Reactions of Thioketones. Part III.[1] Reaction of Chloramine T with Aliphatic and Aromatic Thioketones

By **Malcolm M. Campbell** * and **D. M. Evgenios**, Department of Chemistry, Heriot–Watt University, Edinburgh EH1 1HX

Chloramine T reacted readily with aliphatic and aromatic thiones, acting as a nucleophilic and as an oxidizing reagent. The non-thioenolizable thiones, thioadamantanone and thiobenzophenone afforded thio-ozonide products. Thiocamphor, however, gave an unsaturated disulphide dimer which on heating underwent a stereospecific Cope-type rearrangement.

CHLORAMINE T (p-$MeC_6H_4SO_2NNaCl,3H_2O$) reacts with organosulphur compounds [2] to afford a range of interesting adducts and rearrangement products. We have been studying the reactions of thiones and in a preliminary communication [3] have reported a novel reaction of thiobenzophenone (3) with chloramine T which produced the thio-ozonide 3,3,5,5-tetraphenyl-1,2,4-trithiolan (14). We now describe our extended studies of the reactivity of chloramine T with aliphatic and aromatic thiones. The stable aliphatic thiones, thioadamantanone (1) and thiocamphor (2) were investigated, the former being non-thioenolizable, whereas the latter has labile α-methylene protons. Thiobenzophenone (3), Michler's thione (4), and xanthenethione (5) were chosen as representative aromatic thioketones.

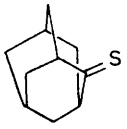
Reactions of Chloramine T with Thioadamantanone.

[1] Part II, M. M. Campbell and D. M. Evgenios, preceding paper.

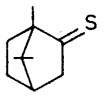
[2] (*a*) F. G. Mann and W. J. Pope, *J. Chem. Soc.*, 1922, 1052; (*b*) S. G. Clarke, Y. Kenyon, and H. Phillips, *ibid.*, 1927, 188; (*c*) A. W. Johnson, 'Ylid Chemistry,' Academic Press, New York, 1966, p. 356; (*d*) M. M. Kremlov and I. V. Koval, *Zhur. Org. Khim.*, 1969, **5**, 279; (*e*) J. B. Lambert, C. E. Mixan, and D. S. Bailey, *Chem. Comm.*, 1971, 316; (*f*) D. W. Emerson and H. Wynberg, *Tetrahedron Letters*, 1971, 3445; (*g*) S. Tamagaki and S. Oae, *ibid.*, 1972, 1159.

[3] M. M. Campbell and D. M. Evgenios, *Chem. Comm.*, 1971, 179.

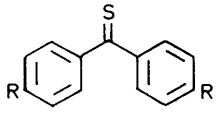
—Chloramine T has been shown to react as a ' nitrene ' precursor in its reaction with sulphides to give stable sulphinilimine ylides.[2] In addition the nucleophilic reaction of chloramine T with epoxides has been described.[4] These ready reactions, together with the



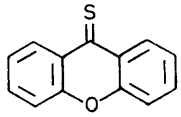
(1)



(2)



(3) R = H
(4) R = NMe_2



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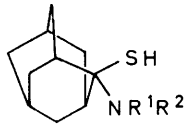
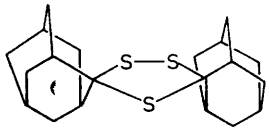


(6) R^1 = Cl
R^2 = $SO_2C_6H_4Me$-*p*



(7)

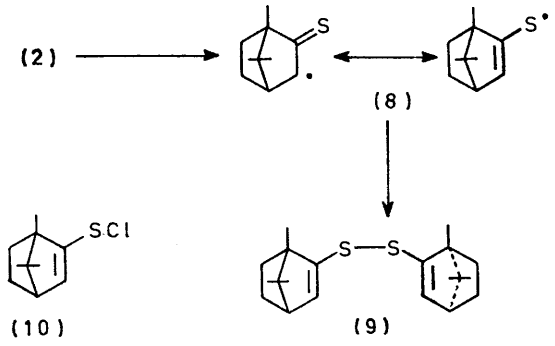
mild conditions under which the products were formed, prompted an investigation of the reactivity of chloramine T towards thioadamantanone in order to establish whether thiocarbonyl ylides * or thiaziridine ring † systems would be formed, or whether reaction would proceed by nucleophilic attack of the *N*-chlorosulphonamidate anion.[4] Further alternative modes of reaction which seemed possible involved reaction *via* chloronium ion or chlorine radical species.

