Tetrahedron Vol. 42, No 20, pp. 5649 to 5656, 1986
Printed in Great Britain.

0040-4020/86 $5.00+.00
Pergamon Journals Ltd.

STEREOSELECTIVE SYNTHESIS OF CIS AND TRANS N-TOSYL SULPHILIMINES AND SULPHOXIDES FROM 2-ALKYLTHIANES AND 2-ALKYLTHIOLANES ASSIGNMENTS OF CONFIGURATIONS AND PREFERRED CONFORMATIONS

I. Jalsovszky, F. Ruff,* M. Kajtár-Peredy,* I. Kövesdi and Á. Kucsman*

Institute of Organic Chemistry, L. Eötvös University, P.O.B. 325, H-1445 Budapest, Hungary; *Central Research Institute of Chemistry, Hungarian Academy of Sciences, P.O.B. 17, H-1525 Budapest, Hungary

(*Received in UK 5 August* 1986)

Abstract - Thiane and thiolane derivatives with 2-methyl, 2-ethyl, 2-isopropyl and 2-tert-butyl groups were prepared and converted to cis and trans sulphilimines and sulphoxides by various stereoselective methods. Cis-sulphilimines were formed by using t-BuOCl and $TsNH^-$ in a two-stage process, while cyclic sulphides were converted by chloramine-T predominantly to trans-sulphilimines. Sulphoxides enriched in cis and trans isomers were obtained by different methods of oxidation. Diastereoisomeric product distributions were measured by hplc and the configurations of diastereoisomers were assigned by ^{13}C NMR spectroscopy. Preferred conformations of sulphilimines were determined by analysis of ^{13}C NMR and X-ray data. As shown by ^{13}C NMR spectra, the conformations of sulphilimines and sulphoxides are analogous.

Previously we reported on the stereochemistry of the conversion of chiral alkyl phenyl sulphides to diastereoisomeric sulphilimines and sulphoxides.[1] This paper[2] describes the first synthesis and configurational assignments of cis and trans sulphilimines derived from 2-alkylthianes and 2-alkylthiolanes, together with the stereoselective oxidation of the same precursors into diastereoisomeric sulphoxides. For both series of compounds we investigated (i) the diastereoselectivity depending on the reactants and reaction conditions, (ii) the conformational preference of polar S-substituents in cyclic sulphilimines and sulphoxides, (iii) the distortion of the thiane ring by bulky vicinal substituents, and (iv) the factors governing the preferred conformations of 1,2-disubstituted thiolanes. Details on the stereochemistry of the conversion of cyclic sulphides,[3a] X-ray analysis[3b,c] and hplc measurements[3d] will be published elsewhere.

SYNTHESIS

Sulphides - 2-Alkylthianes (1a-1d) and 2-alkylthiolanes (4a-4d) (Scheme 1) were prepared by α-alkylation of thiane (1) and thiolane (4). Like 2-methyl and 2-ethyl compounds,[4] 2-isopropyl derivatives were obtained by the reaction of 2-chlorothiane and -thiolane with Grignard reagent; (t-BuO-Cu-t-Bu)Li[5] was used for the preparation of 2-tert-butyl-substituted sulphides.

Sulphilimines -Two methods were elaborated for the stereoselective synthesis of cis- and trans-sulphilimines from α-substituted cyclic sulphides.

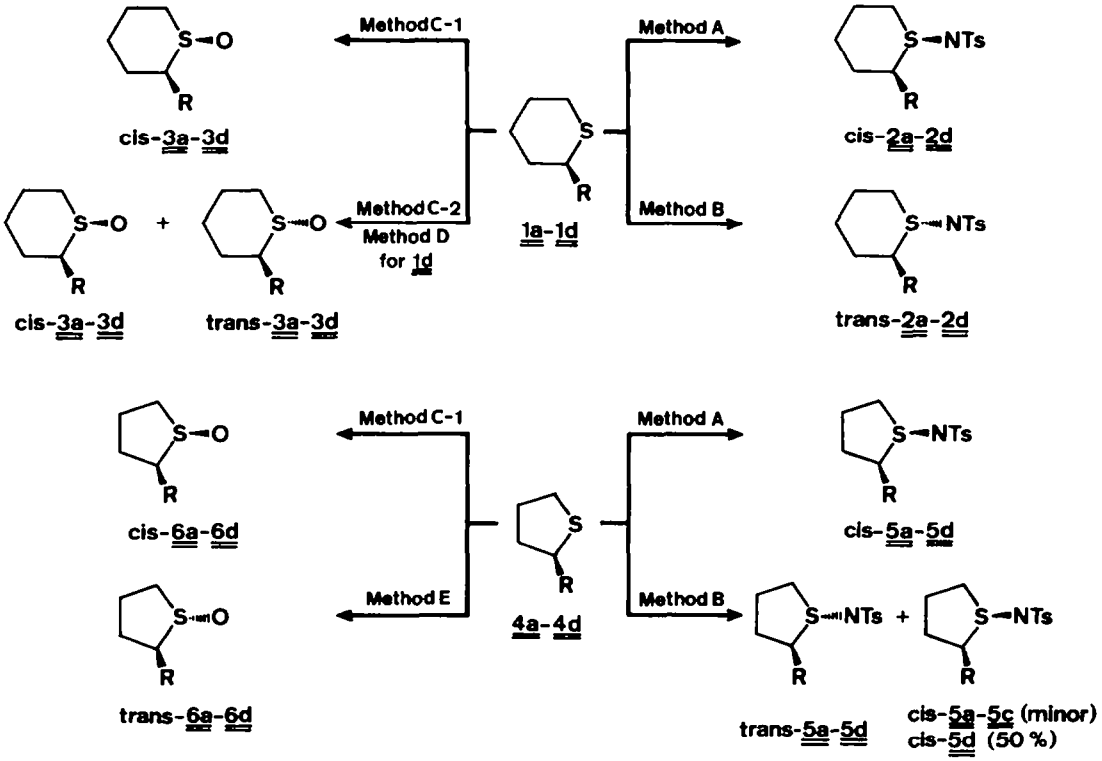
(i) The reactions of 2-alkylthianes and 2-alkylthiolanes with t-BuOCl and $TsNH^-$ were used for the preparation of the corresponding cis-sulphilimines, cis-2a-2d and cis-5a-5d (Method A; Scheme 1, Table 1; cf. Refs 1 and 6). The two steps involving S-chlorination and nucleophilic displacement on sulphur were disconnected. First t-BuOCl was added at -78° to the sulphide dissolved in methanol. A fast reaction occurred despite of the very low reaction temperature (cf. Ref. 7). After 15 min equimolecular amounts of $TsNH_2$ and TEA dissolved in DMF-methanol were poured into the mixture. The pure cis-sulphilimine diastereoisomers were obtained from the crude product by recrystallization. The bulkiness of the 2-alkyl groups did not have any significant influence on the cis:trans product ratio. On the other hand, the stereochemistry was decisively influenced by the order of adding the reactants to the reaction mixture. When $TsNH_2$ and TEA were added to the

