

1088. *The Action of Sulphur Monochloride on Amides of Monocarboxylic Acids.*

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Monocarboxylic acid amides frequently give monosulphides, $(R \cdot CO \cdot NH)_2S$, with sulphur monochloride. Diacyl hydrazides, $(R \cdot CO \cdot NH)_2$, are not formed as was previously supposed. Formamide gives an adduct containing nitrogen but no sulphur. The evolution of hydrogen chloride from the reaction with benzamide shows first-order kinetics in its early stages.

THE reaction of sulphur monochloride, S_2Cl_2 , with carboxyamides has been studied by Naik,¹ and by Naik and Patel.² The products described were:

- (i) monosulphides, $(R \cdot CO \cdot NH)_2S$, from acetamide, monochloroacetamide, n-butyramide, and benzamide,
- (ii) a disulphide, $(NC \cdot CH \cdot CO \cdot NH_2)_2S_2$, from cyanoacetamide,
- (iii) diacyl hydrazides, $(R \cdot CO \cdot NH)_2$, from trichloroacetamide, isobutyramide, n-valeramide, and n-hexanamide.

The authors accounted for the different products in (i) and (iii) by assuming that the course of the reaction depended on the basic strength of the amide, but the illustrations given to support this are contradictory. In particular, the complete elimination of sulphur in the reactions which were stated to give hydrazides was considered to be comparable with that of ammonia and sulphur monochloride to give ammonium chloride and sulphur.

The reaction of amides with sulphur monochloride is not a recognized method for

¹ K. G. Naik, *J.*, 1921, **119**, 1166.

² K. G. Naik and C. S. Patel, *J. Indian Chem. Soc.*, 1924, **1**, 27.

preparing diacyl hydrazides,³ and since the above explanations are inadequate it was decided to repeat the work.

In no case was a diacyl hydrazide (iii) found. The main product was usually a monosulphide, together with free sulphur. Although sulphur monochloride has not previously been observed as a dehydrating agent for amides⁴ it seemed possible that a nitrile might be a by-product and benzonitrile was isolated from benzamide.

Formamide behaved unusually. It gave various adducts of formamide and ammonium chloride and not a sulphide. Addition compounds between formamide and metallic salts, *e.g.*, $5\text{H}\cdot\text{CO}\cdot\text{NH}_2\cdot 2\text{NaBr}$ and $\text{H}\cdot\text{CO}\cdot\text{NH}_2\cdot 2\text{Na}_2\text{HPO}_4$, have been reported.⁵ Formamide reacts with thionyl chloride at ordinary temperatures giving ammonia and carbon monoxide,⁶ so it is understandable that formamide with sulphur monochloride will give ammonium chloride.

We confirm the monosulphides (i) previously obtained.^{1,2} Compounds with the linkage N-S-N often melt with decomposition⁷ so that recorded melting points may differ considerably. With an electrically heated block our specimen of bisacetamido sulphide had m. p. 203—203.5° (Naik,¹ m. p. 192°), but with a Kofler hot bench, which allows very rapid determinations, it had m. p. 229°. This compound was proved by nuclear magnetic resonance spectroscopy to have the structure $(\text{Me}\cdot\text{CO}\cdot\text{NH})_2\text{S}$, and not to be the isomeric compound, 2,2'-thiobisacetamide $(\text{NH}_2\cdot\text{CO}\cdot\text{CH}_2)_2\text{S}$, (m. p. 161—162°), which has been prepared⁸ by the action of sodium sulphide on monochloroacetamide. The spectrum showed methyl groups, and a chemical shift identical with that in acetanilide. The amido sulphides are very readily hydrolysed, and all attempts to prepare sulphones from them were unsuccessful.

