Tetrahedron, 1963, Vol. 19, pp. 695 to 699. Pergamon Press Ltd. Printed in Northern Ireland

CONTRIBUTIONS TO THE CHEMISTRY OF α-SUBSTITUTED SULPHIDES—X*

THE ACID-CATALYSED ADDITION OF TRICHLOROMETHANE-SULPHENYL CHLORIDE TO 2,3-DIHYDROFURAN

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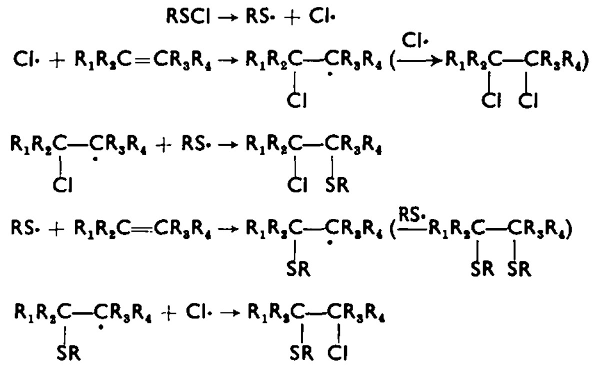
(*Received* 14 *November* 1962)

Abstract—The acid-catalysed addition of trichloromethanesulphenyl chloride to 2,3-dihydrofuran yields 2-chloro-3-trichloromethylthiotetrahydrofuran. This is a useful intermediate for reactions with nucleophilic agents. The mechanism of the addition reaction is discussed and related to the behaviour of other sulphenyl chlorides toward the carbon–carbon double bond.

The available experimental data concerning the addition of sulphenyl chlorides to the carbon–carbon double bond present a rather complex picture. Often the structure of the addition products from the unsymmetrical olefinic compounds is said to be uncertain and equally often a structure is proposed without any experimental proof. It is the merit of a few, newer investigations employing kinetical studies, gas chromatography, infrared spectroscopy and nuclear magnetic resonance that a self-consistent pattern is beginning to emerge. Its complexity may be conceived from the consideration of the structural diversities in a group of compounds comprising *inter alia* SCl_2, S_2Cl_2, ArSCl, AlkSCl, AcSCl, $(RO)_2P(O)SCl$, and $R(R'O)P(O)SCl$ and of the fact that one and the same sulphenyl chloride may react according to different mechanisms, even in the same reaction.

The mechanisms that have been encountered so far are conveniently described in the following Tables:

Table 1. Radical mechanisms



(1) $$RSCl \rightarrow RS\cdot + Cl\cdot$$

(2) $$Cl\cdot + R_1R_2C{=}CR_3R_4 \rightarrow R_1R_2\underset{Cl}{C}{-}\underset{\cdot}{C}R_3R_4 \; (\xrightarrow{Cl\cdot} R_1R_2\underset{Cl}{C}{-}\underset{Cl}{C}R_3R_4)$$

$$R_1R_2\underset{Cl}{C}{-}\underset{\cdot}{C}R_3R_4 + RS\cdot \rightarrow R_1R_2\underset{Cl}{C}{-}\underset{SR}{C}R_3R_4$$

(3) $$RS\cdot + R_1R_2C{=}CR_3R_4 \rightarrow R_1R_2\underset{SR}{C}{-}\underset{\cdot}{C}R_3R_4 \; (\xrightarrow{RS\cdot} R_1R_2\underset{SR}{C}{-}\underset{SR}{C}R_3R_4)$$

$$R_1R_2\underset{SR}{C}{-}\underset{\cdot}{C}R_3R_4 + Cl\cdot \rightarrow R_1R_2\underset{SR}{C}{-}\underset{Cl}{C}R_3R_4$$

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[*] Part IX.: A. Senning and S.-O. Lawesson, *Acta Chem. Scand.* **16**, 1175 (1962).