solution of sulphide before t-BuOCl, trans-sulphilimines were formed predominantly (cf. Ref. 6b). In this case, e.g., the cis:trans product distributions 22:78 and 25:75 were observed for the sulphilimines 2b and 5b, respectively.

(ii) 2-Alkylthianes (1a-1d) treated with chloramine-T in methanol yielded trans-sulphilimines (trans-2a-2d) as major products (Method B; Scheme 1, Table 1; cf. Ref. 8). Diastereoisomeric product distributions were not controlled noticeably by the nature of 2-alkyl groups. Pure trans-compounds were obtained from the crude products by recrystallization.

The reactions of 2-alkylthiolanes (4a-4d) with chloramine-T, leading to trans-sulphilimines (trans-5a-5d) were also investigated and a decrease of stereoselectivity was observed with the increase of the size of 2-alkyl group from methyl to tert-butyl. Thus, the conversion of 2-tert-butylthiolane (4d→5d) gave a 1:1 mixture of cis- and trans-sulphilimines. Owing to the high solubility of trans-5d, the yield was far better for cis-5d. The cis-5b-5c compounds were also less soluble than the trans-isomers and could be prepared from the reaction mixture.

Sulphoxides - Cyclic sulphides were converted to cis- and trans-sulphoxides by stereoselective oxidation (Scheme 1, Table 2). When 2-alkylthianes (1a-1d) and 2-alkylthiolanes (4a-4d) were treated in methanol with t-BuOCl at -78° in the presence of Na_2CO_3 (Method C-1), cis-sulphoxides (cis-3a-3d and cis-6a-6d) were obtained as major products. Using CH_2Cl_2 solvent (Method C-2), 1:1 mixtures of cis/trans-sulphoxides were formed from the corresponding 2-alkylthianes. A considerable amount of trans-3d was formed from 2-tert-butylthiane when the oxidizing agent was $NaIO_4$ in water (Method D). The oxidation of 2-alkylthiolanes with CrO_3 in pyridine (Method E) gave products enriched in the trans-isomer (trans-6a-6d). Samples were analysed by hplc and purified by distillation and/or by the recrystallization of the $HgCl_2$ adduct. In the latter case, an appreciable shift in cis:trans product distribution was observed. Since cis-trans mixtures enriched in one of the isomers were suitable for NMR studies, pure diastereoisomers were not prepared. Similar results were reported earlier in the literature[9] for the oxidation of 2-methylthiolane (4a) and 4-substituted thianes.



Scheme 1. Major products obtained in stereoselective conversions of 2-R-thianes and 2-R-thiolanes into cis/trans-1-tosylimides and -1-oxides; R = Me (a), Et (b), i-Pr (c) and t-Bu (d). Method A: t-BuOCl, MeOH, -78°, then $TsNH_2$-TEA in DMFA-MeOH, -78°. Method B: TsNClNa, MeOH, 20°. Method C-1: t-BuOCl, MeOH, Na_2CO_3, -78°. Method C-2: t-BuOCl, CH_2Cl_2, -78°, then cold NaOH aq. Method D: $NaIO_4$, H_2O, 0°. Method E: CrO_3, pyridine, 0°.

Table 1. Preparation of diastereoisomeric sulphilimines from 2-alkylthianes and 2-alkylthiolanes