It was established that adamantanethione reacted immediately at room temperature in ethanol with an excess of chloramine T. The major product was isolated in 37% yield as a crystalline solid which was shown to be the new thio-ozonide (7) described in the preceding paper.

Mechanistic pathways, in which chloramine T acts initially as a nucleophile to give the intermediate (6) may be invoked. Subsequent oxidative dimerization as described in the preceding paper could then lead to the thio-ozonide (7). Any *N*-chloroimmonium by-product would be unstable under the reaction conditions and could account for the formation of adamantanone which was also isolated. Studies of the oxidation step were not feasible because of complicating reactions of chloramine T or thione with many inhibiting or trapping additives, but the addition of hydroquinone, for example, did not significantly affect the reaction.

Reaction of Chloramine T *with* D-*Thiocamphor*.—When chloramine T was added under nitrogen to a stirred solution of D-thiocamphor in ethanol at room temperature, the red colour of the thione was rapidly discharged. One major, non-polar product was isolated as a crystalline solid by cautious column chromatography, together with toluene-*p*-sulphonamide.

Elemental and spectroscopic analysis indicated bis-(1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl) disulphide (9), a compound previously reported [5] as resulting from the iodine oxidation of the sodium thioenolate of thiocamphor. The possibility thus arose that chloramine T formed the sodium thioenolate and thence the disulphide (9). However, a brief study of the thioenolisation of (2) showed that on the same time scale as the chloramine T reaction no deuterium was incorporated into thiocamphor in the presence of D_2O–HBr in D_2O, or in the presence of Et_3N–D_2O. Thus, during this short period, in aqueous solution between pH 1 and 9 no detectable thioenolization occurs. The reaction may therefore proceed by initial abstraction of a labile α-methylene hydrogen atom by a chlorine radical derived from chloramine T, or a related disproportionation product, to give the resonance-stabilized thiyl radical (8), and thence the disulphide (9). This process would exemplify the inherent tendency of the thioketone group to acquire single-bond character, and provide a driving force for the chlorine radical abstraction of 3-H. In order to provide support for the mechanism several related reactions were examined.



(2) (8) (10) (9)

It was observed, for example, that D-thiocamphor reacted instantaneously in benzene with the weak nucleophile, *NN*-dichlorotoluene-*p*-sulphonamide (dichloramine T) affording (9) in 46% yield. In addition, reaction with *N*-bromosuccinimide rapidly afforded (9). This reaction was unaffected by aqueous potassium chlorate which was added to scavenge halogen acid.[6] Disulphide (9) was also obtained by the photochemical reaction of D-thiocamphor with bromine or iodine (4 × 250 W sunlamps). The bromine reaction was terminated before completion because of the build-up of by-products, but the iodine reaction was clean. No reaction with bromine or iodine occurred in the dark.

* After completion of this work, the formation of a thiocarbonyl ylide by the reaction of chloramine T with 1,2-benzodithiol-3-thione was reported.[2g]

† No stable thiaziridine ring has been isolated.

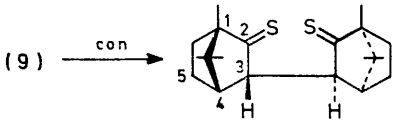
[4] F. E. Hardy, *J. Chem. Soc.* (*B*), 1971, 1899.

[5] D. C. Sen, *J. Indian Chem. Soc.*, 1937, **14**, 214; *Science and Culture*, 1938, **4**, 134; P. C. Ray, *Nature*, 1936, **138**, 548.

