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Short Communications

N''-Sulfonylformamidrazones, Methylation, Tosylation, Hydrolysis and Reaction with Amines

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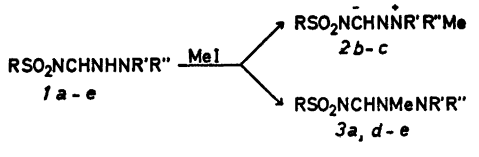
In connection with our interest in sulfonylformamidrazones [1] we have investigated the chemical reactivity of *N''*-sulfonylformamidrazones by their reactions with methyl iodide, tosyl chloride, amines and aqueous acid and base.

The methylation of benzamidrazones has been investigated by Smith [2,3] who found that ylides ($RC(\bar{N}-R')N\dot{N}^+(R'')_3$) were not formed on direct methylation, whereas they recently have been prepared in another reaction sequence.[4] *N',N'*-Dimethyl-*p*-toluenesulfonohydrazide has, however, been reported to give *N,N,N*-trimethylated ylides on direct methylation with methyl iodide.[5] Amidrazones undergo hydrolysis on prolonged heating with acid or base,[2,3] and are reported to form new amidrazones on reaction with amines.[6] Tosylation of formamidrazones has not been described.

Results. Methylation of *N''*-sulfonylformamidrazones was carried out by reflux in excess methyl iodide without solvent or with benzene, toluene or ethanol as solvent. Subsequently the product was triturated with aqueous base and the methylated product was extracted from the mixture by means of dichloromethane giving yields of *2* from 70 to 80 % and of *3* from 12 to 50 %.



Scheme 1. Compound *a*, R = R' = R'' = Me; *b*, R = Ph, R' = R'' = Me; *c*, R = *p*-MeC_6H_4, R' = R'' = Me; *d*, R = R' = Ph, R'' = Me; *e*, R = *p*-MeC_6H_4, R' = Ph, R'' = Me.

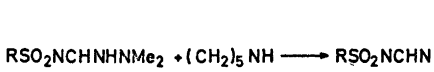
For compound *1b* methylation was also carried out with methyl iodide and sodium ethoxide in benzene and in ethanol solution giving the same products as found without ethoxide. This is different from observations with methylation of benzhydrazides where the solvent polarity influenced the position of methylation.[9] Compound *1a* could only be methylated with the use of sodium ethoxide. As shown in Scheme 1, the products formed depend on the *N*-substituents [2,3] and the RSO_2-moiety. Thus for compounds *1b* and *1c* only the ylides *2b* and *2c* were isolated, while for the amidrazones with an *N*-phenyl substituent and for *1a* only compounds *3* were isolated.

The ylides *2* are colourless crystalline compounds. The IR, NMR and mass spectral data (given in the experimental part) are in accordance with the proposed structure. Both the ^1H and ^{13}C NMR spectra show only one signal for the $-N^+(Me)_3$ group, deshielded compared to the $N(Me)_2$ signal in the amidrazones (*1b*, *1c*),[1] and an upfield shift of the *CH*=N signal. The IR spectrum of *2c* showed absorptions at 3019 and 2964 cm^{-1} characteristic for the stretching vibrations in an *N*-trimethylammonium group.[7,8] The SO_2-stretching vibrations show no particular changes from those of compound *1c*. The change in IR absorption from *N*-(3-pyridyl)-sulfonamides to 1-sulfonyliminopyridinium ylides has been ascribed to delocalization of the ylide nitrogen lone pair into the sulfonyl group.[10] The absence of such changes for compounds *2* can be explained by the fact that the negative charge may be spread over a greater part of the molecule in *2* than in the sulfonylimides.

Hydrolysis experiments. Compounds *1b* and *1c* were treated with 1 M HCl and 1 M NaOH at room temperature. The treatment with base resulted in recovery of the starting material when hydrolysed overnight, while hydrolysis for 4 days resulted in formation of sulfonamide and recovery of *ca.* 70 % of the starting material. Acid hydrolysis for one night resulted in almost quantitative formation of sulfonamide. These results are analogous to those found for benzamidrazones [2] which, however, often required prolonged heating.

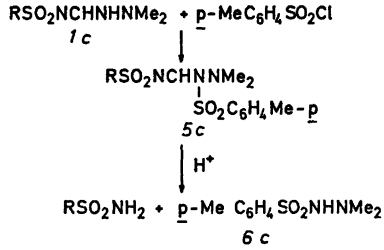
Other reactions. The *N''*-sulfonylformamidrazones *1b* and *1c* were treated with *p*-toluenesulfonamide, *p*-toluenesulfonohydrazide, anilinium chloride and aniline by reflux for several days in benzene or toluene solution, but only starting materials and some decomposition products were isolated.

Treatment of *1c* with piperidine by reflux for two days in benzene resulted in formation of the sulfonylformamidine *4c* in 94 % yield. For *1b* reflux for 4 days with piperidine resulted in formation of benzenesulfonamide and the sulfonylformamidine *4b*.



Scheme 2.

