Cyanamides. Part VII. Synthesis of Arenesulphonylmelamines and Arenesulphonylammelides.*

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The structure of triarenesulphonylmelamines, previously suggested on the evidence of degradation (Part VI *), is confirmed by the synthesis of these compounds from cyanuric chloride and sodium arenesulphonamides. Under suitable conditions, this reaction affords *N*-sulphonylammelides. The ultra-violet absorption spectra of the new derivatives are recorded.

The action of arenesulphonyl chlorides on *N*-aryl-*N'*-cyanoureas, *N*-arylbiurets, or *N*-arenesulphonyl-*N'*-cyanoguanidines yields trisulphonylmelamines (Kurzer and Powell, *Chem. and Ind.*, 1953, 195; *J.*, 1953, 2531), the structure (III) of which was established by hydrolytic degradation. The structural proof is now completed by an unequivocal synthesis of triarenesulphonylmelamines from a preformed triazine nucleus.

A number of acylmelamines, including the tribenzoyl derivative, have been synthesised by treatment of melamine with acid anhydrides at high temperatures (Ostrogovich, *Gazzetta*, 1935, **65**, 566; Cason, *J. Amer. Chem. Soc.*, 1947, **69**, 495; Emerson and Patrick, *ibid.*, 1948, **70**, 343). Our efforts to extend this method to the production of sulphonylmelamines by employing arenesulphonic anhydrides under various conditions, however, were not successful.

Arenesulphonamido-groups were introduced directly into the triazine ring by interaction of cyanuric chloride with sodium salts of arenesulphonamides in non-ionising solvents. Phillips (*J.*, 1941, 9) synthesised arenesulphonylpyrimidines by refluxing halogenopyrimidines with sulphanilamide in the presence of potassium carbonate and copper powder, and ascribed this condensation involving the sulphonamido- rather than the amino-group of sulphanilamide to the intermediate formation of its potassium salt. The present results are in agreement with this.

In the temperature range 140—190°, the action of 6—7 mols. of sodium sulphonamide on 1 mol. of cyanuric halide (I) resulted in the replacement of all three halogen atoms, triarenesulphonylmelamines (III) being conveniently obtained as sole products in good yields. For example, cyanuric chloride in boiling xylene or decahydronaphthalene yielded tritoluene-*p*-sulphonylmelamine (III; R = *p*-$C_6H_4Me\cdot$) as its sodium salt. The observation that triarenesulphonylmelamines thus synthesised were identical with specimens obtained by the less obvious routes (*loc. cit.*) confirms the structures previously suggested.

The interaction of cyanuric chloride with ammonia, amines, and alcohols may be controlled by a suitable choice of the reaction conditions in such a way that one, two, or all three halogen atoms are successively replaced (Fierz-David and Matter, *J. Soc. Dyers and Col.*, 1937, **53**, 424; Kaiser, Thurston, and their co-workers, *J. Amer. Chem. Soc.*, 1951, **73**, 2981, and subsequent papers). Attempts were therefore made to limit the replacement in the present reaction. Treatment, at lower temperatures, of cyanuric chloride with only 2—2·5 equivalents of sulphonamide introduced one sulphonamido-residue and afforded *N*-monoarenesulphonylammelides (V). For example, the primary product on use of sodium toluene-*p*-sulphonamide in boiling benzene, though not obtained pure, was obviously the sodium salt of 2 : 4-dichloro-6-toluene-*p*-sulphonamidotriazine (II; R = *p*-$C_6H_4Me\cdot$), and when warmed in alkali afforded good yields of *N*-toluene-*p*-sulphonylammelide.

The structures of the *N*-arenesulphonylammelides (V) were confirmed by the methods that have proved reliable in the triarenesulphonylmelamine series (Part VI, *loc. cit.*). Hydrolysis by ethanolic hydrochloric acid afforded cyanuric acid and the sulphonamide; treatment with concentrated sulphuric acid, on the other hand, gave appropriate proportions of ammelide and the sulphonic acid.

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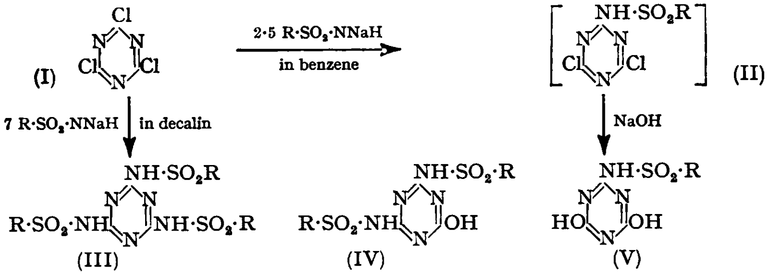
* Part VI, *J.*, 1953, 2531.