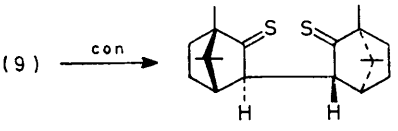
[6] H. D. House, ' Modern Synthetic Reactions,' Benjamin–Interscience, New York, 1965, p. 144.

A reaction with chlorine was very complex, but afforded a 16% yield of (9). These studies indicate that for D-thiocamphor, the formation of an α-radical may be followed by very rapid bimolecular coupling to form the unsaturated disulphide. We cannot at this stage, however, preclude the intermediacy in the chloramine T reaction of an unsaturated sulphenyl chloride (10) formed by nucleophilic attack by the thioketone on an *N*-chloro-species.

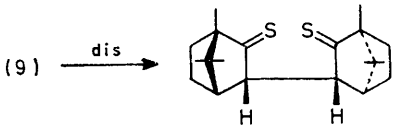
Knowing that the unsaturated disulphide on heating or prolonged standing afforded the valence bond isomer (11) [5] it was apparent that this rearrangement would afford a subtle stereochemical probe into the hetero-Cope reaction (12) ⟶ (13). Thus, a sample of the



(11a)



(11b)



(11c)

(12) (13)

unsaturated disulphide (9) was converted by heating, into a stereochemically homogeneous 1,4-dithione which could have three possible structures (11a—c). Structures (11a and b) would arise from the two possible antarafacial 3,3-sigmatropic rearrangements, whereas (11c) would result from a suprafacial 3,3-sigmatropic process. A detailed n.m.r. study indicated (11b) as the product structure; 3- and 3′-H appeared as a singlet at τ 7·49. *endo*-Stereochemistry was therefore assigned, since no coupling to 4-H was observed, indicating a dihedral angle of *ca.* 90° between 3- and 4-H. *exo*-3-H would have coupled both to *exo*-4- and -5-H. 3- and 3′-H were apparently magnetically equivalent, since no coupling was observed. Thus (11b) is the preferred structure. In the alternative product (11a), 3- and 3′-H would also be magnetically equivalent, but a study of molecular models indicates that coupling of 3- and 4-H superimposed on coupling between 3- and *exo*-5-H would be apparent, *i.e.* *exo*-3-H in (11a) would appear as a multiplet. Structure (11c) was ruled out since 3- and 3′-H are magnetically equivalent.

Thus, the unsaturated disulphide (9) cyclizes in a

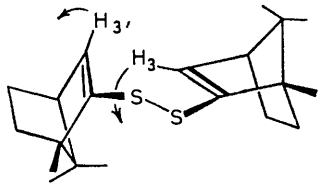
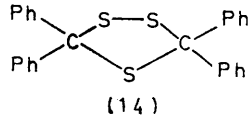


FIGURE Transition state for the antarafacial formation of (11b)

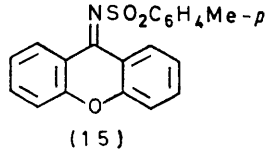
3,3-sigmatropic antarafacial process (Figure). The alternative antarafacial product would have resulted in appreciable steric interaction between the developing *exo*-3-H and a methyl group on C-7. Molecular models indicate that the transition state for each of these conrotatory modes is ' chair-like,' giving 3- and 3′-H *trans* to one another. The suprafacial product (11c) would have required a ' boat-type ' transition state, affording 3- and 3′-H *cis* to one another.

Reaction of Chloramine T *with Aromatic Thioketones.*—Chloramine T reacted rapidly with thiobenzophenone (3) in homogeneous polar solution (*e.g.* ethanol) or in suspension in non-polar solvents (*e.g.* benzene). An excess of reagent was required. The principal non-polar product was isolated in high yield as an unstable white crystalline material, identified as the thio-ozonide, 3,3,5,5-tetraphenyl-1,2,4-trithiolan (14), by comparison with an authentic sample. Column chromatography of the mother liquors afforded thiobenzophenone and benzophenone by-products. No difference in the reaction was observed when the reaction was carried out in air or under nitrogen, in the daylight, or in the dark. Additives such as quinone and hydroquinone did not appear to affect the reaction. A reaction mechanism similar to that proposed for the formation of the bis-adamantane thio-ozonide (7) possibly operates.

