155. *A Synthesis of Guanidine Derivatives.*

By W. V. FARRAR.

Potassium ferricyanide, sodium toluene-*p*-sulphinate, and an aliphatic primary amine in aqueous solution give the guanidine derivative (Ia or Ib; R = Alkyl). Some diamines give cyclic guanidines (II) and (III).

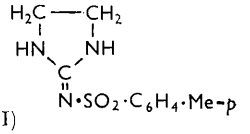
THIS work began as an attempt to discover a chemical system which would convert aliphatic amines into sulphonamides in homogeneous aqueous solution. For this purpose, a study was made of the action of oxidising agents on an aqueous solution containing sodium toluene-*p*-sulphinate and morpholine. Only two oxidising agents, out of a large number tried, gave a precipitate of *N*-toluene-*p*-sulphonylmorpholine; they were chloramine-T and potassium ferricyanide.

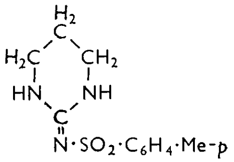
Repetition of the experiment with chloramine T, omitting morpholine, gave toluene-*p*-sulphonyl chloride which is undoubtedly the intermediate in the reaction with morpholine.

With potassium ferricyanide and secondary amines the reaction was straightforward, and yields of >80% (based on sulphinate) were obtained. The hindered di-isopropylamine did not react. Primary amines, however, gave precipitates containing only minor amounts (or none) of the expected alkyl toluene-*p*-sulphonamide; the major products were alkali-insoluble compounds whose elementary analyses indicated that they were guanidine derivatives of general formula (Ia or Ib; R = Alk).

$(RNH)_2C{:}N{\cdot}SO_2{\cdot}C_6H_4{\cdot}Me\text{-}p$ (Ia)

$RNH{\cdot}C({:}NR){\cdot}NH{\cdot}SO_2{\cdot}C_6H_4{\cdot}Me\text{-}p$ (Ib)


(II)


(III)

This was confirmed by comparison of the product from benzylamine, sodium toluene-*p*-sulphinate, and potassium ferricyanide with the product from *NN'*-dibenzylguanidine [1] and toluene-*p*-sulphonyl chloride; they were identical (Ia or Ib; R = $PhCH_2$).

The formation of guanidines proceeded smoothly from the majority of simple aliphatic primary amines, including ethylenediamine and 1,3-diaminopropane, which gave the cyclic compounds (II) and (III), respectively.

No definite products were obtained from glycine or ethanolamine, although a reaction took place; urea and amides did not react. None of the reactions described in this Paper is applicable to aromatic amines, which are usually oxidised to coloured products.

The mechanism by which guanidines are formed must be a matter for conjecture. Potassium ferricyanide appears not to react with either primary amines or sulphinate alone, under conditions which readily produce guanidines when all three reactants are present. There is, however, some indirect evidence for the presence of $C_7H_7{\cdot}SO_2^+$ ions in sulphinate–ferricyanide mixtures; in presence of fluoride or azide ions, such mixtures gradually deposit moderate yields of toluene-*p*-sulphonyl fluoride or azide. Since the presence of F^+ or N_3^+ is extremely unlikely, the presence of $C_7H_7{\cdot}SO_2^+$ may be assumed. It is not clear, however, why the reaction should follow an entirely different course with secondary amines.

[1] J. Strakosch, *Ber.*, 1872, **5**, 692.

EXPERIMENTAL

*Reaction of Sodium Toluene-*p*-sulphinate with Chloramine-*T.—Sodium toluene-*p*-sulphinate (dihydrate, 4·3 g.) in water (25 c.c.) was mixed with chloramine-T (trihydrate; 5·6 g.) in water (25 c.c.) at 0—10°. Toluene-*p*-sulphonyl chloride (1·77 g., 47%) was immediately precipitated, m. p. and mixed m. p. 67°. The filtrate, after acidification, gave toluene-*p*-sulphonamide (2·9 g.).

Repetition of this experiment, in the presence of morpholine (2·0 g.), precipitated *N*-toluene-*p*-sulphonylmorpholine (4·10 g., 85%), m. p. and mixed m. p. 147° (lit.[2] gives 147°).

*Reaction between Sodium Toluene-*p*-sulphinate, Morpholine, and Potassium Ferricyanide.*—Sodium toluene-*p*-sulphinate (dihydrate; 4·3 g.) and potassium ferricyanide (dihydrate; 29·2 g.) were dissolved in water (200 c.c.) at 50° and morpholine (4·0 g.) was added. The solution became deep green, then orange, with crystallisation of *N*-toluene-*p*-sulphonylmorpholine, m. p. 147° (3·95 g., 81%).

