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SIMPLE PREPARATION OF EPIMERIC 2,6-DIMETHYL-4-(N'-SUBSTITUTED THIOUREIDO)-1,3-DIOXANES AND CRYSTAL STRUCTURE OF *rel*-2S,4S,6S--2,6-DIMETHYL-4-(N'-BENZYLTHIOUREIDO)-1,3-DIOXANE

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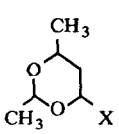
One-pot reaction of acetaldehyde, KSCN and $POCl_3$ affords 2,6-dimethyl-4-isothiocyanato-1,3-dioxane **4** in good yield. Compound **4** reacts with primary amines to give crystalline *rel*-2S,4R,6S-2,6-dimethyl-4-(N'-substituted thioureido)-1,3-dioxanes **5**. The obtained thioureas **5** with axial thioureido group are spontaneously epimerised in acetone solution under formation of *rel*-2S,4S,6S-2,6-dimethyl-4-(N'-substituted thioureido)-1,3-dioxanes **6**. These compounds form dimers containing relatively strong intermolecular hydrogen bonds -N-H...S- as confirmed by X-ray diffraction analysis. Treatmenat of isothiocyanate **4** with secondary amines is accompanied by epimerisation during the reaction and leads to a mixture of diastereoisomeric **5** and **6** or to pure diastereoisomers **6**.

Acid-catalysed condensations of aldehydes or ketones with suitable 1,3-diols belong to the most frequently used methods of preparation of substituted 1,3-dioxanes. These reactions are often utilized for the protection of aldehydes, ketones or 1,3-diols because the arising 1,3-dioxanes, like others acetals, are acid-labile and can be readily decomposed back to the starting compounds. Another popular approach to 1,3-dioxanes is the Prinse reaction[1]. However, in the synthesis of 1,3-dioxane derivatives relatively little has been used the fact that in the usual preparation of acetaldol the arising product easily adds to the unreacted acetaldehyde and the formed open-chain hemiacetal is further converted to 2,6-dimethyl-4-hydroxy-1,3-dioxane (aldoxane) **1**[2]. The aldoxane **1** itself is of no great preparative use because it is relatively thermolabile and decomposes easily back into acetaldol and acetaldehyde, however, its acylation leads to the stable ester **2**[3]. Recently, the preparation of related ethers **3** by reaction of paraldehyde, the corresponding alcohol and sulfuric acid



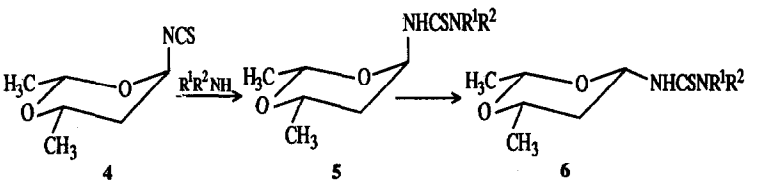
1 X= -OH
2 X= -OCOR
3 X= -OR

has been described[4].

The results of our present communication show that a similar compound, i.e. 2,4-dimethyl-4-isothiocyanato-1,3-dioxane **4**, can be prepared by a simple one-pot reaction from $POCl_3$, KSCN and acetaldehyde.

RESULTS AND DISCUSSION

Dropwise addition of $POCl_3$ to a suspension of KSCN in acetaldehyde at -40°C, followed by slow warming to room temperature, extraction of the product with ether and distillation afforded the isothiocyanate **4** in a more than 50% (Scheme 1). The obtained compound **4** is more stable than aldoxane **1**, can be chromatographed on alumina and distilled, however, it gradually decomposes on standing. The presence of an -NCS group in **4** was confirmed by the IR spectrum (characteristic band at 2040 cm^{-1} with shoulder at 2080 cm^{-1}) and ^{13}C NMR spectrum (signal of -NCS group at δ 138.9). Its mass spectrum displayed molecular ion (m/z 173) and a significant peak at m/z 115, corresponding to the dimethyldioxane skeleton $C_6H_{11}O_2$. The position and shape of signals in the ^1H NMR spectrum of **4** agreed well with those of



