Intermolecular Stereoselective Pummerer Reactions of 4-(*p*-Chlorophenyl)thiane 1-Oxides and *trans*-1-Thiadecalin 1-Oxides and 2-Thiadecalin 2-Oxides with Acetic Anhydride

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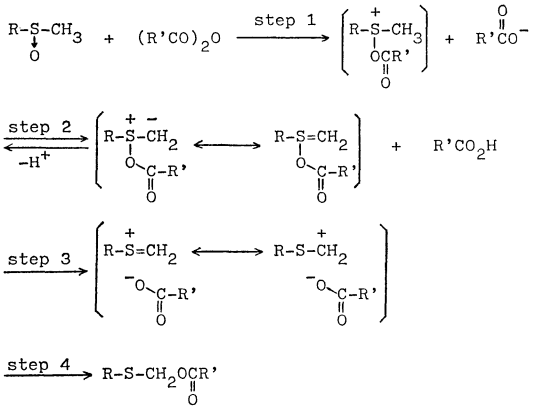
The Pummerer reactions of conformationally fixed 4-(*p*-chlorophenyl)thiane 1-oxides and *trans*-1-thiadecalin 1-oxides and *trans*-2-thiadecalin 2-oxides with acetic anhydride are either stereoselective or stereospecific, both in the absence and in the presence of a scavenger of acetic acid formed, such as dicyclohexylcarbodiimide (DCC) or 2,6-lutidine. However, the ^{18}O-tracer experiments with the ^{18}O-labeled sulfoxide revealed the reaction to be an intermolecular rearrangement, while the kinetic experiment with α-deuterated 4-(*p*-chlorophenyl)thiane 1-oxides gave sizable values of kinetic isotope effect, *i.e.*, 2.8 for the *cis* isomer and 3.4 for the *trans* isomer. In the reaction of 4-arylthiane 1-oxides with acetic anhydride, the thermodynamically controlled product is axial 2-acetoxy-4-(*p*-chlorophenyl)thiane while the kinetically controlled product is the equatorial isomer which is formed in the presence of the acid scavenger, DCC. In the Pummerer reaction of the thiadecalins *S*-oxides the equatorial α-acetoxy sulfides are the preferential products, however, the isomer preference is more pronounced in the reaction with DCC. These observations, along with other pertinent data seem to suggest that the rate-determining step in the Pummerer reaction of these simple heterocyclic sulfoxides is E2 elimination of acetic acid from the acetoxysulfonium intermediates.

Since Horner proposed[1] to call the reaction between alkyl sulfoxides with acetic anhydride leading to the formation of corresponding α-acetoxy sulfides as the Pummerer reaction fifty years after the original works of Pummerer,[2] numerous investigations have been carried out to clarify the mechanism of this interesting rearrangement and the mechanistic studies on the Pummerer reaction have been well-documented in many reviews in recent years.[3–10]

The general scheme of the Pummerer reaction is believed to be shown in the following four sequential steps of elemental reactions and the rate-determining step is known to vary with changes of both the acylating agent and the sulfoxide.[8,9] Many of the early examples of the Pummerer reactions of open chain alkyl sulfoxides with acetylating reagents were shown by ^{18}O-tracer studies to be intermolecular rearrangements which have the rate-determining step at step 2 and no stereoselectivity or specificity was observed.[11,12]



Recently, however, several examples of the Pummerer reactions which proceed through intramolecular migration to afford stereoselective (or stereospecific) products have been reported.[13–17] In most of these intramolecular rearrangements, the slowest step has been shown to be the S–O bond cleavage at step 3 with a few exceptions in which the step 1 is the rate-determining.[18,19] Among several examples of the Pummerer reaction of *S*-oxides of sulfur-heterocycles with acetic anhydride, stereoselectivity was observed in only two cases of five-membered sulfur-heterocycles, *i.e.*, *S*-oxides of thiosugar derivatives[20] and *S*-oxides of 1,3-oxathiolane derivatives.[21] However, no legitimate observation was made as to the nature of acetoxyl migration. Thus, the only example of intermolecular stereoselective Pummerer reaction of the *S*-oxide of a simple sulfur-heterocycle has been that of 4-(*p*-chlorophenyl)thiane 1-oxide (**1**) with acetic anhydride.[22] We now have found that another example of intermolecular stereoselective Pummerer reaction, *i.e.*, the reaction of conformationally rigid *trans*-1-thia- and 2-thiadecalin *S*-oxides (**3** and **5**) with acetic anhydride. This paper gives a full account of our mechanistic investigation on the Pummerer reactions of *cis*- and *trans*-4-(*p*-chlorophenyl)thiane 1-oxides (**1c** and **1t**) and *trans*-1-thiadecalin 1-oxides (axial **3a** and equatorial **3e**) and 2-thiadecalin 2-oxides (axial **5a** and equatorial **5e**) with acetic anhydride.

Results and Discussion

*Reaction of 4-(*p*-Chlorophenyl)thiane 1-Oxides with Acetic Anhydride.* Configurationally fixed *cis*- and *trans*-4-(*p*-chlorophenyl)thiane 1-oxides (**1c** and **1t**) were allowed to react with excess acetic anhydride with or without DCC or 2,6-lutidine, the acetic acid scavenger, both the axial 2-acetoxy-4-(*p*-chlorophenyl)thiane (**2a**), and the equatorial isomer (**2e**), were obtained along with the elimination product, *i.e.*, 4-(*p*-chlorophenyl)-3,4-dihydro-2*H*-thiopyran (**2o**) in the ratios as summarized in Table 1.

When the sulfoxides, **1c** and **1t** were heated with a large excess of acetic anhydride at 100 °C, only the corresponding axial α-acetoxy sulfide **2a** and the olefinic product **2o** were obtained in 72—73% and 20% yields, respectively (runs 1 and 2). The axial α-acetoxy sulfide **2a** was found to be formed stereoselectively (**2e**:**2a**=1:15) from both the *trans*-sulfoxide **1t** and the *cis* isomer **1c**. Whereas, when the sulfoxides (**1t** and **1c**) were allowed to react with excess acetic anhydride in the presence of dicyclohexylcarbodiimide (DCC) or 2,6-lutidine at 100 °C for 4—6 h, the pre-

Table 1. The pummerer reaction of the thiane 1-oxides **1t** and **1c** with acetic anhydride at 100 °C

Run	Sulfoxide	Acid-scavenger (ratio)[a]	t/h	Products and yields/%	
				2(**2e**:**2a**)[b]	**2o**
1	**1t**	—	3	70(1:15)	23
2	**1c**	—	3	71(1:15)	21
3	**1t**	—	0.75[c]	40(1:1)	
4	**1c**	—	0.75[c]	40(1:1)	
5	**1t**	DCC(1)	4	78(2:1)	20
6	**1c**	DCC(1)	4	77(2:1)	20
7	**1t**	DCC(3)	4	85(9:1)	11
8	**1t**	DCC(5)	4	83(13:1)	9
9	**1c**	DCC(5)	6	83(14:1)	12
10	**1c**	2,6-Lutidine(5)	4.5	81(5:2)	15
11	**1c**	2,6-Lutidine(10)	4.5	86(5:1)	12

a) Ratio = acid scavenger/sulfoxide. b) The ratio (**2e**:**2a**) was determined by NMR measurement. c) The sulfoxide **1** was recovered in *ca.* 50% yield.

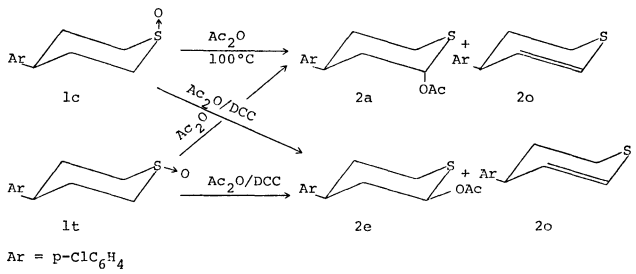


Fig. 1.

