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ON THE STRUCTURE OF N-SULPHONYLFORMAMIDINES

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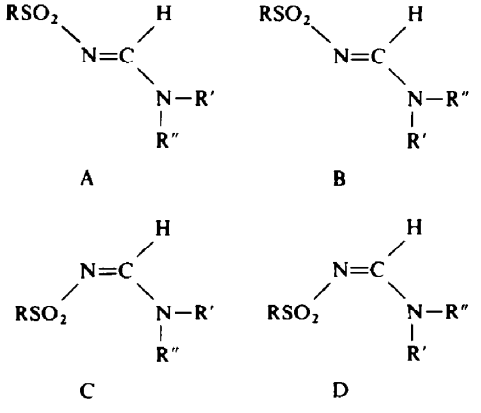
Abstract—The structure of N^2-sulphonylformamidines has been investigated by means of IR, ^1H and ^{13}C NMR spectroscopy. The compounds are shown to exist as two rotamers in solution. A previous report on the isolation of *Z* and *E* isomers (regarding the C=N^2-bond) for one N^2-methane-sulphonylformamidine is shown to be dubious, the spectroscopical data indicating the two isomers to be rotamers at the C–N^1-bond.

The conformational status of formamidine and benzamidine systems have attracted interest in connection with structure activity and mode of action studies for, e.g. pesticides[1] and pharmaceuticals.[2]

Some controversy exists on the structure of amidine systems. Thus reports on the existence of different tautomers and geometrical isomers in benzamidine systems[3,4] were later shown to be wrong.[5] A recent report on the existence of isolable *Z*/*E* isomers (regarding the C=N double bond) of one N-methanesulphonylformamidine[6] seem to be contradicted by newer investigations on *Z*/*E* isomerism of formamidines, where it was shown that above room temperature only the *E* form was present.[7]

To try to solve this structure problem in the field of N-sulphonylformamidines we have prepared representative compounds, including the one reported to exist in isolable *Z*/*E* isomers and investigated them by means of IR and NMR spectroscopy, as this method earlier has been used with success.[8]

Sulphonylformamidines of the type $RSO_2NCHNR'R''$ can theoretically exist in the forms **A**–**D**:



If one of the groups R′, R″ is hydrogen the possibility of additional tautomeric forms exists. For the compounds investigated here the actual tautomeric form was estimated from the ^{13}C NMR chemical shift values.[8]

RESULTS

Compounds **1**–**10** were investigated by means of ^1H, ^{13}C NMR and IR spectra.

$RSO_2NCHNR'R''$

1–**10**

(Compound: R, R′, R″): **1**; Me, Ph, $C^aH_2C^bH_2NHPh$. **2**; Me, Me, Me. **3**; Me, Et, Et. **4**; Me, Ph, Ph. **5**; Me, H, *p*-C_6H_4-Me. **6**; Me, Me, Ph. **7**; *p*-C_6H_4-Me, Ph, $C^aH_2C^bH_2NHPh$. **8**; Ph, Me, Ph. **9**; Ph, H, *p*-C_6H_4-Me. **10**; *p*-C_6H_4-Me, H, Me.

Compound **1**, which is reported to exist as *Z* and *E* isomeric species[6] could be obtained in two different forms, **1a** with m.p. 112° and **1b** with m.p. 140°, while all the other sulphonylformamidines prepared only gave one crystalline species. By the preparation of **1** according to the literature[6] a compound with m.p. 125–130° was normally obtained. On recrystallization from benzene, toluene or ethanol the two different species could be obtained, but not in a reproducible way. **1a** normally precipitated first in colourless crystals while **1b** precipitated on standing for longer time. On melting **1a** the higher melting **1b** was formed. **1a** was more soluble in $CHCl_3$, DMSO, benzene and toluene than **1b**, the low melting often being converted to the high melting species. The behaviour of the two species in solution was identical regarding tlc, IR, ^1H and ^{13}C NMR data, also their mass spectra were identical.

