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Thioformhydroximic Acid *S*-Esters

The Reaction of Fulminic Acid with Thiols

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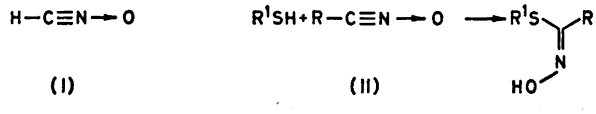
Reactions between fulminic acid and hydrogen sulphide, α-toluenethiol, and tetra-*O*-acetyl-1-thio-D-glucopyranose have been studied.

A product formed in the reaction with hydrogen sulphide, and known for almost a century, is demonstrated to be the thioanhydride (V).

Reaction of fulminic acid with α-toluenethiol affords *S*-benzyl thioformhydroximate, with *anti*-configuration (VI). The ester is identical with a product previously obtained by Cambi *via* a different route. Another product, claimed to possess the structure (VI), is shown to be 1,3-dibenzylthio-3-hydroxyamino-2-azapropene (X).

Fulminic acid reacts with tetra-*O*-acetyl-1-thio-D-glucopyranose to the expected thioformhydroximate (XI).

Fulminic acid, a chemical entity with a long and fascinating history, is now to be regarded as formonitrile oxide (I),** formally the simplest member of the class of nitrile oxides (II).*** These react with thiols to give *S*-esters of thiohydroximic acids (III),[2–4] reportedly with *anti*-configuration (R, OH).[4]



(I) (II) (III)

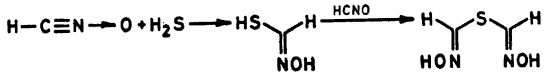
* The work described was taken from the thesis submitted by Dan Kjersgaard in partial fulfillment of the requirements for the doctor's degree (lic.techn.) from the Technical University of Denmark.

** For physical studies of fulminic acid in the gas phase, see Ref. 14 and literature cited therein.

*** For an excellent review of nitrile oxides, including numerous literature references, see Grundman.[1]

We have studied the reactions of fulminic acid (I)* with hydrogen sulphide, α-toluenethiol, and tetra-*O*-acetyl-1-thio-D-glucopyranose, and present the results.

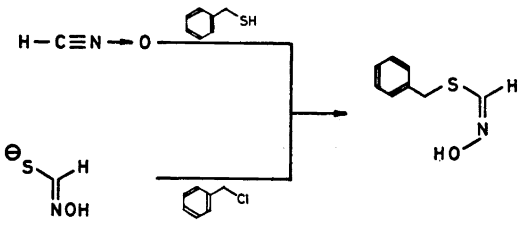
Nearly a century ago, Steiner [7] described a colourless, crystalline compound, $C_2H_4N_2O_2S$, formed upon treatment of an ethereal suspension of mercuric fulminate with hydrogen sulphide. Following his directions, we have prepared the same compound, albeit in low yield, and established its structure as the thioanhydride (V), disregarding stereochemistry, on basis of its molecular weight and spectroscopic properties (IR, NMR, and mass spectra). Most likely, (V) originates from addition of fulminic acid to initially formed thioformhydroximic acid (IV):



(IV) (V)

Analogous thioanhydrides have been described as products of the reaction between aromatic nitrile oxides and hydrogen sulphide.[2]

Equimolecular amounts of fulminic acid and α-toluenethiol reacted in ether solution at 0° to give, in satisfactory yield, *S*-benzyl thioformhydroximate (VI), m.p. 147–148.5°, apparently identical with the product (m.p. 144–6°) previously described by Cambi [8] and prepared by *S*-benzylation of sodium thioformhydroxamate:

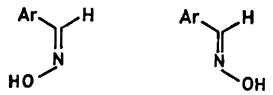


(VI)

The previously unknown configuration of the *S*-benzyl ester is believed to be *anti* (H, OH) (VI), primarily on the basis of NMR-data. In tetrahydrofuran (THF), the methine proton appears as a doublet (J 1.0 cps) at δ 7.18 ppm. In the same solvent, the corresponding signals for aromatic aldoximes typically appear at δ 7.4 and δ 8.1 ppm for the *anti*-(VII) and *syn*-(VIII) isomerides, respectively.[9] Corrected for the differently substituted olefinic systems by means of the 'shielding increments' proposed by Matter *et al.*,[10]

* In all cases, ethereal solutions of fulminic acid were employed, prepared and analyzed by modified literature procedures [5,6] (see Experimental).