Attempts to establish the conditions for the replacement of two chlorine atoms in the triazine system were only partially successful. There was no doubt that diarenesulphonylammelines (IV), arising from intermediate 2-chloro-4 : 6-diarenesulphonamidotriazines, were produced in the reaction with 4—6 equivalents of sodium arenesulphonamides in boiling benzene but they could not be separated completely from the monoarenesulphonylammelides (V) formed simultaneously. Reaction at higher temperatures, *e.g.*, in boiling toluene, followed by the usual treatment with alkali, gave mixtures of the three products (III, IV, and V).



In the formation of both triarenesulphonylmelamines and *N*-arenesulphonylammelides from cyanuric chloride, two molecules of sodium sulphonamide were required, in practice, for the replacement of one halogen atom, the products being obtained as sodium salts. Treatment of cyanuric chloride with 4 instead of 7 equivalents of the arenesulphonamide salt, for example, reduced the yield of arenesulphonylmelamine from 78 to 12%. Triarenesulphonylmelamines (III) [and presumably also dichloroarylsulphonamidotriazines (II)] are stronger acids than the sulphonamides from which they are derived (cf. Table). The reaction does therefore not terminate with the production of the free acids (II or III), but immediately consumes a second equivalent of sulphonamide salt in the formation of sodium salts of the arenesulphonyltriazines (II or III). Similar observations were made in the synthesis of substituted melamines from 2 : 4-diamino-6-chlorotriazines and amines of different strengths (Kaiser, Thurston, Dudley, Schaefer, Hechenbleikner, and Holm-Hansen, *J. Amer. Chem. Soc.*, 1951, **73**, 2985).

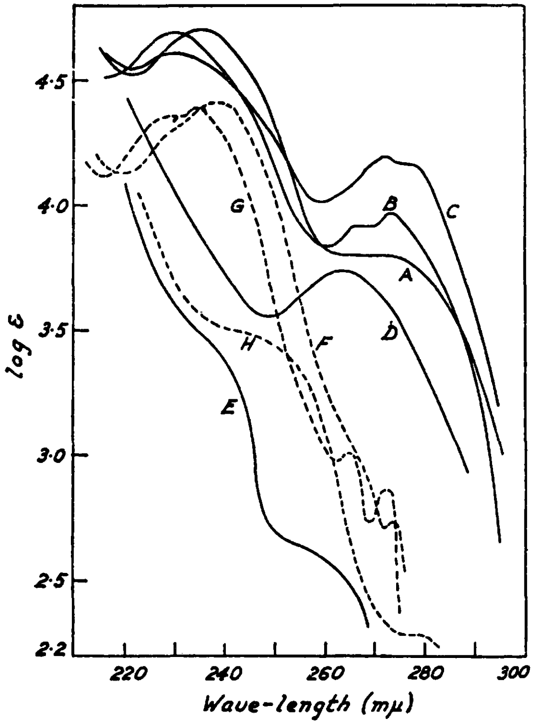
pH *of* 0·005M-*solutions of sulphonamides and trisulphonylmelamines.*

Compound	Me[a]	Ph[b]	*p*-C_6H_4Me[b]
$R{\cdot}SO_2{\cdot}NH_2$	5·25	5·90	5·95
$(R{\cdot}SO_2{\cdot}NH{\cdot}CN)_3$ (III)	2·35	2·50	2·85

[a] Measured in water. [b] Measured in 33% aqueous ethanol.

