

Synthesis of Heterocyclic Compounds. Part 34.¹ Reactions of Chlorosulphonyl Isocyanate with Carbon–Nitrogen Double Bonds

By Hans Suschitzky* and Ralph E. Walrond, The Ramage Laboratories, Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, Lancashire
Roy Hull, Imperial Chemical Industries Limited, Pharmaceuticals Division, Alderley Park, Macclesfield, Cheshire SK10 4TF

Anils react with chlorosulphonyl isocyanate (CSI) to yield triazinediones, whereas azines produce triazolotriazolones. Other compounds containing carbon–nitrogen double bonds (oximes, hydrazones, amidines, and carbodi-imides) also react with CSI giving synthetically useful results. The cycloaddition of CSI to azides is described.

CHLOROSULPHONYL ISOCYANATE ($\text{ClO}_2\text{S}\cdot\text{NCO}$) (CSI) has received considerable attention² owing to its reactivity as a 'uniparticulate' electrophile^{3b} and as a heterocumulene in cycloaddition reactions with olefins,⁴ acetylenes⁵ and bicyclic strained hydrocarbons.³ The initial products from olefins are usually azetidion-2-ones, formed in a reaction possibly involving a $[\pi 2_s + \pi 2_a]$ process, and followed in some cases by rearrangement. By contrast, interaction of the reagent with carbon–nitrogen multiple bonds has, apart from our preliminary communication⁶ concerning anils, been reported only for an alk-1-enylideneamine⁷ (>C=C=N-), which yielded an unstable diazinone. We now enlarge on our note⁶ concerning the interaction of Schiff's bases and CSI, and also describe the first examples of the addition of this reagent to other carbon–nitrogen multiple bonds.

¹ Part 33, R. L. Bentley and H. Suschitzky, *J.C.S. Perkin I*, 1976, 1725.

² (a) H. Bestian, 'Cycloaddition Reactions,' I.U.P.A.C., Butterworth, London, 1971, p. 611; (b) R. Graf, *Angew. Chem. Internat. Edn.*, 1968, 172.

³ (a) E. J. Moriconi and C. P. Dutta, *J. Org. Chem.*, 1970, **35**, 2443; (b) L. A. Paquette, G. R. Allen, jun., and M. J. Broadhurst, *J. Amer. Chem. Soc.*, 1971, **93**, 4503.

As reported,⁶ azomethines [*e.g.* (1; $\text{R}^1 = \text{R}^2 = \text{Ar}$)] yield triazinediones (2; $\text{R}^1 = \text{R}^2 = \text{Ar}$, $\text{R}^3 = \text{SO}_2\text{Cl}$) in high yield when treated with CSI at room temperature in methylene chloride. Conversion of the chlorosulphonyl substituent by conventional methods into various derivatives (2; $\text{R}^3 = \text{SO}_2\text{Me}$, SO_2N_3 , or SO_2NR_2) occurred readily (see Experimental section), as did de(chlorosulphonylation) to give the corresponding cyclic amide (2; $\text{R}^3 = \text{H}$). The latter could be alkylated to give (2; $\text{R}^3 = \text{Me}$), but was resistant to PCl_5 and to reduction (LiAlH_4).

We also carried out reactions of CSI with Schiff's bases containing an *o*-dialkylamino-group (3) in methylene

⁴ L. A. Paquette, T. Kakihana, J. R. Hansen, and J. C. Phillips, *J. Amer. Chem. Soc.*, 1971, **93**, 152; L. A. Paquette, S. Kirschner, and J. R. Malpass, *ibid.*, 1970, **92**, 4330; J. R. Maldass, *J.C.S. Chem. Comm.*, 1972, 1246; J. R. Malpass and N. J. Tweddle, *ibid.*, p. 1247.

⁵ E. J. Moriconi and Y. Shimakawa, *J. Org. Chem.*, 1972, **37**, 196.

⁶ H. Suschitzky and R. E. Walrond, *J.C.S. Chem. Comm.*, 1973, 570.

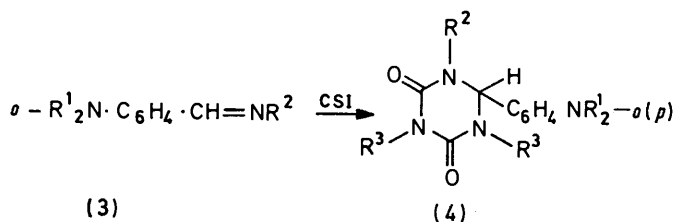
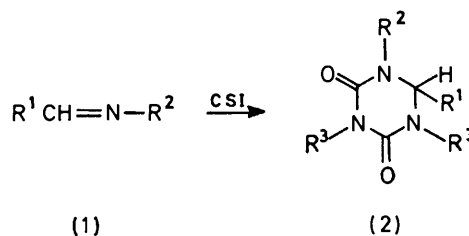
⁷ Nasser-Ud Din, J. Riegl, and L. Skattebøl, *J.C.S. Chem. Comm.*, 1973, 271.