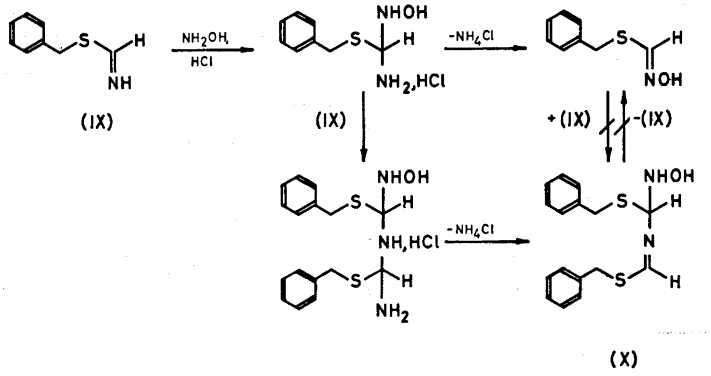
the methine proton in (VI) is expected to appear at about δ 7.1 ppm (*viz.* δ 7.4 ppm for (VII) -0.3), in agreement with the observed value, whereas the *syn*-isomer should exhibit resonance at δ 7.8 ppm (δ 8.1 ppm for (VIII)



(VII) (VIII)

-0.3). In fact, irradiation of (VI) with UV-light in THF-solution resulted in the appearance of a signal at δ 7.88 ppm, suggesting approximately 10 % stereomutation to the energetically less favoured *syn*-isomer which rapidly vanished when irradiation was interrupted. The observations are similar to those recently made by Davies *et al.*[11] in similar systems. The notable coupling (J 1.0 cps) between the H–C= and OH-protons, seemingly unknown in aromatic oximes, may reflect a diminished acidity of the thiohydroximates relative to the oximes.

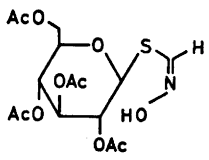
Thirty years ago, Houben and Zivadinovich [12] assigned the above structure (VI), yet without stereochemical specification, to a compound, m.p. 116–7°, resulting from the reaction between benzyl thioformimidate (IX) and hydroxylamine hydrochloride. Repetition of the synthesis, and detailed investigation of the resulting product by spectroscopic analyses (UV, IR, NMR, and mass spectrometry) afforded evidence for its structure being 1,3-dibenzylthio-3-hydroxyamino-2-aza-propene (X). According to chromatographic analysis, minor amounts of *S*-benzyl thioformhydroximate (VI) are formed, apparently concurrently with (X) since control experiments excluded the formation of (X) by reaction between the thioimidate (IX) and thiohydroximate (VI) under acidic, neutral, or basic conditions. Again, neither base nor acid could bring about fragmentation of (X) to (VI). A course of events accommodating all observations is the following:



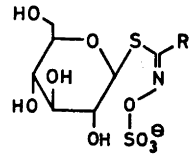
(X)

To what extent products analogous to (X) are formed when the Houben-synthesis is utilized for the production of other *S*-esters of thioformhydroximic acid remains to be clarified. The alleged *S*-ethyl and *S*-butyl esters [12] seem, in fact, to possess the thioformhydroximic ester structures proposed.

Addition of tetra-*O*-acetyl-1-thio-D-glucopyranose to fulminic acid proceeded in the expected fashion to give the *S*-thioformhydroximate (XI). Further conversion of the latter into glucosinolate ion (XII), the parent compound of the extensive series of naturally occurring glucosinolates (XIII),[13] is presently being studied in this laboratory.



(XI)



(XII): R= H

(XIII): R= alkyl, aryl, aralkyl etc.