Attempts to prepare triarenesulphonylmelamines from melamine itself by several methods were unsuccessful. Melamine was recovered unchanged after treatment with toluene-*p*-sulphonyl chloride in pyridine (in which the base, however, was only sparingly soluble); this differs from a claim by Anderson, Faith, Manson, Winnek, and Roblin (*J. Amer. Chem. Soc.*, 1942, **64**, 2902) to have introduced *one* *p*-nitrobenzenesulphonyl residue into melamine by this method. Melamine also failed to yield the desired products when treated with the acid halide in the presence of alkali in water or aqueous acetone. In this respect, amino-(or imino)-groups linked to the *s*-triazine nucleus differ therefore from those of the closely related 2-aminopyridine and 2-aminopyrimidine, both of which react readily with arenesulphonyl chlorides under comparable conditions (Hinsberg and Kessler, *Ber.*, 1905, **38**, 906; Ewins and Phillips, B.P. 530,187, 512,145; Roblin, Williams, Winnek, and English, *J. Amer. Chem. Soc.*, 1940, **62**, 2002). The analogous behaviour of hydroxy-groups was also observed : cyanuric acid, though readily soluble in pyridine, did not react with arenesulphonyl halides in this solvent. The general chemical behaviour of hydroxy-, alkoxy-, amino-, and halogeno-*s*-triazines suggests their classification with acids, esters, amides, and acid halides rather than with aromatic (or, indeed, aliphatic) compounds bearing corresponding substituents (cf., for example, Ponomarev, *Ber.*, 1885, **18**, 3267; Hofmann, *Ber.*, 1886, **19**, 2067; Thurston *et al.*, *J. Amer. Chem. Soc.*, 1951, **73**, 2995, 2999).

As the Figure (curves *A*, *B*, and *C*) shows, in agreement with general experience (Jones, *Chem. Reviews*, 1943, **32**, 11), the introduction of methyl groups into the molecule has little effect on the general outline of the ultra-violet absorption curve of triarenesulphonylmelamines, beyond causing a slight bathochromic displacement of the high-intensity maximum. For comparison, some data for triazines and arenesulphonamides are summarised in the annexed Table. In acid solution (but not in neutral solution, cf. curve *E*), melamine has a peak at 236 mμ (Klotz and Askounis, *J. Amer. Chem. Soc.*, 1947, **69**, 801). Methanesulphonamide is optically transparent in the near-ultra-violet range. The spectrum of trimethanesulphonylmelamine (curve *D*) contained a broad maximum of relatively low intensity at 263 mμ, but lacked the typical features of the absorption curves of the arenesulphonylmelamines. The absorption characteristics of the latter compounds are therefore not likely to be primarily due to the presence of the triazine nucleus. Doub and Vandenbelt (*J. Amer. Chem. Soc.*, 1947, **69**, 2714) have traced the progressive bathochromic displacement of the absorption bands of benzene as a result of substitution in the aromatic nucleus. It is suggested that the high-intensity band of benzene (198 mμ; ε 8000), already intensified and displaced towards the longer wave-lengths in sulphonamide (see Table) by the marked bathochromic influence of sulphonyl substituents (Böhme and Wagner, *Ber.*, 1942, **75**, 606; Kumler and Strait, *J. Amer. Chem. Soc.*, 1943, **65**, 2349), is further modified by additional electronic interaction with the triazine nucleus, so as to appear as the high-intensity maximum in triarenesulphonyl-



Absorption spectra of melamine, triarenesulphonylmelamines (III) *and triarenesulphonylammelides* (V). *Curve E, melamine.*

R	Compound (III)	Compound (V)
p-C_6H_4Me	*A*	*F*
Ph	*B*	*G*
o-C_6H_4Me	*C*	—
Me	*D*	*H*

	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{max.}$ (mμ)	log ε
Benzenesulphonamide [a]	217·5	3·99	264·5 [e]	2·87
Toluene-*p*-sulphonamide [b]	226	4·12	262·5	2·73
Melamine [c]	236	3·99	—	—
Cyanuric chloride [d]	238	3·34	—	—

Measured in [a] water, [b] 0·1N-hydrochloric acid (Doub and Vandenbelt, *loc. cit.*), [c] water at pH 1—2·8, and [d] methanol (Klotz and Askounis, *loc. cit.*). [e] For more detailed resolution see Koch, *J.*, 1949, 410.

melamines. The less well-defined bands between 262 and 278 mμ may originate from the low-intensity benzenoid absorption near 255 mμ (cf. Gillam and Stern, "Electronic Absorption Spectroscopy," Arnold, London, 1954, pp. 116, 124). As with the triarenesulphonylmelamines (III), differences in the absorption properties of aromatic and non-aromatic sulphonylammelides (V) (cf. Figure, broken curves) were very marked.

EXPERIMENTAL

Benzene and xylene were dried by azeotropic distillation. The stated yields were obtained only when the heterogeneous mixtures were rapidly stirred by means of a Hershberg stirrer (*Org. Synth.*, 1943, Coll. Vol. 2, p. 117). Ultra-violet absorption measurements were made with a Unicam S.P. 500 photoelectric spectrophotometer, absolute ethanol being used as solvent.

