Research and Development Center, Armstrong Cork Company

The Synthesis and Characterization of Some

2,4,6-Triaryl and Alkylsulfonylhydrazido-*s*-Triazines (1)

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2,4,6-Trialkyl- and triarylsulfonylhydrazido-*s*-triazines (I) have been synthesized by the reaction of cyanuric chloride with a variety of sulfonylhydrazides in a hydrocarbon solvent. The subject compounds (I) were characterized by elemental analysis, molecular weight and spectroscopy.

The behavior of cyanuric chloride as a pseudo acid chloride and its reactivity toward various nucleophilic reagents (amines, alcohols, etc.) is well known (2). Of particular interest to us was the reaction of cyanuric chloride with sulfonylhydrazides to form 2,4,6-trisubstituted sulfonylhydrazido-*s*-triazines (I).

D'Alelio and Becker (3a) carried out the reaction of cyanuric chloride with arylsulfonylhydrazides in the presence of sodium bicarbonate at 0-10° and obtained 2,4-dichloro-6-arylsulfonylhydrazido-*s*-triazines (II) in 60-75% yield. The intermediates (II) were difficult to purify and, consequently, no elemental analyses were given. The crude 2,4-dichloro-6-arylsulfonylhydrazido-*s*-triazines (II) were subsequently converted to 2,4-diamino-6-arylsulfonylhydrazido-*s*-triazines. Di- and tri-substitution on the *s*-triazine ring by arylsulfonylhydrazido groups was apparently not investigated. Earlier D'Alelio and Underwood (3b) claimed the preparation of a variety of 2,4,6-triarylsulfonylhydrazido-*s*-triazines (I) by reaction of 2,4,6-trihydrazino-*s*-triazine with the corresponding arylsulfonyl halide; detailed reaction conditions were not given nor were the products (I) characterized.

Kurzer and coworkers (4) have prepared the analogous 2,4,6-triarylsulfonamido-*s*-triazines. Initially (4a-b) these compounds were isolated as primary reaction products in apparently unsuccessful attempts to prepare *N*-cyano-*N*,*N'*-disulfonylguanidines by interaction of *N*-cyano-*N'*-sulfonylguanidines and sulfonyl chlorides in pyridine. The *s*-triazine structure was assigned on the basis of molecular weight determinations, elemental analysis and hydrolytic degradation. Subsequently, further confirmation was obtained when Kurzer and coworkers (4c-d) synthesized the 2,4,6-triarylsulfonamido-*s*-triazines from cyanuric chloride and sodium arylsulfonamides.

In view of the ability of cyanuric chloride to undergo reaction with various nucleophiles by a stepwise replacement of its chlorine atoms and in light of its reactions (3,4) with sulfonamides and sulfonylhydrazides, the preparation of 2,4,6-tri-substituted sulfonylhydrazido-*s*-triazines (I) seemed reasonable.

A variety of aryl and alkylsulfonylhydrazides (Table I) were reacted with cyanuric chloride under moderate conditions to give the previously unidentified 2,4,6-trisubstituted sulfonylhydrazido-*s*-triazines (I) in high yields (Table I). In most cases the reaction was effected by heating a stirred slurry or solution (5) of the sulfonylhydrazide in a dried hydrocarbon solvent (benzene or toluene) under a positive nitrogen pressure until hydrogen chloride evolution essentially ceased (*ca*. 24 hours). The reaction was also carried out successfully in the polar solvents, tetraethylene glycol dimethyl ether and tetrahydrothiophene 1,1-dioxide (sulfolane). Reaction temperatures (*ca*. 80°) were governed by the thermolability of the requisite sulfonylhydrazide. The sulfonylhydrazide was present in at least 10% excess over that required to react with the three chlorine atoms of cyanuric chloride. That some (*ca*. 10%) of the sulfonylhydrazide was evidently consumed by the decomposition route was ascertained by the isolation of the corresponding thiolsulfonate (Table I). Sulfonylhydrazides are known (6) to give rise to thiosulfonates and disulfides upon thermal decomposition.

