Acta Chemica Scandinavica B 28 (1974) 1—4

The Reaction between 5-(*p*-Toluenesulfonamido)tetrazole and *p*-Toluenesulfonyl Chloride

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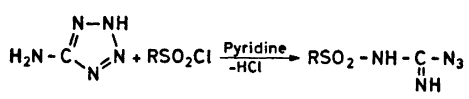
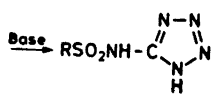
5-(*p*-Toluenesulfonamido)tetrazole reacts with *p*-toluenesulfonyl chloride and pyridine at room temperature with spontaneous evolution of nitrogen and formation of the dipolar compound II. This reacts with nucleophiles with elimination of pyridine. During the reactions with ethanol or ammonia an infrared absorption band near 2200 cm^{-1} appears for a short time, indicating that a carbodiimide, $RSO_2N=C=N-NHSO_2R$, is formed as an intermediate. Compound II also eliminates pyridine on heating or in solution, probably forming dimers (or polymers) of the carbodiimide.

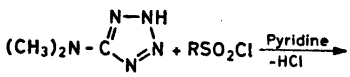
The primary product of the reaction between 5-aminotetrazole and *p*-toluenesulfonyl chloride in pyridine at temperatures below 70°C is known to be *p*-toluenesulfonylguanyl azide.[1] Under the influence of a base this is rearranged to the isomeric 5-(*p*-toluenesulfonamido)-tetrazole.

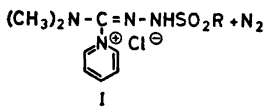
When, however, the temperature of the pyridine solution is raised above 90°C a violent reaction takes place with evolution of nitrogen.[2] Since we found [2] that 5-dimethylaminotetrazole reacted with *p*-toluenesulfonyl chloride in pyridine with evolution of nitrogen and formation of (1-*p*-toluenesulfonyl-4,4-dimethylcarbamohydrazonoyl)pyridinium chloride (I; semicarbazide numbering) it was anticipated





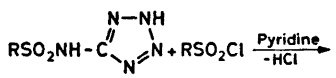
that a similar reaction had taken place between 5-(*p*-toluenesulfonamido)tetrazole and excess *p*-toluenesulfonyl chloride with the formation of compound II.

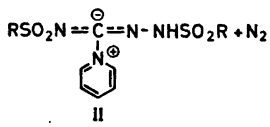




I

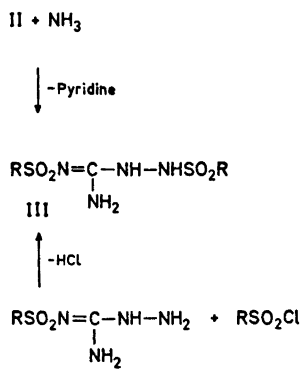
No compound corresponding to II could, however, be isolated from the solution. A possible reason for this negative result might be that the buffer solution pyridine/pyridinium chloride is too acid to induce a ring closure of the initially formed guanyl azide and that the nitrogen evolution originates from a thermal decomposition of the latter. However, the guanyl azide is not decomposed under the conditions of the experiment and it does not react with the sulfonyl chloride. It must therefore be concluded that some 5-(*p*-toluenesulfonamido)-tetrazole is actually formed and reacts with ex-





II

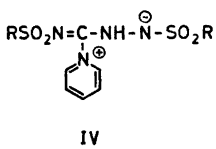
cess sulfonyl chloride under nitrogen evolution and formation of II, which, however, is unstable at the high temperatures used. We have now found that 5-(*p*-toluenesulfonamido)tetrazole in fact reacts with *p*-toluenesulfonyl chloride in pyridine solution with instantaneous release of nitrogen and the formation of a product which analytically corresponds to formula II. Chemical evidence in support of this structure is furnished by the reaction of II with ammonia. The product of this reaction was found to be in all respects identical with 1-(*p*-toluenesulfonamido-2-(*p*-toluenesulfonyl)guanidine (III), prepared from 2-(*p*-toluenesulfonyl)-1-aminoguanidine and *p*-toluenesulfonyl chloride.