Xanthenethione (5) when treated under similar conditions yielded no detectable thio-ozonide, affording instead the *p*-tolylsulphonylimine (15),[7] together with



(14)



(15)

sulphur. The imine may have been formed by nucleophilic attack on the thione by *N*-chlorotoluene-*p*-sulphonamide (formed by disproportionation of chloramine T) followed by elimination of H_2S. It is also possible to invoke the intermediacy of a thiaziridine. Michler's thione (4) afforded a highly complex reaction mixture when treated with chloramine T, the major reaction product isolated being the new imine, *N*-[bis-(*p*-dimethylaminophenyl)methylene]toluene-*p*-sulphonamide.

[7] A. Schonberg and E. Sinzer, *Chem. Ber.*, 1968, **101**, 3445.

EXPERIMENTAL

General experimental details are as described in Part II.[1]

Reaction of Thioadamantanone with Chloramine T. *Formation of* (7).—Thiodamantanone (1 g) dissolved in ethanol (10 ml) was added to a stirred solution of chloroamine T (1·692 g) in ethanol (20 ml) under nitrogen. The red colour of the thione was rapidly discharged and a yellow solution resulted. Toluene-*p*-sulphonamide precipitated out of the solution. The solution was filtered, the solvent removed *in vacuo* and the resultant solid, which included toluene-*p*-sulphonamide, was extracted with cold light petroleum. The extract was subjected to column chromatography on silica gel, eluting with petroleum ether, affording pure dispiro[adamantane-2,3′-(1,2,4-trithiolan)-5′,2″-adamantane] (7) [1] (270 mg, 37%), m.p. 189—191°. Sulphur, adamantanone, and trispiro-[1,3,5-trithian-2,2′:4,2″:6,2‴-triadamantane] [8] were also isolated in very small quantities.

A similar reaction was carried out in the presence of hydroquinone (0·25 g) but the results were unaltered.

Reaction of D-*Thiocamphor with Chloramine* T. *Formation of* (9).—D-Thiocamphor (370 mg) was dissolved in ethanol (10 ml) and chloramine T (350 mg) in ethanol (15 ml) was added with stirring. The red colour of the thione was immediately discharged. T.l.c. (light petroleum) indicated one major product, together with toluene-*p*-sulphonamide. On concentration of the solution, toluene-*p*-sulphonamide precipitated and was filtered off. Further concentration afforded an unstable oil which was rapidly adsorbed onto a silica gel chromatographic column. Elution with petroleum ether afforded *bis*-(1,7,7-*trimethylbicyclo*[2.2.1]*hept*-2-*en*-2-*yl*) *disulphide* (9) [5] (184 mg, 50%), m.p. 68·5—69° (Found: C, 71·45; H, 9·1. $C_{20}H_{30}S_2$ requires C, 71·85; H, 9·0%), $\nu_{max.}$ (KBr) 2980, 1470, 1385, 1375, 1365, 1295, 1228, 1100, 975, 875, 820, and 712 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 277 (ε 11,000) nm, τ ($CDCl_3$) 4·05 (2H, d, *J* 4 Hz), 7·15 (2H, two overlapping d, $J_{3,4}$ 4 Hz), and 8·4—9·2 (26H, m), *m/e* 334 (M^+, 8%), 332 (4), 319 (30), 301 (8), 168 (20), 85 (60), and 83 (100). The reaction was repeated on a degassed solution under nitrogen, with no change in product formation.

A similar reaction was achieved by adding a benzene suspension of chloramine T to a stirred benzene solution of D-thiocamphor.