In general, our reaction conditions (excess of sulfonylhydrazide and relatively long reaction times) precluded the isolation of mono and/or dichloro-*s*-triazine derivatives. However, in several reactions of cyanuric chloride with benzenesulfonylhydrazide small amounts of 2,4-dichloro-6-benzenehydrazido-*s*-triazine (II, R = Ph) were isolated. Identification was made by elemental analysis and melting point (3a).

I

II
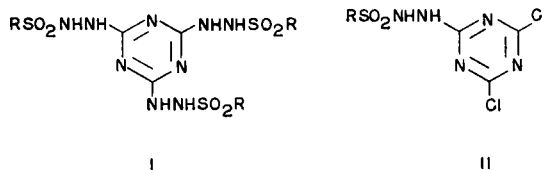
The amorphous, white, solid, 2.4.6-trisubstituted sulfonylhydrazido-s-triazines (I), with the exception of the n-butane derivative (If), were insoluble in conventional solvents, e.g. alcohol, benzene, etc. The compounds were soluble to varying degrees in polar solvents such as dimethylformamide, dimethyl sulfoxide, tetrahydrofuran, etc. Purification was effected in most cases by recrystallization from dioxane or precipitation from dimethylformamide solution on addition to water (Table I). Drying in vacuo (< 0.1 mm.) at ca. 110° was necessary to remove polar solvents used in purification. The presence of solvent usually manifested itself by broad melting points and preliminary softening. Dilute aqueous alkali dissolved the compounds (I) to give colored solutions.

The reaction products were formulated as 2,4,6-trisubstituted sulfonylhydrazido - s - triazines (I) on the basis of their elemental analysis, molecular weight (where solubility in THF allowed), infrared absorption and n.m.r. spectra. In the case of 2,4,6 - tribenzenesulfonylhydrazido - s - triazine (Ia), hydrolytic degradation with concentrated sulfuric acid afforded 2,4,6 - trihydrazino - s - triazine and benzenesulfonic acid. Kurzer and Powell (4c) obtained melamine and the arylsulfonic acid upon similar treatment of the analogous 2,4,6-triaryl-sulfonamido-s-triazines.

The infrared spectra of (I) exhibited NH absorption at 2.9-3.0 μ. In addition, strong absorption, usually three well-defined bands, occurred in the 6.2-7.0 μ region; a band of medium intensity was also present at 12.3-12.4 μ. These absorptions may be attributed (7) at least in part to in-plane and out-of-plane vibrations of the triazine ring, respectively. Characteristic (7.4-7.6 and 8.6-8.7 μ) strong sulfonyl absorption was present for all compounds (I).

The n.m.r. spectra of the 2,4,6 - trisubstituted sulfonylhydrazido-s-triazines (I) exhibited two generally broad NH singlets of approximately equal intensity at low field (τ = 0-1.1 p.p.m.) (Table II). The lower field proton (H_a) was assigned to the NH adjacent to the s-triazine ring and the upfield proton (H_b) as the NH adjacent to the sulfonyl group. Assignment of the low field proton as H_a follows from evidence that it is bonded. The exchange process with deuterium oxide was followed for one of the compounds (Ie) and the low field proton (H_a) exchanged only about half as rapidly as the upfield proton (H_b). In addition, the position of (H_a) in (Ie) exhibited little or no change on dilution while (H_b) undergoes a definite shift. The chemical shift values for the aromatic and aliphatic protons of the 2,4,6 - trisubstituted sulfonylhydrazido - s - triazines (I) were consistent with expectation. In summary, the chemical shift values and their corresponding integrals supported the assigned structure for (I).

The reaction of cyanuric chloride with several sulfonylhydrazides in the presence of a base as a hydrogen chloride acceptor was briefly investigated. Use of both aqueous alkali and triethylamine was considered initially; however, examination of the

literature and our own experimentation showed these to be impractical. Cyanuric chloride has been shown (8) to hydrolyze in aqueous alkali. Several workers (9) have demonstrated the reaction of tertiary alkyl, aryldialkyl, and N-alkyl saturated nitrogen heterocyclics with cyanuric chloride under relatively mild conditions to yield among other products alkyl halides and amino substituted triazines.