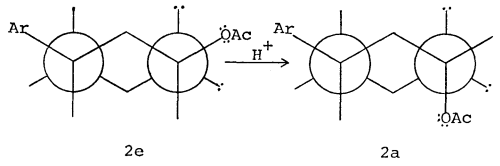


Fig. 2.

ferential product, obtained in 77—80% yield, was the equatorial α-acetoxy sulfide **2e**. Thus, the stereoselectivity of the reaction was found to be changed drastically by addition of DCC or 2,6-lutidine into the reaction mixture (runs 5—11). For example, treatment of the two isomeric sulfoxides with acetic anhydride in the presence of 5 equiv. amounts of DCC gave the corresponding crystalline equatorial α-acetoxy sulfide **2e** as the main product (runs 8 and 9) as shown in Fig. 1.

These interesting stereoselectivities in the Pummerer reaction suggest that the equatorial α-acetoxy sulfide **2e** is the kinetically controlled product and the equatorial α-acetoxy sulfide **2e** is isomerized in the presence of acetic acid formed to the axial isomer **2a** when there is no acid scavenger such as DCC or 2,6-lutidine. Indeed, in the presence of acetic acid, the equatorial α-acetoxy sulfide was found to isomerize readily to the axial isomer **2a** which is considered to be more stable than the equatorial isomer **2e** due mainly to the less electron repulsion between the lone electron pairs of sulfur atom and those of terminal oxygen in **2a** than that in **2e**, as illustrated in Fig. 2.

When one compares runs 1 and 2 with 3 and 4,

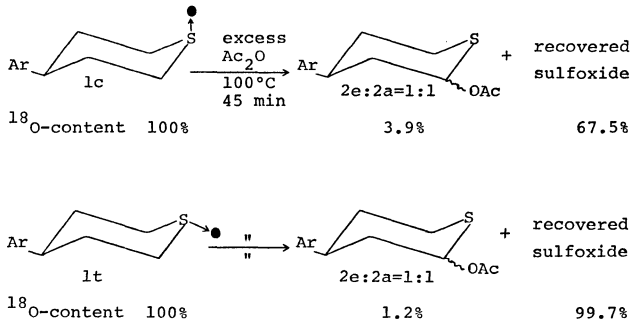


Fig. 3.

the isomerization is found to be multiplied by acetic acid formed in the reaction mixture. Upon treatment of the equatorial isomer **2e** with hot acetic anhydride in the presence of acetic acid at 100 °C for 3 h, the axial isomer **2a** and the olefinic product **2o** were obtained in 70 and 20% yields, respectively. The olefinic sulfide **2o** would obviously be formed by 1,2-elimination of acetic acid from the axial isomer **2a**.

In order to scrutinize the nature of acetoxyl migration, our usual ^{18}O-tracer experiments were carried out using the ^{18}O-labeled sulfoxides and the acetoxyl migration was found to proceed intermolecularly based on the following observations. Namely, when the ^{18}O-labeled *trans*-sulfoxide **1t** [1.092 ex. atom%] was treated with 60 mol equivalents of acetic anhydride at 100 °C for 45 min, during when the reaction was at about half completion, the recovered sulfoxide, [1.089 ex. atom% of ^{18}O], was contaminated with no *cis* sulfoxide **1c**, while the sulfoxide recovered was found to have retained the original ^{18}O-content nearly completely. Whereas, the Pummerer rearrangement product, the α-acetoxy sulfide **2**, was found to retain only 0.013 ex. atom% of ^{18}O which corresponds to 1.2% incorporation of ^{18}O from the starting sulfoxide **1t**-^{18}O. The ^{18}O-labeled *cis* sulfoxide **1c**-^{18}O, [0.495 ex. atom% of ^{18}O] under the same conditions gave the recovered sulfoxide and the Pummerer rearrangement product of which ^{18}O-contents were found to be 0.334 and 0.019 ex. atom% of ^{18}O, which corresponds to 3.9% incorporation of ^{18}O from the starting sulfoxide **1c**-

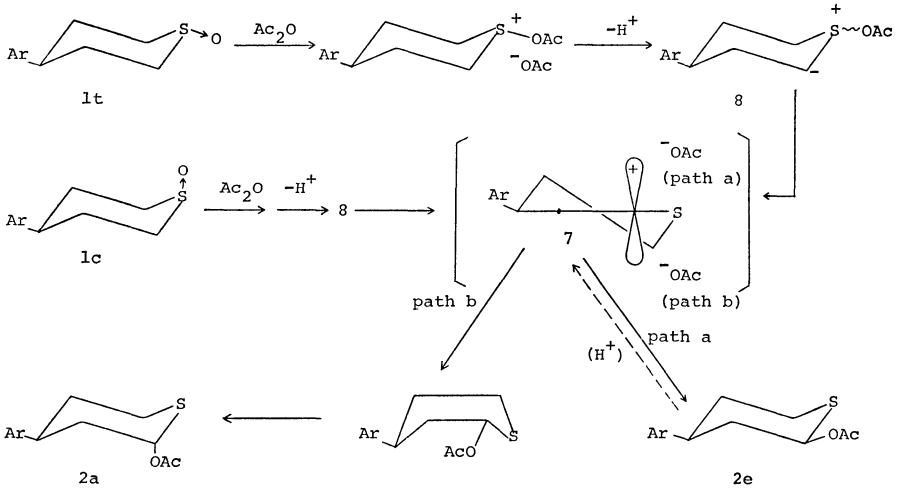


Fig. 4.

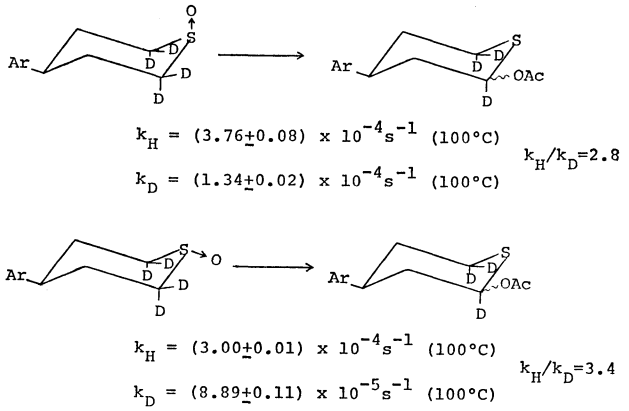


Fig. 5.

^{18}O respectively. The *cis*-sulfoxide **1c**-^{18}O was shown to undergo concurrent oxygen exchange in acetic anhydride[23] to the extent of 35% as illustrated in Fig. 3. All these ^{18}O-tracer data reveal clearly the acetoxyl migration is intermolecular, and the rearrangement is considered to proceed through the formation of the α-sulfenyl carbenium ion intermediate **7** which is then attacked by external acetoxyl group preferentially from the direction (path a) to give the equatorial α-acetoxy sulfide **2e**. The acid-catalyzed isomerization of the α-acetoxy sulfide **2e** to the other isomer **2a** is also considered to proceed via the formation of the carbenium ion intermediate **7** as shown in Fig. 4.

In the Pummerer reaction of most alkyl sulfoxides with acetic anhydride, the rate-determining step seems to be the proton-removal, *i.e.*, step 2, or E2 type elimination of acetic acid in the general scheme of the reaction, as revealed in a few sizable values of kinetic isotope effect, k_H/k_D, found in the rearrangements.[12,24] In order to find out the rate-determining step of the Pummerer reaction of 4-(*p*-chlorophenyl)thiane 1-oxides with acetic anhydride, kinetic experiments with 4-(*p*-chlorophenyl)thiane-2,2,6,6-d_4 1-oxides were carried out, and the values of the kinetic isotope effect (k_H/k_D) were found to be 2.8 for the *cis* isomer and 3.4 for the *trans* isomer. The sizes of the kinetic isotope effects are similar to that in the Pummerer reaction of methyl phenyl sulfoxide with acetic anhydride as illustrated in Fig. 5. Thus the rate-determining step of this reaction is clearly the step 2. If the subsequent S–O bond cleavage is very fast, as was found to be the case, the proton-removal could actually be a part of the E2 reaction, which was found to be the most likely in view of the stereochemistry of the Pummerer reaction of more rigid *trans*-1-thia- and 2-thiadecalin *S*-oxides (**3** and **5**) with acetic anhydride, (*vide infra*).

