The electronic absorption spectra were recorded with a Pye–Unicam 8800 spectrophotometer. The mass spectra were recorded with a Varian MAT CH-6 spectrometer with direct introduction of the samples at an electron-ionization energy of 70 eV and a sample-vaporization temperature of 150-200°C. The high resolution PMR spectra of solutions in $CDCl_3$ (10^{-3} M) were recorded with a Bruker WM-360 spectrometer (360 MHz) with tetramethylsilane as the internal standard. The signals were accumulated using a 90° pulse (7 μsec) into a memory of 16K at a scan width of 6024 Hz.

The mixture of randomers of tetra(tert-butyl)porphyrazine was obtained in accordance with [3], whereas the samples of the individual randomers for the PMR and mass spectra were obtained by micropreparative HPLC.

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CONDENSED THIOLANE 1,1-DIOXIDE SYSTEMS.

2.* BROMINATED cis-PERHYDROTHIENO[3,4-d]OXAZOLES AND IMIDAZOLES

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Bromocyclization of 2-bromo-4-ureido-2-thiolene 1,1-dioxide has given perhydrothieno[3,4-d]oxazol-2-imino 5,5-dioxide, in which hydrogen atoms are absent from one of the α-methylene groups. In weakly basic media, this undergoes conversion into the corresponding aminooxazoline. Treatment of an aqueous solution of 2-bromo-4-ureido-2-thiolene 1,1-dioxide with bases gives a mixture of perhydrothieno[3,4-d]imidazol-2-one 5,5-dioxides in which the bromine atoms have the exo- and endo-orientations. In all the bicyclic compounds, the two rings are cis-fused.

Derivatives of thiolan 1,1-dioxide containing a substituent bonded to the heterocyclic ring via an oxygen atom are cleaved in dilute solutions of caustic alkali [2]. Thiolan 1,1-dioxides which do not bear a good leaving group or which cannot form an α-sulfonylcarbanion are more stable to bases [3]. The aim of the present investigation was to synthesize such compounds from the readily accessible 4-ureido-2-thiolene 1,1-dioxides (I).

In order to avoid the possible formation of an α-sulfonylcarbanion in the β-position to the good leaving group, we decided to replace both hydrogen atoms in this position by bromine. Such compounds have not previously been described. Ellis and Sammes [4] synthesized a compound with one bromine atom by bromocyclizing (I) in acetic acid. They showed that, as would be expected, the oxazolidine (II) was readily cleaved to the urea (III) on basification. We have repeated these reactions, and found that the yields from both

*For Communication 1, see [1].

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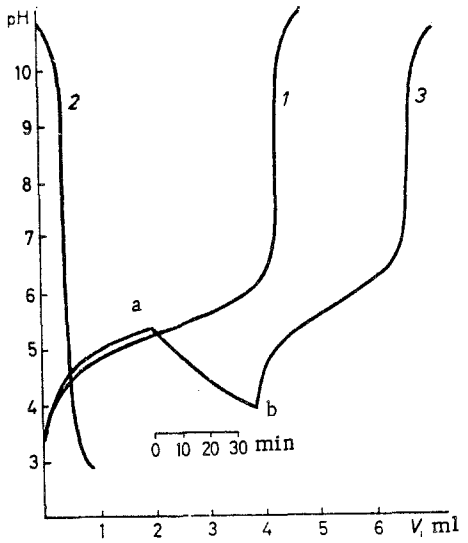


Fig. 1. Titration curves for an aqueous solution of (II). 1) 0.106 N NaOH without keeping; 2) 0.1 N HCl after titration with NaOH; 3) 0.106 N NaOH after keeping: a) addition of titrant stopped; b) titration continued.