Tosylation of *1c* was carried out by stirring equimolar amounts of tosyl chloride, *1c* and excess triethylamine in toluene solution for 2 days, which resulted in formation of the ditosylated product *5c* in a yield of 25 %. The structure of *5c* was confirmed by the spectral data and by hydrolytic degradation which formed *p*-toluenesulfonamide and 1,1-dimethyl-2-*p*-toluenesulfonyl hydrazine *6c*.



Scheme 3.

Experimental. The instrumental equipment is the same as reported earlier.[1]

Methylation of N²,N²-*dimethylformohydrazide methylsulfonylimide* 1a. Sodium (0.019 mol) was dissolved in absolute ethanol (10 ml); *1a* (0.019 mol) and methyl iodide (0.038 mol) were added and the mixture refluxed for 4 days The precipitate was filtered off and recrystallized from ethanol giving an iodide salt, m.p. 189–190 °C, yield 1.7 g. ^{13}C NMR (DMSO-d_6): δ 153.8, 56.2, 40.0, 31.1 data which probably correspond to an impure iodide salt of dimethylated *1a*. Attempts to isolate an ylide by addition of base and subsequent extraction with CH_2Cl_2, resulted in decomposition of the compound. The mother liquor from the reaction mixture was evaporated, extracted with CH_2Cl_2, giving 15 % yield of *3a*, identified by IR and NMR spectra identical with those of the authentic compound.[1]

Methylation of N²,N²-*dimethylformohydrazide phenylsulfonylimide* 1b. Methyl iodide (30 ml) and *1b* (0.017 mol) were refluxed for 2 days. The precipitate was filtered off and treated with 25 % NaOH. The basic layer was extracted with CH_2Cl_2, the CH_2Cl_2-layer was dried over K_2CO_3, filtered and evaporated to dryness. Yield 70 % of N-*trimethylammonio*-N′-*phenylsulfonylformamidinate* 2b m.p. 136 °C (from ethanol). Anal. $C_{10}H_{15}N_3O_2S$: C, H, N, S. MS *m/e* (% of base peak): 241(4)M⁺, 184(1), 141(3), 84(2), 77(18), 59(50), 58(100), 51(10), 43(6), 42(7). ^{1}H NMR ($CDCl_3$): δ 7.2–7.8 (6 H, m), 3.37 (9 H, s).

Methylation of N²,N²-*dimethylformohydrazide 4-methylphenylsulfonylimide* 1c. Methylation was carried out analogous to *1b*. Yield 80 % of N-*trimethylammonio*-N′-*4-methylphenylsulfonylformamidinate* 2c, m.p. 158 °C (from ethanol). Anal. $C_{11}H_{17}N_3O_2S$: C, H, N, S. MS *m/e* (% of base peak): 255(6)M⁺, 92(4), 91(36), 89(3), 84(4), 65(15), 59(98), 58(100), 57(6), 44(5), 43(16), 42(19). ^{1}H NMR (DMSO-d_6): δ 7.67 (1 H, s), 7.3–7.8 (4 H, m), 3.40 (9 H, s), 2.40 (3 H, s). ^{13}C NMR (DMSO-d_6): δ 155.7, 142.4, 140.6, 129.1, 125.3, 54.2, 20.8. IR (KBr, cm^{-1}): 3056w, 3045w, 3020w, 2925w, 1581s, 1554m, 1461m, 1348m, 1280s, 1258m, 1140s, 1082m, 728s, 699m, 548m.

Methylation of *1c* in ethanol solution was carried out by dissolution of sodium (0.006 mol) in ethanol (20 ml); *1c* (0.006 mol) and methyl iodide (0.012 mol) were added and the mixture refluxed for 30 min. After evaporation the residue was treated with saturated Na_2CO_3-solution and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried over K_2CO_3, evaporated, and the crystals recrystallized from ethanol. Yield of *2c* 50 %.

Methylation of N²-*methyl*-N²-*phenylformohydrazide phenylsulfonylimide* 1d. A mixture of *1d* (0.008 mol) and methyl iodide (20 ml) was refluxed for 2 days. Working up the mixture analogous to *1b* gave a yield of 50 % of N¹,N²-*dimethyl*-N²-*phenylformohydrazide phenylsulfonylimide 3d*, which was identified by IR and NMR spectra.[1] ^{1}H NMR ($CDCl_3$): δ 8.64 (1 H, s), 8.2–6.7 (10 H, m), 3.17 (3 H, s), 3.05 (3 H, s).