Sulphur monochloride is known to replace a hydrogen atom of active methylene groups by sulphur,^{9,10} and we agree with Naik and Patel² that cyanoacetamide (ii) reacts in this manner, although their formulation of the disulphide as a branched chain, >C-S-S , is no longer acceptable.¹¹ The compound readily loses hydrogen cyanide, and we were unable to obtain good analytical figures. The evidence for substitution of hydrogen by sulphur at the methylene group and not at the amide group is indirect. Aliphatic amides which have an electron-attracting group substituted in the alkyl radical (*e.g.*, trichloroacetamide) react very slowly with sulphur monochloride. In contrast cyanoacetamide reacts vigorously. The sulphide shows an infrared absorption band at 746 cm^{-1} probably indicating the C-S stretching frequency.

The diacylhydrazides (iii) previously claimed by Naik and Patel² have been prepared by ourselves, or by other workers, from the reaction of hydrazine on a carboxylic acid, acid chloride, or acid anhydride, and, as the following Table shows they, have totally different melting points.

Melting points of diacylhydrazides.

Hydrazide R in $(\text{R}\cdot\text{CO}\cdot\text{NH})_2$	Naik and Patel ²	Other workers
Cl_3C	148—149°	195° ¹²
Me_2CH	120—121	244—245 ¹³ 238—239 ¹⁴
$\text{Me}[\text{CH}_2]_3$	123	163 (this paper)
$\text{Me}[\text{CH}_2]_4$	111—112	159 ¹⁵

³ A. W. Johnson, C. E. Dalglish, and J. Walker in "Chemistry of Carbon Compounds," ed. E. H. Rodd, Elsevier, 1st edn., 1951, 1A, p. 600.

⁴ J. C. Thurman, *Chem. and Ind.*, 1964, 752.

⁵ L. Kahovec and H. Wassmuth, *Z. phys. Chem.*, 1941, 48, 70.

⁶ L. Bert, *Compt. rend.*, 1946, 222, 666.

⁷ C. H. Anderson and E. F. Degering, *Proc. Indiana Acad. Sci.*, 1946, 56, 134.

⁸ J. Schurz and G. Kromer, *Chem. Ber.*, 1955, 88, 1631.

⁹ F. Magnani and A. Angeli, *Gazzetta*, 1894, 24, 342.

¹⁰ F. Konek-Norwall, *Ber.*, 1918, 51, 391.

¹¹ O. Foss in "Organic Sulfur Compounds," ed. N. Kharasch, Pergamon, 1st edn., 1961, p. 75.

¹² L. Spiegel and P. Spiegel, *Ber.*, 1907, 40, 1737.

¹³ H. Stetter and H. Spangenberg, *Chem. Ber.*, 1958, 91, 1982.

¹⁴ R. M. Herbst and J. A. Garrison, *J. Org. Chem.*, 1953, 18, 875.

¹⁵ W. Autenreith and P. Spiess, *Ber.*, 1901, 34, 189.

Some remarks on the possible course of the reactions can be made. The experimental facts are

(a) the order of reactivity of amides with sulphur monochloride ran parallel to their relative basic strengths,¹⁶ *i.e.*, Me > Ph > ClCH₂ ≫ Cl₂CH and Cl₃C,

(b) the reaction with acetamide rapidly precipitated two-thirds of the amide as the hydrochloride, 2Me·CO·NH₂·HCl,

(c) the reaction with benzamide evolved hydrogen chloride in a first-order reaction for 1.5 hours (subsequently the kinetics became more complex),

(d) the quantity of hydrogen chloride evolved during this first-order reaction was greater than would be obtained by the decomposition of benzamide hydrochloride, Ph·CO·NH₂·HCl¹⁷ or 3Ph·CO·NH₂·2HCl,¹⁸

(e) the total quantity of hydrogen chloride evolved is consistent with the reaction of 1 mole of amide with 1 mole of sulphur monochloride,

(f) the amido sulphides formed have the bonding, N-S-N.