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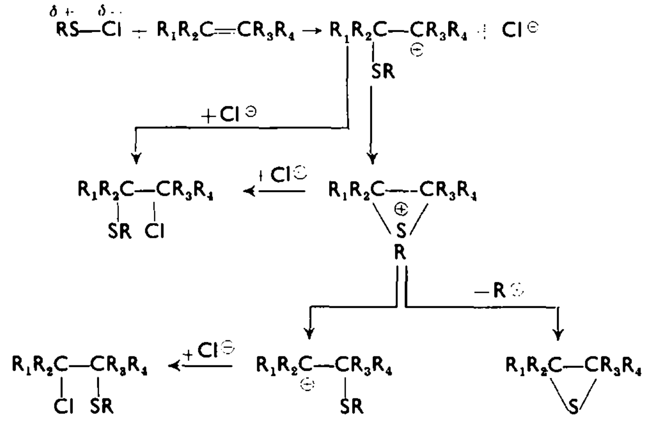
TABLE 2. CRYPTOIONIC MECHANISMS



Thus N. Kharasch and his school investigated the addition of aromatic sulphenyl chlorides to unsymmetrical olefins and characterized it as a cryptoionic reaction which in most cases leads to the Markovnikoff adduct[1,2] (the terminology based upon the assumption that in the sulphenyl chloride the sulphur atom bears a fractional positive and the chlorine atom a fractional negative charge). In a few instances, however, minor amounts of the anti-Markovnikoff adduct were encountered together with the expected product and this fact was explained in terms of a cyclic sulphonium ion intermediate which could break up at either new carbon-sulphur bond. Gundermann *et al.*,[3] reinvestigated the addition of aliphatic sulphenyl chlorides to acrylic ester, the product of which had been previously claimed by one author to be the Markovnikoff adduct[4] and the anti-Markovnikoff adduct by another.[5] Careful degradation of the product showed it to consist of about equal parts of both isomers, indicating a random break-down of the new carbon-sulphur bonds in the three-membered sulphonium ring intermediate. Adding acetyl sulphenyl chloride to olefins, Böhme *et al.*[6] were surprised to find a disulphide linkage in the product rather than a sulphide linkage. Their explanation was that the sulphonium ion intermediate detached the residue originally present in the sulphenyl chloride to yield an episulphide which in turn reacts with excess sulphenyl chloride to form the observed product. To complete the picture, radicaloid additions of aliphatic sulphenyl chlorides were studied by Prey *et al.*,[7,8] and by Harris, Jr.[9] According to Prey *et al.*, trichloromethanesulphenyl chloride with unsymmetrical olefins gave the adducts one would expect if the chlorine radical were the chain-propagating species. This statement, however, was rigorously proved only

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[1] N. Kharasch and C. M. Buess, *J. Amer. Chem. Soc.* **71**, 2724 (1949).

[2] W. L. Orr and N. Kharasch, *J. Amer. Chem. Soc.* **75**, 6030 (1953); **78**, 1201 (1956).

[3] K.-D. Gundermann and R. Huchting, *Chem. Ber.* **95**, 2191 (1962).

[4] I. L. Knunyants, N. D. Kuleshova and M. G. Lin'kova, *Doklad. Akad. Nauk USSR* **135**, 81 (1960).

[5] H. Brintzinger and M. Langheck, *Chem. Ber.* **87**, 325 (1954).

[6] H. Böhme, H. Bezzenberger and H. D. Stachel, *Liebigs Ann.* **602**, 1 (1957).

[7] V. Prey and E. Gutschik, *Monatsh.* **90**, 551 (1959).

[8] V. Prey, E. Gutschik and H. Berbalk, *Monatsh.* **91**, 794 (1960).

[9] J. F. Harris, Jr., *J. Amer. Chem. Soc.* **84**, 3148 (1962).

in the case of styrene. Harris, Jr., added trifluoromethanesulphenyl chloride to a number of unsymmetrical olefins and, in most cases, identified both possible isomers. This finding was interpreted as due to two competing reactions with the chlorine radical and the trifluorothiyl radical as chain-propagating species, respectively. This hypothesis was further corroborated by the identification of adducts containing two chlorine atoms or two trifluoromethylthio groups in the same molecule. The possibility of a competing cryptoionic reaction was excluded.

