

Intramolecular Stereospecific Pummerer Reactions of Aryl (Substituted-methyl) Sulfoxides Bearing Electron-withdrawing Groups with Acetic Anhydride

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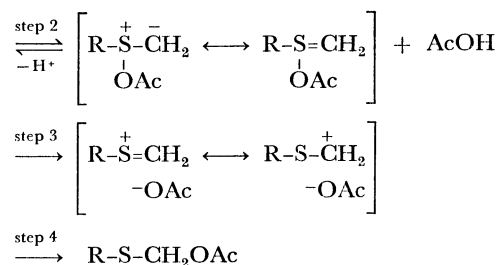
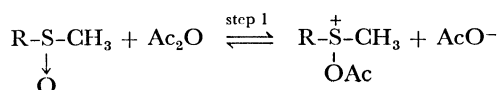
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The Pummerer reaction of optically active cyanomethyl aryl sulfoxides with acetic anhydride gave the corresponding α -acetoxy sulfides which were induced with a partial asymmetry nearly 30% at α -carbon, while the ^{18}O -label of the original sulfoxides was retained in more than 85% in the resulting ester, the Pummerer reaction product. Kinetic experiments with cyanomethyl (*p*-substituted phenyl) sulfoxides and α,α -dideuterated cyanomethyl *p*-tolyl sulfoxide in the reaction with acetic anhydride containing a small amount of acetic acid revealed that the rates were correlated with Hammett σ -values and ρ -value of -0.70 was obtained, while the kinetic isotope effect was practically nil, *i.e.*, $k_{\text{H}}/k_{\text{D}}=1.01$. These observations indicate clearly that the rearrangement is intramolecular and proceeds via forming a very intimate ion-pair and the rate-determining step is believed to be the S–O bond cleavage after the initial reversible acylation and deprotonation. Elimination of acetic acid proceeds through the Elcb type process. The uneven distribution of ^{18}O in the two oxygens of the resulted ester, *i.e.*, ether and carbonyl oxygens, suggests the recombination of the α -sulfenyl carbonium ion and acetate ion to be very rapid. The Pummerer reaction of optically active *N,N*-dimethyl-*p*-tolyl-sulfinylacetamide with excess acetic anhydride also gave the corresponding α -acetoxy sulfide in optically active form. In the presence of dicyclohexylcarbodiimide (DCC), the Pummerer reaction was found to be highly stereoselective affording the corresponding α -acetoxy sulfide with 65% e.e. Other optically active α -carbonyl-substituted alkyl sulfoxides, *i.e.*, ethyl *p*-tolylsulfinylacetate and ω -(*p*-tolylsulfinyl)acetophenone also gave the corresponding highly optically active Pummerer rearrangement products in the treatment with acetic anhydride/DCC system. The Pummerer reaction of the ^{18}O -labeled sulfoxides with acetic anhydride/DCC system gave the corresponding α -acetoxy sulfides which retained much of the original ^{18}O -labels of the sulfoxides. These observations reveal clearly that in the Pummerer reaction of these compounds the acetoxy migration is intramolecular and takes place through intimate ion-pairs.

The reaction of sulfoxides bearing α -methylene protons with acetic anhydride to afford the corresponding α -acetoxy sulfides was named by Horner²⁾ half a century after the discovery by Pummerer.¹⁾ One earliest investigation of the mechanism of this reaction was our ^{18}O -tracer study using dimethyl sulfoxide and uniformly ^{18}O -labeled acetic anhydride in diethyl ether.³⁾ On the basis of our finding that all of the oxygen atoms were completely scrambled during the reaction, we suggested the involvement of intermolecular attack of acetate at the α -carbon and also the possible involvement of the acyloxysulfonium ylide. Because of the possible involvement of the Pummerer reaction in the enzymatic demethylation of methionine⁴⁾ and the growing potential for versatile organic syntheses,⁵⁾ mechanism of this reaction has been investigated quite extensively and well-reviewed.^{6,7)}