chloride at room temperature. A transitory red colour developed which we ascribe to quaternisation of the anil. In every case the expected *s*-triazinedione (4; $R^3 = \text{SO}_2\text{Cl}$) was obtained, which gave the corresponding amide (4; $R^3 = \text{H}$) as set out in Table 1. No interaction between the dialkylamino nitrogen atom and the intermediate dipole during the cycloaddition had thus taken place. However, the product from *N*-benzylidene-*o*-piperidinoaniline (5) was not the expected triazinedione (2; $R^2 = \text{C}_6\text{H}_4\text{NC}_5\text{H}_{10}\text{-}o$, $R^1 = \text{Ph}$, $R^3 = \text{SO}_2\text{Cl}$). Elemental analysis indicated again a 2 : 1 addition of CSI to the anil, but the i.r. spectrum showed a well defined band at 1660 cm^{-1} typical of an unstrained amide rather than of a triazinedione⁶ ($\text{C}=\text{O}$ *ca.* $1770\text{--}1790\text{ cm}^{-1}$). Owing to instability of the compound, attempts to remove the SO_2Cl group and to prepare a cognate derivative have failed so far. The *p*-piperidino-analogue (5; $\text{C}_5\text{H}_{10}\text{N}^-$ in *p*-position) gave the expected *s*-triazinedione (2; $R^1 = \text{Ph}$, $R^2 = \text{C}_6\text{H}_4\text{NC}_5\text{H}_{10}\text{-}p$, $R^3 = \text{SO}_2\text{Cl}$) as did other *p*-dialkylamino-substituted anils (Table 1), whereas the *o*-dialkylamino-isomer (5) did not follow the 'normal' path. This difference is rationally ascribed to the intervention of the *o*-dialkylamino-group, as we have observed in analogous situations (*t*-amino effect).⁸ Tentatively we assign the tricyclic structure (8) to our product, which is supported by its n.m.r. spectrum, its analytical data, and a rational mechanism for its formation (Scheme 1): interception of a dipolar intermediate (6) by the *o*-*t*-amino-group leads to the transient ammonium structure (7) in which one of the reactive α -methylene groups suffers nucleophilic attack by the internal anion with simultaneous fission of the piperidine ring. The formation of structure (8) can be regarded as chemical evidence for the existence of a dipolar intermediate in the reaction of anils with CSI. Work is in progress to find suitable conditions for producing stable 1,3-bridged dihydrobenzimidazoles of type (8) by this remarkable one-step conversion of *o*-dialkylamino-substituted Schiff's bases.

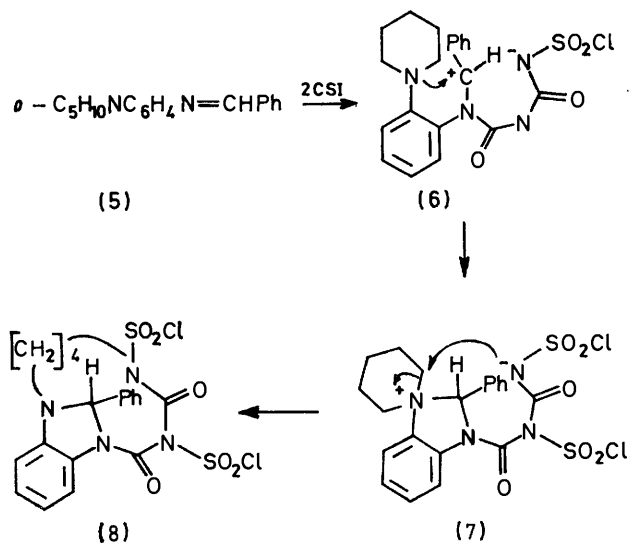
Attempts at trapping a transitory 1,4-dipolar species in the formation of the *s*-triazinedione (2; $R^1 = R^2 = \text{Ph}$) from benzylideneaniline (1; $R^1 = R^2 = \text{Ph}$) and CSI in presence of a large excess of phenyl isocyanate led only to the triazine (2). The lack of competition between these two isocyanates is, however, not unexpected, in view of the very high reactivity of CSI.^{2a}

Azines, which can be regarded formally as bis-anils are versatile partners in cycloaddition reactions. Both azomethine groups may react with dipolarophiles in 'criss-cross' additions⁹ or, as recently observed only one of the azomethine groups will engage in a [2 + 2] addition with cyano-(*t*-butyl)keten¹⁰ to give an aze-tidin-2-one or with an alkoxydiazonium salt as a dipolarophile in a [2 + 3] cycloaddition to produce 1,2,4-tri-

azoles.¹¹ With CSI 'criss-cross' adducts were obtained in high yields at ambient temperature. For instance



benzaldehyde azine (9; $\text{R} = \text{Ph}$) gave the stable diphenyltriazolotriazolone (10; $\text{R} = \text{Ph}$, $\text{R}' = \text{SO}_2\text{Cl}$). On heating or prolonged storage decomposition occurred with liberation of sulphur dioxide and hydrogen chloride.



SCHEME 1

Removal of the chlorosulphonyl group (with sodium sulphite or potassium iodide) gave the cyclic amide (10; $\text{R} = \text{Ph}$, $\text{R}' = \text{H}$). Structural assignment followed from spectral data as well as from acidic hydrolysis to give benzaldehyde and hydrazodiformamide,¹² ($\text{NH}_2\cdot\text{CO}\cdot\text{NH}$)₂, and from oxidation with nitric acid to 5-hydroxy-3-phenyltriazole. Electron-donating or withdrawing substituents in the phenyl ring of (9; $\text{R} = \text{Ph}$) and other aromatic analogues gave analogous products (Table 3). The introduction of another reactive site into the azine such as an *o*-dialkylamino-group (9; $\text{R} = o$ -

⁸ O. Meth-Cohn and H. Suschitzky, *Adv. Heterocyclic Chem.*, Academic Press, New York and London, 1972, **14**, 211.

⁹ (a) T. Wagner-Jauregg, *Ber.*, 1930, **63**, 3213; (b) J. R. Bailey and A. T. McPhearson, *J. Amer. Chem. Soc.*, 1917, **39**, 1322; (c) M. Horing and T. Wagner-Jauregg, *Helv. Chim. Acta*, 1957, **40**, 852.