Reaction of trans-*1-Thiadecalin 1-Oxides (**3**) and* trans-*2-Thiadecalin 2-Oxides (**5**) with Acetic Anhydride.* In the Pummerer reaction of conformationally rigid 4-(*p*-chlorophenyl)-thiane 1-oxides (**1c** and **1t**) with acetic anhydride, the kinetically controlled initial product was the equatorial α-acetoxy thiane **2e**, although the rearrangement was shown to be intermolecular. The stereoselectivity is expected to be more pronounced in the Pummerer reaction of more rigid heterocyclic sulfoxides. Our choice sulfoxides are *trans*-1-thiadecalin 1-oxides (axial **3a** and equatorial **3e**) and *trans*-2-thiadecalin 2-oxides (axial **5a** and equatorial **5e**) which are conformationally more rigid six-membered cyclic sulfoxides than 4-(*p*-chlorophenyl)thiane 1-oxides (**1c** and **1t**). When *trans*-1-thiadecalin 1-oxides (**3a** and **3e**) were allowed to react with excess acetic anhydride at 100 °C for 3—4 h, both in the absence and in the presence of DCC, both the corresponding axial α-acetoxy sulfide **4a** and the equatorial isomer **4e** were obtained, respectively. Similarly, in the reactions between *trans*-2-thiadecalin 2-oxides (**5a** and **5e**) and acetic anhydride at 100 °C for 3 h, both the corresponding axial and equatorial α-acetoxy sulfides [(**6a1**:**6a3**=1:1) and (**6e1**:**6e3**=1:1)] were obtained, respectively both in the absence and in the presence of DCC, as illustrated in Fig. 6.

These data reveal clearly that there is a preferential direction for acetate ion to attack the α-sulfenyl stabilized carbenium ion, *i.e.*, the attack of acetate takes place at the opposite side of γ-axial hydrogen to avoid the steric repulsion of the γ-axial hydrogen. The preferential formation of the equatorial acetoxy sulfides is more pronounced in the Pummerer reactions of these

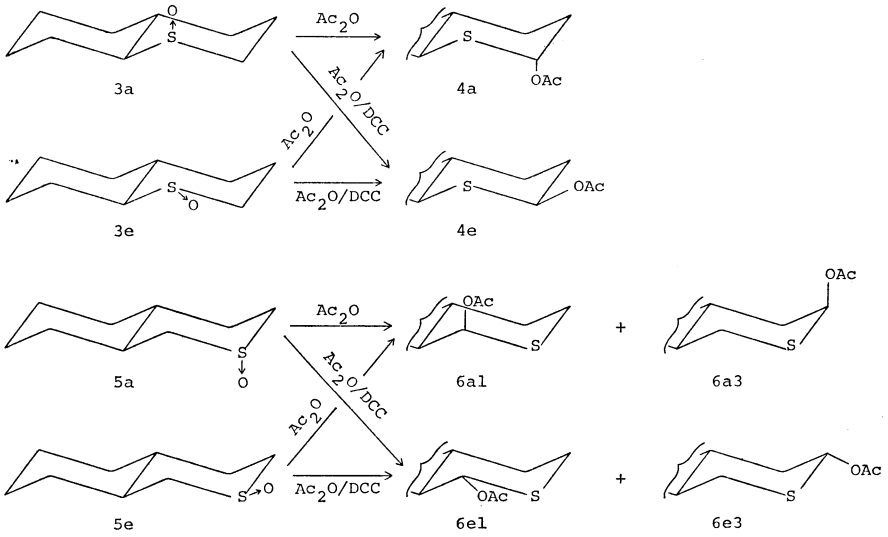


Fig. 6.

Table 2. ^{18}O-Experiments in the reaction of *trans*-1-thiadecalin-1-oxides with acetic anhydride

Sulfoxide (ex. atom% of ^{18}O)	Reaction conditions t/°C	t/min	Pummerer products Yield %	(ex. atom%)	Incorporation %	Recovered sulfoxide Yield %	(ex. atom%)	Retention %
3a (0.856)	Ac_2O		28	**4e** (0.057)[a]	13	25	(0.710)	83
	100	45	(**4e**:**4a**=6:1)	**4a** (0.043)[a]	10			
3a (0.856)	Ac_2O/DCC		51	(0.068)[b]	16	30	(0.574)	67
	100	75	(**4e**:**4a**=19:1)					
3e (0.955)	Ac_2O		37	(0)[b]	0	53	(0.774)	81
	100	45	(**4e**:**4a**=8:1)					
3e (0.955)	Ac_2O/DCC		34	(0)[b]	0	59	(0.812)	85
	100	75	(**4e**:**4a**=19:1)					

a) Axial and equatorial acetoxy sulfides were separated through silica-gel column chromatography, and their ^{18}O-contents were analyzed. b) A mixture of axial and equatorial acetoxy sulfides was subjected to ^{18}O-analysis.

highly rigidly fixed *trans*-1- and 2-thiadecalin *S*-oxides. Addition of DCC, the scavenger of acetic acid, was also found to slow down the reaction but the isomeric preference is more remarkable in favor for the equatorial acetoxy sulfides.

The usual ^{18}O-tracer experiments were carried out with ^{18}O-labeled *trans*-1-thiadecalin 1-oxides (**3a**-^{18}O and **3e**-^{18}O) with acetic anhydride both in the absence and in the presence of DCC and the results are shown in Table 2.

The results are quite interesting. The Pummerer reaction of the equatorial sulfoxide **3e** is obviously an intermolecular rearrangement since the acetoxyl group of the resulted ester was found to be completely diluted with oxygen of excess acetic anhydride, while the sulfoxide recovered retained more than 80% of original ^{18}O-label both in the absence and in the presence of DCC. The Pummerer reaction of the axial sulfoxide **3a** is also an intermolecular rearrangement, though the incorporation of 13% or 16% of ^{18}O of the original sulfoxide in the 2-acetoxy-1-thiadecalin (**4**) and the sulfoxide recovered have 83% or 67% of original ^{18}O-label mean that the rearrangement is partially intramolecular. When one looks at the preferential conformations and conformational changes required for the rate-determining elimination of acetic acid and the subsequent rapid recombination for the Pummerer reactions of both isomeric sulfoxides, it is quite evident that both E2 type elimination of acetic acid and recombination with acetate in the reaction of the axial sulfoxide requires less conformational change, and hence the reaction of the axial sulfoxide would be more facile than that of the equatorial sulfoxide which would have to undergo conformational change for E2 elimination and also in the product formation. Perhaps, the facile E2 reaction of acetic acid and recombination would have increased the chance of intramolecular rearrangement for the axial sulfoxide **3a**.

One interesting observation we made was the stereochemistry of proton-removal and cleavage of acetate in this rearrangement. Thus, *trans*-1-thiadecalin-2e-*d* 1a-oxide (D:59%) (**9**), *trans*-1-thiadecalin-2a-*d* 1a-oxide (D:57%) (**10**), and *trans*-1-thiadecalin-2a-*d* 1e-oxide (D:57%) (**11**) were subjected to the Pummerer reaction with excess acetic anhydride in the presence of 5 equivalent amounts of DCC. The deuterium contents of the corresponding 2e-acetoxy sulfides were found to be 59, 13, and 50%, respectively, upon measurement of the NMR spectra using 14% of Eu(dpm)$_3$ shift reagent, to the α-acetoxy sulfides. As

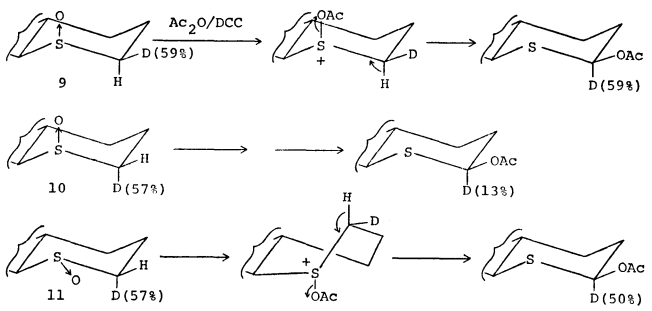


Fig. 7.