Sulphide No.	Method[a]	Sulphilimine crude product No.	Yield %	cis:tr[b]	Cryst.solvent (v/w) MeOH	Et_2O	Sulphilimine pure product No.	Yield %	m.p. (°C)	IR in KBr (cm^{-1}) ν(SNS)	ν(SO_2)
1a	A	2a	42	90:10	4.0	12.6	cis-2a	24	140-6	968,757	1272,1138
1a	B	2a	70	10:90	2.8[c]	8.4[c]	trans-2a	23	73-88	977,750	1279,1135
1b	A	2b	47	92:8	8.6	0	cis-2b	36	155-7	950,754	1272,1131
1b	B	2b	80	5:95	(d)		trans-2b[e]	73	oil	978,755	1280,1138
1c	A	2c	42	94:6	13.0[f]	30.8[g]	cis-2c	29	148-50	960,750	1270,1131
1c	B	2c	80	6:94	0.6[h]	145.0[h]	trans-2c	13	106-8	969,759	1276,1134
1d	A	2d	15	92:8	5.0	30.0	cis-2d	7	148-50	956,753	1272,1131
1d	B	2d	58	5:95	2.1	5.8	trans-2d	40	131-3	963,745	1272,1129
4a	A	5a	19	87:13	3.3	4.0	cis-5a	6[i]	119-21	978,754	1260,1132
4a	B	5a	51	30:70	1.6	19.3	trans-5a	22[i]	97-100	975,750	1268,1130
4b	A	5b	50	92:8	4.2	13.8	cis-5b	28	119-23	982,755	1266,1129
4b	B	5b	59	38:62	1.8[j]	14.2[j]	cis-5b	11[d]	121-4	982,755	1266,1129
4b	B	5b	59	38:62	0.8	10.0	trans-5b	21[d]	86-9	978,745	1276,1135
4c	A	5c	47	85:15	1.8[k]	21.2[k]	cis-5c	20	122-4	975,748	1274,1131
4c	B	5c	66	38:62	1.2[l]	12.0[l]	cis-5c	6[d]	122-4	975,748	1274,1131
4c	B	5c	66	38:62	0.5[l]	8.0[l]	trans-5c[m]	10[d]	78-80	950,747	1270,1125
4d	A	5d	40	81:19	5.0	21.0	cis-5d	16	151-4	968,760	1278,1140
4d	B	5d	65	50:50	3.7	7.4	cis-5d	32	151-4	968,760	1278,1140
4d	B	5d	65	50:50	(d)		trans-5d	7	110-5	970,742	1271,1141

(a) See Scheme 1. Method A: t-BuOCl, MeOH, -78°, then $TsNH_2$-TEA, DMFA-MeOH, -78°. Method B: TsNClNa, MeOH, 20°. (b) Determined by hplc. (c) 2.5 (MeOH) and 10 (Et_2O) for repeated cryst. (d) See Experimental. (e) Cis:trans 5:95. (f) Methanol-dioxane (82:18) was used. (g) Ether-petroleum ether (50:50) was used. (h) 0.7 (MeOH) and 130 (Et_2O) for repeated cryst. (i) Crystallization was repeated. (j) 2.0 (MeOH) and 14.2 (Et_2O) for repeated cryst. (k) 1.2 (MeOH) and 15.5 (Et_2O) for repeated cryst. (l) 0.7 (MeOH) and 15.5 (Et_2O) for repeated cryst. (m) Cis:trans 20:80.

Table 2. Stereoselectivity in oxidations of 2-alkylthianes and 2-alkylthiolanes

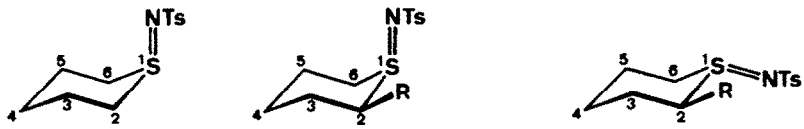
Sulphide No.	Method[a]	Sulphoxide crude product[b] No.	Yield %	cis:tr	Sulphoxide purification Method[a]	Yield %	b.p. (°C/133 Pa)	IR in film (cm^{-1}) ν(SO)
1a	C-1	3a	88	90:10	F	63	85-90	1049
1a	C-2	3a	85	73:27	F	50	85-90	1049,1033
1b	C-1	3b	88	94:6	F	40	94-8	1029
1b	C-2	3b	87	44:56	F	37	94-8	1040,1031
1c	C-1	3c	90	94:6	F	45	107-9	1031
1c	C-2	3c	92	47:53	F	48	107-9	1042
1d	C-1	3d	50	92:8	G	30	(c)	1031,1014
1d	D	3d	36	58:42	(d)		(c)	1031,1014
4a	C-1	6a	51	73:27[e]	H	14	72-4[f]	1023
4a	E	6a	31	16:84[g]	H	14	72-4	1023
4b	C-1	6b	86	79:21	F	40	82-4[f]	1028
4b	E	6b	38	18:82	F	20	82-4	1017
4c	C-1	6c	85	83:17[h]	H	9	86-8	1022
4c	E	6c	55	15:85	F	30	86-8	1019
4d	C-1	6d	50	82:18	F	20	120[i]	1037,1022
4d	E	6d	50	5:95	F	30	120[i]	1037,1022

(a) See Scheme 1. Method C-1: t-BuOCl, MeOH, Na_2CO_3, -78°. Method C-2: t-BuOCl, CH_2Cl_2, -78°, then cold 5% NaOH aq. Method D: $NaIO_4/H_2O$. Method E: CrO_3, pyridine, 0°. Method F: distillation in vacuo with no change in diastereoisomeric product distribution. Method G: recrystallized from petroleum ether (twice). Method H: through $HgCl_2$ complex. (b) Determined by hplc. (c) Low melting solid. (d) Used without purification. (e) 65:35 in Ref. 9a; after purification 88:12. (f) B.p. for a cis-trans mixture, see in Ref. 19. (g) Taken from Ref. 9a; after purification 0:100. (h) After purification 100:0. (i) Temperature of the bath.

ASSIGNMENTS OF CONFIGURATIONS, PREFERRED CONFORMATIONS

a) *Thiane derivatives.* The cis or trans configuration of sulphilimine (2a-2d) and sulphoxide (3a-3d) diastereoisomers were identified by ^{13}C NMR spectroscopy (Table 3). In all cases, the chemical shifts of C-2/C-6 and C-3/C-5 ring carbon atoms of the cis compounds are smaller than those of the corresponding trans derivatives (cf. Refs. 10 and 11). These data also reveal that the substituent effects [$\Delta\delta$ = δ(sulphide-1-X) - δ(sulphide)] of axial and equatorial X groups in thiane-1-tosylimide (2, X = NTs) and thiane-1-oxide (3, X = O) are almost the same as those observed by us for the corresponding 1-X-2-alkyl derivatives. Therefore we may conclude that all stereoisomers are conformationally homogeneous with the 2-alkyl group lying in the equatorial position (cf. Refs. 11a and 12); the 1-X substituent is axial in the cis and equatorial in the trans compounds. (The chemical shifts calculated for compounds with an axial 2-methyl group[12] differ vastly from the experimental values found for 2a and 3a).

