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REATIONS OF DIAZOMETHANE WITH SULFONYL-ACTIVATED DOUBLE BONDS

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(Received in UK 4 December 1972; Accepted for publication 8 January 1973)

Abstract—The cyclo-addition reaction of diazomethane with \( \alpha,\beta \)-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 carboxyl, nitro and nitrile is a well-documented route to substituted pyrazolines.\(^1\) However, the addition of diazomethane to \( \alpha,\beta \)-unsaturated sulfones is scarcely mentioned. Parham et al.\(^2\) reported the formation of two types of pyrazolines from \( \alpha,\beta \)-unsaturated sulfones and diazomethane viz a normal addition product in which the C atom of the diazomethane is attached to the \( \beta \)-C of the vinyl sulfone and an abnormal product with the diazocarbon attached to the \( \alpha \)-C of the unsaturated system. It is generally accepted\(^1\) 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.\(^1\) 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 \( A_2B_2 \) pattern for the protons at C\(_4\) and C\(_5\) 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 R\(^1\)—SO\(_2\)—CH\(=\)CHR\(^2\). With R\(^2\) being aryl, they found normal as well as abnormal addition products. With R\(^2\) 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.\textsuperscript{2} did, a 2-pyrazoline (5), erroneously denoted as 6 by these authors.

\[
\begin{array}{c}
\text{PhSO}_2 \quad \text{PhSO}_2 \\
\text{H} \quad \text{N} \\
\end{array}
\]

\[
\begin{array}{c}
\text{PhSO}_2 \quad \text{PhSO}_2 \\
\text{H} \quad \text{N'} \\
\end{array}
\]

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-3-(5)-p-tolylsulfonylpyrazole (compare 11 and 12) could be isolated in 57% yield. Product formation is rationalized by Meek and Fowler assuming sulfamate 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\textsuperscript{4} 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\textsuperscript{†} of 9 showed a NH absorption at 3370 cm\textsuperscript{-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)-
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\textsuperscript{a} to isolate or detect intermediate 1- or 2-pyrazolines in the reaction of cis- and trans-\( \beta \)-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 CH\(_2\)Cl\(_2\) (m, 2 H on C4); IR: no NH absorption. Compound 2 was obtained pure; NMR (CDCl\(_3\)):
- \( \delta 7.51\) (d, 1 H, J 2 cm\(^{-1}\)),
- \( \delta 8.40\) (broad s, NH) and
- \( \delta 2.05\) (m, 2 H on C2); IR: no NH absorption.

**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 1 M CH\(_2\)Cl\(_2\) in ether. Immediate decolorization of the first part of the CH\(_2\)Cl\(_2\) 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 CH\(_2\)Cl\(_2\)-ether-pentane gave analytically pure 4, m.p. 101-5-103-5° (15-0 mmole) of 1 in 50 ml ether was added at 0° 20 ml 0.4 M ethereal CH\(_2\)N\(_2\) and 30 ml ether was added 100 ml 0.5 M ethereal CH\(_3\)N\(_2\). After standing for 1 week at 5° the CH\(_3\)N\(_2\) had disappeared. Solvents were removed under diminished pressure. The resulting oil was chromatographed over Al\(_2\)O\(_3\) (activity II-II, 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, 20-02%). NMR (CDCl\(_3\)):
- \( \delta 7.51\) (d, 1 H, J 2 cm\(^{-1}\)),
- \( \delta 8.65\) (d, 1 H, J 2 cm\(^{-1}\)),
- \( \delta 4.16\) (s, 3 H, N-Me) and
- \( \delta 3.17\) (s, 3 H, SO\(_2\)-Me); 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, 28-35%). NMR (CDCl\(_3\)):
- \( \delta 7.48\) (d, 1 H, J 2-5 cm\(^{-1}\)),
- \( \delta 6.75\) (d, 1 H, J 2-5 cm\(^{-1}\)),
- \( \delta 4.00\) (s, 3 H, N-Me) and
- \( \delta 3.17\) (s, 3 H, SO\(_2\)-Me); IR: no NH absorption.

3,4-Di(methylsulfonyl)-2-pyrazoline (9). To 736 mg (4 mmole) of 7 in 20 ml CH\(_2\)Cl\(_2\) and 20 ml ether was added at 0° 8 ml 0-5 M CH\(_3\)N\(_2\) in ether. After cooling to -20° 810 mg (90%) of 5 could be filtered off. Washing with CH\(_2\)Cl\(_2\) ether and pentane gave analytically pure 4, m.p. 130-133° (dec). (Found: C, 37-34; H, 4-86; S, 28-35%). The IR showed a NH absorption (3370 cm\(^{-1}\)). An attempt to obtain 9 analytically pure by recrystallization 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 C\(_9\)H\(_8\)N\(_4\)O\(_2\): 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 dioxide was added at 0° 10 ml 0-5 M CH\(_2\)N\(_2\) in ether and 600 mg Et\(_3\)N. After standing for 48 hr at 0° the solvents were evaporated under diminished pressure. The resulting oil was chromatographed (silica gel, EtOAc) giving 685 mg (94%) of 10. Two crystallizations from EtOH gave analytically pure product, m.p. 99-103°. (Found: C, 32-84; H, 4-15; N, 19-36; S, 22-08. Calc. for C\(_9\)H\(_8\)N\(_4\)O\(_2\): C, 32-86; H, 4-14; N, 19-17; S, 21-94%); NMR (CDCl\(_3\)):
- \( \delta 7.90\) (d, 1 H, J 2-5 cm\(^{-1}\)),
- \( \delta 8.63\) (d, 1 H, J 2-5 cm\(^{-1}\)) and
- \( \delta 3.15\) (s, 3 H); IR 3340 cm\(^{-1}\) (NH).

The reaction of cis- and trans-1,2-bis(methylsulfonyl)-ethene and 10 with CH\(_3\)N\(_2\) under identical conditions. To 92 mg of 7 in 5 ml CH\(_2\)Cl\(_2\) was added at 0° 15 ml of 0-5 M CH\(_3\)N\(_2\) 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 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 C\(_9\)H\(_8\)N\(_4\)O\(_2\): C, 51-41; H, 4-79; N, 13-33; S, 15-25%); NMR (CDCl\(_3\)):
- \( \delta 7.75\) (m, 5 H),
- \( \delta 5.75\) (m, 1 H on C3),
- \( \delta 4.57\) (m, 2 H on C4) and
- \( \delta 2.05\) (m, 2 H on C2); IR: no NH absorption.

3-Phenylsulfonyl-1-pyrazoline (4). To 840 mg (5 mmole) phenyl vinyl sulfone\textsuperscript{e} in 20 ml dry ether was added at 0° 35 ml 0-4 M ethereal CH\(_2\)N\(_2\). After 48 hr at -20° 790 mg (75%) of 4 was filtered off. Two crystallizations from CH\(_2\)Cl\(_2\)-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 C\(_9\)H\(_8\)N\(_4\)O\(_2\): C, 51-41; H, 4-79; N, 13-35; S, 15-25%); NMR (CDCl\(_3\)):
- \( \delta 7.75\) (m, 5 H),
- \( \delta 5.75\) (m, 1 H on C3),
- \( \delta 4.57\) (m, 2 H on C4) and
- \( \delta 2.05\) (m, 2 H on C2); IR: no NH absorption.

3-Phenylsulfonyl-2-pyrazoline (5). To 840 mg (5 mmole) phenyl vinyl sulfone\textsuperscript{e} in 20 ml dry ether was added at 0° 20 ml 0-4 M ethereal CH\(_2\)N\(_2\) and 30 mg Et\(_3\)N. After 48 hr
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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