4 **5** **6**

a: R^1 = H, R^2 = n-butyl-
b: R^1 = H, R^2 = 1-adamantyl-
c: R^1 = H, R^2 = Ph-CH_2-
d: R^1 = H, R^2 = Ph-
e: R^1 = H, R^2 = 4-CH_3-Ph-
f: R^1 = H, R^2 = 4-Br-Ph-
g: R^1 = H, R^2 = HO-CH_2-CH_2-
h: R^1 = R^2 = C_2H_5-
i: R^1 = CH_3, R^2 = Ph-
j: R^1, R^2 = morpholino-

Scheme 1

analogous compound **3**[4]. Since some minor signals (probably belonging to decomposition products) in some regions overlapped with the signals of compound **4**, it was not possible to determine the coupling constants and thus also the relative configuration of the dominant stereoisomer. Nevertheless, comparison of the ^1H and ^{13}C NMR chemical shifts with those of the thioureas **5** and **6** (Table 5 and 6) showed that the relative configuration of this diastereoisomer is the same as the configuration of derivatives **5** discussed below.

The isothiocyanate **4** reacted readily with aliphatic as well as aromatic amines in ethereal solution, affording in good yields stable crystalline thioureas. Reaction with primary amines **a-g** afforded compounds of configuration **5**, the reaction with diethylamine **h** led to a mixture of stereoisomers **5** and **6**, whereas with

amines **i** and **j** we obtained solely the isomer **6**. The isomers **5** and **6** differed markedly in the ^{13}C chemical shifts of skeletal carbon atoms of the 1,3 dioxane ring (Table 5).

The configuration of compound **5** was determined in the following way. First, we tried to determine the spatial arrangement of substituents on the atoms $C_{(4)}$ and $C_{(6)}$ from the vicinal coupling constants of protons in the fragment $C_{(4)}H\text{-}C_{(5)}H_2\text{-}C_{(6)}H$ of the dioxane ring. Unfortunately, this system afforded spectra of the 2.order (even at 300 MHz) from which the key values of $J_{(H,H)}$ were not directly obtainable. For compound **5c** it was possible to obtain the $J_{(H,H)}$ values by the simulation of ABX systems, using iterative procedure, after decoupling the $C_{(4)}$-H or $C_{(6)}$-H protons. The obtained values 11.9 Hz and 2.4 Hz for the coupling of proton $C_{(6)}$-H with the methylene protons $C_{(5)}$-H_2 indicate an equatorial position of the methyl $C_{(6)}$-CH_3. For the coupling of proton $C_{(4)}$ with the methylene protons $C_{(5)}$-H_2 we found the values 3.9 Hz and cca 0 Hz indicating an axial position of the thioureido group on $C_{(4)}$. The configuration at $C_{(2)}$ was derived from comparison of the ^{13}C chemical shift of the methyl group $C_{(2)}$-CH_3 (the methyl carbon atom signals were assigned by selective INEPT) with the data for similar compounds available in the literature. Signals of equatorial methyl $C_{(2)}$-CH_3 in cis-2,4-dimethyl-1,3-dioxane[5] or the corresponding diastereoisomers of 2,4,6-trimethyl-1,3-dioxane[6] and 2,6-dimethyl-cholesteryloxy-1,3-dioxane[4] appear in the narrow region of δ 21.0-21.4 whereas axial $C_{(2)}$-CH_3, e.g. in trans-4,6-dimethyl-1,3-dioxane[6] exhibits chemical shift δ 16.7. As seen from Table 5, the chemical shift of $C_{(2)}$-CH_3 in thioureas **5a-h** ranges between δ 20.8-21.3 which indicates its axial position. This result was confirmed by measurement of differential NOE spectra (at 500 MHz) of derivative **5b**. At selective saturation of the signal of axial proton $C_{(6)}$-H at 3.99 we observed a 14% NOE enhancement of the $C_{(2)}$-H signal and a weaker NOE for $C_{(6)}$-CH_3 (6.5%) and NH (4.5%). In the 500 MHz ^1H NMR spectrum of compound **5b** the protons of the $C_{(5)}H_2$ group are well resolved enabling thus an easy extraction of all coupling constants on the 1,3-dioxane ring (for data see Table 6). It follows from these data that the reaction of isothiocyanate **4** with primary amines affords diastereoisomers **5** with relative configuration *rel*-2S,4R,6S. Pure diastereoisomers can be obtained by crystallization of the crude product from acetonitrile-hexane.