^{13}C NMR *data*. The data in Table 1 show doubling of most signals for the CH=N carbon atom and the NR′R″ groups while the RSO_2 groups only exhibit one set of signals. This indicates the existence of two isomers with differences in the CHNR′R″ moiety of the molecule and not in the RSO_2 part, as it is known that the differences in chemical shift for C atoms in isomers is dependent on the distance from the center of isomerism.[9,10]

In $CDCl_3$ solution, **1** shows only one set of signals and in a mixture of $CDCl_3$ and DMSO-d_6 (1/1) the isomer ratio was different from that in pure DMSO-d_6.

The ^{13}C NMR data thus indicates that it is compounds **A** and **B** or compounds **C** and **D** which exist in solution, but does not give information about which one of the pairs. From a steric viewpoint it is most likely the *E* forms (**A** and **B**) which is in accordance with recent results found by Hegarthy and Chandler[7] who showed the *E* form of some formamidines to be the stable one (the only one existing after heating to above room temperature).

^1H NMR *data*. Compounds **1a** and **1b** were investigated in benzene-d_6, toluene-d_8, acetone-d_6, chloroform-d_1, methanol-d_4 and DMSO-d_6 and showed identical spectra for the two modifications in the different solvents. Only in DMSO-d_6 solution two sets of signals were seen for the CH_2CH_2 NHPh and

Table 1. ^{13}C NMR chemical shift values (DMSO-d_6) in ppm

Compound	CHN	R				R'				R"					
		C1	C2	C3	C4	C1	C2	C3	C4	C[a]	C[b]	C1	C2	C3	C4
1	160.9 159.4	41.8				142.5	126.9 129.3	129.9 129.5	128.0 127.5	53.9 47.8	40.6 39.6	148.4	112.3	123.6	116.3
2	159.7	42.0				40.8				34.9					
3	158.1	41.4				47.5	13.7			39.6	11.2				
4	159.3	41.3				143.3 140.9	129.6 127.1	129.7 129.6	128.1 127.1						
5	157.4 154.6	41.7										135.9 135.6	120.4 117.8	130.6 129.4	134.3 134.1
6	158.2	40.8				34.4						142.4	121.1	128.8	125.9
7	161.0 158.7	139.0	126.1	129.1	142.4	142.5	129.3 126.5	129.9 129.7	128.0 127.5	54.0 48.3	40.8 39.6	148.2	112.1	123.6	116.1
8	160.3 158.6	141.9	126.4	129.6	132.2	42.4 35.6						142.9	122.0	129.0	126.9
9	157.2 152.7	140.9	126.3	129.4	132.2							135.2	120.8 118.1	130.0 129.2	134.6
10	158.3	140.0	125.9	129.3	141.9					27.6					

the CH_3SO_2 group, while the CH=N proton was seen as a somewhat broad singlet. The differences from the ^{13}C NMR spectra, where the CH_3SO_2 signal appeared as a single signal and the CH=N signal as two signals, may be explained from the fact that ^{13}C NMR shows differences in the skeleton while ^{1}H NMR spectra rather reflect the outer sphere of the molecule.

On heating the DMSO-d_6 solution of **1** the two methyl singlets collapsed around 100°, while cooling to −50° did not cause any changes from the room temperature spectra.

The data for compounds **2–10** (Table 2) clearly indicates the existence of hindered rotation around the CHN single bond as seen from the nonequivalence of the R' and R" groups in compounds **2** and **3** and from the doubling of signals for compounds **5**, **8–10**. Compound **6** mainly exists as one isomer probably because of steric reasons. The magnitude of the coupling constants for compounds **5** and **9** indicates the two isomers as *cis* and *trans*.

The ^{1}H data thus supports the ^{13}C data indicating that the investigated compounds exists as two rotamers in solution due to hindered rotation around the CHN single bond showing no sign on the existence of *Z*/*E*-isomers.