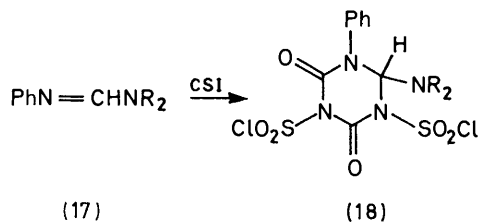
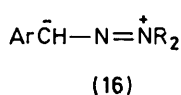
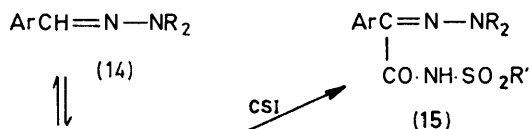
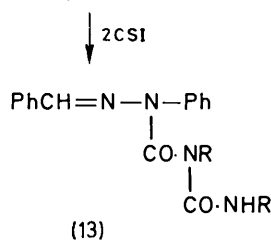
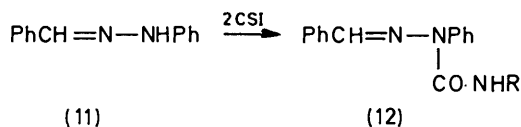
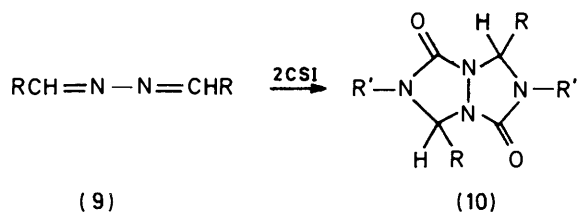
¹⁰ D. Johnson and H. Suschitzky, unpublished results.

¹¹ S. S. Mathur and H. Suschitzky, *J.C.S. Perkin I*, 1975, 2474.

¹² T. Curtius and K. Heidenreich, *Ber.*, 1894, **27**, 55.

$R_2N \cdot C_6H_4$) or an allyloxy-group (9; $R = o\text{-CH}_2 \cdot \text{CH} \cdot \text{CH}_2 \cdot \text{O} \cdot C_6H_4$) still produced only 'criss-cross' adducts of type (10) even with an excess of CSI. Aromatic ketone azines did not interact with CSI, which is reminiscent of their inertness towards aryl, acyl, and alkyl isocyanates.^{9b,13} The chlorosulphonyl compound (10; $R = \text{Ph}$ $R' = \text{SO}_2\text{Cl}$) provided other derivatives ($R' = \text{SO}_2 \cdot \text{NPh}$, SO_2N_3 , SO_2OMe , Ac, Me, or Et) by conventional methods.

Arylhydrazones (11) contain an NH as well as an azomethine group and might be expected to react with CSI at both positions. With 1 equiv. of the reagent the *N*-carbamoylhydrazone (12; $R = \text{SO}_2\text{Cl}$) and with 2 equiv. the biuret compound (13; $R = \text{SO}_2\text{Cl}$) were obtained, in reactions analogous to those of simple



amines. Removal of the SO_2Cl group occurred with sodium sulphite to give the corresponding amides ($R = \text{H}$). We thought that dialkylhydrazines of type (14)

¹³ O. Tsuge and S. Kanemasa, *Bull. Chem. Soc. Japan*, 1972, **45**, 3591.

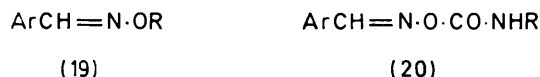
¹⁴ R. Brehine and H. E. Nikolajewski, *Tetrahedron*, 1969, **25**, 1159.

might provide an azomethine group and yield triazine systems in reactions analogous to those of Schiff's bases. However, we obtained the *C*-carbamoylhydrazones (15; $R' = \text{Cl}$) from a variety of hydrazones (see Experimental section). The products were readily converted into the corresponding esters (15; $R' = \text{OEt}$) on boiling for a few minutes in ethanol, and attempted reduction in an aqueous ethanolic solution of potassium iodide gave only the corresponding ester. On the basis that hydrazones can be regarded as aza-enamines¹⁴ a rational mechanism for the result can be advanced [(14) \rightarrow (16) \rightarrow (15)].

By contrast dialkylamidines (17) reacted in a way analogous to that of anils (1), thus providing a convenient route to the stable 6-dialkylaminohexahydrotriazine-2,4-diones (18) (Table 5).

The benzaldehyde oximes (19; $R = \text{H}$, $\text{Ar} = 4\text{-ClC}_6\text{H}_4$ or $4\text{-MeC}_6\text{H}_4$) with CSI reacted like alcohols to give the corresponding unstable carbamoyloximes (20; Ar as before, $R = \text{SO}_2\text{Cl}$), which could be reduced with aqueous sodium sulphite to give (20; $R = \text{H}$). The oxime ether (19; $\text{Ar} = \text{Ph}$, $R = \text{Me}$) did not react with CSI even in boiling benzene.

Cycloadditions of carbodi-imides (21) with various isocyanates have been investigated extensively.¹⁵ Aryl