The obtained thioureas **5** were thermally stable substances which,similarly to other acetals,decomposed in an acidic medium. Thus, e.g. 15 minutes after addition of 0.1 mol of acetic acid to a solution of 1 mol of thiourea **5c** in acetone we isolated only N-benzylthiourea. A very much slower decomposition of **5c** was observed on several hours standing of its solution in unpurified chloroform. No decomposition took place in pure acetone; however, the compounds **5** were gradually converted into isomers **6** that had the same stereochemistry as the products **6i** and **6j** obtained directly by reaction of secondary amines with isothiocyanate **4**.

Structural arguments for the isomeric thioureas **6** were again obtained from their NMR spectra. The ^1H NMR spectrum of **6c** exhibited the $C_{(4)}$-H proton coupling constants 10.1 Hz and 2.3 Hz for coupling with the $C_{(5)}$-H2 protons, indicated an equatorial position of the thioureido group on $C_{(4)}$. Similar constants (11.1 and 2.4 Hz) have been found for the coupling of $C_{(5)}H_2$ with $C_{(6)}$-H showing thus the equatorial

position of the methyl group on $C_{(6)}$. Chemical shifts of the $C_{(2)}$-CH_3 group in the ^{13}C NMR spectra of thioureas **6a-j** range from δ 20.7 to 21.0 and show (vide supra) its equatorial position. This conclusion was confirmed again by the differential ^1H NOE spectrum of isomer **6b** : irradiation of the $C_{(6)}$-H proton at 3.83 resulted in marked NOE peaks for the protons $C_{(2)}$-H (12%) and $C_{(4)}$-H (14%), together with a weaker one for the $C_{(6)}$-CH_3 (5.5%). The coupling constants $J_{(H,H)}$ from the 500 MHz spectrum of **6b** are given in Table 6. Contrary to the spectra of compounds **5**, there is a marked widening of the $C_{(4)}$-H proton signal (which does not disappear on deuterium exchange on NH) and partially also of the $C_{(5)}$-H_{eq} signal in the spectra of isomers **6**. This interesting fact is obviously due to the tendency of compounds **6** to dimerize which was indicated in the mass spectra and proven in the crystalline state (vide infra).

Electron impact mass spectra of the isomeric thioureas **6** were almost identical with those of the thioureas **5** ; however, chemical ionization mass spectra (as well as spectra obtained by the FAB or FD technique) in some case exhibited marked peaks corresponding to dimeric structures. Thus, e.g. the CI-mass spectra of thiourea **6a** displayed, in addition to the $M^+ + 1$ ion of m/z 247 (100%), also a $2M^+ + 1$ ion at m/z 493 (27%). Similarly, under the same conditions, the spectrum of **6c** contained an $M^+ + 1$ ion (m/z 281;100%) along with a $2M^+ + 1$ peak (561;7%). It is known[7] that unsubstituted 1,3-dioxane in the presence of anhydrous $HClO_4$ dimerises to the energetically more advantageous 1,3,7,9-tetraoxacyclododecane. This fact, together with the mass spectral results, led us originally to the assumption (published in a preliminary form[8]) that also in our case the thioureas **5** dimerize to 1,3,7,9-tetraoxacyclododecane derivatives. On the other hand when we determined osmometrically the molecular weight of some