In previous work with sulphur monochloride,^{19,20} aromatic compounds containing the reactive chlorodithio-group (S₂Cl) have been isolated. The reagent therefore causes electrophilic substitution by the chlorodithio-cation. Acylation^{21,22} and protonation²³ of amides occurs at the carbonyl oxygen atom, and presumably this holds for other electrophilic species. Amides exist largely in the oxo-form and the initial change may be tautomerism to the imino-form, R·CO·NH₂ ⇌ R·C(OH):NH, followed by reaction with sulphur monochloride, R·C(OH):NH + S₂Cl₂ ⇌ R·C(OS₂Cl):NH + HCl. The tautomeric change will occur most readily with electron-donating substituents since these will assist the protonation of the oxygen atom [(a) above]. One-third of the acetamide must have reacted rapidly with sulphur monochloride to give sufficient hydrogen chloride for the immediate precipitation of the amide hydrochloride (b). The quantity of hydrogen chloride liberated in the first-order reaction (c) cannot be accounted for by a single process (d). The equation 2R·CO·NH₂ + S₂Cl₂ → (R·CO·NH)₂S + S + 2HCl does not express the reaction correctly (e). Since the sulphides formed have nitrogen linked to sulphur, there must be a rearrangement from O to N, probably of the chlorodithio-compound (f), R·C(OS₂Cl):NH → R·CO·N(S₂Cl)H. Chlorodithio-compounds readily break down to sulphides,¹⁹ and the product is (R·CO·NH)₂S.

There are three first-order reactions which may be the rate-determining step for the evolution of hydrogen chloride, (i) the tautomeric change of the amide, (ii) the decomposition of the amide hydrochloride, (iii) the rearrangement from O to N of the chlorodithio-compound.

The immediate precipitation of acetamide hydrochloride indicates that the tautomeric change of the amide, and the subsequent attack by sulphur monochloride, are both fast reactions, and we therefore eliminate (i). The hydrogen chloride comes from two simultaneous reactions, the decomposition of the amide hydrochloride and of the *N*-chlorodithio-compound. *O*-Chlorodithio-compounds are unlikely to be stable under the reaction conditions, and we suggest that rearrangement (iii) determines the rate of evolution of hydrogen chloride.

EXPERIMENTAL

Sulphur monochloride was purified as previously described.²⁴ Melting points were determined on a Kofler hot block. The infrared spectra were measured for mulls in hexachlorobutadiene on a Perkin-Elmer Infracord spectrophotometer.

¹⁶ T. Higuchi, C. H. Barnstein, H. Ghassemi, and W. E. Perez, *Analyt. Chem.*, 1962, **34**, 400.

¹⁷ M. V. Dessaignes, *Ann. Chim. (France)*, 1852, **34**, 147.

¹⁸ E. von Meyer, *J. prakt. Chem.*, 1844, **30**, 122.

¹⁹ Z. S. Ariyan and L. A. Wiles, *J.*, 1962, 1725.

²⁰ Z. S. Ariyan and L. A. Wiles, *J.*, 1963, 755.

²¹ D. Davidson and H. Skovronek, *J. Amer. Chem. Soc.*, 1958, **80**, 376.

²² R. Gompper and O. Christmann, *Chem. Ber.*, 1959, **92**, 1935.

²³ A. R. Katrikzky and R. A. Y. Jones, *Chem. and Ind.*, 1961, 722.

²⁴ Z. S. Ariyan and L. A. Wiles, *J.*, 1961, 4510.

Reaction of Sulphur Monochloride with Formamide.—Formamide (4.5 g., 1 mole) and sulphur monochloride (13.5 g., 1 mole) were refluxed in benzene (100 ml.) until hydrogen chloride was no longer evolved (24 hr.). The granular product was extracted with pyridine and then with carbon disulphide leaving a white solid (m. p. 190° decomp.) (67%); ν_{\max} . 3260, 3050, and 1410 (NH_4^+), and 1700 cm^{-1} (CO). It was soluble in water, and the solution gave a precipitate of silver chloride with silver nitrate solution. The solid had a variable constitution (Found, in one experiment: C, 6.8; H, 6.7; Cl, 52.2; N, 25.9. Calc. for $3\text{H}\cdot\text{CO}\cdot\text{NH}_2, 7\text{NH}_4\text{Cl}$: C, 7.1; H, 7.3; Cl, 48.8; N, 27.4%).