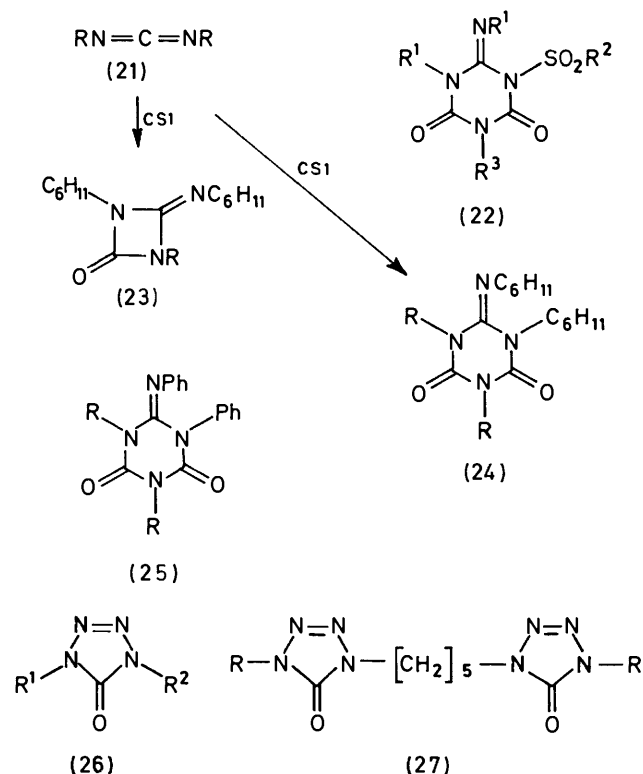
isocyanates give an unstable [2 + 2] addition product, and acyl and thioacyl isocyanates were recently shown to undergo a [4 + 2] reaction, not the [2 + 2] addition originally reported.¹⁶ A more complex reaction pattern has been reported for sulphonyl isocyanates¹⁷ ($\text{R}^2\text{SO}_2\text{-NCO}$) with dialkylcarbodi-imides: an intermediate polar 1 : 1 adduct which can react with another molecule of isocyanate to form a 2 : 1 adduct (22; $\text{R}^3 = \text{SO}_2\text{R}^2$) or can be intercepted by sulphonylcarbodi-imide ($\text{R}^2\text{SO}_2 \cdot \text{N} \cdot \text{C} \cdot \text{NR}^1$, arising from disproportionation of a 1 : 1 addition product) to give the cycloadduct (22; $\text{R}^3 = \text{R}^1$). The mode of addition was said to influence the product distribution. On this basis we expected an analogous sequence of events for the interaction of CSI and dialkylcarbodi-imides. However, by contrast the addition of CSI to dicyclohexylcarbodi-imide (21; $R = \text{C}_6\text{H}_{11}$) which occurred at 0 °C in a mixture of ether-benzene yielded one of two products, depending on the mode of addition. Adding CSI dropwise to the di-imide (21; $R = \text{C}_6\text{H}_{11}$) in the solvent gave the diazetidinone (23; $R = \text{SO}_2\text{Cl}$), reduceable to (23; $R = \text{H}$). When the mode of addition was reversed the product formed from 2 molecules of CSI and 1 molecule of the di-imide (21; $R = \text{C}_6\text{H}_{11}$) was the triazinedione (24; $R = \text{SO}_2\text{Cl}$) giving on reduction (24; $R = \text{H}$). The formation of the two products (23) and (24) was solely dependent on

¹⁵ H. Ulrich, 'Cycloaddition Reactions of Heterocumulenes,' Academic Press, New York and London, 1967.

¹⁶ O. Tsuge and K. Sakai, *Bull. Chem. Soc. Japan*, 1972, **45**, 1534.

¹⁷ H. Ulrich, *Accounts Chem. Res.*, 1969, **2**, 186.

the sequence of addition and was in no way influenced by a change in the molar ratio of reagent and substrate. By contrast, diphenylcarbodi-imide (21; R = Ph) gave only a single product, the triazinedione (25; R = SO₂Cl), regardless of the mode of addition or the quantities of reactants.



Azides are well-known dipolar species¹⁸ and CSI was expected to be a suitable dipolarophilic partner. However, aryl azides did not react at room temperature, and in boiling chloroform charring occurred. The formation of a tetrazolone (26; R¹ = Ph, R² = SO₂Cl) was inferred from the i.r. spectrum of the products, which were probably in equilibrium with the reactants owing to cycloreversion as reported for related reactions.¹⁹ Alkyl azides reacted instantaneously at ambient temperature in a variety of solvents to give alkyl(chlorosulphonyl)-tetrazolones (26; R¹ = alkyl, R² = SO₂Cl) in high yield as hygroscopic liquids which decomposed unless kept under nitrogen. Recently¹⁹ the n-butyl derivative (26; R¹ = Buⁿ, R² = SO₂Cl) was observed to decompose spontaneously to an unidentified viscous material. Other isocyanates furnish similar products on prolonged reaction and at higher temperatures. We prepared various alkyltetrazolones from CSI (26; R² = SO₂Cl), which on removal of the chlorosulphonyl group (aqueous

sodium sulphite at pH 7–8) gave the stable cyclic amides (26; R² = H). Although some of these have been made by a different method,²⁰ the CSI route is convenient especially for the preparation of alkyl and alicyclic derivatives (26; R¹ = alkyl, R² = H). These alkyltetrazolones are soluble in aqueous alkali and show weak acid titration curves (potentiometric determination; 50% ethanol). Their u.v. spectra in both acidic and basic media are similar to those observed for the 1-aryl systems.²¹ The 1,4-dimethyl derivative (26; R¹ = R² = Me) is reported to eliminate nitrogen photochemically²² but our 1-alkyltetrazol-5-ones (26; R² = H) proved stable to irradiation and also to thermolysis, in accord with the Woodward-Hoffmann rules. With 1,5-diazidopentane (N₃[CH₂]₅N₃) the bistetrazolone was obtained (27; R = SO₂Cl or H); trimethylsilyl azide gave only equilibrium mixtures similar to those from the aryl azides. Acyl and sulphonyl azides (RCON₃, RSO₂N₃) proved unreactive even in benzene or chloroform.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 instrument, ¹H n.m.r. spectra with a Varian A60 or HA100 spectrometer (Me₄Si as standard), and mass spectra with an A.E.I. MS12 or MS9 (for high resolution work) instrument. Alumina used was type H (B.D.H.) and chlorosulphonyl isocyanate (CSI) was obtained from Hoechst A.G.