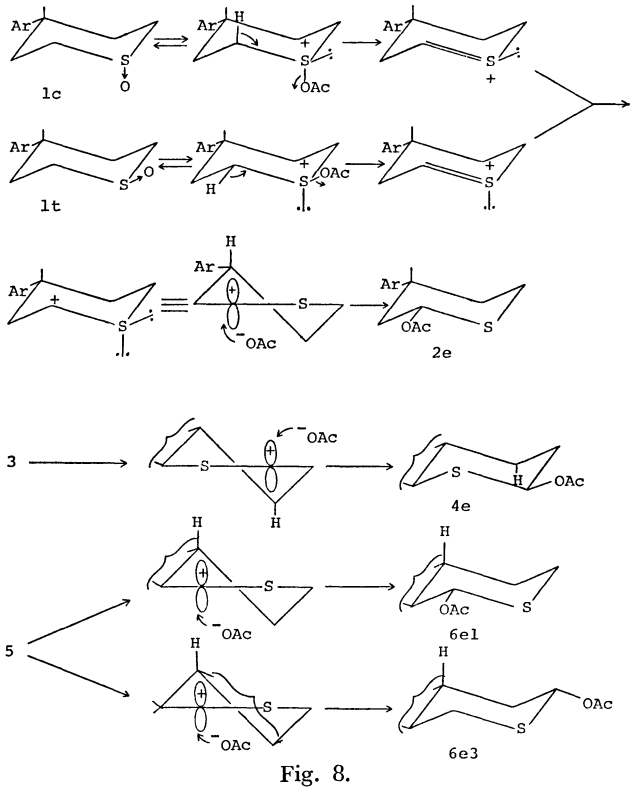


Fig. 8.

the mechanistic scheme indicates, the reaction of each isomer of 2-monodeuterated *trans*-1-thiadecalin 1-oxides gave only the corresponding each one product formed by the E2 elimination of acetic acid from the corresponding acetoxysulfonium intermediate as illustrated in Fig. 7. This is the first clean-cut example of *trans* E2 type elimination of acetic acid from the acetoxysulfonium intermediate in the Pummerer reaction, although E2 elimination was suggested early by us[6,9] and also Wolfe and Kazmeier.[25]

Conclusion

The Pummerer reaction of conformationally rigid six-membered thiane 1-oxides with acetic anhydride is stereoselective and the rearrangement is mainly intermolecular, while the rate-determining step appears to be the E2 1,2-elimination of acetic acid from the acetoxysulfonium intermediates formed in the initial acetylation of the sulfoxides. Meanwhile, the preferential formation of the equatorial α-acetoxy sulfides in the initial rearrangement is considered to be due to the facile sterically access of the acetate to the equatorial position, whereas the isomerization to the more stable axial α-acetoxy sulfide in the case of 4-arylthiane derivatives is catalyzed by acetic acid present in the system. Thus, the overall mechanism of the Pummerer reaction of these conformationally rigid thiane 1-oxides may be illustrated as shown in Fig. 8.

Experimental

General. All melting points were uncorrected. IR spectra were taken on a Hitachi 260-50 spectrometer. NMR spectra were recorded with a Hitachi Perkin-Elmer R-20 spectrometer in $CDCl_3$ using TMS as an internal standard. Mass spectra were determined with a Hitachi RMU-6MG mass spectrometer. Acetic anhydride was purified by stirring with sodium metal for 7 d, followed by a refluxing under reduced pressure below 50 °C for 5 h and then distillation under reduced pressure, bp 47—48 °C/20 mmHg.**

^{18}O-Analysis. ^{18}O-Analysis was carried out by the method developed by Rittenberg and Ponticorvo,[26] with a modification which involves the use of $Pb(OAc)_2$ to remove H_2S gas from the gas produced by the thermolysis of sample: about 20 mg of sample was pyrolyzed with 250 mg each of purified $HgCl_2$ and $Hg(CN)_2$, respectively in an evacuated sealed Pyrex tube at *ca.* 500 °C for 12 h. Then the tube was broken in a vacuum line and CO_2 gas formed was purified by distillation and the mass peaks of *m/e* 44 and 46 which correspond to $C^{16}O_2$ and $C^{16}O^{18}O$, respectively, were recorded on a mass spectrometer.

Materials. The NMR shift reagent $Eu(dpm)_3$ (tris-(dipivaloylmetanato)europium) is Dotite Reagents purchased from Wako Pure Chemical Co.

cis-*4*-(p-*Chlorophenyl)thiane 1-Oxide (**1c**)*: To a stirred solution of 4-(*p*-chlorophenyl)thiane[27] (1.06 g, 5 mmol) in 50 ml of dry methanol cooled to −70 °C in an acetone–Dry Ice bath was added an equimolar amount of *t*-butyl hypochlorite. When the temperature of the bath reached −40 °C, anhydrous sodium carbonate was added. The mixture was allowed to warm up to room temperature and methanol was removed under vacuum. The residue was washed three times with 50 ml portion of chloroform and the chloroform solution was dried. The solvent was evaporated to give a solid product **1c** containing a very small amount of *trans*-4-(*p*-chlorophenyl)thiane 1-oxide (**1t**). The product was recrystallized from ethyl acetate to afford a pure **1c**: mp 171—172 °C (lit,[27] 172.5—173 °C).

trans-*4*-(p-*Chlorophenyl)thiane 1-Oxide (**1t**)*: To a stirred solution of 4-(*p*-chlorophenyl)thiane[27] (1.06 g, 5 mmol) in 50 ml of dichloromethane cooled in an ice bath was added 1.05 equiv. of *m*-chloroperbenzoic acid. The solution was washed with saturated sodium hydrogencarbonate, and the aqueous layer was extracted with 50 ml of chloroform three times. The whole solution was washed with water, dried ($MgSO_4$) and evaporated to afford solid products which were separated through alumina column chromatography with ethyl acetate–chloroform (2:1) as the eluent giving *cis*-4-(*p*-chlorophenyl)thiane 1-oxide from the former solution, *trans*-4-(*p*-chlorophenyl)thiane 1-oxide from the latter solution. Then the solvent was removed to give the *cis* derivative (634 mg, 60%) and the *trans* derivative (372 mg, 35%). The *trans* derivative was recrystallized from ethyl acetate–hexane to afford a colorless crystals: mp 120—120.5 °C (lit,[27] 120—120.5 °C).

** 1 mmHg=133.3 Pa.

trans-*1-Thiadecalin*:[28] *trans*-1-Thiadecalin was prepared by the reported procedure.[28,29] After 4.86 g (30 mmol) of *trans*-2-allylcyclohexanethiol in 200 ml of dry benzene was refluxed in the presence of 1% benzoyl peroxide to the thiol for 10 h, the solvent was removed under reduced pressure. The resultant residue was separated through silica-gel column chromatography with hexane as an eluent to give an oily product (4.05 g, 86%).

trans-*1-Thiadecalin 1-Oxides (**3a** and **3e**)*: The sulfoxides **3a** and **3e** were prepared by the following three methods.

1) To a stirred solution of the corresponding sulfide (156 mg, 1 mmol) in 10 ml of dry methanol cooled to −70 °C with an acetone–Dry Ice bath was added 1 equiv. of *t*-butyl hypochlorite. When the temperature of the bath reached −40 °C, anhydrous sodium carbonate was added. The mixture was allowed to come up to room temperature and then methanol was removed under vacuum. The residue was washed four times with 20 ml portion of chloroform and the chloroform solution was dried and concentrated to afford an oily product which was purified through alumina column chromatography with ethyl acetate as an eluent, giving crystalline *trans*-1-thiadecalin 1-oxide (**3a**) (123 mg, 71% yield).

2) To a stirred solution of the sulfide (2.34 g, 15 mmol) in 150 ml of acetone cooled with an ice bath was added dropwise 1.05 equiv. of sodium periodate dissolved in the least amount of water in which the metaperiodate is soluble. Then the solution was stirred at room temperature for 2 h and poured into 100 ml of water. The solution was extracted with 100 ml of chloroform seven times. The combined solution was dried and concentrated to afford oily substances which were separated through alumina column chromatography with ethyl acetate–benzene as an eluent giving *trans*-1-thiadecalin 1a-oxide (**3a**, 947 mg) from the former solution, *trans*-1-thiadecalin 1e-oxide (**3e**, 374 mg) from the latter solution.