TABLE 1. ^{13}C NMR Spectra of Compounds Prepared

Compound	Solvent	Chemical shifts of carbon atoms relative to TMS, ppm				
		$C_{(6)}$	$C_{(6a)}$, d	$C_{(3a)}$, d	$C_{(4)}$, t	$C_{(2)}$, s
II	D_2O	58,0 d	88,5	56,7	52,1	165,2
IV	H_2O	63,4 s	84,6	52,3	45,4	161,1
	DMSO-D_6	62,4 s	82,6	50,4	44,0	158,9
V	CD_3OD	70,0 s	86,7	62,7	49,2	—
	DMSO-D_6	67,4 s	81,8	59,7	45,9	157,8
endo-VII	CF_3COOH	59,0 d	51,9	55,9	51,1	165,3

reactions were near-quantitative, and the oxazolidine moiety of the salt (II) was cleaved even by aqueous sodium acetate at room temperature.

We obtained an oxazolidine which did not bear hydrogen atoms in the 4-position in a similar way, by bromocyclizing the urea (III) in acetic acid. Treatment of the hydrobromide (IV) with one equivalent of sodium hydroxide or excess sodium carbonate at room temperature did not result in cleavage of the oxazolidine ring, but gave the free base (V).

The differing behavior of oxazolidines (II) and (IV) towards dilute sodium hydroxide is illustrated by the titration curves for the salt (II) (Fig. 1). It will be seen that when the sodium hydroxide is added relatively rapidly, the dependence of the pH on the volume of titrant added (curve 1) is very similar to that for the titration of a weak acid with $pK_a \sim 5.2$. However, titration of the resulting alkaline solution with acid resulted in neutralization of the excess alkali only (curve 2). Consequently, in the course of titrating the oxazolidine (II) with alkali, it decomposed completely. The decomposition proceeded at a significant rate even in weakly acid solution (curve 3). In the case of the salt (IV), the usual titration curves for a weak base and its conjugate acid (pK_a 5.1-5.2) were obtained. The equality of the equivalents of sodium hydroxide and hydrochloric acid consumed in the successive titration of a weighed amount of the salt (IV) indicates the stability of the bicyclic compound (V) under these conditions.

Under more severe conditions, however (heating with an excess of NaOH or sodium carbonate), this compound decomposed to colored products of unknown structure. We therefore decided to replace one of the hydrogen atoms of the methylene group in the alkali-stable cis-perhydrothieno[3,4-d]imidazol-2-one 5,5-dioxide (VI) by bromine [4, 5] and examine the behavior of the product with bases.

Attempts to bromocyclize the urea (I) in neutral media or in the presence of HBr acceptors (DMF, sodium carbonate, or urea) gave only the oxazolidine (II) or its cleavage product (III). Treatment of an aqueous solution of (I) with bromine in the presence of K_2HPO_4 afforded 4-(N'-bromo)ureido-2-thiolene 1,1-dioxide. The required product,

TABLE 2. PMR Spectra of Solutions of Bicyclic Compounds in DMSO-D_6

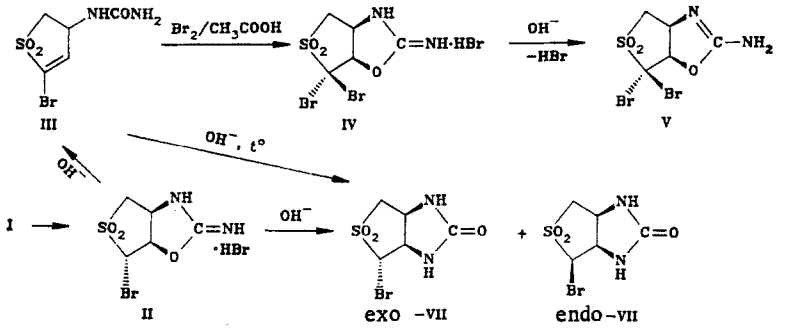
Compound	Chemical shifts of protons relative to HMDS, ppm						Vicinal coupling constants, Hz			
	6	6a	3a	^{4}exo	^{4}endo	NH	6a6	3a6a	$^{3a}4_{endo}$	$^{3a}4_{exo}$
II	6,12	5,95	5,16	3,86	3,70	9,35; 9,60; 10,29	1,8	9,3	1,9	6,8
IV	—	6,11	5,20	3,96	3,80	9,47*	—	9,0	1,2	6,6
V	—	5,46	4,81	3,88	3,33	6,33	—	8,9	2,7	7,8
endo-VII	5,42	4,6...4,4		3,53	3,28	6,89; 6,76	5,0	—†	2,0	6,0
exo-VII	5,33	4,6...4,4		3,72	3,28	6,90; 7,19	3,5	—†	—†	6,5

*One very broad, low intensity signal; exchange with traces of D_2O in the solvent occurred.

