REACTIONS OF DIAZOMETHANE WITH SULFONYL-ACTIVATED DOUBLE BONDS

R. HELDER, T. DOORNBOS, J. STRATING AND B. ZWANENBURG

Department of Organic Chemistry, The University, Zernikelaan, Groningen, The Netherlands

(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 carbonyl, 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\(_2\)B\(_2\) 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 tautomeration 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.\(^4\) 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. did, a 2-pyrazoline (5), erroneously denoted as 6 by these authors.

Having studied so far the addition of diazo-methane 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 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-methylsulfonyl-pyrazoles (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 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 sulfonic 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- 

\[ \text{DNA} \rightarrow \text{RNA} \]

\[ \text{beta-S} \] 

chloroacetates 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 (75%) of 4 was filtered off. Two crystallizations from 20 ml dry ether and 20 ml ether was added at 0° 24 ml (dec). (Found: C, 35-78; H, 5-14; N, 27-58; S, 15-88%). NMR (CDCl₃): \( \delta 7-75 \) (m, 5 H), \( \delta 6-30 \) (broad s, NH) and \( \delta 3-30 \) (A₂B₂ pattern, 4 H); IR: 3380 cm⁻¹ (NH).

**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 ethereal CH₂N₂. After standing for 1 week at 5° the CH₂N₂ 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 C₈H₇NO₄S₉: C, 37-88; H, 4-98; N, 17-83; S, 20-22%). NMR (CDCl₃): \( \delta 7-71 \) (J 2-5 c/s), \( \delta 8-65 \) d, 1 H, J 2 c/s), \( \delta 4-16 \) (s, 3, H, N-Me) and \( \delta 3-17 \) (s, 3, H, S-O₂Me); 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; N, 17-57; S, 20-22%); NMR (CDCl₃): \( \delta 7-48 \) (d, 1 H, J 2 c/s), \( \delta 6-75 \) (d, 1 H, J 2 c/s), \( \delta 4-00 \) (s, 3 H, N-Me) and \( \delta 3-17 \) (s, 3, H, S-O₂Me); IR: no NH absorption.

3,4-Di(methylsulfonyl)-2-pyrazoline (9). To 736 mg (4 mmole) of 7 in 20 ml CH₂Cl₂ and 20 ml ether was added at 0° 8 ml 0-5 M CH₂N₂ in ether. After cooling to -20° 810 mg (90%) of 9 could be filtered off. Washing with CH₂Cl₂ ether and pentane gave analytically pure 9, m.p. 130-133° (dec). (Found: C, 32-84; H, 4-15; N, 19-36; S, 22-08. Calc. for C₇H₁₁NO₄S₉: C, 32-84; H, 4-15; N, 19-36; S, 22-08%); NMR (CDCl₃): \( \delta 4-91 \) (s, 3 H, N-Me) and \( \delta 3-17 \) (s, 3, H, S-O₂Me).

**Reactions of diazomethane with sulfonyl-activated double bonds**. In strong contrast to the stability of pyrazoline 9 with subsequent elimination of sulfonic 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.

The reaction of 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.
When 35 mg of 10 in 5 ml CH₂Cl₂ was treated with 15 ml 0.45 M CH₂N₂, the ratio of 11 and 12 amounted to 4.5:1.

REFERENCES

1. Houben-Weyl, Methoden der organischen Chemie (Vierte Auflage) Stickstoffverbindungen 1, Teil 4, p. 804 e.f. (1968);
5. L. G. Tensmeyer and C. Ainsworth, J. Org. Chem. 31, 1878 (1966);