This short survey, together with older, less accurate work, shows that both radicaloid and cryptoionic addition of sulphenyl chlorides to the carbon–carbon double bond is a well-established reaction, with the exception of radicaloid addition reactions of aromatic sulphenyl chlorides where we lack accurate quantitative data.

As far as trichloromethanesulphenyl chloride is concerned, addition reactions have been reported with isobutylene, pentene-2, hexene-1, cyclohexene, diisobutylene, styrene, indene, vinylcyclohexene, hendecenoic acid, tetradecene-1, allyl ether, allyl acetate, allyl chloride, cumarone, and hexachlorodihydrothiophene.[7,8,10,11] Ethylene failed to react with trichloromethanesulphenyl chloride, even at elevated temperature and pressure.[11] Much of the older work was mainly devoted to developing practical fungicidal formulations and much less to the chemistry of the reactions. More often than not there is not only doubt as to the reaction, but also to the identity of the products. Recently clear-cut experiments were carried out by Prey *et al.*[8] The radicaloid character of the addition reaction was established by the judicious use of radical initiators and radical scavengers, the orientation in the adducts was determined by means of comparative infrared spectroscopy and the chlorine radical found to be the chain-propagating species. The reaction of trichloromethanesulphenyl chloride with saturated hydrocarbons to give chloroalkanes and hexachlorodimethyldisulphide was another example of the homolytic scission of the sulphur-chlorine bond in trichloromethanesulphenyl chloride.[12]

As indicated in two preliminary communications,[13,14] the present authors encountered a cryptoionic reaction of trichloromethanesulphenyl chloride when adding it to 2,3-dihydrofuran. The adduct is 2-chloro-3-trichloromethylthiotetrahydrofuran as evident from the reactivity of the chlorine atom, α to the ether linkage. At room temperature there was a vigorous reaction with alcohols to yield 2-alkoxy-3-trichloromethylthiotetrahydrofurans. The adduct is, in fact, the Markovnikoff product one would expect from a cryptoionic addition of a sulphenyl chloride to a polarized carbon–carbon double bond, provided that the sulphur atom bears a positive and the chlorine atom, a negative fractional charge. This is customarily assumed to be correct and virtually all experimental evidence corroborates this assumption. Though there are isolated instances where authors postulated an opposite polarization of the sulphur–chlorine bond in trichloromethanesulphenyl chloride, it would seem sound to disregard such theories as the experimental evidence in their favour is scarce and

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[10] G. Sosnovsky, *Chem. Revs.* **58**, 509 (1958).

[11] F. Drahowzal in N. Kharasch (editor), *Organic Sulphur Compounds*, Pergamon Press 1961, Vol. 1, p. 361.

[12] V. Prey, E. Gutschik and H. Berbalk, *Monatsh.* **91**, 556 (1960).

[13] A. Senning and S.-O. Lawesson, *Acta Chem. Scand.* **15**, 1203 (1961).

[14] A. Senning and S.-O. Lawesson, *11th Nordic Chemists' Meeting*, Turku, Finland, August 20–25, 1962.

since the conventional approach leads to reasonable and useful working hypotheses. Strictly speaking, there might be little physical reality behind either picture and the common confusion of the molecules' ground states with their excited states, as present in the activated complex, makes the terminology ambiguous, if not misleading. The actual electron distribution might well differ from reaction to reaction as the activated complex changes its character.

The addition of trichloromethanesulphenyl chloride to 2,3-dihydrofuran appears to be the first example of an acid-catalyzed addition reaction of a sulphenyl chloride. The acid-catalyzed "pyranylation" of alcohols with the closely related 2,3-dihydropyran is a standard procedure in organic chemistry. The addition of trichloromethanesulphenyl chloride to 2,3-dihydrofuran is a remarkably fast reaction, at 0° complete after a few minutes as judged by the disappearance of the yellow colour of the sulphenyl chloride.