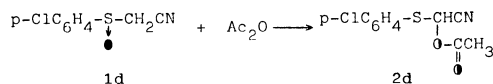
The general scheme of the reaction is believed to be shown in the following four sequential elemental reactions with the rate-determining step varying with changes of both the acylating agent and the sulfoxide. In some cases, the reaction of the steps 2 and 3 became simultaneous, to result in E2 process, as in the Pummerer reaction of *trans*-1- and 2-thiadecalin S-oxides with acetic anhydride.⁸⁾

Although there has been no clear-cut example of the Pummerer reaction in which the last recombination step 4 is the rate-determining, we have found all the three examples of the reactions in which each of the three steps is rate-determining.^{7c–e)}

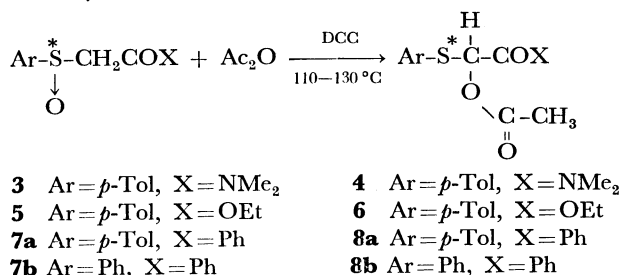


While the first example of the Pummerer reaction which results in a substantial asymmetric induction⁹⁾ was the novel cyclization of *o*-carboxyphenyl alkyl sulfoxide with acetic anhydride and dicyclohexylcarbodiimide (DCC)¹⁰⁾ to give cyclized 3*H*-4-thiaisocoumarin in 11.2 and 29.9% e.e., respectively, the rate-determining step of this reaction seems to be the initial acylation (step 1). The second example of the Pummerer reaction which leads to the formation of asymmetrically induced α -acetoxy sulfide was the reaction of open-chain optically active cyanomethyl *p*-tolyl sulfoxide (**1b**) with acetic anhydride.¹¹⁾ The rate-determining step of this reaction appears to be the heterolysis of the S–O linkage of the sulfonium-ylide-ylene intermediate formed by the initial reversible acylation of the sulfoxide and subsequent reversible deprotonation, while the rearrangement seems to proceed predominantly through intramolecular migration of acetoxy group when the reaction of the ^{18}O -labeled sulfoxide was carried out.

Other examples of the Pummerer reaction which affords the corresponding asymmetrically induced α -acetoxy sulfides are all with optically active open-chain aryl methyl sulfoxides bearing some electron-



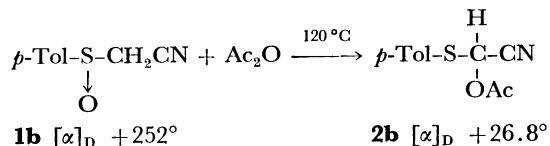
withdrawing groups on methyl group,¹²⁻¹⁴⁾ while the reaction of aryl 2-propynyl sulfoxide with acetic anhydride gives not only the Pummerer rearrangement product but also the thio-Claisen type rearrangement product, and hence it will be dealt separately.¹⁴⁾ All these optically active aryl (carbonyl-substituted methyl) sulfoxides **3**, **5**, and **7a** were found to react with acetic anhydride affording the corresponding α -acetoxy sulfides **4**, **6**, and **8a** which are substantially induced with optical activities on the α -carbons. In the presence of DCC, scavenger of acetic acid formed, the amounts of asymmetric induction were markedly increased in the resulting Pummerer products. Meanwhile, the usual ^{18}O -tracer experiments with ^{18}O -labeled sulfoxides **3**, **5**, and **7b** revealed that the rearrangements are predominantly intramolecular in view of the high retentions of ^{18}O -label in the resulted corresponding α -acetoxy sulfides **4**, **6**, and **8b**.



This paper describes detailed accounts of these interesting intramolecular stereoselective Pummerer reactions of aryl (substituted methyl) sulfoxides bearing electron-withdrawing group with acetic anhydride.