3) To a stirred solution of the sulfide (2.50 g, 6 mmol) and methanesulfonic acid (1.54 g, 8 mmol) in a 30 ml of methanol cooled with ice bath was added 1.1 equiv. of hydrogen peroxide in 30 wt%. The mixture was stirred at room temperature until the sulfide disappeared. The resulting mixture was extracted, dried over K_2CO_3 and then concentrated to give oily products which were separated as in the above-mentioned case. Sulfoxides **3a** and **3e** were obtained in 35% (985 mg) and 38% (1080 mg) yields, respectively. **3a**: mp 87—88 °C (lit,[30,31] 82.5—86.0 °C); IR (KBr) 2930 and 1027 cm^{-1}; Found: C, 62.67; H, 9.45%. **3e**: mp 71—72 °C (lit,[30,31] 72.0—74.0 °C); IR (KBr) 2930 and 1035 cm^{-1}; Found: C, 62.80; H, 9.39%.

trans-*2-Thiadecalin*: *trans*-2-Thiadecalin was synthesized by a similar method as reported by Birch *et al.*[32] from *trans*-1-bromomethyl-2-(2-bromoethyl)cyclohexane prepared by the following procedure which is different from that of Brich *et al.*

1-Ethoxycarbonyl-trans-*hexahydro-2-indanone.* A solution of 32.0 g (0.125 mol) of diethyl *trans*-1,2-cyclohexanediacetate in 840 ml of dry toluene and 3.73 g of sodium ethoxide was heated at 110 °C for 8 h, ethanol formed was removed and then the residue was poured into 200 ml of water. The solution was neutralized with ammonium chloride. The toluene layer was separated and the aqueous layer was extracted with 200 ml of benzene twice. The combined organic solution was dried and the solvent was evaporated to give an oily product which was distilled (14.7 g, 56% yield). Bp 102 °C/12 mmHg; IR (neat) 1753 and 1720 cm^{-1}; NMR (CCl_4) δ=4.14 (2H, q), 2.88—1.00 (13H, m), 1.28 (3H, t).

trans-*2-Oxadecalin-3-one.* A solution of 14.7 g (70.6 mmol) of 1-ethoxycarbonyl-*trans*-hexahydro-2-indanone in 50 ml of 25% sulfuric acid was refluxed for 1.5 h and poured into 50 ml of water. The solution was extracted with 100 ml of ether three times and the ether solution was neutralized with diluted sodium hydroxide, then washed with water and dried. The solvent was evaporated to afford an oily *trans*-hexahydro-2-indanone[33] which was added into 500 ml of dichloromethane. To the dichloromethane solution, 22.5 g of *m*-chloroperbenzoic acid was added gradually under stirring over night. The solution was filtered and the filtrate was neutralized with diluted sodium hydroxide, washed with water and dried. The solvent was evaporated and the residue was distilled to give an oily *trans*-2-oxadecalin-3-one (5.6 g, 52% yield): bp 114—116 °C/4 mmHg (lit,[34] 102—104 °C/0.1 mmHg).

trans-*1-Bromomethyl-2-(2-bromoethyl)cyclohexane*: To a slurry of 1.5 g (40 mmol) of lithium aluminum hydride in 100 ml of dry ether was added dropwise while stirring the solution of 5.6 g (36 mmol) of *trans*-2-oxadecalin-3-one in 50 ml of ether. When the addition was complete, the mixture was refluxed for an additional 1 h and then treated successively with 1.5 ml of water, 1.5 ml of 15% aqueous sodium hydroxide, and 4.1 ml of water under stirring while cooling in an ice bath. The mixture was filtered and the filtrate was dried and concentrated. The residue was dried thoroughly under vacuum to give oily *trans*-2-(hydroxymethyl)-cyclohexaneethanol.[35] A portion of 10.7 g (39 mmol) of phosphorus tribromide was slowly dropped into 30 ml of dichloromethane solution of the oil under cooling in an ice bath. After dichloromethane was removed at 60 °C, the solution was heated at 100 °C for 6 h, cooled in an ice bath, and water was carefully added. Then the solution was extracted with dichloromethane, washed, dried, and concentrated. The residue was distilled with Kugelrohr (6.5 g, 63% yield); bp 115 °C/2 mmHg (lit,[32] 104—106 °C/0.8 mmHg).

trans-*2-Thiadecalin*: To a refluxing solution of sodium sulfide nonahydrate (4.15 g, 17.5 mmol) in 50 ml of 50% aqueous ethanol was added dropwise 6.5 g of the dibromide and an additional 50 ml of the sodium sulfide (4.15 g) solution at such a rate that the addition of both was complete in 1 h. After refluxing for 8 h, the mixture was extracted with ether. The combined organic extract was dried over anhydrous magnesium sulfate, the solvent was removed by evaporation and the residue was purified through silica-gel chromatography with hexane as an eluent (2.135 g, 38% yield).

trans-*2-Thiadecalin 2-Oxides (**5a** and **5e**)*: 1) To a stirred solution of *trans*-2-thiadecalin (156 mg, 1 mmol) in 10 ml of dry methanol cooled to −70 °C with an acetone–Dry Ice bath was added 1 equiv. of *t*-butyl hypochlorite. When the temperature of the bath reached −40 °C, anhydrous sodium carbonate was added. The mixture was allowed to come up to room temperature and then methanol was removed under reduced pressure. The residue was washed three times with 20 ml portion of chloroform and the chloroform solution was dried and concentrated to give an oily product which was separated through alumina column chromatography with ethyl acetate as an eluent, giving crystalline *trans*-2-thiadecalin 2a-oxide (**5a**) (97 mg) in 56% yield.

2) To a stirred solution of the sulfide (80 mg, 5 mmol) in 50 ml of acetone cooled with an ice bath was added dropwise 1.05 equiv. of sodium periodate dissolved in the least amount of water. When the addition was complete, the solution was stirred at room temperature for 2 h and poured into 50 ml of water. The solution was extracted with 100

ml of chloroform four times. The organic solution was dried and concentrated to give oily substance which was separated through alumina column chromatography with ethyl acetate–benzene (1:1) as an eluent giving *trans*-2-thiadecalin 2a-oxide (**5a**, 611 mg) from the former solution and *trans*-2-thiadecalin 2e-oxide (**5e**, 162 mg) from the latter solution.

3) To a stirred solution of the sulfide (5 mmol) in 50 ml of dichloromethane cooled with an ice bath was added 1.05 equiv. of *m*-chloroperbenzoic acid. The solution was washed with saturated sodium hydrogencarbonate, and the aqueous layer was extracted with chloroform three times. The combined organic layer was washed with water, dried and concentrated to afford oily product which was separated as in the above-mentioned case. The sulfoxide **5a** and **5e** were given in 31% (265 mg) and 57% (492 mg) yields, respectively. **5a**: mp 98—99 °C; IR (KBr) 1029 and 2930 cm^{-1}; Found: C, 62.61; H, 9.23%. Calcd for $C_9H_{16}OS$: C, 62.74; H, 9.36%. **5e**: mp 53—54.5 °C; IR (KBr) 1036 cm^{-1}; Found: C, 62.39; H, 9.20%. Calcd for $C_9H_{16}OS$: C, 62.74; H, 9.36%.