The addition product, 2-chloro-3-trichloromethylthiotetrahydrofuran, is reasonably stable in ether solution at room temperature, but at attempted distillation *in vacuo* a vigorous exothermic evolution of hydrogen chloride sets in. 3-Trichloromethylthio-4,5-dihydrofuran is obtained in low yield, the main product being a tarry residue. In situ, 2-chloro-3-trichloromethylthiotetrahydrofuran reacts smoothly with alcohols to give 2-alkoxy-3-trichloromethylthiotetrahydrofurans in fair to good yields. Primary alcohols are more reactive and give higher yields than secondary alcohols. While methanol, ethanol, isopropanol, allyl alcohol, and benzyl alcohol reacted at a convenient rate at room temperature, cyclohexanol required a temperature of 40°. Though t-butanol reacted in the same fashion as the other alcohols, the product decomposed when distilled *in vacuo* and yielded 3-trichloromethylthio-4,5-dihydrofuran. The instability is probably due to the presence of two adjacent bulky groups in the molecule. The formation of 3-trichloromethylthio-4,5-dihydrofuran proceeded much more smoothly than from the decomposition of 2-chloro-3-trichloromethylthiotetrahydrofuran and is to be preferred as a means of preparation of this compound. The analyses of 3-trichloromethylthio-4,5-dihydrofuran and of 2-allyloxy-3-trichloromethylthiotetrahydrofuran gave somewhat low values for chlorine and it would appear that trichloromethylthiofurans containing an olefinic double bond in the molecule cannot be purified satisfactorily by means of distillation *in vacuo* due to addition reactions of the double bond.

The 2-alkoxy-3-trichloromethylthiotetrahydrofurans are stable colourless oils or colourless solids with a characteristic aromatic odour. Usually, some yellow impurities are present and, to prevent extensive discolouration, the liquid compounds should be stored in the refrigerator.

As some of the trichloromethyl aryl sulphides prepared by us[15] exhibited interesting cytostatic properties, the compounds described in the present paper were tested against Walker carcinoma in the rat. These tests indicate that the cystotatic activity is negligible.

Acknowledgements—Our thanks are due to Professor Arne Fredga for facilities put at our disposal. The project was sponsored by the Swedish Agricultural Research Council (Jordbrukets Forskningsråd) and by the Faculty of Mathematics and Natural Sciences, University of Uppsala, Sweden. We are indebted to Badische Anilin- & Soda-Fabrik AG, Ludwigshafen am Rhein, Germany, for a gift of 2, 3-dihydrofuran and Farbenfabriken Bayer AG, Leverkusen, Germany, for the biological tests.

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[15] A. Senning and S.-O. Lawesson, *Acta Chem. Scand.* **14**, 2230 (1960); **16**, 117 (1962).

EXPERIMENTAL

The microanalyses were carried out at the Institute of Medicinal Chemistry, University of Uppsala. The b.p.s. and m.p.s. are uncorrected.

Trichloromethanesulphenyl chloride is a toxic substance with an obnoxious odour and should be handled with due care. All experiments were conducted in a well-ventilated hood. To eliminate the possibility of contamination of the reaction products with trichloromethanesulphenyl chloride (which would have rendered the work-up hazardous and cumbersome), experiments usually were conducted with a 100% excess 2,3-dihydrofuran and alcohol. The by-product, the corresponding 2-alkoxytetrahydrofuran, did not interfere with the isolation and purification of the desired product.

General procedure. 2,3-Dihydrofuran (28·0 g, 0·4 mole) was placed in a flask and cooled to 0°. While stirring, a few drops of conc hydrochloric acid were added and then 37·2 g (0·2 mole) trichloromethanesulphenyl chloride were added dropwise. The yellow colour of the sulphenyl chloride disappeared within a few min. After 15 min, 0·4 mole of the alcohol was added dropwise and the reaction mixture kept at room temp (in the case of cyclohexanol the reaction mixture had to be warmed to 40°). After 2 hr, the reaction product was dissolved in ether, extracted twice with sodium bicarbonate solution and twice with water, and finally dried ($MgSO_4$). After removal of the solvent, the product was distilled *in vacuo*. Towards the end of the distillation there appeared oily drops in the condenser and in order to avoid extensive decomposition and tar formation in the distillation flask, the distillation had to be discontinued at this point. The oily drops could be conveniently removed by filtering the liquid through ordinary filter paper.