Bisacetamide Hydrochloride.—Acetamide (5.9 g., 1 mole) was dissolved in chloroform (100 ml.) and sulphur monochloride (13.5 g., 1 mole) added. An immediate exothermic reaction occurred, and a hygroscopic white solid was precipitated. After extraction with hot ethyl acetate it had m. p. 119—120° (77%) (lit.,²⁵ sinters 123°) (Found: C, 31.4; H, 7.4; Cl, 22.2; N, 17.0. Calc. for $\text{C}_4\text{H}_{11}\text{ClN}_2\text{O}_2$: C, 31.1; H, 7.1; Cl, 23.0; N, 18.2%).

Bisacetamido Sulphide.—Acetamide (10 g., 1 mole) was dissolved in boiling benzene (200 ml.) and sulphur monochloride (25 g., 1.1 mole) dissolved in benzene (50 ml.) was slowly added. Bisacetamide hydrochloride was immediately precipitated. The mixture was refluxed until hydrogen chloride ceased to be evolved (24 hr.). A dark *solid* separated which, crystallised from ethanol, gave white needles, m. p. 229° (50%); ν_{\max} . 3310 (NH), 2920 and 2710 (CH_3), 1670 (CO), and 1560 cm^{-1} (CONH) (Found: C, 32.9; H, 5.6; N, 18.7; S, 21.7. $\text{C}_4\text{H}_8\text{N}_2\text{O}_2\text{S}$ requires C, 32.9; H, 5.4; N, 18.9; S, 21.6%). Unchanged acetamide (1 g.) was recovered.

Bis(dichloroacetamido) Sulphide.—Dichloroacetamide (6.4 g., 1 mole) and sulphur monochloride (6.75 g., 1 mole) were refluxed in benzene (50 ml.) for 24 hr. Concentration of the solution gave white *crystals*, m. p. 208° (decomp.) (41%); ν_{\max} . 3300 (NH), 1680 (CO), and 1560 cm^{-1} (CO·NH) (Found: C, 17.2; H, 1.9; N, 9.8; S, 11.3. $\text{C}_4\text{H}_4\text{Cl}_4\text{N}_2\text{O}_2\text{S}$ requires C, 16.8; H, 1.4; N, 9.8; S, 11.2%). Unchanged dichloroacetamide (2 g.) was recovered.

Bis(trichloroacetamido) Sulphide.—Trichloroacetamide (8.1 g., 1 mole) and sulphur monochloride (6.75 g., 1 mole) were refluxed in benzene (100 ml.) for 5 days. White *crystals* separated on cooling, and when recrystallised from ethanol had m. p. 201—202° (24%) (Found: C, 14.2; H, 0.9; Cl, 59.5; N, 7.5; S, 9.2. $\text{C}_4\text{H}_2\text{Cl}_6\text{N}_2\text{O}_2\text{S}$ requires C, 13.5; H, 0.6; Cl, 60.0; N, 7.9; S, 9.0%). Unchanged trichloroacetamide (2.0 g.) was recovered.

Di(carbamoylcyanomethyl) Disulphide.—Cyanacetamide (5 g., 1 mole) and sulphur monochloride (6.75 g., 1 mole) were refluxed in benzene (50 ml.) for 4 hr. Hydrogen chloride was vigorously evolved, and a sticky mass (6.7 g.) containing sulphur was precipitated. Extraction with carbon disulphide gave a brown *solid*, m. p. 129° (decomp.); ν_{\max} . 3200 (broad, NH), 2260 (CN), 1675 (CO), and 746 cm^{-1} (C-S) (Found: C, 29.9; H, 3.1; N, 21.5; S, 24.4. $\text{C}_6\text{H}_6\text{N}_4\text{O}_2\text{S}_2$ requires C, 31.3; H, 2.6; N, 24.2; S, 27.9%).