Table 1. Atomic coordinates (x 10^4) with e.s.d's. in parentheses

atom	x/a	y/b	z/c	atom	x/a	y/b	z/c
S41	-1751(4)	1693(1)	5210(1)	H2	5767(16)	2523(6)	1305(5)
O1	5112(10)	1081(4)	1006(3)	H4	5589(14)	1651(5)	3221(4)
O3	2358(9)	1992(3)	2106(3)	H5A	3696(15)	-336(5)	2762(5)
N41	2034(11)	1121(4)	3864(4)	H5B	6737(15)	-375(5)	3460(5)
N42	1100(10)	3022(4)	3822(4)	H6	8662(16)	678(6)	1958(5)
C2	4027(16)	2139(6)	1204(5)	H21A	3397(18)	3016(6)	-395(5)
C4	3936(14)	1272(5)	3031(4)	H21B	1317(18)	3692(6)	468(5)
C5	5321(15)	124(5)	2822(5)	H21C	486(18)	2466(6)	224(5)
C6	6894)16)	322(6)	1833(5)	H41	1681(11)	266(4)	4216(4)
C21	2181(18)	2879(6)	314(5)	H42	2701(10)	3104(4)	3229(4)
C41	583(12)	1977(5)	4255(4)	H42A	-1135(13)	3815(5)	4870(5)
C42	-316(13)	4054(5)	4088(5)	H42B	1211(13)	4582(5)	4068(5)
C43	-2724(12)	4749(5)	3365(4)	H44	-3581(14)	6033(5)	4192(5)
C44	-4172(14)	5766(5)	3538(5)	H45	-7363(16)	7293(6)	3029(5)
C45	-6319(16)	6436(6)	2829(5)	H46	-8922(16)	6634(7)	1572(6)
C46	-7173(16)	6111(7)	2067(6)	H47	-6347(16)	4839(6)	1227(5)
C47	-5750(16)	5094(6)	1887(5)	H48	-5239(13)	3603(5)	2398(5)
C48	-3573(13)	4408(5)	2532(5)	H61A	9343(19)	-1382(7)	2124(6)
C61	7973(19)	-784(7)	1516(6)	H61B	9126(19)	-603(7)	795(6)
				H61C	6207(19)	-1150(7)	1408(6)

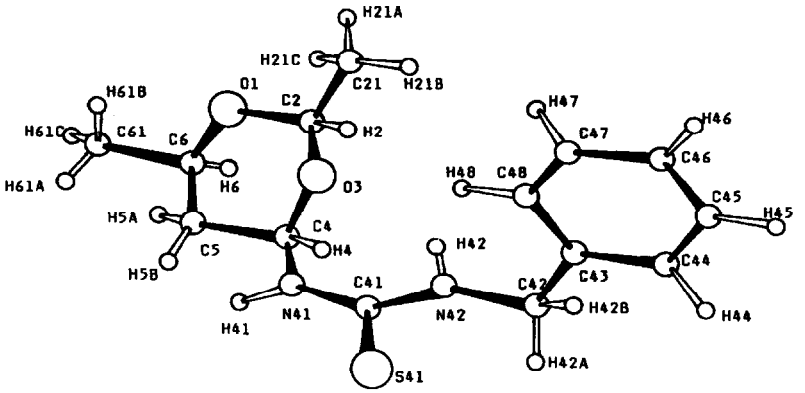


Figure 1.

thioureas, we obtained for **6a** the value 276 ± 14 and for **6c** 291 ± 15 which corresponded to the monomeric structures. To decide unequivocally whether the thioureas **5** on dissolution in acetone dimerize to derivatives of 1,3,7,9-tetraoxacyclododecane or undergo a mere isomerisation to another stereoisomer,we determined the structure of thiourea **6c** by X-ray diffraction.

The perspective view of a molecule of **6c** with atom numbering is depicted in Fig.1. Table 1 contains

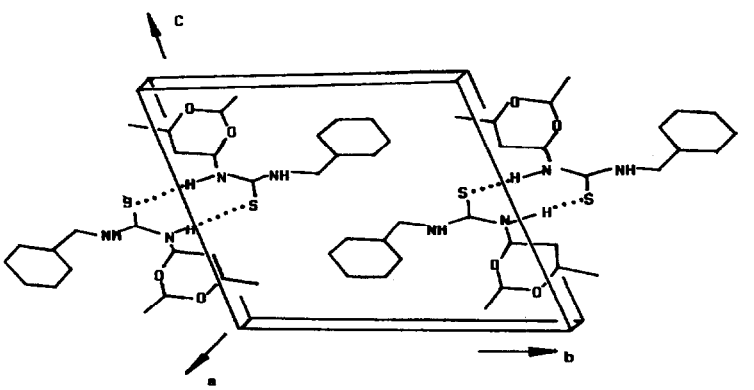


Figure 2.