Tritoluene-p-*sulphonylmelamine*.—A stirred suspension of the sodium salt of toluene-*p*-sulphonamide (6·75 g., 0·035 mole) in a solution of cyanuric chloride (0·93 g., 0·005 mole) in xylene (60 ml.) was refluxed during 3 hr. After several hours at room temperature the flocculent solid was collected (xylene filtrate A), air-dried, and dissolved in water (100 ml.) at 60—80°, with addition of a few drops of aqueous sodium hydroxide if necessary. The cooled (25—35°) stirred solution was acidified (Congo-red) with concentrated hydrochloric acid (6 ml.). Much of the resulting precipitate redissolved when the suspension was slowly heated, with good stirring, to 80°; the aqueous phase (extract B) was readily decanted from the granular residue. The residue was stirred with water (3 × 30 ml., at 80—90°; washings added to extract B) and redissolved in aqueous sodium hydroxide (3% w/v; 100 ml.) at 60—70°. Acidification (Congo-red) of the filtered warm solution with 3N-hydrochloric acid gave a precipitate, which was collected at 0° and washed with water. Addition of the dried pale-yellow powder (2·75—3·5 g.) to boiling ethanol (50 ml.) gave a clear orange solution, which rapidly deposited a white crystalline solid. This was collected after 2 days at 0° (m. p. 274—277°; 2·1—2·3 g., 71—78%) (ethanolic filtrate C) and afforded, after further crystallisation from ethanol, prisms of tritoluene-*p*-sulphonylmelamine, m. p. 282—283° alone or mixed with material obtained by the interaction of toluene-*p*-sulphonyl chloride with (*a*) *N*-cyano-*N'*-toluene-*p*-sulphonylguanidine (cf. Part VI, *J.*, 1953, 2531), (*b*) *N*-cyano-*N'*-phenylurea, or (*c*) 1-phenylbiuret (*Chem. and Ind.*, 1953, 195) (Found: C, 49·0; H, 4·3. Calc. for $C_{24}H_{24}O_6N_6S_3$: C, 49·0; H, 4·1%).

The ethanol filtrate C, when evaporated to 10 ml., deposited further quantities of the triarenesulphonylmelamine (up to 0·2 g.). Complete removal of the solvent under reduced pressure gave an acidic resin which was dissolved in dilute aqueous sodium hydroxide, and reprecipitated with hydrochloric acid. When collected it formed an amorphous pale yellow or pink powder (0·4—0·6 g.) of indefinite m. p. The aqueous extract B, when cooled to 0°, deposited lustrous plates (2·60 g., 0·015 mole), which gave toluene-*p*-sulphonamide, m. p. and mixed m. p. 135—137°, on crystallisation from water. Evaporation of the xylene filtrate A under reduced pressure gave only traces of a residue consisting chiefly of toluene-*p*-sulphonamide.

Reactions in boiling decahydronaphthalene (190°) gave substantially the same yields. Use of 5 or 4 mols. of sodium toluene-*p*-sulphonamide reduced the yields to 22 or 12%, respectively. Cyanuric chloride (0·01 mole) with toluene-*p*-sulphonamide (0·04 mole) in pyridine at 90—95° during 30 min. gave ill-defined products.

Tribenzenesulphonylmelamine.—The sodium derivative of benzenesulphonamide (6·25 g., 0·035 mole) and cyanuric chloride (0·93 g., 0·005 mole) in boiling xylene (60 ml.) afforded, as above, a crude product (2·5 g.) which was dropped into boiling chloroform (25 ml.). The clear solution rapidly deposited a crystalline solid (2·0 g.), which gave, on crystallisation from ethanol, prisms (1·65 g., 60%) of solvated tribenzenesulphonylmelamine, m. p. 149—152° undepressed on admixture with specimens prepared by methods (*a*), (*b*), and (*c*) (Found: C, 47·0; H, 4·1; N, 13·9; S, 15·9. Calc. for $C_{21}H_{18}O_6N_6S_3,C_2H_6O$: C, 46·6; H, 4·05; N, 14·2; S, 16·2%). Benzenesulphonamide (1·55 g., 0·01 mole; m. p. and mixed m. p. 151—153°) was recovered from the appropriate aqueous extracts (see above).