Di-isobutyramido Sulphide.—Isobutyramide (8.7 g., 1 mole) and sulphur monochloride (13.5 g., 1 mole) were refluxed in benzene (100 ml.) for 6 hr. Concentration of the solution gave white *crystals* which, recrystallised from ethanol, had m. p. 218° (68%); ν_{\max} . 3300 (NH), 3010, and 2890 (CH_3), 1670 (CO), and 1560 cm^{-1} (CO·NH) [Found: C, 47.2; H, 8.0; N, 13.1; S, 15.4%; *M* (Rast) 188. $\text{C}_8\text{H}_{16}\text{N}_2\text{O}_2\text{S}$ requires C, 47.1; H, 7.8; N, 13.7; S, 15.4%; *M*, 204].

Di-n-valeramido Sulphide.—*n*-Valeramide (10.1 g., 1 mole) and sulphur monochloride (13.5 g., 1 mole) were refluxed in benzene (100 ml.) for 6 hr. A white *solid* separated which, recrystallised from ethanol, had m. p. 173° (67%); ν_{\max} . 3300 (NH), 2960 and 2890 (CH_3), 1660 (CO), and 1560 cm^{-1} (CONH) [Found: C, 51.4; H, 8.6; N, 12.6; S, 14.0%; *M* (Rast), 212. $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ requires C, 51.7; H, 8.6; N, 12.1; S, 13.8%; *M*, 232].

Divalerylhydrazide.—Prepared by the method of Stetter and Spangenberg,¹³ this crystallised as white needles (from ethanol), m. p. 163° (38%) [Found: C, 60.0; H, 10.1; N, 13.8%; *M* (Rast), 209. $\text{C}_{10}\text{H}_{20}\text{N}_2\text{O}_2$ requires C, 60.0; H, 10.0; N, 14.0%; *M*, 200].

Di-n-hexanamido Sulphide.—*n*-Hexanamide (5.8 g., 1 mole) and sulphur monochloride (6.75 g., 1 mole) were refluxed in benzene (50 ml.) for 16 hr. The *solid* which separated was recrystallised from ethanol as white needles (m. p. 167.5°) (17%); ν_{\max} . 3220 (NH), 2900 and 2830 (CH_2), 1660 (CO), and 1560 cm^{-1} (CO·NH) (Found: C, 55.6; H, 9.0; N, 10.6; S, 12.4. $\text{C}_{12}\text{H}_{24}\text{N}_2\text{O}_2\text{S}$ requires C, 55.4; H, 9.2; N, 10.8; S, 12.3%).

Di-benzamido Sulphide.—(a) Benzamide (10 g., 1 mole) and sulphur monochloride (11 g., 1 mole) were refluxed in benzene (200 ml.) for 16 hr. The *solid* which separated crystallised from ethanol as white needles, m. p. 221° (71%); ν_{\max} . 3260 (NH), 1650 (CO), and 1560 cm^{-1} (CO·NH) [Found:

²⁵ L. Kahovec and K. Knollmuller, *Z. phys. Chem.*, 1942, 51, 49.

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C, 61.9; H, 4.6; N, 10.0; S, 11.6%; *M* (Rast), 173. $C_{14}H_{12}N_2O_2S$ requires C, 61.8; H, 4.4; N, 10.3; S, 11.8%; *M*, 201]. Unchanged benzamide (1 g.) was recovered.

(b) Benzamide (0.1 mole) and sulphur monochloride (0.1 mole) were refluxed in benzene in a stream of nitrogen for 19 hr. The hydrogen chloride evolved was absorbed in water and estimated by titration with 0.1N-sodium hydroxide solution. The following Table shows that for the first 105 min. the evolution of hydrogen chloride followed first-order kinetics [t = time (min.); a = initial concentration of amide; x = equivalents of hydrogen chloride evolved].

t	0	15	30	45	60	75	90	105	120	135	165
x	0	0.020	0.036	0.048	0.057	0.066	0.072	0.078	0.085	0.087	0.093
$\log a/(a-x)$	0	0.098	0.194	0.283	0.371	0.462	0.556	0.652	0.829	0.893	1.155

Steam-distillation of the reaction mixture gave benzonitrile (20%) confirmed by its infrared spectrum.

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