All assumptions about conformation have been supported by X-ray data obtained for thiane-1-tosylimide and some of its 2-alkyl derivatives.[3b] Solid state conformations together with relevant geometry data are shown in Scheme 2. In agreement with ^{13}C NMR studies, X-ray analysis clearly points to the following facts. (i) The polar NTs group prefers the axial orientation, while 2-alkyl groups occupy exclusively the equatorial position. (ii) The chair conformation of thiane derivatives do not change significantly with the variation of 2-alkyl substituents; ring puckering and the orientation of ring substituents are not exceptional. To avoid steric crowd, only the thiane rings with bulky 2-alkyl groups are somewhat distorted. (iii) In cis-1,2- and trans-1,2-disubstituted thiane derivatives the "substituent torsion angles" ϑ(N-S^1-C^2-R) do not differ significantly resulting in similar chemical shifts of the C-21 side chain carbon atoms in both cis and trans derivatives. The rather high ϑ values in both cis and trans series may be ascribed to a considerable repulsion between vicinal groups.



	2	cis-2a	cis-2c	trans-2a	trans-2d
R	H	Me	i-Pr	Me	t-Bu
φ(av)	60	58	58	59	59
$\Delta\varphi1/\Delta\varphi2$	108/114	106/112	108/117	110/116	105/113
η/ζ	50/-53	55/-51	52/-53	-159/167	-155/164
ρ/ς		-178/-179	-175/179	-178/179	-174/-177
ϑ		-71	-74	77	79

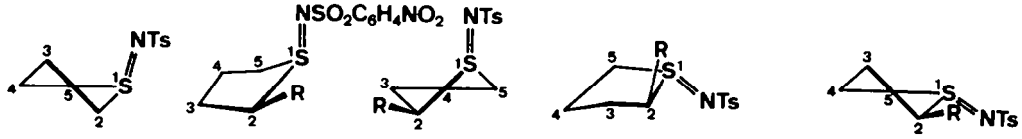
Scheme 2. Preferred conformations and relevant solid state geometry data[3b] for 2-R-thiane-1-tosylimides. φ(av) is average ring torsion angle (deg.). $\Delta\varphi1$ = φ(6,1) - φ(1,2) and $\Delta\varphi2$ = φ(1,2) - φ(2,3) characterize ring puckering at S1 and C2 atoms. η(N-S1-C2-C3), ζ(N-S1-C6-C5), ρ(R-C2-C3-C4), ς(R-C2-S1-C6) and ϑ(N-S1-C2-R) are torsion angles related with ring substituents (deg.).

b) *Thiolane derivatives.* The thiolane ring is less puckered than thiane, and so the substituent effects on the ^{13}C chemical shifts of thiolane ring carbon atoms (other than C-2), exerted by S-substituents in axial-like and equatorial-like positions, may be expected not to differ to such a large extent as with the thiane derivatives. In further contrast with thianes, the preferred conformations of thiolanes may differ significantly, depending on the nature, number and relative positions of the ring substituents. It is characteristic of thiolanes, however, that cis-vicinal substituents are in all conformations markedly nearer to each other than trans-vicinal groups (cf. Ref. 13). Thus the cis and trans diastereoisomers of thiolane-1-tosylimides 5a-5d and thiolane-1-oxides 6a-6d could be unequivocally identified by ^{13}C NMR spectroscopy, examining the β- and γ_g-effects produced on C-2 ring atom and C-21 side-chain atom, respectively (Table 3). Due to the polar 1-NTs and 1-O substituents, C-2 is less deshielded and C-21 is more shielded in the cis-compounds than in the trans-analogues (cf. Ref. 14).

Table 3. ^{13}C Chemical shifts (δ) of 2-R-thiane-1-X and 2-R-thiolane-1-X derivatives[a]