Analytical data for all the compounds in Tables 1–5 are available as Supplementary Publication No. SUP 21880 (8 pp.).*

Anils.—Those used for making the triazinediones previously described⁶ were made as detailed in the literature; the dialkylamino-substituted anils were prepared as recorded by us.¹

Hexahydro-s-triazine-2,4-diones (2) and (4).—In a typical preparation, benzylideneaniline (1 g, 0.005 mol) in dry dichloromethane (5 ml) was added dropwise to CSI (1 ml, 0.011 mol) in the same solvent (3 ml) with stirring while the temperature was maintained at 10 °C. The mixture was then diluted with ether (15 ml) and kept for 15 min in ice. The product was filtered off, washed with ether, and air-dried. General spectral features (i.r., ¹H n.m.r., and mass) have been discussed.⁶ De(chlorosulphonylation) was carried out by any of the following three methods. (a) To the N-chlorosulphonyl compound (2; R³ = SO₂Cl) (0.005 mol) in acetone (10 ml) and benzenethiol (2.5 g, 0.022 mol) was added dropwise at –5 °C a solution of pyridine (1.35 g, 0.02 mol) in acetone (5 ml), and the mixture was then allowed to reach room temperature. The product was filtered off and recrystallised. (b) The N-chlorosulphonyl derivative (0.005 mol) was added piecemeal to methanol (20 ml) containing aqueous potassium iodide (10 ml). During reduction the pH was maintained between 1 and 3 by adding aqueous potassium hydroxide (20%) as required, and when the reaction was complete the pH was adjusted to neutrality. The product was filtered off and recrystallised. (c) The N-chlorosulphonyl compound (0.005 mol) dissolved

* For details of Supplementary Publications see Notice to Authors No. 7, *J.C.S. Perkin I*, 1976, Index issue.

¹⁸ 'The Chemistry of The Azido Group,' ed. S. Patai, Interscience, London and New York, 1971, p. 373.

¹⁹ J.-M. Vandersavel, G. Smets, and G. L'Abbe, *J. Org. Chem.*, 1973, **38**, 675.

²⁰ R. Stolle and Fr. Henke-Starke, *J. prakt. Chem.*, 1930, **124**, 283.

²¹ J. P. Harwitz, B. E. Fischer, and A. J. Tomaszewski, *J. Amer. Chem. Soc.*, 1959, **81**, 3076.

²² W. S. Wadsworth, *J. Org. Chem.*, 1969, **34**, 2994.

in a small volume of dichloromethane was added dropwise to a mixture of aqueous sodium sulphite (4%; 5 ml) and dichloromethane (5 ml). During addition the pH was maintained between 7 and 8 (aqueous NaOH) and the product was obtained as in (b). All these methods gave high yields. Method (b) proved best for compounds insoluble in dichloromethane. Details of some of the triazinediones have been given; * the dialkylamino-derivatives are set out in Table 1.

TABLE 1
Triazinediones (2) and (4) from CSI and dialkylamino-substituted Schiff's bases

R ¹	R ²	o- or p-NR ₂	M.p. (°C)	Yield (%)	R ¹	R ²	o- or p-NR ₂	M.p. (°C)	Yield (%)
Ph	SO ₂ Cl	o-Me ₂ N	182	100	Ph	SO ₂ Cl	p-NMe ₂	146	85
Ph	SO ₂ Cl	o-C ₆ H ₄ N	102	85	Ph	H	p-NMe ₂	>300	70
Ph	SO ₂ Cl	o-C ₆ H ₄ N	105	90	Ph	SO ₂ Cl	p-C ₆ H ₄ N-C ₆ H ₄	195	95
Ph	SO ₂ Cl	o-C ₆ H ₄ N	150	90	Ph	H	p-C ₆ H ₄ N-C ₆ H ₄	>300	85
Ph	SO ₂ Cl	o-Morpholino	135	85	Ph	SO ₂ Cl	p-C ₆ H ₄ N-C ₆ H ₄	265	85
Ph	H	o-Me ₂ N	280	75	Ph	H	p-C ₆ H ₄ N-C ₆ H ₄	>300	80
Ph	H	o-C ₆ H ₄ N	255	60	Ph	SO ₂ Cl	p-Morpholino-C ₆ H ₄	160	85
Ph	H	o-C ₆ H ₄ N	182	85	Ph	H	p-Morpholino-C ₆ H ₄	>300	82
Ph	H	o-C ₆ H ₄ N	145	80					
Ph	H	o-Morpholino	>300	75					

Derivatives of the Triazinediones (2).—(a) *The 3,5-bis-sulphonyl azide (2; R² = R¹ = Ph, R³ = SO₂N₃).* A mixture containing dichloromethane (10 ml), the sulphonyl chloride (2; R² = R¹ = Ph, R³ = SO₂Cl) (1.85 g, 0.004 mol), sodium azide (1.1 g), and water (10 ml) was stirred for 30 min at room temperature. The dichloromethane layer was separated and evaporated to leave 2,4-dioxo-5,6-diphenylhexahydro-s-triazine-1,3-bis-sulphonyl azide (0.5 g), m.p. 96—98°, from light petroleum (b.p. 40—60 °C), ν_{\max} 2 120 (N₃) and 1 650 cm⁻¹ (C=O) (Found: C, 37.7; H, 2.5; N, 26.5). C₁₅H₁₁N₉O₆S₂ requires C, 37.7; H, 2.3; N, 26.4%.

(b) *Dimethyl 2,4-dioxo-5,6-diphenylhexahydro-s-triazine-1,3-disulphonate.* A solution of the sulphonyl chloride (2; R¹ = R² = Ph, R³ = SO₂Cl) (1.84 g) in acetone (10 ml) was treated with saturated methanolic sodium hydroxide until pH 9 was recorded. The precipitate was dissolved by addition of water and the product extracted with chloroform. The ester (0.9 g), m.p. 174°, showed ν_{\max} 1 710 cm⁻¹ (C=O), τ 2.8 (10 H, s), 4.1 (s, CH), and 6.5 (s, 2 Me) (Found: C, 45.1; H, 3.7; N, 9.45). C₁₇H₁₇N₃O₈S₂ requires C, 44.8; H, 3.7; N, 9.2%.