Qualitatively similar results were obtained by replacing morpholine by dimethylamine, piperidine, and hexamethyleneimine. Di-isopropylamine did not react; diethanolamine gave a green colour, but no precipitate.

*Reaction between Toluene-*p*-sulphinate, Methylamine, and Potassium Ferricyanide.*—To sodium toluene-*p*-sulphinate (dihydrate; 4·3 g.) and potassium ferricyanide (dihydrate; 14·6 g.) in water (100 c.c.) at 50°, methylamine (6 c.c. of 40% aqueous solution) was added. A deep green colour was followed by precipitation; the solid was collected after 4 hr. Extraction with dilute sodium hydroxide left almost pure guanidine derivative (I; R = Me) (0·95 g.), as prisms from acetic acid, m. p. 207—208° (Found: C, 49·9, 49·8; H, 6·4, 6·1; N, 17·7; S, 12·9. $C_{10}H_{15}N_3O_2S$ requres C, 49·8; H, 6·3; N, 17·4; S, 13·3%). The alkaline extract on acidification gave *N*-methyl toluene-*p*-sulphonamide (0·35 g.), m. p. 75°.

Qualitatively similar results were obtained from other amines as shown in the Table.

Amine	Product	Molecular formula	M. p.	Recryst. from	Found (%)	Required (%)
Ethylamine	I; R = Et	$C_{12}H_{19}N_3O_2S$	132°	EtOH	C 53·1 H 7·3	C 53·5 H 7·1
Isopropylamine	I; R = Pr^i	$C_{14}H_{23}N_3O_2S$	109	Toluene–petroleum	C 56·8 H 7·5 N 14·0 S 10·3	C 56·6 H 7·8 N 14·1 S 10·8
t-Butylamine	I; R = Bu^t	$C_{16}H_{27}N_3O_2S$	93—95	Petroleum	C 59·4 H 8·4 N 12·5 S 9·7	C 59·1 H 8·4 N 12·9 S 9·9
Benzylamine	I; R = $PhCH_2$	$C_{22}H_{23}N_3O_2S$	143—144	EtOH	C 66·9 H 6·1 N 10·7 S 8·3	C 67·2 H 6·0 N 10·7 S 8·1
Cyclohexylamine	I; R = C_6H_{11}	$C_{20}H_{31}N_3O_2S$	161	EtOH	C 63·5 H 7·9	C 63·6 H 8·3
Ethylene diamine	II	$C_{10}H_{13}N_3O_2S$	232—233	EtOH	C 50·2 H 6·0 N 17·4 S 13·6	C 50·2 H 5·9 N 17·6 S 13·4
1,3-Diamino-propane	III	$C_{11}H_{15}N_3O_2S$	270—271	Bu^nOH	C 52·7 H 5·9 N 15·9 S 12·6	C 52·2 H 6·0 N 15·8 S 12·6

The product from benzylamine was identical (mixed m. p.) with the produt of the aqueous Schotten–Baumann reaction between *NN'*-dibenzylguanidine[1] and toluene-*p*-sulphonyl chloride.

*Reaction between Sodium Toluene-*p*-sulphinate, Sodium Fluoride and Potassium Ferricyanide.*—Sodium toluene-*p*-sulphinate (dihydrate; 2·15 g.), sodium fluoride (2·0 g.) and potassium ferricyanide (dihydrate; 7·3 g.), dissolved in water (60 c.c.) and kept at 20—25° for

[2] J. Sand, *Ber.*, 1901, **34**, 2908.

48 hr., deposited crystals of toluene-*p*-sulphonyl fluoride (0·75 g., 43%), m. p. and mixed m. p. 43—44°.

Substitution of sodium azide for sodium fluoride similarly gave toluene-*p*-sulphonazide (0·4 g.), m. p. 22° (lit.,[3] m. p. 22°).

Miscellaneous Experiments.—Qualitative observations were made of the behaviour of the following amines with a solution of sodium toluene-*p*-sulphinate (2·15 g.) and potassium ferricyanide (7·3 g.) in water (100 c.c.). Ethanolamine, glycine, and thiourea, gave deep green colours, but no solid product. No reaction took place with urea, acetamide, triethylamine, and toluene-*p*-sulphonamide. Hydroxylamine, hydrazine, and toluene-*p*-sulphonhydrazide gave effervescence. Ammonia slowly yielded a trace of toluene-*p*-sulphonamide. Phenylhydrazine smoothly gave 1-phenyl-2-toluene-*p*-sulphonylhydrazine, m. p. and mixed m. p. 156° (decomp.). Trimethylamine slowly gave *NN*-dimethyl toluene-*p*-sulphonamide, m. p. and mixed m. p. 80° in small yield.

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[3] J. Curtius and W. Klavehn, *J. prakt. Chem.*, 1926, **112**, 65.