Attention was next turned to pyridine as a hydrogen chloride acceptor. Pyridine, in the presence of water and also in acetone, has been shown (10a) to react with cyanuric chloride. However, Saure (10b) did not observe reaction with anhydrous pyridine even on boiling. We failed to obtain any of the desired 2,4,6-triarylsulfonylhydrazido-s-triazine (I) on reacting cyanuric chloride with a slurry of an aromatic sulfonylhydrazide in anhydrous benzene containing pyridine in amounts sufficient to combine with the hydrogen chloride that could form.

Finally, an alternate route to the 2,4,6-triaryl-sulfonylhydrazido-s-triazines (I) was investigated. The procedure entailed reaction of an arylsulfonyl chloride, specifically the benzene analog, with 2,4,6-trihydrazino-s-triazine in the presence of aqueous alkali. This approach is similar to that of D'Alelio and Underwood (3b) who employed a tertiary amine as a hydrogen chloride acceptor. A small amount of crude trisubstituted s-triazine (Ia) was obtained. Concurrent hydrolysis of the benzenesulfonyl chloride and possibly of the 2,4,6-trihydrazino-s-triazine, under the conditions used, appeared to be major obstacles to the reaction. Kurzer and coworkers (4c) had earlier reported the failure of the analogous reaction of melamine with arylsulfonyl chlorides in the presence of base.

EXPERIMENTAL (11)

Materials.

Cyanuric chloride (American Cyanamid) was purified by recrystallization from benzene (53.4 g. per 100 ml. of boiling solvent); m.p. 146-148° [lit. (12) m.p. 154°]. The sulfonylhydrazides were prepared in 60 to 90% yield by one of two general procedures: (A) addition of a benzene solution of the sulfonyl chloride to a slurry of hydrazine or hydrazine hydrate in benzene at 10 ± 5° or (B) by the procedure given in Organic Syntheses (13). The purity of the sulfonylhydrazides synthesized was ascertained by brominetric analysis (14,15).

Preparation of 2,4,6-Trisubstituted Sulfonylhydrazido-s-Triazines (I) by Reaction of Cyanuric Chloride with Sulfonylhydrazides.

In general, the 2,4,6-trisubstituted sulfonylhydrazido-s-triazines (I) (Table I) were prepared according to the procedure given below for the benzene derivative (Ia). Toluene was utilized as the reaction solvent in the reaction involving benzylsulfonylhydrazide and a reaction temperature of 100 ± 5° was maintained. In the case of n-butane-sulfonylhydrazide a lower reaction temperature (70 ± 5°) was maintained in benzene as the reaction solvent.

Reaction of Cyanuric Chloride with Benzenesulfonylhydrazide.

(A) To a stirred solution of cyanuric chloride (18.5 g., 0.1 mole) in 525 ml. of dry benzene was added benzenesulfonylhydrazide (60 g., 0.35 mole). The stirred reaction mixture was heated at 80 ± 3° under a positive nitrogen pressure. Exit gases were scrubbed by passage through aqueous 10% sodium hydroxide. Ten to fifteen minutes after

TABLE I

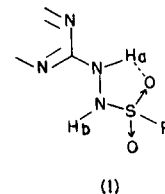### 2,4,6-Trisubstituted Sulfonylhydrazido-s-Triazines (I)