^{18}O-*Labeled* trans-*4-(*p-*Chlorophenyl)thiane 1-Oxide (**1t**-^{18}O)*: The title sulfoxide **1t**-^{18}O was prepared by the usual oxidation of the corresponding sulfide with bromine.[36] The sulfide (1 g, 4.7 mmol) was dissolved in a mixture of acetic acid (30 ml), pyridine (5 ml) and ^{18}O-enriched water (3 ml) (1.6 ex. atm%). To the cooled solution was added bromine (753 mg) in 5 ml of acetic acid at 0 °C. After the mixture was kept standing for 2 h at 0 °C, the reaction mixture was quenched with 50 ml of water and extracted with 50 ml of chloroform four times. The chloroform solution was washed with aqueous $Na_2S_2O_3$ solution, diluted aqueous hydrochloric acid, water and then dried ($MgSO_4$). After evaporation of chloroform with a rotary evaporator, a resulting substance was separated through alumina column chromatography with ethyl acetate–chloroform (2:1) as the eluent, giving ^{18}O-labeled corresponding equatorial sulfoxide **1t**-^{18}O (750 mg) and ^{18}O-labeled *cis*-sulfoxide **1c**-^{18}O (108 mg). The ^{18}O-labeled *trans*-4-(*p*-chlorophenyl)thiane 1-oxide was recrystallized from ethyl acetate–hexane and found to contain 1.092 ex. atom% of ^{18}O.

^{18}O-*Labeled* cis-*4-(*p-*Chlorophenyl)thiane 1-Oxide (**1c**-^{18}O)*: To a stirred solution of the *trans*-sulfoxide **1t** (600 mg, 2.63 mmol) in dichloromethane (3 ml) *ca.* 0.9 g (4.73 mmol) of triethyloxonium tetrafluoroborate (Et_3OBF_4) was added. After the mixture was stirred at room temperature for 1 h, 40 ml of anhydrous ether was added at 0 °C to give the oily ethoxysulfonium salt as a precipitate. After the mixture was kept standing for 2 h, the solvent was removed by decantation, and to the residue was added 5 ml of a 2 mol dm^{-3} $Na^{18}OH$ solution which was prepared by treating sodium metal with $H_2{}^{18}O$ (1.5 ex. atm%) under nitrogen atmosphere. The mixture was then extracted with dichloromethane. The solution was dried over $MgSO_4$ and the solvent was evaporated. The residue was then chromatographed on alumina with ethyl acetate–chloroform (2:1) as the eluent. The solvent of the former elution was removed to afford colorless crystals which were recrystallized from ethyl acetate (294 mg, 49%). The title sulfoxide (**1c**-^{18}O) was found to contain 0.4295 ex. atom% of ^{18}O.

^{18}O-*Labeled* trans-*1-Thiadecalin 1e-Oxide (**3e**-^{18}O)*: The *trans*-1-thiadecalin was similarly oxidized with bromine and ^{18}O-enriched water to give an oily substance which was separated through alumina column chromatography with ethyl acetate as the eluent to give the corresponding ^{18}O-labeled equatorial sulfoxide from the latter elution and the corresponding axial sulfoxide from the former one. The ^{18}O-labeled *trans*-1-thiadecalin 1e-oxide (**3e**-^{18}O) (654 mg, 69% yield) was recrystallized from hexane and found to contain 0.955 ex. atom% of ^{18}O.

^{18}O-*Labeled* trans-*1-Thiadecalin 1a-Oxide (**3a**-^{18}O)*: After a solution of 1e-sulfoxide **3e** (900 mg, 5.2 mmol) and Et_3OBF_4 (1.89 g, 9.4 mmol) in dichloromethane (**3** ml) was stirred at room temperature for 1 h, 30 ml of anhydrous ether was added at 0 °C. Then the mixture was kept standing for 2 h, the solvent was removed by decantation, and to the residue was added 3 ml of a 2 mol dm^{-3} $Na^{18}OH$ solution. The usual work-up and alumina chromatography gave the ^{18}O-labeled title sulfoxide **3a** which was recrystallized from hexane, and found to contain 0.856 ex. atom% of ^{18}O.

trans-*1-Thiadecalin-2e-*d *1a-Oxide (**9**)*:[37] After a solution of 1.1 ml of lithium (0.1 g/ml in hexane) was added to a stirred solution of a *trans*-1-thiadecalin 1a-oxide (**3a**) (253 mg, 1.47 mmol) in 5 ml of a freshly distilled THF cooled at −78 °C in an acetone–Dry Ice bath for 1 h, 2 ml of MeOD was added to the cooled solution at −78 °C under stirring for 0.5 h. The reaction mixture was quenched with 20 ml of water and neutralized with 10 ml of aqueous ammonium chloride and extracted with 30 ml of chloroform seven times. The whole solution was dried with $MgSO_4$ and the solvent was evaporated to afford the D-labeled product **9** which was recrystallized from hexane. Thus the title sulfoxide **9** obtained (250 mg, 99% yield) was found to contain 59% of D-atom at α-equatorial position upon treatment with 1 equiv. molar mixture of the lanthanoids shift reagent, Eu(dpm)$_3$ and the sulfoxide.

trans-*1-Thiadecalin-2a-*d *1e-Oxide (**11**)*: The title sulfoxide **11** was synthesized from the equatorial sulfoxide (344 mg) by the work-up as mentioned above (337 mg, 97%). The title sulfoxide **11** was found to contain 57% of D-atom at α-axial position upon treatment with 1 equiv. molar of Eu(dpm)$_3$.

trans-*1-Thiadecalin-2a-*d *1a-Oxide (**10**)*: The title sulfoxide **10** was prepared by the same chemical transformation of *trans*-1-thiadecalin-2a-*d* 1e-oxide (**11**). A solution of **11** (104 mg, 0.6 mmol) and (342 mg, 1.8 mmol) of triethyloxonium tetrafluoroborate in dichloromethane (2 ml) was stirred at room temperature for 1 h and 30 ml of anhydrous ether was added at 0 °C to give the oily ethoxysulfonium salt. After the mixture was kept standing for 2 h, the solvent was removed by decantation twice. Then to the residue was added 10 ml of a 0.5 M NaOH solution. The solution was neutralized with 10 ml of aqueous ammonium chloride solution and extracted with chloroform seven times. The solvent was dried with $MgSO_4$ and evaporated to afford a residue, which was then chromatographed through alumina with ethyl acetate–chloroform (2:1) to give the sulfoxide **10** (12.8 mg, 80%) which was found to contain 57% of D-atom at α-axial position upon treatment with an equimolar amount of Eu(dpm)$_3$.

*Reaction of 4-(*p-*Chlorophenyl)thiane 1-Oxides (**1c** and **1t**) with Acetic Anhydride.* The *trans* **1t** or *cis*-sulfoxide **1c** (45.7 mg, 0.2 mmol) was heated with 1 ml of acetic anhydride at 100 °C for 3 h until the sulfoxide disappeared upon monitoring with TLC. Then after evaporation of excess acetic anhydride and any volatile product *in vacuo*, the remaining residue was separated through silica-gel column chromatography with hexane–ether (4:1) as the eluent, in a low-temperature room at 0—4 °C. The corresponding axial α-acetoxy sulfide **2a** and olefinic product **2o** were obtained in 72—73% and 20% yields, respectively. **2a**: IR (neat) 1740 and 1223 cm^{-1}; NMR ($CDCl_3$) δ=7.15 (4H, aromatic), 5.98 (1H, t-like J=3.0 Hz), 2.12 (3H, s). Oxidation of **2a** gave the corresponding sulfone: mp 204—204.5 °C; IR (KBr) 1755, 1330, 1210, and 1140 cm^{-1}; Found: C, 51.44; H,

4.94%. Calcd for $C_{13}H_{15}ClO_4S$: C, 51.57; H, 4.99%. **2o**: bp 110 °C/5 mmHg (Kugerohr); Found: C, 62.98; H, 5.24%. Calcd for $C_{11}H_{11}ClS$: C, 62.69; H, 5.26%.

*Reaction of 4-(p-Chlorophenyl)thiane 1-Oxides (**1c** and **1t**) with Acetic Anhydride in the Presence of DCC or 2,6-Lutidine. 1)*: The *trans*- or *cis*-sulfoxide **1t** or **1c** (45.7 mg, 0.2 mmol) was heated with 1 ml of acetic anhydride in the presence of 1 equiv. of DCC to the sulfoxide at 100 °C for 4 h. When the reaction mixture was treated according to the above-mentioned procedure, the Pummerer products (the corresponding equatorial α-acetoxy sulfide **2e** and axial α-acetoxy sulfide **2a** in the ratio of 2:1 respectively) and olefinic product **2o** were obtained in 77% and 21% yields, respectively.