EXPERIMENTAL

Melting points are uncorrected and determined in an electrically heated oil bath. Mass spectra are recorded on a Perkin-Elmer model 270 mass spectrometer (ionizing potential: 70—80 eV, solid inlet temperature: 70°). NMR-spectra are recorded on a Varian A 60-instrument. IR- and UV-spectra are recorded on a Perkin-Elmer 421 grating infrared spectrophotometer, and a Perkin-Elmer 402 ultraviolet-visible spectrophotometer, respectively.

Fulminic acid. All operations are carried out in a 5° room. 1.42 g of mercuric fulminate, suspended in 17 ml of water, and 4.0 g of 6.1 % sodium amalgam are reacted under magnetic stirring. After *ca.* 20 min, the clear solution of sodium fulminate is removed by decanting and dropwise added, with magnetic stirring, to 20 ml of 1 N nitric acid, at −2°. The solution is now extracted twice with 35 ml-portions of ether. Yield: 67 ml of an ether solution containing 7.0 mmoles of fulminic acid (yield 70 %), *i.e.* a 0.1 M solution. *Titration*: 10.0 ml of the solution is transferred to about 20 ml of 0.1 M silver nitrate. After stirring for 5 min, the precipitated silver fulminate is removed by filtration * and washed with a little water. A few ml of 6 N nitric acid, 1 ml of 1 M iron ammonium sulphate, and a few ml of nitrobenzene are added to the filtrate, and the excess of silver ions is titrated with 0.1 M ammonium thiocyanate.

Thioformhydroximic acid thioanhydride (V). Following the directions of Steiner,[7] mercuric fulminate (1.42 g) was suspended in anhydrous ether (15 ml) at −5°, and anhydrous hydrogen sulphide was bubbled through for about 1 h. After filtration, and concentration at 0° to a small volume, colourless crystals separated (about 50 mg). They were filtered off, dried, and used for further studies. M.p. 100° (decomp.). The *mass spectrum* exhibited conspicuous peaks at the following *m/e* values (relative abundance in parentheses): 120 (M^+) (36), 103 (17), 102 (16), 88 (31), 85 (9), 77 (65), 76 (23), 61 (28), 60 (30), 59 (100), 58 (20), 57 (12), 46 (12), 45 (47), 44 (63), 43 (23), and 42 (10). The *NMR-spectrum* (in $CDCl_3$) disclosed the presence of the methine proton at δ 7.54 ppm. The *infra-red spectrum* (KBr) exhibited strong bands at 1607 (C=N), 1405 (OH), and 1242 (CH?) cm^{-1}.

* *Caution!* The silver fulminate must be destroyed at once (*e.g.* with thiosulfate), since the dry salt may explode violently on touching.

anti *Thioformhydroximic acid* S-*benzyl ester (VI)*. An ethereal solution of fulminic acid (prepared from 4.75 g of mercuric fulminate) and α-toluenethiol (3.5 ml) is left at 4° for 30 min. After 24 h at −25°, crystals have separated. After concentration and filtration, colourless crystals (2.9 g) are obtained. After two recrystallizations from ethanol, an analytical specimen is obtained, m.p. 147−148.5° (Found: C 57.65; H 5.50; N 8.55; S 19.10. Calc. for C_8H_9NOS: C 57.46; H 5.42; N 8.38; S 19.17). *Mass spectrum:* 167 (M^+) (13), 150 (22), 124 (5), 123 (7), 121 (5), 92 (10), 91 (100), 89 (5), 77 (5), 65 (16), 63 (5), 51 (6), 45 (10), and 39 (6). *NMR-spectrum:* (δ-values for OH and =CH, respectively), in $CDCl_3$: 7.95 and 7.3 ppm; in DMSO: 11.23 and 7.52 ppm (*J* 1.0 cps); in THF: 10.25 and 7.18 ppm (*J* 1.0 cps). *IR-spectrum* (KBr): 1601 (C=N), 1384 (OH), and 920 (NO) cm^{-1}.

S-*Benzyl thioformimidate (IX) hydrochloride*. This salt was prepared in 60 % yield, according to directions in the literature.[12] Colourless crystals, m.p. about 180° (decomp). IR-spectrum (KBr): 1625 cm^{-1} (C=N).