(c) *3,5-Sulphonamides.* A solution of the sulphonyl chloride (2; R¹ = R² = Ph, R³ = SO₂Cl) (1.85 g) in dichloromethane (10 ml) was added dropwise to the appropriate amine (5 molar excess) in the same solvent (5 ml) with stirring and cooling during 30 min. Removal of the solvent left a solid which was dissolved in ethanol. The solution was added to water (100 ml) and stirred for 2 h. The products (Table 2) were crystallised from methanol.

TABLE 2

Sulphonamides of the triazinediones (2; R ¹ = R ² = Ph)					
R ³ in (2)	Yield (%)	M.p. (°C)	R ³ in (2)	Yield (%)	M.p. (°C)
PhNH-SO ₂	30	147	C ₆ H ₄ N-SO ₂	28	114
PhCH ₂ NH-SO ₂	30	183—184	2-Pyridyl-NH-SO ₂	20	210
Morpholino-SO ₂	30	140			

(d) *3,5-Dialkyl-1,6-diphenylhexahydro-s-triazine-2,4-diones.* The triazinedione (2; R¹ = R² = Ph, R³ = H) (1 g, 0.004 mol) was added piecemeal to dry dimethylformamide containing sodium hydride (0.3 g) with stirring. The mixture was heated on a water-bath until a clear solution resulted. Alkyl iodide [MeI or EtI (0.01 mol)] was then added, and after 10 min the mixture was poured into water and the product filtered off and recrystallised from ethanol.

The 3,5-dimethyl compound (2; R¹ = R² = Ph, R³ = Me) (80%) had m.p. 112°, ν_{\max} 1 710 and 1 670 cm⁻¹, τ 2.6 (10 H, m), 3.9 (1 H, s), 3.0 (s, CH₃), and 3.25 (s, CH₃) (Found: C, 69.6; H, 5.6; N, 14.4). C₁₇H₁₇N₃O₂ requires C, 69.2; H, 5.8; N, 14.25%. The 3,5-diethyl compound (2; R¹ = R² = Ph, R³ = Et) (85%), m.p. 136°, had the expected i.r. and n.m.r. spectra (Found: C, 70.1; H, 6.1; N, 13.5). C₁₉H₂₁N₃O₂ requires C, 70.65; H, 6.55; N, 13.0%.

Reaction of N-Benzylidene-2-piperidinoaniline (5) with CSI.—The aniline (1.5 g, 0.005 5 mol) in dichloromethane (5 ml) was added dropwise to CSI (1 ml, 0.01 mol) at 0 °C and the mixture worked up as above. 1,2,3,4,5,6,7,8,9,10-Decahydro-2,4-dioxo-15-phenyl-1,10-methano-1,3,5,10-benzotetra-azacyclododecine-3,5-bis-sulphonyl chloride (8) (3 g), m.p. 136°, showed ν_{\max} 1 645 cm⁻¹ (C=O), τ 2.0—2.4 (10 H, m), 7.3—7.7 (4 H, m), and 7.9—8.3 (4 H, m) (Found: C, 43.0; H, 4.0; N, 9.5). C₂₀H₂₀Cl₂N₄O₆S₂ requires C, 42.5; H, 3.5; N, 9.9%.

3,7-Diaryltetrahydro-s-triazolo[1,2-a]-s-triazole-1,5-diones (10; R' = SO₂Cl or H).—The procedure was analogous to that described for the anils. The required azines were made as described in the literature, those with an allyloxy-group²³ and dialkylamino-substituents as reported recently.¹¹ Reduction was carried out by the sodium sulphite or the potassium iodide method (see above) to give compounds (10; R' = H). Details of new triazolotriazolediones are in Table 3. Hydrolysis of the triazolotriazole (10; R = Ph,

TABLE 3

Triazolo[1,2-a]triazole-3,7-diones (10) from CSI and azines

R	R'	M.p. (°C)	Yield (%)	R	R'	M.p. (°C)	Yield (%)
Ph	SO ₂ Cl	150	60	2-Thienyl	SO ₂ Cl	118—120	75
Ph ²⁴	H	232	90	2-Thienyl	H	252	60
p-MeO-C ₆ H ₄	SO ₂ Cl	80	83	2-Allyloxy-C ₆ H ₄	SO ₂ Cl	132—134	70
p-MeO-C ₆ H ₄	H	180	80	2-Allyloxy-C ₆ H ₄	H	>300	75
p-Tolyl	SO ₂ Cl	160	85	1-C ₁₀ H ₇	SO ₂ Cl	175	73
p-Tolyl	H	225	85	1-C ₁₀ H ₇	H	268—270	60
m-NO ₂ -C ₆ H ₄	SO ₂ Cl	135	78	o-Me ₂ N-C ₆ H ₄	SO ₂ Cl	170	60
m-NO ₂ -C ₆ H ₄	H	250	80	o-Me ₂ N-C ₆ H ₄	H	>360	70
p-Cl-C ₆ H ₄	SO ₂ Cl	160	65	p-Me ₂ N-C ₆ H ₄	SO ₂ Cl	153	73
p-Cl-C ₆ H ₄	H	240	85	p-Me ₂ N-C ₆ H ₄	H	>360	85
o-MeO-C ₆ H ₄	SO ₂ Cl	137—138	65	o-C ₆ H ₁₃ N-C ₆ H ₄	SO ₂ Cl	240	65
o-MeO-C ₆ H ₄	H	>350	75				
o-MeO-C ₆ H ₄	H	>350	75				
p-NO ₂ -C ₆ H ₄	SO ₂ Cl	262	69	o-C ₆ H ₄ N-C ₆ H ₄	SO ₂ Cl	240	70
p-NO ₂ -C ₆ H ₄	H	>300	70	o-C ₆ H ₄ N-C ₆ H ₄	H	>360	75
o-FC ₆ H ₄	SO ₂ Cl	154	75	o-C ₆ H ₁₃ N-C ₆ H ₄	SO ₂ Cl	190	65
o-FC ₆ H ₄	H	235	85	o-C ₆ H ₁₃ N-C ₆ H ₄	H	207	68
2-Furyl	SO ₂ Cl	118	85				
2-Furyl	H	160—162	60				

R' = H) in boiling hydrochloric acid gave benzaldehyde and ureidourea, m.p. 246°, and treatment with nitric acid at 10 °C gave 5-hydroxy-3-phenyltriazole, m.p. 321° (lit.,²⁴ 321—322°).