No.[b]	R	X	Isomer	C-2	C-3	C-4	C-5	C-6	C-21	C-22	
1[c]	H	l.p.		29.1	27.8	26.5	27.8	29.1			
2[d]	H	NTs	ax.	41.2	16.3	23.2	16.3	41.2			
	H	NTs	eq.	47.6	23.8	23.2	23.8	47.6			
3[e]	H	O	ax.	45.1	15.5	24.7	15.5	45.1			
	H	O	eq.	52.1	23.3	24.7	23.3	52.1			
1a[f]	Me	l.p.		37.3	36.6	26.4	26.9	29.3	21.9		
2a	Me	NTs	cis	48.7	25.1	23.6	15.3	42.9	16.7		
	Me	NTs	trans	55.5	31.6	23.7[g]	23.3[g]	47.9	16.4		
3a[h]	Me	O	cis	50.7	24.5	24.7	15.1	46.1	16.7		
	Me	O	trans	58.3	30.6	24.5	22.7	50.7	16.0		
1b	Et	l.p.		44.5	34.4	26.3	27.6	29.2[g]	29.1[g]	11.5	
2b	Et	NTs	cis	56.3	23.9[g]	23.7[g]	15.6	42.7	24.1[g]	10.3	
	Et	NTs	trans	61.2	27.9	23.2	23.8	48.0	22.3	9.6	
3b	Et	O	cis	58.0	22.7	25.0	15.5	45.9	24.2	11.0	
	Et	O	trans	64.4	27.0	24.5	22.6[g]	50.7	22.4[g]	10.4	
1c	i-Pr	l.p.		50.2	31.5	26.9	27.6	29.4	33.0	19.8	19.9
2c	i-Pr	NTs	cis	61.7	21.0	24.3	15.2	43.0	28.5	19.3	20.0
	i-Pr	NTs	trans	66.2	24.2	23.6	23.1	48.7	25.1	15.7	19.6
3c	i-Pr	O	cis	63.2	19.9	25.6	15.1	46.3	29.6	19.9	20.5
	i-Pr	O	trans	69.6	23.1	25.1	22.6	51.6	25.4	16.8	20.1
1d	t-Bu	l.p.		55.2	29.5	27.5[g]	27.6[g]	29.8	34.1	27.6	
2d	t-Bu	NTs	cis	65.1	19.1	25.3	15.5	44.4	34.7	27.6	
	t-Bu	NTs	trans	69.6	21.0	24.3	23.2	48.1	35.0	28.3	
3d	t-Bu	O	cis	67.1	17.6	26.4	15.3	47.2	34.2	28.2	
	t-Bu	O	trans	73.3	24.7	25.7	23.7	53.1	34.6	28.6	
4[i]	H	l.p.		31.7	31.2	31.2	31.7				
5[i]	H	NTs		51.2	26.3	26.3	51.2				
6[i]	H	O		54.3	25.4	25.4	54.3				
4a[j]	Me	l.p.		43.3	39.6	30.4	32.9		22.8		
5a	Me	NTs	cis	57.2	33.2	25.3	51.9		12.0		
	Me	NTs	trans	64.9	34.3	26.0	49.7		15.9		
6a[k]	Me	O	cis	58.6	32.4	24.9	54.8		11.5		
	Me	O	trans	64.3	33.1	24.7	52.4		15.1		
4b	Et	l.p.		51.2	37.0	30.7[g]	32.1		30.4[g]	13.4	
5b	Et	NTs	cis	65.1	31.1	24.6	51.0		20.1	12.5	
	Et	NTs	trans	72.5	32.5	26.3	49.8		24.3	12.3	
6b	Et	O	cis	66.7	30.3	24.5	53.9		20.0	13.1	
	Et	O	trans	73.1	31.6	25.2	52.6		23.7	12.6	
4c	i-Pr	l.p.		57.4	35.2	31.2	32.1		34.9	21.3	22.1
5c	i-Pr	NTs	cis	71.5	29.7	24.7	50.8		26.3	20.9	22.3
	i-Pr	NTs	trans	79.3	30.8	26.8	50.2		29.8	20.5	21.0
6c	i-Pr	O	cis	73.0	28.7	24.7	53.5		26.5	21.3	22.7
	i-Pr	O	trans	80.8	30.2	25.8	53.0		29.3	20.7	21.4
4d	t-Bu	l.p.		61.6	31.9[g]	31.8[g]	32.3		33.9	27.8	
5d	t-Bu	NTs	cis	73.3	26.0	23.5	50.8		33.4	28.9	
	t-Bu	NTs	trans	84.6	28.2	27.1	50.5		33.2	27.8	
6d	t-Bu	O	cis	75.2	25.0	23.9	53.7		33.1	29.3	
	t-Bu	O	trans	86.7	28.9	26.4	53.2		32.6	28.2	

(a) In $CDCl_3$ solutions. Shifts are in ppm relative to internal TMS. Side chain carbon atoms linked to S(VI) and C-2 atoms are numbered as C-11 and C-21, the following as C-12 and C-22, etc., respectively. Mean values of the chemical shifts (±0.2 ppm) found for the N-tosyl carbon atoms in sulphilimines with thiane and thiolane ring, respectively: C-11, 141.9 and 141.7; C-12/16, 125.1 and 126.3; C-13/15, 129.2; C-14, 141.5; C(Me), 21.3 ppm. (b) See Scheme 1. (c) See Ref. 11a. (d) Data were taken from Refs. 11a and 11c. (e) See Ref. 10a. (f) See Ref. 12. (g) Assignments may be reversed. (h) See Ref. 10c. (i) See Ref. 10b. (j) See Ref. 14a. (k) See Ref. 14c.



	5 ($^3T_2$)	cis-5a (^1E)	cis-5d ($^1T_2$)	trans-5a (E_4)	trans-5b (E_4)	trans-5d ($^3T_2$)
R	H	Me	t-Bu	Me	Et	t-Bu
φ(av)	26	28	27	31	26	proposed
Δφ1/Δφ2	49/75	80/62	69/77	14/40	15/32	geometry*
η/ζ	71/-86	67/-62	65/-77	-114/80	-110/85	-137/128†
ρ/ς		150/-166	171/-173	158/-133	159/-140	174/-168‡
ϑ		-61	-69	120	115	88¶

Scheme 3. Preferred conformations and relevant solid state geometry data[3c] for 2-R-thiolane-1-tosylimides and proposed geometry for trans-5d. T = half-chair; E = envelope. φ(av) is average ring torsion angle (deg.). $\Delta\varphi 1 = \varphi(5,1) - \varphi(1,2)$ and $\Delta\varphi 2 = \varphi(1,2) - \varphi(2,3)$ characterize ring puckering at S1 and C2 atoms. η(N-S1-C2-C3), ζ(N-S1-C5-C4), ρ(R-C2-C3-C4), ς(R-C2-S1-C5) and ϑ(N-S1-C2-R) are torsion angles related with ring substituents.

†-143/137 for $^1T_2$. ‡171/-173 for $^1T_2$. ¶82 for $^1T_2$. *Geometry data for $^3T_2$ and $^1T_2$ conformations of trans-5d were calculated by using experimental values found for 5 and cis-5d.