Table 2. Bond lengths (Å) with e.s.d.'s in parentheses

S41 - C41	1.674(6)	N41 - C4	1.405(8)	C4 - C5	1.539(9)	C43 - C48	1.395(8)
O1 - C2	1.402(9)	N41 - C41	1.363(8)	C5 - C6	1.480(1)	C44 - C45	1.360(1)
O1 - C6	1.462(8)	N42 - C41	1.336(8)	C6 - C61	1.530(1)	C45 - C46	1.370(1)
O3 - C2	1.406(8)	N42 - C42	1.450(8)	C42 - C43	1.507(9)	C46 - C47	1.390(1)
O3 - C4	1.450(7)	C2 - C21	1.490(1)	C43 - C44	1.386(9)	C47 - C48	1.380(1)

Table 3. Bond angles (°) with e.s.d.'s in parentheses

C2 - O1 - C6	112.3(5)	O3 - C4 - C5	108.8(4)	N42 - C42 - C43	114.3(5)
C2 - C3 - C4	112.4(5)	N41 - C4 - C5	111.4(5)	C42 - C43 - C44	118.7(5)
C4 - N41 - C41	124.7(5)	C4 - C5 - C6	110.2(5)	C42 - C43 - C48	122.8(5)
C41 - N42 - C42	125.1(5)	O1 - C6 - C5	110.1(5)	C44 - C43 - C45	118.5(5)
O1 - C2 - O3	110.3(5)	O1 - C6 - C61	107.2(5)	C43 - C44 - C45	120.9(5)
O1 - C2 - C21	109.2(5)	C5 - C6 - C61	112.1(6)	C44 - C45 - C46	121.2(6)
O3 - C2 - C21	107.4(5)	S41 - C41 - N41	119.9(4)	C45 - C46 - C47	118.5(6)
O3 - C4 - N41	107.5(4)	S41 - C41 - N42	123.6(4)	C46 - C47 - C48	121.0(6)
		N41 - C41 - N42	116.5(5)	C43 - C48 - C47	119.9(5)

the obtained atomic fractional coordinates, Table 2 bond lengths and Table 3 bond angles in the molecule of **6c**. The bond lengths and angles have usual values and are in good accord with those published[9] for 2-(4-chlorophenyl)-1,3-dioxane. Supplementary data (thermal parameters and structure factors) are available from the Cambridge Crystallographic Data Centre or the British Library,Lending Division, on request.

The X-ray diffraction analysis confirmed unequivocally that the thiourea **6c** is an epimer of thiourea **5c** and not a 1,3,7,9-tetraoxacyclododecane derivative. This 1,3-dioxane exists in an almost ideal chair conformation with all the three substituents in equatorial positions.

In the crystalline state (see Fig.2),its molecules form dimeric structures linked by two centrosymmetric hydrogen bonds N41 - H41....S with bond lengths N-H 1.08, H....S 2.33(2) 9 and NH....S angle 168(3)°. All other intermolecular contacts are close to or longer then the sum of the van der Waals radii of the atoms involved. The dimers are arranged parallel to the bc plane,explaining thus the strong mechanical anisotropy of the crystals. It is very probable that the mentioned stable dimers manifest themselves also in the mass spectra of thioureas **6**, suggesting erroneously that these compounds are derivatives of 1,3,7,9-tetraoxacyclododecane. Now all the evidence shows that thioureas **5** on dissolution in acetone undergo spontaneous epimerisation on C(4) to give the diastereoisomers **6** of configuration *rel*-2S,4S,6S. According to the NMR spectroscopy,the equilibrium mixture contains at least 95% of diastereoisomer **6** which can be isolated in the pure state by one crystallization from acetone-hexane.