1,3-Dibenzylthio-3-hydroxyamino-2-aza-propene (X). Following the procedure of Houben and Zivadinovich,[12] the thioformimidate (IX) salt (5.0 g) is converted into the free base. An ethereal solution (65 ml) of the latter is vigorously stirred, for 1 h, with a solution of hydroxylamine hydrochloride (2.0 g) in water (2.5 ml). From the ether phase, a colourless crystalline crop (1.1 g) is isolated, consisting, according to TLC analysis (silicagel, ethyl ether: benzene (1:4)), of a mixture of (X) (major product) (R_F 0.3) and (VI) (R_F 0.5). An analytical specimen of (X) is produced by recrystallization from ether: hexane. Colourless crystals, m.p. 115° (reported:[12] m.p. 116−7°) (Found: C 60.28; H 5.74; N 8.62; S 19.96. Calc. for $C_{16}H_{18}N_2OS_2$: C 60.34; H 5.70; N 8.80; S 20.13). *Mass spectrum:* no molecular ion is observed. The spectrum is dominated by peaks at 142 and 91, corresponding to α-toluenethiol. Running the spectrum quickly, peaks (1−2 % relative abundance) are observed at *m/e*: 195, 178, 177, 151, and 150. *NMR-spectrum* δ-values in DMSO): 7.22 (arom.), 3.75 (CH_2), 6.86 (=CH), 5.22 (CH) (doublet, *J* 6.5 cps), 6.92 (NH) (doublet, *J* 6.5 cps), and 9.61 ppm (OH). In $CDCl_3$: 7.21 (arom.), 3.76 (CH_2), 6.67 (=CH), 4.80 (CH), and about 5.6 ppm (NH, very flat). On lowering the temperature, the =CH-signal splits up into two (spaced by 0.18 ppm), possibly indicating the existence of *syn-anti*-isomers. The coalescence temperature seems to be about 30°. Employing 1,3,5-trinitrobenzene as an internal standard,* an approximate molecular weight was determined by NMR-technique. Found: 326±15; Calc. for $C_{16}H_{18}N_2OS_2$: 318.5. *IR-spectrum* (KBr): 1667 (C=N); ($CDCl_3$): 1662 (C=N), 3400 (NH), and 3595 (OH) cm^{-1}. *UV-spectrum* (CH_3CN); 217-218 nm (shoulder) (ε 23 000) (−S−C=N-chromophor).

Thioformhydroximic acid S-*(tetra-O-acetyl-β-D-glucopyranosyl) ester (XI)*. Equimolecular amounts of fulminic acid and tetra-*O*-acetyl-1-thio-D-glucopyranose are permitted to react in ether at 5° for 20 h. A small amount of a crystalline deposit is removed by filtration, and the filtrate is concentrated to dryness. TLC chromatography reveals that the residue consists of a major reaction product, contaminated with 4−5 minor components. Column chromatography on silicagel, with methanol:benzene 1:9 as the mobile phase, yields the major product in virtually pure form. Two recrystallizations from chloroform:hexane (3:5) afford an analytical specimen: m.p. 146−8°; $[\alpha]_D^{24}$ −23.4° (*c* 2.9, $CHCl_3$). (Found: C 43.98; H 5.22; N 3.37; S 7.81. Calc. for $C_{15}H_{21}NO_{10}S$: C 44.22; H 5.20; N 3.44; S 7.87). *Mass spectrum:* peaks at very low intensity are observed at *m/e* 407 (M^+) and 390 (M−17). Otherwise the fragmentation pattern is that expected from the tetraacetylglucopyranosyl moiety. In the *NMR-spectrum*, signals due to the OH and =CH are observed at δ 9.33 and δ 7.48 (in $CDCl_3$), and δ 10.53 and δ 7.39 ppm (in THF), respectively. The observed coupling (in THF) is 0.8 cps. A medium intensity band in the *IR-spectrum* (KBr) is present at 1592 cm^{-1} (C=N).

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