Derivatives of the Triazolotriazolediones (10).—The bis-methoxysulphonyl derivative (10; R = Ph, R' = SO₂Me) had m.p. 73° (Found: C, 57.3; H, 2.9; N, 9.0). C₁₈H₁₈N₄O₈S₂ requires C, 57.5; H, 2.9; N, 8.9%. The bisanilino-sulphonyl derivative (10; R = Ph, R' = SO₂NHPh), m.p. 158—160°, had ν_{\max} 3 260 and 1 695 cm⁻¹ (Found: C, 55.8; H, 4.2; N, 13.6). C₂₈H₂₄N₆O₆S₂ requires C, 55.6; H, 4.0; N, 13.9%. Alkylation of the reduced compound (10; R = Ph, R' = H) with methyl iodide or ethyl iodide in dimethylformamide in the presence of sodium hydride gave

²³ S. Mathur and H. Suschitzky, *J.C.S. Perkin I*, 1975, 2479.
²⁴ J. R. Bailey and N. H. Moore, *J. Amer. Chem. Soc.*, 1917, **39**, 279.

the *dimethyl compound* (10; R = Ph, R' = Me), m.p. 170° (Found: C, 67.2; H, 6.0; N, 17.5. C₁₈H₁₈N₄O₂ requires C, 67.1; H, 5.6; N, 17.4%), or the *diethyl compound* (10; R = Ph, R' = Et), m.p. 165° (Found: C, 68.8; H, 6.45; N, 15.9. C₂₀H₂₂N₄O₂ requires C, 68.6; H, 6.3; N, 16.0%).

Reaction of Hydrazones with CSI.—An ethereal solution (5 ml) of the reagent (1 ml) was added dropwise to benzaldehyde phenylhydrazone (1.95 g, 0.01 mol) in ether (30 ml) to give the sulphonyl chloride (12; R = SO₂Cl), m.p. 120°, as a white solid (2.4 g), ν_{\max} 3 295, 1 725, and 1 620 cm⁻¹ (C=O). Reduction with aqueous sulphite gave the amide (12; R = H), m.p. 150°, ν_{\max} 3 400 (NH), 1 680, and 1 620 cm⁻¹ (C=O). With 2 mol. equiv. of CSI the biuret (13; R = H) was produced on reduction (NaSO₃) of the first precipitated sulphonyl chloride (13; R = SO₂Cl); its i.r. spectrum showed ν_{\max} 3 240 (NH) and 1 750 and 1 700 cm⁻¹ (C=O).

In the case of the dialkyl-substituted hydrazones the solvent was benzene. The sulphonyl chlorides (15; R' = Cl) were converted without purification into the *esters* by boiling the chloride (1 g) in the appropriate alcohol (10 ml) (Table 4).

TABLE 4

Sulphonyl esters (15) from the hydrazones (14) and CSI in methanol

R ₂	R'	Ar	M.p. (°C)	Yield (%)
[CH ₂] ₄	Me	<i>p</i> -NO ₂ -C ₆ H ₄	146	45
[CH ₂] ₄	Et	<i>p</i> -NO ₂ -C ₆ H ₄	155	75
[CH ₂] ₅	Me	Ph	112	40
[CH ₂] ₆	Me	Ph	145	60
[CH ₂] ₆	Me	<i>p</i> -NO ₂ -C ₆ H ₄	152	70

Reaction of Amidines with CSI.—The amidines (17) were prepared according to the literature.²⁵ By adding CSI (1 ml, 0.001 mol) in dichloromethane (5 ml) dropwise with stirring to the amidine (0.005 mol) in dichloromethane (5 ml) the various 6-*dialkylamino*hexahydro-*s*-triazine-2,4-*diones* (18) were obtained (Table 5). Yields were *ca.* 70% and

TABLE 5

6-Dialkylaminohexahydro-*s*-triazine-2,4-*diones* (18) from amidines (17) and CSI

R ₂	M.p. (°C)	Yield (%)	τ
Me ₂	90	65	2.2—2.6 (5 H, m), 4.1 (CH, s), 7.6—7.5 (2 Me, s)
[CH ₂] ₄	110	60	2.2—2.6 (5 H, m), 4.1 (CH, s), 6.0 (4 H, m), 9 H (4 H, m)
[CH ₂] ₅ ·O·[CH ₂] ₂	97	68	2.2—2.6 (5 H, m), 4.2 (CH, s), 7.2 (4 H, m), 7.8 (4 H, m)
[CH ₂] ₅	116	70	2.2—2.6 (5 H, m), 4.2 (CH, s), 6.1 (4 H, m), 9.4 (6 H, m)

purification was achieved by washing the crude product with ether.

Reactions of Benzaldehyde Oximes with CSI.—The oximes (19; R = H) were treated in ether with CSI in equimolar amounts at room temperature to yield the unstable sulphamoyl chlorides (20; R = SO₂Cl, Ar = *p*-ClC₆H₄ or *p*-MeC₆H₄). Compound (20; R = SO₂Cl, Ar = *p*-ClC₆H₄) showed ν_{\max} 3 160 (NH) and 1 775 and 1 630 cm⁻¹ (C=O), τ 2.2—2.6 (4 H, m), 1.6 (s, CH), and -2.3 (s, NH). Reduction with aqueous sodium sulphite gave the corresponding *carbamoyloximes* (20; R = H, Ar = *p*-ClC₆H₄), m.p. 176° ν_{\max} 3 300 (NH) and 1 740 and 1 620 cm⁻¹ (C=O) (Found:

²⁵ H. Bredereck, R. Gompper, K. Klemm, and H. Rempfer, *Chem. Ber.*, 1959, **92**, 837; A. Lazizza, G. Brancaccio, and G. Letterei, *J. Org. Chem.*, 1964, **29**, 3697.