The conformation of thiolane derivatives in the literature has been studied by ^{13}C NMR spectroscopy (see e.g. Ref. 14). We decided, however, that our conformational analysis can be more firmly based on X-ray diffraction.[3c] Relevant geometry data and solid state conformations given in idealized perspective representations for thiolane-1-tosylimide and some of its 2-alkyl derivatives are shown in Scheme 3. (Since the crystals of cis-2-methylthiolane-1-tosylimide could not be used for XD, a p-nitrophenylsulphonyl derivative was investigated.)

The structures of both cis and trans compounds are governed by the equatorial preference of the 2-alkyl group and by the repulsion between vicinal substituents. All these result in different basic conformations for 1-monosubstituted (5), 1,2-cis-disubstituted (cis-5a and cis-5d) and 1,2-trans-disubstituted thiolanes (trans-5a and trans-5b). The polar NTs group is axial in the cis-derivatives, pseudoaxial in thiolane-1-tosylimide, and endo-isoclinal in the investigated trans-derivatives, revealing the axial preference of NTs group in compounds with a five-membered thiolane ring. 2-Alkyl groups occupy a pseudoequatorial or equatorial position in cis-sulphilimines with maximum staggering around S^1-C^2 bond, while they are exo-isoclinal in the planar part of the 2-methyl and 2-ethyl substituted trans-sulphilimines with maximum ϑ(N-S^1-C^2-R) torsion angle.

For preferred conformations in solution it may be assumed that they correspond to the solid state conformations, although the neighbouring conformers in the pseudorotational circuit may also be present as minor equilibrium component (cf. the identical conformational preference of thiane-1-tosylimide in solution[11] and solid state[3b]). The conformational change $^1E \rightarrow {}^1T_2$ (cis-5a→cis-5d) observed in the cis-series can be ascribed to the greater equatorial preference of tert-butyl group and the increase of steric repulsion between vicinal substituents. With increasing the bulkiness of 2-alkyl group, the axiality of the polar S-substituent becomes more pronounced, which is also indicated in the ^{13}C NMR spectra by the gradual change in Δδ(C-4) values.

It seems very likely that a conformational change should also occur in the trans-series of sulphilimines when the bulkiness of the 2-alkyl group is increased. Starting from the above experience we suppose that trans-2-tert-butylthiolane-1-tosylimide (5d) would assume the $^3T_2$ half-chair conformation with equatorial tert-butyl and pseudoequatorial NTs group and with a relatively large ϑ(N-S^1-C^2-R) torsion angle. ^{13}C NMR data also support that the NTs group in the trans-series is not tilted toward the axial position as Δδ(C-3) and Δδ(C-4) values associated with γ_g-effect do not change markedly with increasing bulkiness of 2-alkyl groups.

Finally, it should be noted that the very similar pattern of ^{13}C NMR shifts found for sulphilimines and sulphoxides in both thiane and thiolane series suggests an analogy in their preferred conformations.

EXPERIMENTAL

Preparation of Sulphides - Compounds 1a[4,15] (10%, b.p. 151°), 1b[16] (30%, b.p. 177-180°), 4a[4,15] and 4b[17] (18%, b.p. 155-160°) were obtained by cyclization of a dibromoalkane or by α-alkylation of a cyclic sulphide (cf. Ref. 4). The purification procedure was improved. As detected by NMR spectroscopy, thiane derivatives were contaminated by compounds formed from 2-chlorothiane by elimination (cf. Ref. 18). The unsaturated by-products were removed by boiling with 20% HCl aq then with 30% NaOH aq. Separation from unchanged thiane or thiolane could be achieved through repeated distillation in vacuo. Yields were rather low, owing to multistage purification processes.

2-Isopropylthiane (1c) *and -thiolane* (4c). These compounds were prepared from thiane (1)[15] and thiolane (4)[15] by α-chlorination with NCS, followed by alkylation with Grignard reagent by Ref. 4, and purified as given above (for 1c: 35%, b.p. 76-7°/1.75 kPa; for 4c: 25%, b.p. 180-5°).

2-tert-Butylthiane (1d) *and -thiolane* (4d). To a suspension of Cu_2I_2 (38 g, 200 mmol) in dry THF (400 ml) were added, under stirring at 0°, 175 ml of a 1.14 M t-BuOLi-THF soln (200 mmol) prepared from Li (1.5 g), a boiling mixture of THF (160 ml; freshly distilled from $LiAlH_4$) and t-BuOH (14.8 g). After 15 min the mixture was cooled to -78°, to the vigorously stirred soln were dropwise added, under an argon atmosphere, 134 ml of a 1.5 M t-BuLi-pentane soln (200 mmol) and, after 10 min, a benzene soln (120 ml) of 2-chlorothiane or -thiolane prepared from 100 mmol of the corresponding sulphide by Ref. 4. The cooled mixture was stirred for additional 2 hr, then mixed with methanol (25 ml) and allowed to warm to room temp. The soln was washed with cc. NH_4OH aq, and the aqueous layer was extracted two times with 300 ml of ether. The solns containing sulphide were mixed, dried ($MgSO_4$) and the solvents were removed under reduced pressure.

Crude 1d was boiled with 20% HCl aq, then with 30% NaOH aq, and finally purified by crystallization of the $HgCl_2$ derivative (cf. Ref. 15). To a soln of $HgCl_2$ (10.9 g, 40 mmol) in hot 96% EtOH (30 ml) was added 1d (6.2 g, 39 mmol). After refluxing for 10 min the mixture was cooled, the crystals were filtered, washed with cold EtOH (8.5 g) and recrystallized from 8 ml of 96% EtOH (6.5 g, m.p. 120-35°). 1d was regenerated by steam distillation from 15% HCl aq. The steam distillate was extracted with ether, dried ($MgSO_4$). The solvent was removed and the residue was distilled in vacuo (10%, b.p. 136-8/12.6 kPa). Crude 4d was purified by repeated (eight times) distillation in vacuo (22%, b.p. 115-6°/11.7 kPa).