Table 4. Characteristics of 1,3-dioxane derivatives **5** and **6**

Compound	Yield	M.p.	Calcd / Found			mol. ion
	%	°C	%C	%H	%N	(%)[a]
5a	73	115-118	53.63 / 53.42	9.00 / 9.32	11.37 / 11.13	246
5b	97	148-150	62.73 / 63.04	8.98 / 9.11	9.60 / 8.45	324
5c	63	149-151	59.97 / 60.15	7.18 / 7.42	9.99 / 9.73	280
5d	77	141-144	58.61 / 58.43	6.81 / 7.14	10.51 / 10.29	266
5e	69	147-149	59.97 / 60.03	7.18 / 7.24	9.99 / 10.12	280
5f	45	169-171	45.22 / 44.91	4.96 / 4.73	8.11 / 7.82	345
5g	77	154-156	46.13 / 46.33	7.74 / 8.02	11.95 / 11.77	234
5h	60[b]	127-129	53.63 / 53.42	9.00 / 9.13	11.37 / 11.56	246
6a	70	96-97	53.63 / 53.38	9.00 / 8.85	11.37 / 11.53	247(100); 493(23)
6b	72	95-98	62.73 / 62.94	8.98 / 9.13	8.60 / 8.52	324(22); 648(0.1)
6c	60	135-137	59.97 / 60.23	7.18 / 7.32	9.99 / 10.15	281(100); 561(7)
6d	74	155-157	58.61 / 58.42	6.81 / 6.53	10.51 / 10.36	267(100); 532(1)
6e	65	141-143	59.97 / 59.74	7.18 / 7.02	9.99 / 9.73	281(100); 560(1)
6f	50	127-130	45.22 / 45.01	4.96 / 5.12	8.11 / 7.93	346(8)
6g	70	137-139	46.13 / 45.98	7.74 / 7.51	11.95 / 12.03	235(67); 468(0.3)
6h	60[b]	99-101	53.63 / 53.42	9.00 / 8.72	11.37 / 11.15	247(39); 492(4)
6i	60	135-136	59.97 / 60.18	7.18 / 7.32	9.99 / 9.73	281(100); 560(0.3)
6j	69	138-140	50.74 / 51.08	7.74 / 8.03	10.79 / 10.93	261(100); 520(1.5)

[a] For compounds **5** by EI at 70 eV ; for compounds **6** by CI

[b] Mixture of **5h** and **6h**

Table 5. ^{13}C - chemical shifts of 1,3-dioxane derivatives **4**, **5**, and **6** in $CDCl_3$

Compound	$C_{(2)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	$C_{(2)}$ -CH_3	$C_{(6)}$ - CH_3	C=S	Other carbons
4	93.5	82.0	37.6	67.9	20.6	21.1	138.9	
5a	91.4	78.8	34.9	68.2	20.8	21.4	183.1	Bu: 13.7; 20.0; 31.1; 45.0
5b	91.2	78.8	35.2	67.9	20.8	21.5	181.4	Adm: 54.5; 41.5; 29.5; 36.2
5c	91.5	77.8	35.3	67.9	20.8	21.5	183.4	CH_2Ph: 48.8; 127.4; 127.7; 128.6;138.0
5d	92.0	78.8	35.0	68.2	21.0	21.4	182.3	Ph: 124.7; 126.5; 129.1; 138.0
5e	91.9	78.6	34.9	68.1	21.0	21.4	182.2	CH_3Ph: 21.0; 125.0; 129.7; 135.2; 136.5
5f	91.8	77.3	35.5	67.8	21.1	21.5	181.8	BrPh: 117.7; 125.6; 131.3; 138.2
5g	92.0	78.1	36.4	68.2	21.3	21.8	184.4	CH_2CH_2OH: 47.6; 60.1
5h	92.5	78.5	36.2	68.3	20.9	21.5	180.2	Et: 12.7; 45.4
6a	97.4	81.5	37.4	72.1	21.0	21.3	182.7	Bu: 13.7; 20.1; 30.1; 44.7
6b	97.2	81.8	37.5	71.6	20.9	21.3	180.8	Adm: 54.4; 41.8; 29.4; 36.1
6c	97.4	81.4	37.3	71.9	20.7	21.2	182.8	CH_2Ph: 48.8; 127.7; 127.8; 128.7; 137.2
6d	97.2	81.9	37.9	71.6	20.7	21.1	180.2	Ph: 127.5; 130.5; 133.2; 138.9
6e	97.7	81.9	38.5	71.6	20.9	21.4	180.6	CH_3Ph: 21.1; 125.6; 130.7; 133.3; 137.7
6f	97.5	81.3	38.0	71.6	21.0	21.4	181.2	BrPh: 126.1; 132.0; 137.3
6g	97.1	81.1	37.9	71.6	20.9	21.4	183.2	CH_2CH_2OH: 46.8; 60.7
6h	97.7	82.2	37.0	71.6	20.9	21.5	180.2	Et: 12.7; 45.4
6i	97.6	82.2	38.2	71.6	20.9	21.3	181.3	NCH_3: 43.6, Ph: 126.9; 128.8; 130.7; 142.4
6j	97.7	83.1	37.7	72.1	20.9	21.4	181.9	Morf: 48.0; 66.1

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. NMR spectra were measured on Tesla BS 567-A, Varian XL-200,Varian XL-300 and Varian UNITY-500 (compounds **5b** and **6b**) spectrometers in deuterochloroform with tetramethylsilane as internal standard. Mass spectra were obtained with a Jeol DX 303/DA 5000 instrument at 70 eV or using the chemical ionization method (CI).