For compound **1** especially the investigations in benzene and toluene, from which the two modifications could be crystallized, were interesting in showing

Table 2. ^{1}H NMR chemical shift values[a,b] in DMSO-d_6 solution

Compound	CH	R	R'	R"
1[c]	8.30(1H,s,b)	3.03(4/5·3H,s) 2.82(1/5·3H,s)	7.47(5H,s)	4.08(4/5·2H,t) 4.03(1/5·2H,t) 3.1–3.5(2H,m,b) 6.3–7.3(5H,m) 5.7(1H,t,b)
2	8.10(1H,s)	2.98(3H,s)	3.18(3H,s)	2.92(3H,s)
3	8.07(1H,s)	2.88(3H,s)	3.45(2H,q) 1.18(3H,t)	3.38(2H,q) 1.12(3H,t)
4	8.50(1H,s)	3.00(3H,s)	7.6–7.2(5H,m)	7.6–7.2(5H,m)
5[d]	8.12(2/3H,d), J= 6Hz 8.53(1/3H,d), J=12Hz	3.03(3H,s)	10.5(2/3H,d,b), J= 6Hz 11.0(1/3H,d,b), J=12Hz	7.1–7.7(4H,m) 2.32(3H,s)
6	8.30(1H,s)	3.03(3H,s)	3.40(3H,s)	7.4(5H,s,b)
7	8.45(1H,s)	6.3–8.0(4H,m) 2.43(3H,s)	7.48(5H,s)	4.05(2H,t) 3.0–3.5(2H,m,b) 6.3–8.0(5H,m) 5.65(1H,t,b)
8	8.45(6/7H,s) 8.50(1/7H,s)	7.0–8.0(5H,m)	3.40(6/7·3H,s) 3.53(1/7·3H,s)	7.0–8.0(5H,m)
9	8.21(2/3H,d), J= 5Hz 8.61(1/3H,d), J=12Hz	7.0–8.0(5H,m)	11.08(1/3H,d), J=12Hz 10.63(2/3H,d), J= 5Hz	2.28(3H,s) 7.0–8.0(4H,m)
10	8.15(10/11H,d), J=2Hz 8.18(1/11H,s b)	2.40(3H,s) 7.2–7.7(4H,m)	8.3–8.8(1H,b)	2.97(1/11·3H,d), J=5Hz 2.83(10/11·3H,d), J=5Hz

a Centers of multiplets, intensity and multiplicity given in parenthesis.

b Cooling to −50 °C in $CDCl_3$ caused no changes from the room temperature spectra.

c Coalescence of the Me-signals at 100 °C.

d Coalescence of the CH-signals at 110 °C.

only one set of signals although the low melting compound on standing in the NMR tube changed to the high melting modification which could be isolated from the tube.

Infrared data. The two modifications of **1** gave identical IR spectra in solution as reported in the literature.[6] The NH stretching frequency was found concentration dependent for compounds **5** and **10** indicating the presence of intermolecular H-bond, which is compatible with forms **A** and **B** while the *Z* isomer would tend to form an intramolecular H-bond.

Regarding the two modifications of **1** the KBr spectra were quite different over the whole area from 3500 to 600 cm^{-1}. It was therefore possible to use the IR data to find the difference between the two forms.

IR data for sulphonamides[11] show the position of the $\nu_s SO_2$ around/1150 cm^{-1} and the $\nu_s SO_2$ around 1300 cm^{-1} to be dependent on the steric requirements of the groups connected to the N atom. Tosolini[12] reported the stretching vibrations of the SO_2 group to depend on the substituents in a study of N-sulphonyl formamidines. The CH_3SO_2 methyl rocking mode is reported as a medium to strong band around 965 cm^{-1} and the (C–S) band is found around 760 cm^{-1} variable in intensity.[11]

For the two modifications of **1** the two SO_2 stretching vibrations are found at 1125 and 1272/1275 cm^{-1}, the CH_3SO_2 methyl rocking mode is found at 965/966 cm^{-1} and the C–S stretching frequency is found at 780 cm^{-1}. As these frequencies are almost identical for the two modifications the differences in the two molecules must be found in the other part of the molecule than the CH_3SO_2NCH part. The major differences between **1a** and **1b** are found in the areas 1370–1340, 1224–1210, 1008–978 and 860–800 cm^{-1}. Vibrations connected with the N=C–N (C–N) stretching vibration, also called the amidine II′ band[13] or the amidine III band[14] are reported for amidines in the area 1415–1380 cm^{-1}. This is probably the same band reported as the δCH band for N-sulphonylformamidines[12] in the area 1362–1342 cm^{-1}. Grivas *et al.*[15] reported the amidine III band in the region 1340–1230 for some trichloroacetamidines dependent on the type of substitution on the N atom, and the R–N–CH=N (R–N) stretching vibration at 1340–1320 or 1170–1090 cm^{-1} (R aryl or alkyl). The CH out of plane vibration is possibly to find in the area 1000–800 cm^{-1} in accordance with data for alkenes.[16,17]