C, 48.0; H, 3.5; N, 14.8. C₈H₇ClN₂O₂ requires C, 48.2; H, 3.55; N, 14.65%), and (20; R = H, Ar = *p*-MeC₆H₄), m.p. 320° (Found: C, 60.5; H, 5.75; N, 15.6. C₉H₁₀N₂O₂ requires C, 60.7; H, 5.6; N, 15.7%).

Reactions of Carbodi-imides with CSI.—CSI (1 ml, 0.11 mol) in ether-benzene (5 ml) was added dropwise to dicyclohexylcarbodi-imide²⁶ (1.2 g, 0.011 mol) in ether-benzene (10 ml), with the temperature maintained at 0°C. 3-Cyclohexyl-2-cyclohexylimino-4-oxo-1,3-diazetidone-1-sulphonyl chloride (23; R = SO₂Cl) was precipitated; m.p. 120° (2.7 g), ν_{\max} 1 780 and 1 695 cm⁻¹ (C=O) (Found: C, 48.8; H, 6.4; N, 12.2. C₁₄H₂₂ClN₂O₃ requires C, 48.6; H, 6.35; N, 12.1%). Reduction (KI) gave the cyclic *amide* (23; R = H), m.p. 286°, ν_{\max} 3 200 (NH) and 1 740 and 1 680 cm⁻¹ (C=O) (Found: C, 69.1; H, 9.5; N, 17.3. C₁₄H₂₃N₃O requires C, 69.2; H, 9.5; N, 17.3%). Use of inverse addition with 2 ml of CSI gave the *dioxohexahydro-triazinesulphonyl chloride* (24; R = SO₂Cl), m.p. 91° (2.6 g), ν_{\max} 1 800, 1 755, 1 745, and 1 695 cm⁻¹ (Found: C, 37.1; H, 4.6; N, 11.4. C₁₅H₂₂Cl₂N₄O₆S₂ requires C, 36.8; H, 4.5; N, 11.5%). Reduction as before gave the cyclic *amide* (24; R = H), m.p. 248°, ν_{\max} 3 260, 1 740, and 1 660 cm⁻¹ (Found: C, 61.8; H, 8.4; N, 19.1. C₁₅H₂₄N₄O₂ requires C, 61.7; H, 8.3; N, 19.2%). Diphenylcarbodi-imide (0.6 g, 0.006 mol) in ether (5 ml) was added dropwise to CSI (1 ml, 0.011 mol) in ether (10 ml) to give the pale-yellow triazinedione (25; R = SO₂Cl) (0.8 g), m.p. 120° (Found: C, 37.1; H, 1.9; N, 11.3. C₁₅H₁₀Cl₂N₄O₆S₂ requires C, 37.7; H, 2.1; N, 11.7%). Reduction (KI) gave the *amide* (25; R = H), m.p. 160° (Found: C, 64.5; H, 4.4; N, 19.65. C₁₅H₁₂N₄O₂ requires C, 64.3; H, 4.3; N, 20.0%).

Reactions of Azides with CSI.—Azides were made by established methods, *i.e.* aromatic azides from arene diazonium salts and sodium azide, and acyl, alkyl, sulphonyl, and alicyclic azides from the corresponding halogeno-compounds and sodium azide. Various acyl and sulphonyl azides did not react even in hot solvents; aryl azides and trimethylsilyl azide gave equilibrium mixtures (see Discussion section).

In a typical reaction with an alkyl azide, cyclohexyl azide (1.4 g, 0.011 mol) in diethyl ether (10 ml) was treated dropwise with an ethereal solution (10 ml) of CSI (1 ml, 0.011 mol) at 0—5 °C. The solvent was then removed *in vacuo* under nitrogen to yield the tetrazol-5-one (26; R¹ = cyclohexyl, R² = SO₂Cl), almost pure and in quantitative yield. It was stable under nitrogen but gave an unsatisfactory elemental analysis. Reduction occurred on adding the chlorosulphonyl compound (26) in dichloromethane to aqueous sodium sulphite (pH maintained at 8—9 with potassium hydroxide). Work-up as before gave the tetrazole (26; R² = H) in over 90% yield. The *n*-butyl derivative (26; R¹ = Buⁿ, R² = H) showed ν_{\max} 1 710 cm⁻¹ (CO) (Found: C, 42.7; H, 7.2; N, 39.4. C₉H₁₀N₄O requires C, 42.3; H, 7.1; N, 39.4%), and the *phenethyl compound* (26; R¹ = PhCH₂·CH₂, R² = H) ν_{\max} 1 720 cm⁻¹ (CO) (Found: C, 57.0; H, 5.1; N, 29.1. C₉H₁₀N₄O requires C, 56.9; H, 5.3; N, 29.4%). Other tetrazoles (26; R² = H, R¹ = C₆H₅, C₆H₁₁, Ph, *p*-ClC₆H₄, *p*-MeOC₆H₄), obtained by similar methods, are known compounds.^{19,21}

We thank the S.R.C. for a CASE award (to R. E. W. with I.C.I. Pharmaceuticals), and Dr. G. Seidl, Hoechst (Frankfurt), for a gift of CSI.

[6/973 Received, 21st May, 1976]

²⁶ Y. Ohshiro, Y. Mori, T. Minami, and T. Agawa, *J. Org. Chem.*, 1970, **35**, 2076.