2): The *trans*-sulfoxide **1t** was heated with 1 ml of acetic anhydride in the presence of 3 equiv. of DCC at 100 °C for 4 h. The Pummerer products **2e** and **2a** (ratio of 9:1, respectively) and the olefinic product were obtained in 85% and 11% yields, respectively.

3): The *trans*-sulfoxide **1t** was heated with 1 ml of acetic anhydride in the presence of 5 equiv. of DCC at 100 °C for 4 h. The Pummerer products **2e** and **2a** (ratio of 13:1, respectively) and the olefinic product were obtained in 83% and 9% yields, respectively. **2e**: mp 78.5—80 °C; IR (KBr) 1745 and 1225 cm^{-1}; NMR ($CDCl_3$) 7.15 (4H, aromatic) 5.88 (1H, dd, J=9.9 and 3.3 Hz) 2.04 (3H, s); Found: C, 57.75; H, 5.57%. Calcd for $C_{13}H_{15}ClO_2S$: C, 57.66; H, 5.58%.

4): The *cis*-sulfoxide **1c** was heated with 1 ml of acetic anhydride in the presence of 5 equiv. of DCC at 100 °C for 6 h. The Pummerer products (**2e** and **2a** ratio of 14:1, respectively) and the olefinic product were obtained in 83% and 12% yields, respectively.

5): The *cis*-sulfoxide **1c** was heated with acetic anhydride in the presence of 5 or 10 equiv. of 2,6-lutidine at 100 °C for 4.5 h. The Pummerer products (**2e** and **2a** ratio of 5:2 or 5:1, respectively) and the olefinic product were obtained in 81 or 86% and 15 or 12% yields, respectively.

*Isomerization Reaction of 2e-Acetoxy-4-(p-Chlorophenyl)thiane (**2e**) with Acetic Anhydride in the Presence of Acetic Acid.* After the sulfide **2e** (60 mg) was heated with 1 ml of acetic anhydride in the presence of 1 equiv. of acetic acid to the acetoxy sulfide at 100 °C for 3 h and then evaporation of excess acetic anhydride and any volatile substance *in vacuo*, an oily product was purified through silica-gel column chromatography with hexane–ether 4:1 as an eluent at 0—4 °C to afford the corresponding 2a-acetoxy sulfide (**2a** 42 mg, 70% yield) and the olefinic compound **2o** (13 mg, 28%).

Reaction of trans-*1-Thiadecalin 1-Oxides (**3e** and **3a**) with Acetic Anhydride.* The sulfoxide **3e** or **3a** (71.2 mg, 0.4 mmol) was heated with 2 ml of acetic anhydride at 100 °C for 3 or 4 h until the sulfoxide completely disappeared upon monitoring with TLC of alumina. Then after evaporation of excess acetic anhydride and any volatile product *in vacuo*, the remaining residue was separated through silica-gel column chromatography with hexane–ether (5:1) as an eluent in a low temperature room at 0—4 °C. The corresponding equatorial and axial α-acetoxy sulfides **4e** and **4a** (ratio of 1:19, respectively) were obtained in 40—50% yield. To the trapped volatile products in an acetone–Dry Ice bath was added a saturated sodium hydrogencarbonate solution until the solution became alkaline and then the solution were extracted with dichloromethane. The dichloromethane solution was washed with water, dried, and concentrated to afford the olefinic product. **4a**: oil; IR (neat) 2930, 1700, and 1220 cm^{-1}; NMR 5.81 (1H, t, J=3.3 Hz), 2.01 (3H, s). Oxidation of **4a** with *m*-CPBA gave the corresponding sulfone: mp 86—86.5 °C; IR (KBr) 2930, 1760, 1750, and 1215 cm^{-1}; NMR ($CDCl_3$) δ=5.70 (1H, t, J=3 Hz), 2.15 (3H, s); Found: C, 53.63; H, 7.30%. Calcd for $C_{11}H_{18}O_4S$: C, 53.63; H, 7.36%.

Reaction of trans-*1-Thiadecalin 1-Oxides (**3e** and **3a**) with Acetic Anhydride in the Presence of DCC.* The sulfoxide **3a** or **3e** (71.2 mg, 0.4 mmol) was heated with 2 ml of acetic anhydride in the presence of 5 equiv. of DCC to the sulfoxide at 100 °C for 4 h. When the reaction mixture was treated according to the above-mentioned procedure, the corresponding equatorial and axial α-acetoxy sulfides **4e** and **4a** (ratio of 19:1, respectively) were obtained in 45—52% yield. To the trapped volatile products cooled in an acetone–Dry Ice bath was added a saturated sodium hydrogencarbonate solution until the solution became alkaline and then the solution was extracted with dichloromethane. The dichloromethane solution was washed with water, dried $Mg(SO_4)$, and concentrated to give an olefinic product. **4e**: mp 41—42 °C; IR (KBr) 1740 and 1240 cm^{-1}; NMR ($CDCl_3$) δ=5.69 (1H, dd J=9.9 and 3.3 Hz), 2.04 (3H, s); Found: C, 61.75; H, 8.49%. Calcd for $C_{11}H_{18}O_2S$: C, 61.64; H, 8.46%. The olefinic product was converted to the corresponding sulfone: mp 106—7.5 °C; IR (KBr) 2930, 1620, 1300, and 1110 cm^{-1}; Found: C, 57.86; H, 7.53%. Calcd for $C_9H_{14}O_2S$: C, 58.03; H, 7.57%.

Reaction of trans-*2-Thiadecalin 2-Oxides (**5e** and **5a**) with Acetic Anhydride.* The sulfoxide **5e** or **5a** (71.2 mg, 0.4 mmol) was heated with 2 ml of acetic anhydride at 100 °C for 3 h. The usual work-up and silica gel column chromatography with hexane–ether (5:1) as an eluent at 0—4 °C gave 42 mg (48% yield) of a 1:1 mixture of the corresponding 1a- and 3a-acetoxy sulfide **6a1** and **6a3** as main products: oil; IR (neat) 1740, 1230, and 1219 cm^{-1}; NMR ($CDCl_3$) δ=5.67 (t, J=3 Hz, methine proton of **6a1**), 5.88 (d, J=3 Hz, methine protone of **6a3**), 2.13(s). Sulfone: mp 79—80 °C; IR (KBr) 2930, 1760, 1750, and 1215 cm^{-1}; Found: C, 53.75; H, 7.37%. Calcd for $C_{11}H_{18}O_4S$: C, 53.63; H, 7.36%.

Reaction of trans-*2-Thiadecalin 2-Oxides (**5e** and **5a**) with Acetic Anhydride in the Presence of DCC.* The sulfoxide **5e** or **5a** (71.2 mg, 0.4 mmol) was heated with 2 ml of acetic anhydride in the presence of 5 equiv. of DCC to the sulfoxide at 100 °C for 4 h. An about 1:1 mixture of the Pummerer products, the corresponding 1e- and 3e-acetoxy sulfides were obtained as main products (45 mg, 51%): oil; NMR ($CDCl_3$) δ=5.49 (d, J=9.5 Hz, methine proton of **6e1**), 5.82 (dd, J=10.5 and 3.0 Hz, methine proton of **6e3**), and 2.08(s). Sulfone: mp 121—122 °C; IR (KBr) 2970, 1760, 1220, and 1207 cm^{-1}; Found: C, 53.72; H, 7.35%. Calcd for $C_{11}H_{18}O_4S$: C, 53.63; H, 7.36%.

Reaction of ^{18}O-*Labeled* trans-*4-(p-Chlorophenyl)thiane 1-Oxide (**1t**) with Acetic Anhydride.* When the ^{18}O-labeled title sulfoxide **1t** (685.5 mg) was heated with 60 equiv. of acetic anhydride at 100 °C for 0.75 h, the oily residue obtained after evaporation of excess acetic anhydride and any volatile product under vacuum was separated through silica-gel column chromatography with hexane–ether (4:1) as an eluent in a low-temperature room at 0—4 °C and then acetone as eluent to give the Pummerer products **2e** and **2a** (325 mg, 40% yield (e:a/1:1) and the recovered sulfoxide (341 mg, 50% yield), respectively, which was recrystallized from ethyl acetate–hexane. The starting sulfoxide, the Pummerer products and the recovered sulfoxide were subjected to measurement of ^{18}O-content by the routine ^{18}O-analysis technique and the ^{18}O-contents were found to be 1.092, 0.013, and 1.088 ex. atom%, respectively.