The purity of sulphides was checked by elemental analysis (the differences between calculated and obtained C, H and S% values were less than 0.3%), and g.c., using a Hewlett-Packard 5700A chromatograph equipped with an 1m OV-101 column, Chromosorb W (1%); t = 60°.

Preparation of Sulphilimines (Table 1) - *Method A.* To a soln of a sulphide (10 mmol) in MeOH (2 ml) cooled to -78° were dropwise added, under vigorous stirring, t-BuOCl (10.5 mmol) and subsequently (after 20 min) $TsNH_2$ (10 mmol) and TEA (10 mmol) dissolved in the mixture of DMFA (2 ml) and MeOH (0.5 ml). The soln was stirred at -78° for additional 2 hr then allowed to warm up to room temp. 30 ml of cold 5% NaOH aq was added and after standing (0°) the crystalline sulphilimine was filtered off and washed with ice-cold 5% NaOH aq then water. Non-crystalline products were extracted with CH_2Cl_2, dried ($MgSO_4$) and the solvent was evaporated. The crude products were carefully dried in vacuo over P_2O_5, then analysed by hplc.

Method B. To a cooled soln of a sulphide (10 mmol) in MeOH (10 ml) was added chloramine-T ($TsNClNa.H_2O$), 11 mmol) dissolved in MeOH (5 ml) and the mixture was stirred at room temp for 2 hr. After evaporation of the solvent the residue was treated with 30 ml of ice-cold 5% NaOH aq, and the crude product was isolated by Method A.

Purification. Crude products were recrystallized from methanol-ether mixtures as given in Table 1. To samples dissolved in warm (40°) methanol was added an 1/3 part of ether, the soln was filtered then mixed with the remaining 2/3 part of ether. Crystalline products were filtered off and washed with ether then dried. In some cases recrystallization was repeated.

By applying Method B, 2b was formed as a viscous oil (2.4 g). The crude product was boiled with dry ether (150 ml). The ethereal soln was decanted from the precipitated crystals of cis-2b (yield 4%) then evaporated to yield trans-2b as an oily product with a diastereoisomeric purity of 95%. The crystallization of the crude products 5b, 5c and 5d obtained by Method B afforded directly the minor cis isomers. Trans-5b and trans-5c were prepared from the filtrates by evaporation and recrystallization; for trans-5c only a diastereomeric purity of 80% has been attained. Trans-5d was purified by the following procedure: 0.7 g of the crude product was extracted with petroleum ether (three times 10 ml) then with ether (five times 10 ml). The ethereal solns were evaporated, the residue was extracted with ether (two times 20 ml) and the ethereal solns were evaporated again. The residue was recrystallized from 40:60 THF - petroleum ether (0.7 ml).

The purity of all sulphilimine diastereoisomers were checked by elemental analysis (the differences between calculated and obtained C, H, N and S% values were less than 0.3%) and hplc.

Preparation of Sulphoxides (Table 2) - *Method C-1.* To a stirred soln of a sulphide (1a-1d, 4a-4d, 10 mmol) in MeOH (100 ml), cooled to -78° with acetone - dry ice bath, was dropwise added t-BuOCl (1.08 g, 10 mmol) under stirring. After 15 min. anhydrous Na_2CO_3 powder (2.12 g, 20 mmol) was added to the mixture which was allowed to stir for an additional 1 hr at -78°, then to come to room temperature. The solvent was removed under reduced pressure, the residue was extracted with ether (four times 20 ml), dried ($MgSO_4$) and ether was evaporated. *Method C-2.* CH_2Cl_2 and 50 ml of 5% NaOH aq were used instead of MeOH and Na_2CO_3. The obtained crude products (3a-3c) (80-90%) were analyzed by hplc (see Table 2), then submitted to further purification by distillation in vacuo. *Method D* (cf. Ref. 9b). The sulphide 1d (3 mmol) was added to $NaIO_4$ (0.7 g, 3.15 mmol) in water (6.3 ml) at 0°. The mixture was stirred at 0° for additional 12 hr then filtered. The ppt ($NaIO_3$) was washed with CH_2Cl_2 (15 ml), the aqueous filtrate was extracted with CH_2Cl_2 (two times 5 ml). The combined washing was dried ($MgSO_4$) and the solvent was removed. *Method E.* 10 mmol of a sulphide (4a-4d) was converted by CrO_3 as described in Ref. 9. The obtained products were dissolved in dry ether, filtered and ether was removed. - Purification see in Table 2.

Purification via $HgCl_2$ complexes. The sulphoxides cis-6a, trans-6a and cis-6c were purified by applying the method described for 4-tert-butylthiane-1-oxide isomers in Ref. 9b; 5 g of the above sulphoxides were dissolved in EtOH (30, 30, 32 ml) saturated with $HgCl_2$ and the mixtures were refluxed for 1 h, then filtered and evaporated. The residues were crystallized (from 10, 10 and 13 ml of EtOH, MeOH and EtOH, respectively), and recrystallizations were repeated (usually two times) to constant melting points (90–105°, 100° and 144–6°). Sulphoxides were regenerated by Ref. 9b (using 1 g of KCN dissolved in 80 ml of 50% EtOH) and purified further by distillation in vacuo. The purity of sulphoxides was checked by hplc and spectroscopic (NMR, IR) methods.

Hplc[3d] – The chromatograph was a laboratory assembled instrument.[1] Column (250 x 4 mm) was packed with Hypersil silica (5 μm). The following five eluents (v/v): ether-pentane-methanol (70:24:6, 55:36:9, 53:43:4), ether-sec-octylalcohol (90:10) and ether-96% ethanol (96:4) were used for the chromatography of products obtained by the conversion of the sulphides (i) 1c, 1d, 4a and 4b; (ii) 1a and 1b; (iii) 4d; (iv) 4a and (v) 4c, respectively. Samples were dissolved in methanol (2 mg/ml) and 10 μl of the solutions were injected. UV absorption of the column effluents were monitored at 220 nm.