Rearrangement of the Disulphide (9) *to the Dithione* (11).—The diene disulphide (9) (50 mg) was dissolved in benzene (25 ml) and refluxed for 16 h. The colourless solution became orange-red. Removal of solvent *in vacuo*, followed by addition of ethanol, afforded orange-red crystals of {3,3′-*bi*-(1,7,7-*trimethylbicyclo*[2.2.1]*heptane*)}-2,2′-*dithione* (11) [5] (44 mg, 88%), m.p. 174—175° (Found: C, 71·55; H, 9·05; S, 19·35. $C_{20}H_{30}S_2$ requires C, 71·85; H, 9·0; S, 19·2%), $\nu_{max.}$ (KBr) 2985, 1397, 1288, 1272, 1249, 1170, and 1000 cm^{-1}, $\lambda_{max.}$ (ethanol) 244 (ε 18,250), 283 (5000), and 494 (22) nm, τ 7·49 (2H, s), 7·62 (2H, d, *J* 4 Hz), and 8·2—9·4 (26H, m), *m/e* 334 (M^+, 60%), 332 (20), 319 (10), 301 (50), 300 (100), 250 (80), 167 (50), 166 (60), and 85 (40).

This product was also obtained by a very slow crystallization from ethanol (90 h) of the disulphide (9).

Reaction of Thiobenzophenone with Chloramine T.—Thiobenzophenone (500 mg) was dissolved in ethanol (15 ml) and a solution of chloramine T (1·42 g) in ethanol (20 ml) was added with stirring. Immediate loss of the blue thione colour occurred with formation of a precipitate shown to be toluene-*p*-sulphonamide (m.p., i.r.). Concentration of the solution and filtration afforded more toluene-*p*-sulphonamide. The residual solution was evaporated at low temperature *in vacuo*, affording an unstable, greenish oil. Addition of ethanol resulted in crystallization of 3,3,5,5-tetraphenyl-1,2,4-trithiolan (330 mg, 90%), the structure of which was established by spectroscopic comparison with an authentic sample (i.r., u.v., n.m.r.).

The mother liquors were subjected to column chromatography on silica gel (eluant, light petroleum), affording trace quantities of thiobenzophenone and benzophenone, together with a highly polar, unstable, sulphurous compound (150 mg).

The reaction was not inhibited by rigorous exclusion of air, or exclusion of light, and was unaffected by reagents such as hydroquinone (100 mg) and quinone (100 mg).

Reaction of Xanthenethione (5) *with Chloramine* T.—Xanthenethione (320 mg) was dissolved in ethanol–chloroform (3 : 1; 15 ml) and a solution of chloramine T (843 mg) in ethanol (20 ml) was added with stirring. The colour of the solution rapidly changed from purple to orange to green. The reaction solution was filtered and the solvent removed *in vacuo*, affording an oil. Crystallization from ethanol gave *p*-tolylsulphoniminoxanthene [7] (220 mg, 41%) as greenish-yellow plates, m.p. 170—171°. Xanthenethione (70 mg, 22%) was also recovered. The presence of a considerable amount of sulphur was indicated by t.l.c. examination of the crude mixture.

Reaction of Michler's Thione (4) *with Chloramine* T.—Michler's thione (250 mg) was dissolved in ethanol (20 ml) and a solution of chloramine T (495 mg) in ethanol (20 ml) was added with stirring. The colour of the solution was filtered, the solvent removed *in vacuo* and the resultant viscous red oil subjected to chromatography on silica gel, eluting with dichloromethane. Several coloured bands were eluted, an orange band affording the major product as yellow-orange crystals which were shown to be N-[*bis*-(p-*dimethylaminophenyl*)*methylene*]*toluene*-p-*sulphonamide* (212 mg, 57%), m.p. 70—72° (Found: C, 68·3; H, 6·45; N, 9·7; S, 7·65. $C_{24}H_{27}N_3O_2S$ requires C, 68·5; H, 6·45; N, 10·0; S, 7·55%), $\nu_{max.}$ (KBr) 1600 and 1180 cm^{-1}, $\lambda_{max.}$ (ethanol) 225 (ε 18,100) and 392 (43,100) nm, *m/e* 421 (M^+).

[3/1135 *Received*, 4*th June*, 1973]

[8] J. W. Greidanus, *Canad. J. Chem.*, 1970, **48**, 3530.