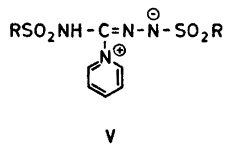
Analogously, the reaction of II with water gives rise to a product the elemental composition of which corresponds to that expected for 1,4-bis(*p*-toluenesulfonyl)semicarbazide. The corresponding thiosemicarbazide could not be obtained from the reaction of II with hydrogen sulfide (neither could it be prepared from *p*-toluenesulfonylhydrazine and *p*-toluenesulfonyl isothiocyanate).

The possibility that compound II should rather be represented by one of the tautomeric forms IV and V is rejected. These correspond to the conjugate base of I, which must be a very strong base since I is neutral. Compound II on the other hand is a very weak base (it does not form a hydrochloride). The structure depicted as II would also appear to be more plausible since it must be resonance-stabilized.

Compound I reacts with nucleophiles as a potential nitrilimine, $R_2N-C\equiv\overset{+}{N}-\overset{-}{N}-SO_2R'$, eliminating pyridinium chloride and forming a semicarbazide, a thiosemicarbazide, and an aminoguanidine with water, hydrogen sulfide, and ammonia, respectively.[2] Compound II, on the other hand, should be able to form a carbodiimide (VI) by elimination of pyridine. The product smells weakly of pyridine but could be recrystallized from acetone without change of composition, although with great loss. By evaporation of the filtrate, or by melting of compound II, a pyridine-free product was obtained the composition of which corresponds approximately to that of the carbodiimide. However, according to its infrared spectrum it cannot be a carbodiimide because there is no absorption near 2200 cm^{-1}. The spectrum exhibits an absorption band at 1725 cm^{-1}, which may originate from the grouping $RSO_2NHN=C$ since acetone *p*-toluenesulfonylhydrazone has a similar band. According to thin-layer chromatography the product contains at least ten compounds, which suggests the presence of four-membered rings since seven structurally isomeric diazetidines, each with several stereoisomers, could be formed by a dimerisation. Attempts at separation of the many compounds were not pursued further. However, the isolation of a small amount of crystalline *p*-tolyl *p*-toluenethiosulfonate, $CH_3C_6H_4SO_2-S-C_6H_4-CH_3$, from the melt shows that a possible dimerisation is accompanied by a more thorough decomposition. Incidentally, the molecular ion of this thiosulfonate and its fragmentation products account for most of the peaks in the mass spectrum of the melt. No ions corresponding to the carbodiimide or its polymers could be detected.

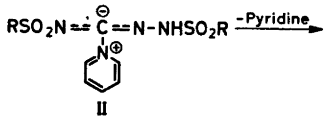


IV



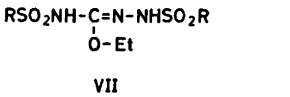
V

Evidence for the fleeting existence of the carbodiimide VI as an intermediate in the reactions of II with nucleophiles has been obtained from the reaction of II with ethanol. In this case products are obtained which initially show a strong infrared absorption in the range 2240–2260 cm^{-1}. This absorption disappears on drying, and the substance left is according to IR and NMR spectroscopic evidence *O*-ethyl 3-(*p*-toluenesulfonyl)-*p*-toluenesulfonimidocar-



II

VI



VII

bazate (VII). Accordingly the reaction of II with ethanol seems to proceed *via* the carbodiimide VI.

With *tert*-butyl alcohol II also gives a product with a strong infrared band at 2240 cm^{-1} which disappears on refluxing for a longer time. The reaction product is, however, not a carbazate but according to its infrared spectrum a similar mixture to that obtained by melting compound II.

During the reaction between compound II and ammonia in ethanol a transient absorption band is observed at 2180 cm^{-1}. The fact that this wavenumber differs somewhat from that observed during the reaction with ethanol may suggest that the carbodiimide forms a molecular complex with the nucleophile before reacting with it.