Spectra – IR spectra were obtained on Zeiss IR-75 instrument in film or KBr pellet. ^1H NMR and ^{13}C NMR were recorded on Varian A-60D and Varian XL-100 instruments in $CDCl_3$ or C_6D_6 solutions at room temperature, using TMS int. stand.

Acknowledgement – The authors thank Dr. H. Medzihradszky-Schweiger and Dr. S. Kutassy for analyses, Dr. M. Mészáros for g.c. measurements, Miss Zs. Szigeti for technical assistance, and Mrs. J. Máthé and Mr. T. Bobák for preparing the manuscript.

This work was supported by the Institute for Science Management and Informatics, Ministry of Education, Budapest, Hungary.

REFERENCES

1. F. Ruff, G. Szabó, J. Vajda, I. Kövesdi and Á. Kucsman, Tetrahedron, 36 (1980) 1631; and refs. therein; Gy. Szókán, F. Ruff, Á. Kucsman, J. Chromatogr. 198 (1980) 207.
2. Preliminary communications were presented at 3rd European Symposium on Organic Chemistry (ESOC III), Canterbury, 1983, and 11th International Symposium on the Organic Chemistry of Sulphur, Lindau, 1984.
3. (a) I. Jalsovszky, F. Ruff, I. Kövesdi, M. Kajtár-Peredy and Á. Kucsman, in preparation;
   (b) I. Jalsovszky, Á. Kucsman, F. Ruff, T. Koritsánszky, Gy. Argay and A. Kálmán, J. Mol. Struct., submitted for publication;
   (c) I. Jalsovszky, Á. Kucsman, F. Ruff, Gy. Argay, T. Koritsánszky and A. Kálmán, J. Mol. Struct., submitted for publication;
   (d) I. Jalsovszky, Gy. Szókán, F. Ruff and Á. Kucsman, J. Chromatogr., submitted for publication.
4. D.L. Tuleen and R.H. Bennett, J. Heterocycl. Chem. 6 (1969) 116.
5. G.H. Posner and J.J. Sterling, J. Am. Chem. Soc. 95 (1973) 3076.
6. (a) P.K. Claus, W. Rieder, P. Hofbauer and E. Vilsmaier, Tetrahedron, 31 (1975) 505; and refs. therein;
   (b) P.K. Claus, W. Rieder and F.W. Vierhapper, Monatsh. Chem. 109 (1978) 609;
   (c) D. Swern, I. Ikeda and G.F. Whitfield, Tetrahedron Letters, (1972) 2635.
7. C.R. Johnson and J.J. Rigau, J. Am. Chem. Soc. 91 (1969) 5398; and refs. therein.
8. (a) C.R. Johnson and J.J. Rigau, J. Org. Chem. 33 (1968) 4340;
   (b) Y. Tamura, Y. Nishikawa, C. Mukai, K. Sumoto and M. Ikeda, J. Org. Chem. 44 (1979) 1684;
   (c) Y. Tamura, C. Mukai, Y. Nishikawa and M. Ikeda, J. Org. Chem. 44 (1979) 3296.
9. (a) J. J. Rigau, C. C. Bacon and C.R. Johnson, J. Org. Chem. 35 (1970) 3655;
   (b) C.R. Johnson and D. McCants, jr., J. Am. Chem. Soc. 87 (1965) 1109;
   (c) C. Barbieri, M. Cinquini, S. Colonna and F. Montanari, J. Chem. Soc., C (1968) 659.
10. (a) G.W. Buchanan and T. Durst, Tetrahedron Letters, (1975) 1683;
    (b) G. Barbarella, P. Dembech, A. Garbesi and A. Fava, Org. Magn. Reson. 8 (1976) 108;
    (c) G. Barbarella, P. Dembech and V. Tugnoli, Org. Magn. Reson. 22 (1984) 402.
11. (a) J.R. DeMember, R.B. Greenwald and D.H. Evans, J. Org. Chem. 42 (1977) 3518;
    (b) P.K. Claus, W. Rieder and F.W. Vierhapper, Monatsh. Chem. 109 (1978) 631;
    (c) P.K. Claus, F.W. Vierhapper and R.L. Willer, J. Org. Chem. 44 (1979) 2863; and refs. therein.
12. R.L. Willer and E.L. Eliel, J. Am. Chem. Soc. 99 (1977) 1925.
13. M. Christl, H.J. Reich and J.D. Roberts, J. Am. Chem. Soc. 93 (1971) 3463.
14. (a) G. Barbarella and P. Dembech, Org. Magn. Reson. 13 (1980) 282;
    (b) G. Barbarella and P. Dembech, Org. Magn. Reson. 15 (1981) 72;
    (c) G. Barbarella, S. Rossini, A. Bongini and V. Tugnoli, Tetrahedron, 41 (1985) 4691.
15. E.W. Whitehead, R.A. Dean and F.A. Figler, J. Am. Chem. Soc. 73 (1951) 3632.
16. D.N. Jones, D.R. Hill, D.A. Lewton and C. Sheppard, J. Chem. Soc., Perkin Trans. 1, (1977) 1575.
17. R.D. Obolentsev and V.G. Bukharov, Chem. Abstr. 55 (1961) 25907.
18. C.G. Kruse, E.K. Poels, F.L. Jonkers and A. van der Gen, J. Org. Chem. 43 (1978) 3548.
19. R.D. Obolentsev, V.G. Bukharov and M.M. Gerasimov, Chem. Abstr. 57 (1963) 5868e.