Compound	R	Yield, % (a)	Solvent of (b) Recrystallization	M.p. °C, dec.	Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found	Mol. Wt. Calcd.	Mol. Wt. Found (c)
Ib	p-CH$_3$C$_6$H$_4$-	85 (d)	DMF-W	232-234	C$_{24}$H$_{27}$N$_9$O$_6$S$_3$	45.48	45.35	4.30	4.38	19.89	19.85	15.18	15.04	633.73	621.4
Ic	p-ClC$_6$H$_4$-	92 (e,f)	D	251-252	C$_{21}$H$_{18}$Cl$_3$N$_9$O$_6$S$_3$	36.29	36.46	2.61	2.55	18.14	18.08	13.84	13.61	694.99	----
Id	p-CH$_3$OC$_6$H$_4$-	94	D	232-233	C$_{24}$H$_{27}$N$_9$O$_9$S$_3$	42.28	42.22	3.99	4.25	18.49	18.34	14.11	12.94	681.73	----
Ie	β-C$_{10}$H$_7$-	92 (g)	D	233-235	C$_{33}$H$_{27}$N$_9$O$_6$S$_3$	53.43	53.24	3.67	3.63	16.99	17.10	12.97	12.80	741.82	732.3
If	C$_6$H$_5$CH$_2$-	100 (h)	DMF-W	232-234	C$_{24}$H$_{27}$N$_9$O$_6$S$_3$	45.48	45.45	4.30	4.29	19.89	19.96	15.18	15.06	633.73	640.8
Ig	CH$_3$(CH$_2$)$_3$-	75	E-W	195-197	C$_{15}$H$_{33}$N$_9$O$_6$S$_3$	33.88	33.67	6.26	6.16	23.71	23.85	18.09	18.06	531.68	530.0

(a) Yields are of the crude reaction product and are based on the amount of cyanuric chloride used. An excess (ca. 10% or more) of the sulfonylhydrazide was employed in each case. Small amounts of the corresponding arylthiolsulfonate were isolated in a number of reactions. (b) DMF = dimethylformamide, W = water, D = dioxane, E = ethyl alcohol. (c) Molecular weights were determined in tetrahydrofuran using a Mechrolab Vapor Pressure Osmometer (Model No. 301, probe No. 1248). Several of the 2,4,6-trisubstituted sulfonylhydrazido-s-triazines (I) were not sufficiently soluble to enable determinations to be made. (d) p-Tolyl-p-toluenethiolsulfonate m.p. 73-74.5° was isolated. Anal. Calcd. for C$_{14}$H$_{14}$O$_2$S$_2$: C, 60.40; H, 5.08; S, 23.03. Found: C, 60.42; H, 5.12; S, 23.20. Reported m.p. 76-77°, [E. Vinkler and F. Klivenyi, Acta. Chim. Acad. Sci. Hung., 5, 159 (1954); Chem. Abstr., 49, 6162e (1955)]. (e) p-Chlorophenyl-p-chlorobenzenethiolsulfonate was identified by m.p. and mixture m.p. with an authentic sample, [reported (d) m.p. 133-134°]. (f) Calcd.: Cl, 15.31. Found: Cl, 15.11. (g) β-Naphthyl β-naphthalenethiolsulfonate was recovered from the benzene solubles, m.p. 97-101° [reported m.p. 106-107°, G. Leandri and A. Tundo, Ann. Chim. (Rome), 47, 575 (1957); Chem. Abstr., 51, 17795e (1957)]. (h) Benzyl benzylthiolsulfonate (m.p. 105-107°) was obtained from the toluene solubles [reported m.p. 108°, B. G. Boldyrev and L. M. Khovalko, Zh. Obshch. Khim., 31, 3729 (1961); Chem. Abstr., 57, 9719e (1962)].

TABLE II

N.m.r. Data (a) for 2,4,6-Trisubstituted Sulfonylhydrazido-s-Triazines (I)

Compound	Chemical Shift (b) Values for N-H Protons τ =	
	H$_a$	H$_b$
Ia	0.79	1.12
Ib	0.88	1.03
Ic	0.58	0.91
Ie	0.73	1.05
If	0.66	0.96
Ig	0.03	0.38

(I)

(a) Spectra were obtained on hexadeuterated dimethyl sulfoxide solutions of (I). (b) Downfield from TMS included as internal standard.

reaching reaction temperature (80 ± 3°), the reaction mixture took on a thick consistency and hydrogen chloride was evolved. After 26 hours, 58% of the available hydrogen chloride was accounted for. Continued heating caused further evolution of hydrogen chloride but at a slower rate (67% after 44 hours and 75% after 66 hours).