2-*Methoxy*-3-*trichloromethylthiotetrahydrofuran*. From 28·0 g (0·4 mole) 2,3-dihydrofuran, 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 12·8 g (0·4 mole) methanol. The yield of crude product was 35·3 g (70%), b.p. 127°–135°/13 mm, n_D^{20} 1·5194. The pure compound had b.p. 128°/12 mm, and n_D^{20} 1·5200. (Found: C 29·26; H 3·88; Cl 42·42; S 12·75. $C_6H_9Cl_3O_2S$ requires: C 28·65; H 3·61; Cl 42·28; S 12·75%.)

2-*Ethoxy*-3-*trichloromethylthiotetrahydrofuran*. The preparation of this compound (b.p. 138°/20 mm, n_D^{20} 1·5101; yield 66%) has been described in a preliminary report.[18]

2-*Isopropoxy*-3-*trichloromethylthiotetrahydrofuran*. From 28·0 g (0·4 mole) 2,3-dihydrofuran, 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 24·0 g (0·4 mole) isopropanol. The yield of crude product was 16·6 g (30%), b.p. 127°–135°/11 mm, n_D^{20} 1·5063. The pure compound had b.p. 134°/11 mm, and n_D^{20} 1·5040. (Found: C 34·28; H 4·33; Cl 38·13; S 11·64. $C_8H_{13}Cl_3O_2S$ requires: C 34·36; H 4·69; Cl 38·04; S 11·47%.)

2-*Cyclohexoxy*-3-*trichloromethylthiotetrahydrofuran*. From 28·0 g (0·4 mole) 2,3-dihydrofuran, 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 40·8 g (0·4 mole) cyclohexanol. The yield of the crude product was 39·4 g (62%), b.p. 155°–164°/0·8 mm, n_D^{20} 1·5198. The pure compound had b.p. 150°/0·8 mm, and n_D^{20} 1·5224. (Found: C 41·77; H 5·41; Cl 32·47; S 9·91. $C_{11}H_{17}Cl_3O_2S$ requires: C 41·33; H 5·36; Cl 33·27; S 10·03%.)

2-*Benzyloxy*-3-*trichloromethylthiotetrahydrofuran*. From 14·0 g (0·2 mole) 2,3-dihydrofuran, 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 21·6 g (0·2 mole) benzyl alcohol. The crude product, which was obtained by distillation at about 190°/0·6 mm, solidified and was immediately recrystallized from pet ether. The yield of pure product was 7·8 g (12%), m.p. 72°–75°. (Found: C 44·13; H 4·07; Cl 32·70; S 10·05. $C_{12}H_{13}Cl_3O_2S$ requires: C 43·99; H 4·00; Cl 32·46; S 9·79)%.

2-*Allyloxy*-3-*trichloromethylthiotetrahydrofuran*. From 28·0 g (0·4 mole) 2,3-dihydrofuran, 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 23·2 g (0·4 mole) allyl alcohol. The yield of crude product was 28·1 g (51%), b.p. 146°–155°/22 mm, n_D^{20} 1·5262. Careful distillation *in vacuo* gave a somewhat impure product, b.p. 152°/22 mm, n_D^{20} 1·5198. (Found: C 35·40; H 4·08; Cl 36·08; S 11·73. $C_8H_{11}Cl_3O_2S$ requires: C 34·61; H 3·99; Cl 38·32; S 11·55%.) (Even repeated careful distillation failed to improve the chlorine analysis.)

3-*Trichloromethylthio*-4,5-*dihydrofuran*. 2,3-Dihydrofuran (28·0 g, 0·4 mole), 37·2 g (0·2 mole) trichloromethanesulphenyl chloride, and 29·6 g (0·4 mole) t-butanol were treated as above. Distillation *in vacuo* gave a product with b.p. 105°–111°/1·5 mm, and n_D^{20} 1·5484 (14·9 g, 34%). A redistilled sample boiled at 124°/23 mm and had n_D^{20} 1·5552. (Found: C 28·35; H 2·44; Cl 44·87; S 14·44. $C_5H_5Cl_3O_2S$ requires: C 27·36; H 2·30; Cl 48·45; S 14·61%.) (Even repeated careful distillation failed to improve the chlorine analysis.)