†Could not be measured.

cis-4-bromoperhydrothieno[3,4-d]imidazol-2-one 5,5-dioxide (VII), was obtained as a mixture of equal amounts (according to PMR) of the endo- and exo-isomers on cyclization of (III) in weakly basic solution. The same mixture was obtained by treating an aqueous solution of the oxazolidine (II) with excess alkali at room temperature or with gentle warming. The yields in both reactions were 35-46%. Most of the urea (III) decomposed under the cyclization conditions, probably with fission of the 1,1-dioxothiolane ring, to give colored, water-soluble products of unknown structure. The appearance of color on boiling with 10% sodium carbonate was seen with the bicyclic compounds (II), (IV), and (V) in addition to the urea (III), and this can be used as a test for these compounds. The imidazolines (VII) gave no coloration under these conditions, and on cooling they crystallized out unchanged. The bromine-free imidazoline (VI) behaved similarly.

The salts (II) and (IV) are regarded as oxazolidines on the basis of the presence in their PMR spectra* of three singlets (II) for the NH protons and the similarity of the chemical shifts for the chemical shifts of the nodal carbon atoms in both compounds (Tables 1 and 2). Bearing in mind the similarity to the PMR spectra of the imidazolidines (VII), we believe it to be reasonable to regard both these salts as 2-iminooxazolidines, as previously suggested by Ellis and Sammes [4] for the salt (II). In the base (V), the signal for the nodal carbon atom bonded to nitrogen is shifted by 10 ppm to lower field than in the salt (IV). In the PMR spectrum of the base, a single broad singlet is present at 6.33 ppm for the amine NH_2 protons, which give rise to absorption in the IR spectrum at 3420 and 3525 cm^{-1}, and we therefore regard the base (V) as a 2-aminooxazoline.



All these bicyclic compounds are regarded as having the cis-orientation of the two rings, since they are obtained by intramolecular cyclization. In the case of compounds (II), (IV), and (V) cis-coupling is confirmed by the high values of the vicinal coupling constants of the protons attached to the nodal carbons. In the imidazolines (VII), the orientation of the bromine atom was established from the values of the vicinal coupling constants for the protons at $C_{(6)}$ and $C_{(6a)}$. It was assumed that the imidazolidine ring is planar, and that the whole molecule has the boat conformation characteristic of cis-coupled bicyclic thiolane 1,1-dioxides [6-8].

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EXPERIMENTAL

NMR spectra were obtained on Bruker WH-90 and Bruker WP-200 spectrometers, and IR spectra on a UR-20 spectrometer in KBr disks. Titration plots were obtained using a Radelkis OP-930/1 automatic buret, titrant flow rate 0.6 ml/min. pK_a values were calculated by the half-neutralization method [9]. The starting 4-ureido-2-thiolene, 1,1-dioxide (I) was obtained as described in [5].

cis-6-exo-Bromo-2-iminoperhydrothieno[3,4-d]oxazole 5,5-Dioxide Hydrobromide (II). In a beaker were placed 30 g (170 mmole) of the urea (I), and glacial acetic acid (160 ml) added followed by 10 ml (190 mmole) of bromine. The mixture was heated to 60-70°C on the water bath. Precipitation of the salt (II) began as soon as all the urea (I) had dissolved. The solution was cooled, and the solid filtered off, washed with acetic acid, and dried to give 55.2 g (96.3%) of pale yellowish crystalline product, mp 195-197°C (decomp.). Literature value [4], mp 190-192°C.