Reaction of ^{18}O-*Labeled* cis-*4-(p-Chlorophenyl)thiane 1-Oxide (**1c**-^{18}O) with Acetic Anhydride.* After the ^{18}O-labeled

title sulfoxide (**1c**-^{18}O) (330 mg) was heated with 60 equiv. of acetic anhydride at 100 °C for 0.75 h, the reaction mixture was treated according to the above-mentioned procedure to afford the mixture of Pummerer products **2e** and **2a** (156 mg) in 40% yield (e:a/1:1) and the recovered sulfoxide (155 mg) in 47% yield, which were recrystallized from ethyl acetate. The ^{18}O-contents of the starting sulfoxide, Pummerer products and the recovered sulfoxide were found to be 0.495, 0.019, and 0.334 ex. atom%, respectively.

Reaction of ^{18}O-*Labeled* trans-*1-Thiadecalin 1e-Oxide (**3e**) with Acetic Anhydride.* When the ^{18}O-labeled title sulfoxide **3e** (152.3 mg) thoroughly dried under vacuum was heated with 60 equiv. of acetic anhydride at 100 °C for 0.75 h, the oily residue, obtained after evaporation of excess of acetic anhydride and any volatile product under vacuum, was separated through silica-gel column chromatography with hexane–ether (5:1) as the eluent to give the Pummerer products **4e** and **4a** (52.7 mg, 28% yield, e:a/6:1) and the recovered sulfoxide (81.4 mg, 53% yield) which was recrystallized from hexane. The ^{18}O-contents of starting sulfoxide, the Pummerer products and recovered sulfoxide were found to be 0.955, 0 and 0.812 ex. atom% of ^{18}O, respectively.

Reaction of ^{18}O-*Labeled* trans-*1-Thiadecalin 1a-Oxide (**3a**-*^{18}O*) with Acetic Anhydride.* The ^{18}O-labeled title sulfoxide (**3a**-^{18}O) (152.3 mg) was heated with acetic anhydride (60 equiv.) at 100 °C for 0.75 h. After the work-up procedure as mentioned above, the Pummerer products **4e** and **4a** (80.6 mg, 43% yield, e:a/8:1) and the recovered sulfoxide (43.3 mg, 28% yield) were obtained and the recovered sulfoxide was recrystallized from hexane. The ^{18}O-contents of the starting sulfoxide, the Pummerer products and the sulfoxide recovered were found to be 0.856, 0.057, and 0.710 ex. atom% of ^{18}O, respectively. The Pummerer products (**4e**:**4a**=6:1) incorporated with 13% of ^{18}O, based on the starting sulfoxide, was recrystallized from hexane to give the pure **4e** (mp 43 °C). Then the filtrate was condensed and separated through silica-gel column chromatography with hexane–ether–ethyl acetate (77:2:1) as an eluent. The ^{18}O-contents of the pure **4e** and **4a** were found to be 0.057 and 0.043 ex. atom%.

Reaction of ^{18}O-*Labeled* trans-*1-Thiadecalin 1e-Oxide (**3e**) with Acetic Anhydride in the Presence of DCC.* When the ^{18}O-labeled sulfoxide (**3e**-^{18}O) (152.3 mg) thoroughly dried was heated with 60 equiv. of acetic anhydride in the presence of 5 equiv. DCC to the sulfoxide at 100 °C for 1.25 h, the residue was obtained after evaporation of excess acetic anhydride and any volatile product under vacuum. To the resultant residue was added 5 ml of ether–hexane and the mixture was filtered. The solvent of the filtrate was removed and the oily residue was separated through silica-gel column chromatography with hexane–ether (5:1) as the eluent at 0—4 °C and then with benzene–acetone (1:1) to give the Pummerer products **4e** and **4a** (97.0 mg, 51% yield, e:a/19:1), and the recovered sulfoxide (45.8 mg, 30% yield) which was recrystallized from hexane. The filtered product was recrystallized from ethyl acetate–hexane giving 650 mg of the *N*-acetyl-*N,N'*-dicyclohexylurea (IR 1600 and 1680 cm^{-1}, NMR δ=2.1, 5.0, 1—2). The ^{18}O-contents of the recovered sulfoxide, the Pummerer products and *N*-acetyl-*N,N'*-dicyclohexylurea were found to be 0.812, 0, and 0 ex. atom%, respectively.

Reaction of ^{18}O-*Labeled* trans-*1-Thiadecalin 1a-Oxide (**1a**-*^{18}O*) with Acetic Anhydride in the Presence of DCC.* The ^{18}O-labeled sulfoxide (**3a**-^{18}O) (152.3 mg) was heated with 60 equiv. of acetic anhydride at 100 °C for 1.25 h. After the work-up procedure as mentioned above, the Pummerer products **4e** and **4a** (65.2 mg, 34% e:a/19:1), recovered sulfoxide (89.9 mg, 59% yield) and the *N*-acetyl-*N,N'*-dicyclohexylurea were obtained. The ^{18}O-contents of the recovered sulfoxide, the Pummerer products and the *N*-acetylurea were found to be 0.574, 0.068, and 0 ex. atom%.

*Hydrogen-Deuterium Kinetic Isotope Effect in the Reaction Between 4-(*p*-Chlorophenyl)thiane-2,2,6,6-*d$_4$ *1-Oxides with Acetic Anhydride.* 4-(*p*-Chlorophenyl)thiane-2,2,6,6-*d$_4$* 1-oxides (*cis* and *trans*) were prepared by the treatment with diethyl 3-(*p*-chlorophenyl)glutarate and lithium aluminum deuteride in the ether and the successive procedures mentioned-above.[27]

Each 4-(*p*-chlorophenyl)thiane 1-oxide (*cis* or *trans*) (0.1 mmol) was dissolved in 10 ml of acetic anhydride. The solution was heated at 100 °C. The solution 10 μl picked up with syringe at time intervals was cooled at 0 °C to stop the reaction. The rate of the reaction was followed by measurement of the GLPC peaks of the Pummerer products (OV1 2% on chromosorb 2 m). The rate constants were obtained from the pseudo-first-order kinetic equation.

Reaction of trans-*1-Thiadecalin-2e-*d *1a-Oxide (**9**) with Acetic Anhydride in the Presence of DCC.* The stereoselectively D-labeled sulfoxide **9** (D, 59%, 103 mg at equatorial position) was heated with 2 ml of acetic anhydride in the presence of DCC (617 mg, 5 equiv. molar to the sulfoxide) at 100 °C for 4 h. After the work-up procedure as mentioned, the 2e-acetoxy sulfide, the Pummerer product, obtained in 39% yield (50 mg) was found to retain 59% of D-content upon measurement of NMR using 14% of Eu(dpm)$_3$.

Reaction of trans-*1-Thiadecalin-2a-*d *1a-Oxide (**10**) with Acetic Anhydride in the Presence of DCC.* When the stereoselectively D-labeled axial sulfoxide **10** (49.4 mg, D, 57% at axial position) was heated with 1 ml of acetic anhydride in the presence of DCC (250 mg) at 100 °C for 4 h, the corresponding 2e-acetoxy sulfide given in 45% yield (27.9 mg) was found to contain only 13% of D-content according to the usual procedure.

Reaction of trans-*1-Thiadecalin-2e-*d *1e-Oxide (**11**) with Acetic anhydride in the Presence of DCC.* After the D-labeled title sulfoxide **11** (108 mg, D, 57% at axial position) was heated with 2 ml of acetic anhydride in the presence of DCC (648 mg) at 100 °C for 6 h, the usual work-up was carried out. The corresponding 2e-acetoxy sulfide obtained in 41% yield (55 mg) had 50% of D-content.

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