EXPERIMENTAL

^1H NMR spectra were recorded in $CDCl_3$ on a Varian A-60 instrument using TMS as internal standard. Chemical shifts are given in δ values (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet). IR spectra were recorded on a Perkin-Elmer Model 337 grating spectrophotometer. Elemental analyses were performed by the analytical laboratory of this department (Mr. Preben Hansen and his staff).

p-*Toluenesulfonylguanyl azide* [2,3] could conveniently be prepared directly by the reaction of the commercially available 5-aminotetrazole hydrate and two equivalents of *p*-toluenesulfonyl chloride in pyridine. The crude azide, which is obtained in almost quantitative yield by pouring the pyridine solution into ice-cold water, still contains traces of pyridine and is specially suited for the following base-catalyzed isomerization. The ring closure to *5-(*p*-toluenesulfonamido)-tetrazole* could thus be achieved merely by refluxing the azide in ethanolic solution for *ca.* 6 h. The tetrazole was obtained by concentrating the ethanolic solution *in vacuo*. The best solvent for recrystallization is water + 15 – 20 % ethanol. Yield *ca.* 25 g of the recrystallized product (m.p. 187 – 189°C) from 20.6 g of 5-aminotetrazole monohydrate (52 %).

Pyridinio-p-*toluenesulfonylhydrazono*-p-*toluenesulfonimidoformate* II. A solution of *p*-toluenesulfonyl chloride (1.6 g) in acetone (10 ml) was added dropwise to a stirred solution of 5-(*p*-toluenesulfonamido)-tetrazole (2 g) and pyridine (2 ml) in acetone (10 ml). The reaction proceeds with evolution of nitrogen; the temperature was kept at 5°C by cooling with ice until all had been added (20 min) and the stirring was continued without cooling. A crystalline precipitate separated eventually or on scratching. The stirring was continued for ½ – 1 h or until the evolution of nitrogen had stopped (usually not more than 80 % of the calculated amount is evolved). The yield is very variable. In one case a yield as high as 70 % was obtained by carrying out the reaction in pyridine solution and adding acetone afterwards but this experiment could not be reproduced. In most cases only 20 – 30 % was obtained. The compound is unstable in contact with the solution and was isolated immediately by centrifugation. After a few washings with acetone, in which the residue is somewhat soluble, the analytically pure substance was obtained as a light yellow solid. (Found: C 54.00; H 4.55; N 12.67; S 14.37. Calc. for $C_{20}H_{20}N_4O_4S_2$: C 54.05; H 4.54; N 12.61; S 14.40). M.p. 121 – 122°C (decomp.). In the infrared spectrum ν(C=N) is found as a strong doublet at 1620 – 1630 cm^{-1}. In the ^1H NMR spectrum the protons of the two methyl groups give rise to a broad singlet at δ 2.40 and the other protons to complicated series of multiplets extending from δ 7 to 9.

On melting it gives off pyridine. According to chromatography ($CHCl_3$, silica gel) the amorphous product formed is a complicated mixture, from which, however, a few percent of *S*-*p*-tolyl *p*-toluenethiosulfonate (m.p. 78 – 79°C, infrared spectrum identical with that of an authentic sample) could be obtained.

The substance is only slightly soluble in benzene or ether, somewhat more soluble in acetone or chloroform. It dissolves in aqueous NaOH with an orange-red colour which disappears on heating. On acidification of the solution 1,4-bis(*p*-toluenesulfonyl)semicarbazide was precipitated; this could, however, be prepared in a purer state without the use of NaOH (see below). When II is dissolved in boiling acetone only a few percent crystallize out again on cooling and when the filtrate is evaporated a pyridine-free substance is obtained with essentially the same spectral properties as the melt. The IR spectrum has characteristic absorptions at 1725 (m), 1600 (s) and 1570 (s) cm^{-1} (difference from II). NMR-spectrum: broadened singlet at δ 2.38, multiplet at δ 7 – 9.

When the acetone solution from the prepara-

tion of II was diluted with water and extracted with chloroform a mixture was obtained which by chromatography (benzene-ethanol, silica gel) was separated into several fractions. One of these was identified as acetone *p*-toluenesulfonylhydrazone by comparison with an authentic sample. M.p. 158°C IR spectra superimposable, NMR spectrum: δ 1.82 (d, 6H); 2.38 (s, 3H); 7.5 (m, 5H). The other fractions were amorphous and apparently polymeric substances with varying N:S ratio (1.5 – 3) but similar infrared spectra except in the 1500 – 1600 cm^{-1} region. No well-defined compounds could be isolated. However, on boiling with water one fraction yielded *p*-toluenesulfonamide and another yielded 1,4-bis(*p*-toluenesulfonyl)-semicarbazide, in addition to insoluble resinous material.