Ether was dried over sodium and distilled. KSCN was dried for 24 h at 120°C prior to use. Other chemicals were commercial products purified by distillation or crystallization.

2,6-Dimethyl-4-isothiocyanato-1,3-dioxane 4

Phosphorus oxychloride (4.6g; 0.03 mol) was added dropwise at -40°C to a suspension of KSCN (8.73g; 0.1 mol) in acetaldehyde (4.4g; 0.1 mol) in a nitrogen atmosphere. The reaction mixture was stirred at -40°C for 1h, allowed to attain room temperature during 1h, set aside overnight and then partitioned between water and ether. The ethereal layer was washed with water to neutral reaction, dried over $CaCl_2$ and the solvent was evaporated. Distillation afforded 1.6g (54%) of isothiocyanate **4**, b.p. 85-87°C/200Pa; IR spectrum ($CHCl_3$): 2040, 2080 cm^{-1}(-NCS); mass spectrum (70 eV): 173(5,M^+), 129(13), 115(28), 71(53),45(100); for the NMR spectra see Tables 5 and 6.

rel-2S,4R,6S-2,6-Dimethyl-4-(N'-substituted thioureido)-1,3-dioxanes 5

The corresponding amine (0.01 mol) in ether (5 ml) was added to a stirred solution of isothiocyanate 4 (0.01 mol) in ether (5 ml) at -10°C. After 1h the reaction mixture was allowed to warm to room temperature, hexane (10 ml) was added and the formed precipitate was filtered and crystallized from acetonitrile-hexane. For yields and characteristics of the obtained thioureas see Table 4, for their NMR spectra see Tables 5 and 6.

rel-2S,4S,6S-2,6-Dimethyl-4-(N'-substituted thioureido)-1,3-dioxanes 6

A solution of thiourea **5** (0.005 mol) in acetone (15 ml) was set aside at room temperature until the starting compound disappeared (10-20 days, monitored by thin-layer chromatography in benzene-acetone 5:1). After evaporation of the solvent, the obtained product was crystallized from acetone-hexane. Thioureas **6i** and **6j** were obtained from isothiocyanate **4** and secondary amines **i** and **j** by the procedure described for the preparation of thioureas **5**. For yields and characteristics of the obtained thioureas **6** see Table 4, their NMR spectra are given in Tables 5 and 6.

Crystal Data of Compound 6c

$C_{14}H_{20}N_2O_2S$, m.w. 280.40, colourless needle shape crystals (vapor diffusion of pentane into a solution in methyl ethyl ketone); the crystals are difficult to handle since they are extremely cleavable along the bc plane.

Triclinic, $P\bar{1}$, a = 4.850(2), b = 12.408(5), c = 13.295(7) Å , α = 74.10(4), β = 87.33(4), γ = 78.25(4)°, V = 753.6(6) Å^3, Z = 2, ρ_m = 1.22(3), ρ_x = 1.235 g.cm^{-3}. An 0.07 x 0.08 x 0.60 mm fragment of a long needle-like crystaal was measured on a CAD4 diffractometer at room temperature.Lattice parameters were determined from 23 reflections in the range $9 < \Theta < 13°$. Intensities were measured between $-5 < h < 5$, $-14 < k < 14$, $-15 < l < 15$ using the ω-4/3Θ scan mode; four standard reflections were monitored every 1h and showed no significant fluctuation. Absorption of the used MoKα radiation (λ = 0.71069 Å) was neglected, μ = 0.22 mm^{-1}. From 2647 symmetrically independent reflections, 1259 fulfilling the $I > 1.96\,\sigma(I)$ were used in the further treatment.

Table 6. Proton NMR parameters of 1,3-dioxane derivatives **4**, **5** and **6** in $CDCl_3$..