As the areas with the greatest differences in the IR spectra for **1a** and **1b** are the areas where the amidine III band, the CH_2-deformation, CH out of plane deformation, and the C–N stretching vibrations are located, also the IR spectra indicate the two modifications to be rotamers regarding the C–N single bond. Similar differences have been found for enamino-ketones[17] where differences could be ascribed to the existence of an *s-cis* and an *s-trans* form one of which existed in melted, the other in crystalline form.

Finally, the combined NMR and IR data indicate the investigated compounds to exist in only one form regarding isomerism at the C=N bond, both in crystalline form and solution. In addition hindered rotation around the C–N bond is seen in solution, with a barrier to rotation of the same magnitude as found for similar systems.[8] For compound **1** the two rotamers by chance can crystallize in either of the rotamers the lower melting being more soluble but thermodynamically unstable.

EXPERIMENTAL

The equipment was reported earlier.[8] The compounds were prepared in accordance with known procedures.[5,8,12]

IR data and analytical data for new compounds.

N^2-*Methanesulphonyl*-N^1-*phenyl*-N^1-2-(*phenylamino*)-*ethylformamidine* **1** IR ($CHCl_3$, cm^{-1}): 1605s, 1580s, 1505m, 1495m, 1430w, 1408w, 1344m, 1320m, 1299s, 1130s, 1077w, 965s, 900w, 852m, 812w, 790m, 690s.

Compound **1a** (KBr, cm^{-1}): 3378m, 1610s, 1580s, 1518m, 1495m, 1458m, 1455m, 1409m, 1342m, 1330m, 1315m, 1296m, 1288m, 1272s, 1211m, 1158m, 1125s, 1008m, 995m, 982m, 965m, 905m, 825m, 800m, 780m, 763m, 754m, 702m, 699m.

Compound **1b** (KBr, cm^{-1}): 3375m, 1610s, 1580s, 1515m, 1498m, 1470m, 1370m, 1360m, 1355m, 1311m, 1275s, 1270m, 1225m, 1125s, 1095m, 978s, 966m, 955m, 909m, 860s, 781m, 748m, 740m, 693s.

N^2-*Methanesulphonyl*-N^1-(4-*methylphenyl*)*formamidine* **5**. m.p. 159°, (Found: C, 51.08; H, 5.80; N, 13.13. Calc. for $C_9H_{12}N_2O_2S$: C, 50.92; H, 5.70; N, 13.20%), yield 60%. IR ($CHCl_3$, cm^{-1}): 1625s, 1595m, 1505w, 1445w, 1315m, 1290s, 1130s, 968s, 915m, 825m, 810m.

N^2-(4-*Methylbenzenesulphonyl*)-N^1-*phenyl*-N^1-2-(*phenylamino*)-*ethylformamidine* **7**. IR ($CHCl_3$, cm^{-1}): 1595s, 1575s, 1500m, 1490m, 1445w, 1335m, 1300m, 1298m, 1280w, 1145s, 1085s, 970m, 900m, 860s, 810m.

N^2-*Benzenesulphonyl*-N^1-(4-*methylphenyl*)*formamidine* **9**. M.p. 179°, (Found: C, 61.11; H, 5.25; N, 10.17. Calc. for $C_{14}H_{14}N_2O_2S$: C, 61.29; H, 5.14; N, 10.21%). Yield 68%. IR ($CHCl_3$, cm^{-1}): 1621s, 1580m, 1435w, 1290s, 1145s, 1085s, 820s.

N^2-4-*Methylbenzenesulphonyl*-N^1-*methylformamidine* **10**. m.p. 102°, yield 68%. IR (KBr, cm^{-1}): 1615s, 1440w, 1405m, 1320s, 1275s, 1265s, 1150s, 1140s, 1085s, 1005w, 965m, 905s, 835w, 810m.

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