2-Bromo-4-ureido-2-thiolene 1,1-Dioxide (III). The oxazolidine (II) (29 g, 86 mmole) was dissolved with gentle warming in 250 ml of water. To the resulting solution was added with stirring a solution of sodium acetate, prepared by mixing 5.2 ml (87 mmole) of 45% sodium hydroxide and 5.0 g (87 mmole) of glacial acetic acid. The mixture was stirred for four hours at room temperature, and the solid which separated was filtered off, washed with water, and dried to give 20.9 g (95%) of a colorless crystalline powder, mp 209-210°C (decomp.) (literature value 222-224°C [4]), IR spectrum identical with that of a sample obtained as described in [4].

cis-6,6-Dibromo-2-iminoperhydrothieno[3,4-d]oxazole 5,5-Dioxide Hydrobromide (IV). To a mixture of 8 g (31 mmole) of the urea (III) and 31 ml of glacial acetic acid was added 1.9 ml (36 mmole) of bromine, and the mixture stirred and heated on the water bath for 40-50 min at 70-80°C, stirring from time to time. The resulting solution was cooled, and the solid which separated was filtered off, washed with acetic acid, and dried in air until all the acetic acid had been removed, to give 12.7 g (97.5%) of a colorless crystalline powder, mp 193-197°C (decomp.). IR spectrum: 1130 and 1340 (SO_2), 1730 (C=N), 3135, 3205, and 3405 cm^{-1} (NH). Found, %: Br 58.0, N 6.7, S 7.5. $C_5H_6Br_2N_2O_3S \cdot HBr$. Calculated, %: Br 57.8, N 6.8, S 7.7.

cis-2-Amino-6,6-dibromo-3a,4,6,6a-tetrahydrothieno[3,4-d]oxazole 5,5-Dioxide (V). To a solution of 3.4 g (8.2 mmole) of the salt (IV) in 25 ml of water was added with stirring 8.2 ml (8.2 mmole) of 1 N NaOH. The solid which separated was worked up in the usual way to give 2.52 g (92%) of a colorless, microcrystalline powder, mp 158-161°C. IR spectrum: 1170 and 1355 (SO_2), 1740 (C=N), 3420 and 3525 cm^{-1} (NH). Found, %: Br 47.9, S 9.6. $C_5H_6Br_2N_2O_3S$. Calculated, %: Br 47.9, S 9.6.

4-(N-Bromo)ureido-2-thiolene 1,1-Dioxide). To a mixture of 1.8 g (10 mmole) of the urea (I), 7.0 g (20 mmole) of $Na_2HPO_4 \cdot 12H_2O$, and 30 ml of water was added dropwise at 55°C over 4 min 0.6 ml (11 mmole) of bromine. The resulting solution was stirred for one hour, cooled to room temperature, and the solid which separated worked up in the usual way to give 1.42 g (54%) of a yellowish-white powder with an odor of bromine. Found, %: Br 27.2, active Br 27.5. $C_5H_7BrN_2O_3S$. Calculated, %: Br 31.4, active Br 31.4.

Mixture of cis-4-endo- and cis-4-exo-Bromoperhydrothieno[3,4-d]imidazole-2-one 5,5-Dioxide (VII). A. The salt (II) (3.36 g, 10 mmole) was dissolved in 30 ml of water with gentle warming, and to the solution was added slowly with stirring 25 ml (25 mmole) of 1 N NaOH. The mixture became colored, and after a short time a colorless, flocculent precipitate began to separate. When no more solid separated, it was filtered off, washed with water, and dried to give 1.16 g (46%) of a mixture of endo-(VII) and exo-(VII). Two recrystallizations from water gave 0.3 g of pure, crystalline endo-(VII), mp 270°C (decomp.). IR spectrum: 1160 and 1342 (SO_2), 1728 (C=O), and 3235 cm^{-1} (NH). Found, %: C 23.5, H 2.7, Br 30.8, S 12.8. $C_5H_7BrN_2O_3S$. Calculated, %: C 23.5, H 2.8, Br 31.4, S 12.6.

B. In a flask fitted with a reflux condenser the urea (III) (1.3 g, 5 mmole) was dissolved at the boil in 30 ml of water, and the solution treated with 1.06 g (10 mmole) of sodium carbonate. The resulting clear, brown solution was boiled for 10 min, cooled and kept overnight. The colored crystals which separated were filtered off, washed with water, and dried to give 0.6 g (46%) of the mixed imidazolidines (VII).

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