1,4-Bis(p-toluenesulfonyl)semicarbazide. When II (100 mg) was boiled with water (8 ml) most of it went into solution. On cooling of the filtered solution and addition of a drop of dilute hydrochloric acid a white solid separated (45 mg). It was purified by crystallization from water-ethanol (10:1). M.p. 197 – 198°C. (Found: C 46.95; H 4.40; N 11.19; S 16.76. Calc. for $C_{15}H_{17}N_3O_5S_2$: C 46.99; H 4.47; N 10.96; S 16.72). Its infrared spectrum exhibits a strong C=O band at 1710 cm^{-1}.

1-(p-Toluenesulfonamido)-2-(p-toluenesulfonyl)guanidine (III). (a) A suspension of 2-(*p*-toluenesulfonyl)-1-aminoguanidine [1] (0.58 g) in pyridine (1 ml) was treated with *p*-toluenesulfonyl chloride (0.48 g) for 30 min at room temperature followed by a few min at 100°C until all had dissolved. On addition of water to the solution a white solid separated, which was filtered off, washed with water and dried over H_2SO_4. Yield 0.80 g. M.p. 240°C after recrystallization from ethanol. (Found: C 47.01; H 4.81; N 14.53; S 16.78. Calc. for $C_{15}H_{18}N_4O_4S_2$: C 47.12; H 4.75; N 14.66; S 16.74). As expected the substance is soluble in aqueous NaOH (to give a colourless solution). It is also soluble in ethanol saturated with ammonia but separates unchanged from the boiling solution as the ammonia escapes.

The infrared spectrum (KBr) exhibits three strong and sharp N – H stretching bands at 3310, 3375 and 3475 cm^{-1} and two strong bands at 1640 and 1560 cm^{-1} (amide I and amide II bands). The presence of some rather pronounced bands in the 2700 – 2800 cm^{-1} range indicates that the compound may in part exist in a dipolar form with an $=NH_2^+$ group.

(b) Compound II (0.30 g) was dissolved in ethanolic ammonia (5 ml). The solution initially had a deep red colour, which faded in 10 – 15 sec. After 1 h at room temperature a quantitative amount of III was obtained on dilution of the solution with ether. According to its m.p. (240°C), analysis (Found: C 46.90; H 4.83; N 14.53; S 16.61), and infrared spectrum this product was identical with that prepared by procedure (a).

O-Ethyl 3-(p-toluenesulfonyl)-p-toluenesulfonimidocarbazate (VII). II (400 mg) was boiled with ethanol (20 ml) until all had been dissolved and the yellow colour had disappeared. The solution was evaporated *in vacuo* and dried over H_2SO_4. Before the latter drying the infrared spectrum of the residue dissolved in $CHCl_3$ exhibited an absorption band at 2260 cm^{-1}, the intensity of which decreased slowly. The substance which had been dried over H_2SO_4 did not exhibit this band but had a strong band at 1602 cm^{-1}, presumably due to ν(C=N). The NMR spectrum was consistent with the expected constitution. The yield was almost quantitative (400 mg) but the product was glassy. It could only be purified with great loss by dissolving it in ethanol-benzene (1:4) and filtering the solution through silica gel; on addition of petroleum ether colourless crystals with m.p. 119 – 120°C were obtained. (Found: C 49.31; H 5.14; N 10.03. Calc. for $C_{17}H_{21}N_3S_2O_5$: C 49.62; H 5.14; N 10.21). NMR spectrum: δ 0.93 (t, 3H); 2.40 (d, 6H); 3.90 (q, 2H); 7.50 (m, 10H).

REFERENCES

1. Jensen, K. A. and Pedersen, C. *Acta Chem. Scand. 15* (1961) 991.
2. Jensen, K. A., Holm, A. and Rachlin, S. *Acta Chem. Scand. 20* (1966) 2795.
3. Dahlbom, R. and Ekstrand, T. *Sv. Kem. Tidskr. 6* (1943) 122.

Received August 18, 1973.