Methylation of N²-*methyl*-N²-*phenylformohydrazide 4-methylphenylsulfonylimide* 1e. (0.0033 mol) *1e* was treated with methyl iodide (10 ml) analogous to *1d*. Yield of N¹,N²-*dimethyl*-N²-*phenylformohydrazide 4-methylphenylsulfonylimide 3e*, 50 %, m.p. 162 °C. Anal. $C_{16}H_{19}N_3O_2S$: C, H, N, S. MS *m/e* (% of base peak): 317 (6)M⁺, 213(28), 135(18), 106(34), 105(100), 91(24), 77(28). IR (KBr, cm^{-1}): 1600bs, 1292w, 1282w, 1145s, 1088s, 890w, 738w, 674m. ^{1}H NMR (DMSO-d_6): δ 8.37 (1 H, broad), 7.8–6.5 (9 H, m), 3.25 and 2.95 (3 H intensity 1/2, s) for the *N′*-methyl signals, 3.15 and 3.03 (3 H intensity 2/1, s) for the *N′*-methyl signals, 2.22 (3 H, s) for the *p*-methyl signal.

Hydrolysis experiments. 1c (1.0 g) was dissolved in 1 M HCl (50 ml) and stirred overnight at room temperature; the mixture was cooled and the precipitate filtered off. Identified as *p*-toluenesulfonamide by IR and NMR spectra. Yield *ca.* 80 %. Treatment of *1c* with 50 ml 1 M NaOH overnight resulted in recovery of *1c*. Acid hydrolysis of *1b* under the conditions

mentioned above resulted in formation of benzenesulfonamide in 90 % yield. Hydrolysis of *1b* (1.0 g) in 1 M NaOH (50 ml) for four days resulted in recovery of *1b* (0.7 g) and formation of benzenesulfonamide, *ca.* 0.2 g.

Reactions with piperidine. 1b (0.015 mol) and piperidine (0.015 mol) were refluxed in benzene (50 ml) for 3 days. On cooling a precipitate was formed; it was filtered off and identified as benzenesulfonamide, yield 40 %. The filtrate was evaporated to dryness, treatment with $CHCl_3$ resulted in a small amount of an unidentified crystalline compound. The filtrate was evaporated and the resulting crystalline mass recrystallized from ethanol, yield 55 % of N²-*phenylsulfonyl*-N¹-*pentamethyleneformamidine 4b*, m.p. 130 °C. MS *m/e* (% of base peak): 252(12)M⁺, 112(8), 111(100), 84(84), 83(11), 77(38), 56(9), 55(9), 51(12), 42(9), 41(8). ¹H NMR ($CDCl_3$): δ 8.07 (1 H, s), 8.0–7.2 (5 H, m), 3.6–3.3 (4 H, broad), 1.7–1.3 (6 H, broad). *1c* (0.04 mol) and piperidine (0.04 mol) were refluxed in benzene (50 ml) for 2 days. Evaporation of the solvent gave N²-*4-methylphenylsulfonyl*-N¹-*pentamethyleneformamidine 4c* yield 90 %. m.p. 153 °C (from ethanol). Anal. $C_{13}H_{18}N_2O_2S$: C, H, N, S. MS *m/e* (% of base peak): 266(14)M⁺, 112(9), 111(100), 91(43), 84(89), 83(13), 65(16), 56(11), 55(10), 42(10), 41(11). ¹H NMR (DMSO-d_6): δ 8.20 (1 H, s), 7.8–7.2 (4 H, m), 3.7–3.3 (4 H, broad), 2.38 (3 H, s), 1.7–1.4 (6 H, broad).

Tosylation experiments. N²,N²-*Dimethyl*-N¹-*4-methylphenylsulfonylformohydrazide 4-methylphenylsulfonylimide* 5c. *1c* (0.0056 mol), *p*-toluenesulfonyl chloride (0.0056 mol) and triethylamine (0.011 mol) were stirred in toluene (15 ml) for 2 days. The precipitate of triethylammonium chloride was filtered off and the filtrate evaporated. The resulting mass was treated with H_2O and CH_2Cl_2, the CH_2Cl_2 layer was separated and dried over K_2CO_3, filtered, evaporated and the crystals recrystallized from ethanol, yield of *5c* 25 %, m.p. 160–161 °C. Anal. $C_{17}H_{21}N_3O_4S_2$: C, H, N, S. MS *m/e* (% of base peak): 395(3)M⁺, 240(38), 155(15), 139(14), 91(56), 85(45), 84(100), 65(18), 59(33), 58(11), 43(36). ¹³C NMR (DMSO-d_6): δ 155.1, 146.2, 143.7, 136.7, 131.7, 130.1, 129.8, 129.1, 126.7, 42.2, 21.2, 21.0. ¹H NMR ($CDCl_3$): δ 9.01 (1 H, s), 7.8–7.1 (8 H, m), 2.57 (3 H, s), 2.47 (3 H, s), 2.42 (3 H, s).

5c (0.4 g) was dissolved in ethanol (30 ml) and 6 M HCl (10 ml) was added. After stirring for 30 min under cooling the solution was made neutral with 6 M NaOH and extracted with CH_2Cl_2 giving a crystalline compound identified as *p*-toluenesulfonamide by means of IR and NMR spectra. The aqueous layer was treated with 6 M NaOH to pH = 10 and extracted with CH_2Cl_2 giving 1,1-dimethyl-2-*p*-toluenesulfonylhydrazine *6c* on evaporation of the solvent. Identified by IR and NMR spectra identical with those of an authentic sample.[11]

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