Compound	$C_{(2)}$-H	$C_{(4)}$-H	$C_{(5)}$-H	$C_{(6)}$-H	$C_{(2)}$-CH_3	$C_{(6)}$-CH_3	NH	Other protons
	q	m	m	m	d	d		
4	5.17	5.58	1.75	4.05	1.28	1.20	-----	
5a	5.15	5.27	1.75	4.07	1.28	1.19	6.90; 7.35	Bu: 0.92t; 1.45m; 3.60dt
5b*	5.17	5.26	1.56; 1.86	3.99	1.30	1.22	6.18; 6.92	Adm: 1.70b; 2.12m; 2.21m; 2.26m
5c	5.13	5.28	1.72	4.02	1.16	1.16	7.20; 7.60	CH_2Ph: 4.80t; 7.40m
5d	5.16	5.62	1.77	3.90	1.33	1.19	7.26; 8.82	Ph: 7.32m
5e	5.15	5.66	1.80	3.92	1.33	1.20	7.40; 8.72	CH_3Ph: 2.35s; 7.22m
5f	5.09	5.91	1.77	4.00	1.31	1.23	8.27; 9.15	BrPh: 7.44m
5g	5.03	5.83	1.71	4.06	1.20	1.10	7.57; 8.31	CH_2CH_2OH: 3.66m
5h	5.14	6.10	1.70	3.90	1.30	1.25	7.50	Et: 1.20t; 3.65q
6a	4.90	5.67	1.77	3.84	1.38	1.27	6.75; 6.92	Bu: 0.94t; 1.50m; 3.48m
6b*	4.85	5.46	1.41; 1.86	3.83	1.38	1.27	6.04; 6.37	Adm: 1.69b; 2.12b
6c	4.72	5.52	1.75	3.80	1.25	1.17	6.95;	CH_2Ph: 4.80t; 7.30m
6d	4.83	5.88	1.88	3.80	1.27	1.20	6.50; 8.48	Ph: 7.30m
6e	4.85	5.88	1.83	3.83	1.30	1.20	6.40; 8.40	CH_3Ph: 2.35s; 7.21m
6f	4.88	5.90	1.83	3.80	1.30	1.23	7.73; 9.28	BrPh: 7.43m
6g	4.80	5.70	1.80	3.80	1.50	0.95	7.22; 8.40	CH_2CH_2OH: 3.60m; 4.40b
6h	4.78	6.00	1.68	3.95	1.30	1.25	7.50	Et: 1.20t; 3.65q
6i	4.82	5.88	1.75	3.70	1.30	1.16	5.63	NCH_3: 3.65s; Ph: 7.30m
6j	4.91	6.15	1.83	3.78	1.35	1.27	5.60	Morf: 3.78m

Coupling constants J (Hz)*

	$H_{(2)}$,CH_3	$H_{(4)}$,NH	$H_{(4)}$,$H_{(5)}$ax	$H_{(4)}$,$H_{(5)}$eq	$H_{(5)}$ax,$H_{(5)}$eq	$H_{(5)}$ax,$H_{(6)}$	$H_{(5)}$eq,$H_{(6)}$	$H_{(6)}$,CH_3
5b	5.2	3.0	5.0	1.0	14.3	12.1	2.4	6.1
6b	5.1	6.9	10.1	2.4	12.7	11.2	2.4	6.2

* The values obtained from 500 MHz spectra.

Structure Solution and Refinement

The structure was solved by direct methods (SHELXS-86)[10] and refined by full-matrix least squares (SHELX 76)[11]. Hydrogen atoms were fixed in calculated positions (sp^2 for N). In the final refinement cycles, scale factor, atomic coordinates of non-H atoms and temperature factors (isotropic for H, anisotropic for non-H) were refined simultaneously. The function minimized was $w = \Sigma w(|F_o| - |F_c|)^2$ where $w = 0.471/(\sigma^2(F_o) + 0.0009 F^2)$. At convergence, R = 0.067, wR = 0.070; the final difference map was featureless with extreme values of 0.19, -0.26 $e\text{Å}^{-3}$. The precision of the structure determination suffers somewhat from the unfavourable shape and mechani cal properties of the crystal but the chemical picture is unequivocal.

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