Other Synthesis Attempts.—Melamine (0·01 mole) was recovered unchanged after treatment with toluene-*p*-sulphonyl chloride (0·04 mole) in pyridine (in which the base was very sparingly soluble) at 100° during 2—3 hr. It failed to yield the triarenesulphonylmelamine when 0·01 mole was treated with the acid chloride (0·04 mole) and potassium hydroxide in water or aqueous acetone (for details, cf. Part VI, *loc. cit.*), or when refluxed with toluene-*p*-sulphonamide in phenol (cf. Thurston, U.S.P. 2,385,766/1945) during 3 hr. Fusion of melamine (0·001 mole) with toluene-*p*-sulphonic anhydride (0·006 mole) (Field, *J. Amer. Chem. Soc.*, 1952, **74**, 394) at 175—200° during ½—1 hr. gave non-crystalline, sometimes infusible products.

N-*Toluene*-p-*sulphonylammelide*.—A solution of cyanuric chloride (3·72 g., 0·02 mole) in benzene (150 ml.) containing suspended sodium toluene-*p*-sulphonamide (7·72 g., 0·04 mole) was refluxed during 3 hr. The voluminous white solid (test for chlorine positive) was collected at 5—10° (filtrate B), dried (10·25 g.), and dissolved in water (150 ml.) at 80°, and the solution acidified to Congo-red with concentrated hydrochloric acid. The resulting oily suspension was stirred at 90° during 5 min., and the aqueous phase decanted (extract A). The residual resin, after further washing with water (3 × 30 ml. at 80°), was converted into a white granular solid (4·85 g.; m. p. 195—200°) by dissolution in aqueous sodium hydroxide (50 ml., 5% w/v) and reprecipitation by 3N-hydrochloric acid at 0—5°. Crystallisation from boiling ethanol (15 ml.) gave a product (m. p. 245—248°; 2·85—3·60 g., 51—64%) which, after two further crystallisations from ethanol (20 ml. per g.; recovery per crystallisation, 50%) formed prisms of N-*toluene*-p-*sulphonylammelide*, m. p. 248—250° (decomp.) (Found: C, 43·3, 42·8; H, 3·5, 3·6; N, 20·3; S, 11·8. $C_{10}H_{10}O_4N_4S$ requires C, 42·55; H, 3·55; N, 19·85; S, 11·35%). The aqueous extract A deposited toluene-*p*-sulphonamide, m. p. and mixed m. p. 136—137° (2·55 g., 0·015 mole, 75%), on cooling. Evaporation of the benzene filtrate B to small volume (10 ml.) gave only traces of toluene-*p*-sulphonamide.

N-*Benzenesulphonylammelide*.—Sodium benzenesulphonamide (14·32 g., 0·08 mole) and cyanuric chloride (7·38 g., 0·04 mole) in boiling benzene (350 ml.) gave, as above (benzenesulphonamide recovered: 5·25 g., 84%), a product which, after reprecipitation from alkaline solution, was dissolved in boiling ethanol (200 ml.). The clear liquid deposited a white solid (m. p. 263—266°; 4·82 g., 45%). Crystallisation from ethanol (70 ml. per g.) afforded platelets of N-*benzenesulphonylammelide*, m. p. 264—267° (decomp.) (Found: C, 39·9; H, 3·1; N, 20·7; S, 11·7. $C_9H_8O_4N_4S$ requires C, 40·3; H, 3·0; N, 20·9; S, 11·9%). The compound was somewhat soluble in water.

N-*Methanesulphonylammelide*.—Sodium methanesulphonamide (4·68 g., 0·04 mole) [prepared by adding an equivalent of sodium dissolved in ethanol to a warm 40% solution (ethanol) of the sulphonamide, and rapidly drying the collected deliquescent salt in a vacuum over phosphoric oxide], when stirred in a boiling benzene solution (100 ml.) of cyanuric chloride (3·69 g., 0·02 mole) gave, after 5 min., a suspended soft plastic mass which became increasingly viscous on continued heating. After 25 minutes' refluxing, the benzene was decanted, and the residual material dissolved in N-sodium hydroxide (10 ml.). After this had been kept at 60° for 20 min., the product was precipitated from the filtered solution at 0° with 3N-hydrochloric acid (dry wt.: 1·65 g., 40%). Two crystallisations from boiling 95% ethanol (70 ml. per g.) gave prisms of solvated N-*methanesulphonylammelide*, m. p. 272—274° (decomp.) after sintering at 266° (Found: C, 20·6; H, 3·5; N, 24·8. $C_4H_6O_4N_4S,H_2O$ requires C, 21·4; H, 3·6; N, 25·0%). After being heated at 220—235° during 1 hr., the *compound* formed a white powder, m. p. 253—254° (decomp.) (Found: C, 22·7; H, 2·95; N, 26·9. $C_4H_6O_4N_4S$ requires C, 23·3; H, 2·9; N, 27·2%).

