70; H, 4-91; N, 11-37; S, 26-04%). IR: no NH absorption.

3-Methylsulfonylpyrazole (10). To 920 mg (5 mmole) of 7 in 10 ml dioxane was added at 0° 10 ml 0-5 M CH₃N₂ in ether and 600 mg Et₃N. After standing for 48 hr at 5° the solvents were evaporated under diminished pressure. The resulting oil was chromatographed (silica gel, EtOAc) giving 685 mg (94%) of 10. Two crystallizations from EtOAc gave analytically pure product, m.p. 99-103°. (Found: C, 32-84; H, 4-15; N, 19-36; S, 22-08. Calc. for C₁₀H₁₀N₂O₂S: C, 32-86; H, 4-14; N, 19-17; S, 21-94%). NMR (CDCl₃): δ 7-90 (d, 1 H, J 2-5 c/s, δ 6-83 (d, 1 H, J 2-5 c/s) and δ 3-15 (s, 3 H); IR 3340 cm⁻¹ (NH). The reaction of cis- resp. trans-2,1-bis(methylsulfonyl)-ethene and 10 with CH₃N₂ under identical conditions. To 92 mg of 7 in 5 ml CH₂Cl₂ was added at 0° 15 ml of 0-5 M CH₃N₂ 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.

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