The cooled reaction mixture was filtered; the filter-cake washed with ether and dried in vacuo gave 68.5 g. of material m.p. 229-233° dec. Distillation of the combined clear colorless washings and benzene filtrate left a weakly acidic oil (1.5 g.) that was unidentified. The main white solid reaction product (68.5 g.) was slurried with water, the resulting acidic slurry filtered, and the filter-cake washed with fresh portions of water until neutral to litmus. The dried filter-cake (61 g.) melted at 241-243° dec. Neutralization of the combined aqueous washings failed to yield any appreciable precipitate.

A warm solution of the reaction product in dimethylformamide (240 ml.) was filtered and the cyanuric hydrazide precipitated by addition to cold water (1500 ml.). After two reprecipitations and final recrystallization from a 1:1 dimethylformamide-benzene mixture, the compound dried in vacuo (< 0.1 mm.) at 110°, melted at 240-243° with decomposition.

Anal. Calcd. for C$_{21}$H$_{21}$N$_9$O$_6$S$_3$ (Ia): C, 42.63; H, 3.58; N, 21.31; S, 16.26. Found: C, 42.47; H, 3.70; N, 21.27; S, 16.18.

(B) The reaction was repeated using 0.66 mole of benzenesulfonylhydrazide, 0.2 mole of cyanuric chloride and 1200 ml. of dry benzene. After 18 hours at 75-80°, the cooled reaction mixture was filtered and the filter-cake treated as described previously gave 137.6 g. of material. Repeated washing of the crude product (137.6 g.) with water left 105 g. (after drying) of (Ia), m.p. 227-230° dec.

Acetone (0.3 mole), added to the combined acidic aqueous washings, precipitated acetone benzenesulfonylhydrazone (18.2 g., 0.086 mole) after drying. The hydrazone was identified by melting point (132-138° dec.) and mixture melting point [lit. (16), m.p. 143-145°].

Distillation of the combined ether washings and benzene filtrate from the original reaction mixture left a pale yellow solid, 5.5 g. (m.p. 155-161° dec.) after drying in vacuo. Recrystallization, once from benzene and twice from aqueous 50% alcohol, raised the melting point to 167-169° with decomposition [reported (3a) m.p. 161-163°].

Infrared absorption (KBr) occurred at 2.29 (m), 2.99 (s), 3.15 (m), 3.35 (m), 6.33 (s), 6.47 (s), 6.60 (s, shoulder), 6.91 (m), 6.99 (s), 7.37 (s), 7.47 (s), 7.64 (s), 8.02 (s), 8.50 (s), 9.17 (m), 10.03 (w), 11.70 (m), 12.53 (m), 13.23 (m), 13.69 (m) and 14.65 (m) μ.

Anal. Calcd. for C$_9$H$_7$Cl$_2$N$_5$O$_2$S (II, R=Ph): C, 33.76; H, 2.21; Cl, 22.15; N, 21.88; S, 10.02. Found: C, 33.92; H, 2.22; Cl, 21.99; N, 22.19; S, 10.15.

Hydrolytic Degradation of 2,4,6-Tribenzenesulfonylhydrazido-s-Triazine (Ia).

A stirred solution of 2,4,6-tribenzenesulfonylhydrazido-s-triazine (Ia) (6.0 g., 0.01 mole) in 15 ml. of concentrated sulfuric acid was heated at 65° for 3 hours. The cooled dark brown solution was added to crushed ice and gave a turbid yellow solution. Addition of alkali to the aqueous acidic solution precipitated a tan solid. The filtered and dried solid (0.9 g.) was identified as 2,4,6-trihydrazino-s-triazine by m.p. (264-267° dec.) and mixture m.p. with authentic material.

Neutralization of the aqueous basic filtrate (255 ml.) and subsequent reaction with s-benzylthiuronium chloride gave the s-benzylthiuronium salt of benzenesulfonic acid (0.02 mole) m.p. 147-149° [lit. (17) m.p. 147.5-148.5°].

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