Hydrolysis of N-*Toluene*-p-*sulphonylammelide*.—(a) *By concentrated sulphuric acid.* The reactant (1·41 g., 0·005 mole) was added to concentrated sulphuric acid (2 ml.) in one portion. The resulting solution, the temperature of which rose spontaneously to 40°, was kept at 70—75° for 30 min. Addition of ice (15 g.) to the almost colourless liquid produced a white microcrystalline precipitate; after storage at 0° for 2 days, this was collected (aqueous filtrate A), washed with cold water (2 × 2 ml.), and dissolved in hot aqueous sodium hydroxide (4% w/v; 15 ml.). From the filtered warm solution, the material was reprecipitated with hydrochloric acid (1 : 1; 5 ml.), collected at 0° (0·52 g., 81%), and crystallised from boiling water (1 l. per g.), giving needles of ammelide (Found: C, 28·0; H, 3·2; N, 44·0, 43·2. Calc. for $C_3H_4O_2N_4$: C, 28·1; H, 3·1; N, 43·75%). The greater part of the free acid in filtrate A was neutralised with aqueous sodium hydroxide (20% w/v; 10 ml.), and the liquid treated with a warm saturated solution of *S*-benzylthiuronium chloride (1·5 g.). The resulting crystalline precipitate, collected at 0°, was crystallised once from ethanol–water (1 : 1), giving benzylthiuronium toluene-*p*-sulphonate, m. p. and mixed m. p. 178—179° (1·22 g., 72%). *N*-Benzenesulphonylammelide gave, under the same conditions, ammelide (Found: N, 43·5%) and benzylthiuronium benzenesulphonate in 84 and 86% yields, respectively.

(b) *By ethanolic hydrochloric acid.* A solution of *N*-toluene-*p*-sulphonylammelide (1·41 g., 0·005 mole) in ethanol (80 ml.) was refluxed, a slow stream of dry hydrogen chloride being continuously passed through the liquid. A white crystalline precipitate appeared after 1 hr. and increased in quantity during subsequent refluxing (total time: 14 hr.). The suspension was evaporated under reduced pressure to one-third of its volume and the solid collected at 5° (0·605 g., 94%) (filtrate A). Crystallisation from water gave cyanuric acid (0·49 g., 75%), identified as copper salt [Found : *M* (volumetrically; cf. Hantzsch, *Ber.*, 1906, **39**, 139), 127. Calc. for $C_3H_3O_3N_3$: *M*, 129]. Filtrate A was evaporated to small volume (8 ml.) and diluted with water (10 ml.); it then deposited toluene-*p*-sulphonamide, m. p. and mixed m. p. 136—137° (0·70 g., 82%).

*Di-*N*-arenesulphonylammelines.*—Interaction of cyanuric chloride (1 mol.) and sodium toluene-*p*-sulphonamide or benzenesulphonamide (4—6 mols.) in boiling benzene gave (after the usual treatment) products, from which small yields (10—20%) of a compound of m. p. 188—192° (decomp.), or 220—226° (decomp.), respectively, were isolated as the most soluble fraction by repeated crystallisation from ethanol. (The less soluble fractions consisted of the appropriate *N*-arenesulphonylammelide.) The composition of these substances, and the results of their hydrolysis by ethanolic hydrochloric acid (80% yield each of cyanuric acid and sulphonamide) or by concentrated sulphuric acid [yield of ammeline (Found : N, 52·8. Calc. for $C_3H_5ON_5$: N, 55·1%) and benzylthiuronium arylsulphonate : 90 and 76%, respectively] are consistent with the view that the products were impure specimens of di-*N*-arylsulphonylammelines.

Interaction of the above reagents in boiling toluene gave varying yields of the monosulphonyl- (V) (~40%) and trisulphonyl-derivatives (III) (~20%) in addition to the above compounds.

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