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).

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 $R^1\text{—SO}_2\text{—CH=CHR}^2$. 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

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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-3(5)-*p*-tolylsulfonylpyrazole (compare 11 and 12) could be isolated in 57% yield. Product formation is rationalized by Meek and Fowler assuming sulfinate 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 data⁴ 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 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 Sinha⁵ 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 1 M CH_2N_2 in ether. Immediate decolorization of the first part of the CH_2N_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_2Cl_2 -ether-pentane gave 600 mg of an equimolar mixture of both diastereomers 2. NMR (CDCl_3): δ 6.44 (m, 1 H on C_3), δ 5.93 (m, 1 H on C_3), δ 4.80 (m, 4 H on C_5) and δ 2.13 (m, 4 H on C_4); IR: no NH absorption. (Found: C, 35.69; H, 5.00; N, 27.72; S, 15.87. Calc. for $\text{C}_6\text{H}_{10}\text{N}_4\text{O}_2\text{S}$: C, 35.63; H, 4.98; N, 27.71; S, 15.85%). After 4 crystallizations one diastereomer 2 was obtained pure; NMR (CDCl_3): δ 5.93 (m, 1 H on C_3), δ 4.80 (m, 2 H on C_5) and δ 2.13 (m, 2 H on C_4); IR: no NH absorption, m.p. 99–104° (dec). (Found: C, 35.43; H, 4.99; N, 27.79; S, 15.83%). Analytically pure 2 (one diastereomer) heated for 15 min in MeCN in the presence of Et_3N 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 1 M CH_2N_2 in ether and 200 mg NaOH. After 18 hr at –5° the mixture was filtered giving 2300 mg (76%) of 3. Two crystallizations from CH_2Cl_2 -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 $\text{C}_6\text{H}_{10}\text{N}_4\text{O}_2\text{S}$: C, 35.63; H, 4.98; N, 27.71; S, 15.85%); NMR (CDCl_3): δ 6.48 (s, 0.8 H, NH) and δ 3.40 (A_2B_2 pattern, 2 H on C_4 and 2 H on C_5); IR: 3330 cm^{-1} (NH).

3-Phenylsulfonyl-1-pyrazoline (4). To 840 mg (5 mmole) phenyl vinyl sulfone² in 20 ml dry ether was added at 0° 35 ml 0.4 M ethereal CH_2N_2 . After 48 hr at –20° 790 mg (75%) of 4 was filtered off. Two crystallizations from CH_2Cl_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 $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_2\text{S}$: C, 51.41; H, 4.79; N, 13.35; S, 15.25%); NMR (CDCl_3): δ 7.75 (m, 5 H), δ 5.75 (m, 1 H on C_3), δ 4.57 (m, 2 H on C_5) and δ 2.05 (m, 2 H on C_4); IR: no NH absorption.

3-Phenylsulfonyl-2-pyrazoline (5). To 840 mg (5 mmole) phenyl vinyl sulfone² in 20 ml dry ether was added at 0° 20 ml 0.4 M ethereal CH_2N_2 and 30 mg Et_3N . 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 $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_2\text{S}$: C, 51.41; H, 4.79; N, 13.33; S, 15.25%); NMR (CDCl_3): δ 7.75 (m, 5 H), δ 6.30 (broad s, NH) and δ 3.30 (A_2B_2 pattern, 4 H); IR: 3380 cm^{-1} (NH).

Conversion of 4 into 5. 420 mg of 4 and 3 mg of Et_3N in 50 ml ether were kept at 5° for 48 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 CH_2Cl_2 and 30 ml dioxane was added 100 ml 0.5 M ethereal CH_2N_2 . After standing for 1 week at 5° the CH_2N_2 had disappeared. Solvents were removed under diminished pressure. The resulting oil was chromatographed over Al_2O_3 (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 $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_2\text{S}$: C, 37.48; H, 5.03; N, 17.49; S, 20.02%); NMR (CDCl_3): 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, $\text{SO}_2\text{-Me}$); 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; N, 17.57; S, 20.22%); NMR (CDCl_3): 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, $\text{SO}_2\text{-Me}$); IR: no NH absorption.

3,4-Di(methylsulfonyl)-2-pyrazoline (9). To 736 mg (4 mmole) of 7 in 20 ml CH_2Cl_2 and 20 ml ether was added at 0° 8 ml 0.5 M CH_2N_2 in ether. After cooling to –20° 810 mg (90%) of 9 could be filtered off. Washing with CH_2Cl_2 , ether and pentane gave analytically pure 9, m.p. 130–133° (dec). (Found: C, 26.50; H, 4.45; N, 12.27; S, 28.06. Calc. for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_4\text{S}_2$: C, 26.54; H, 4.45; N, 12.38; S, 28.35%). The IR showed a 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 $\text{C}_{12}\text{H}_{14}\text{N}_4\text{O}_6\text{S}_4$: 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 CH_2N_2 in ether and 600 mg Et_3N . 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 EtOH gave analytically pure product, m.p. 99–103°. Found: C, 32.84; H, 4.15; N, 19.36; S, 22.08. Calc. for $\text{C}_4\text{H}_6\text{N}_2\text{O}_2\text{S}$: C, 32.86; H, 4.14; N, 19.17; S, 21.94%); NMR (CDCl_3): 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*-1,2-bis(methylsulfonyl)-ethene and 10 with CH_2N_2 under identical conditions. To 92 mg of 7 in 5 ml CH_2Cl_2 was added at 0° 15 ml of 0.45 M CH_2N_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

4·7:1. When 35 mg of **10** in 5 ml CH_2Cl_2 was treated with 15 ml 0·45 M CH_2N_2 the ratio of **11** and **12** amounted to 4·5:1.

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