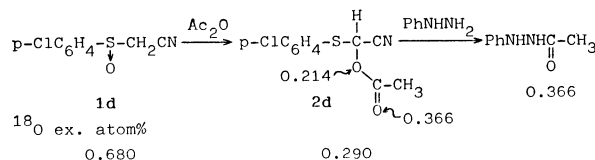
Results and Discussion

Reaction of Aryl Cyanomethyl Sulfoxides with Acetic Anhydride. When optically active cyanomethyl *p*-tolyl sulfoxide (**1b**) [α]_D +252°, was allowed to react with a large excess acetic anhydride at 120 °C for 3.5 h, the resulted acetoxycyanomethyl *p*-tolyl sulfide (**2b**) was found to be optically active, [α]_D +26.8°, which corresponds to 29.0±0.8% of e.e. when determined by NMR using the chiral lanthanoide shift reagent, Eu(hfc), tris(heptafluoropropylhydroxymethyl)-d-camphorato)europium.



In the reaction of ^{18}O -labeled cyanomethyl *p*-chlorophenyl sulfoxide (**1d**) (0.680 ex. atom% of ^{18}O) with a large excess of unlabeled acetic anhydride at 50% conversion (120 °C, 1 h) the unreacted sulfoxide recovered and the Pummerer product **2d** separated by column chromatography were found to be incorporated with 0.655 ex. atom% of ^{18}O (for **1d** recovered) and 0.290 ex. atom% (for **2d**), which correspond to the retention of 96.3% (for **1d** recovered) and 85%

(for **2**), respectively. Thus, the rearrangement proceeded through an intramolecular 1,2-acetoxyl migration at least 85%. In order to shed further light on the nature of the acetoxyl migration, the distribution of ^{18}O in the resulted ester **2d** was determined by treating the ester **2d** with 3 molar excess of phenylhydrazine to convert acetyl group to 1-acetyl-2-phenylhydrazine which had 0.366 ex. atom% of ^{18}O . Thus the following ^{18}O distribution in the ester **2d** was ob-



served. This uneven distribution of ^{18}O , rich in favor for carbonyl oxygen, means that the recombination of acetoxyl group to α -carbon after the heterolysis of the S-O linkage is very rapid while the heterolysis of the S-O linkage is partly assisted by the neighboring group effect of carbonyl oxygen at the transition state of the 1,2-acetoxyl migration.

Meanwhile, in the reaction of cyanomethyl-*d*₂ *p*-tolyl sulfoxide with acetic anhydride containing a small amount of acetic acid, the recovered sulfoxide was found to have lost the D-label completely within a few minutes of the reaction at 120 °C, suggesting strongly that the initial acetylation (step 1) and the deprotonation to form the ylide **9** (step 2) are both fast and reversible, and the rate-determining step is the subsequent S-O bond heterolysis followed by very fast recombination of the resulting α -sulfenyl carbenium ion with acetate within the ion-pair **10a** and **10b**.

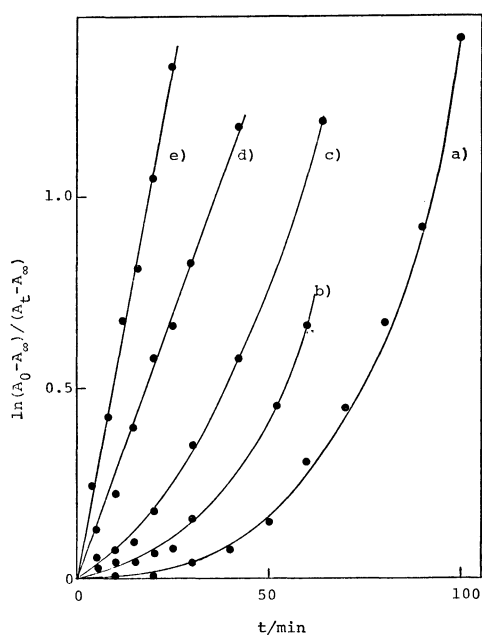
Kinetic experiments of the Pummerer reactions of cyanomethyl *p*-substituted phenyl sulfoxides in a large excess acetic anhydride containing a small amount of acetic acid (0–13.8 mmol) were carried out by following the UV absorption spectra of the starting sulfoxides. The rate of the Pummerer reaction was found to increase as the amount of acetic acid increased as shown in Fig. 1 which illustrates the rate change *vs.* the concentration of acetic acid used. When an equimolar amount of DCC was added into the reaction mixture, the Pummerer reaction was extremely slowed down and could have hardly been seen after heating the reaction mixture for a few hours. Acetic acid is undoubtedly acting as a catalyst in the initial acetylation step (step 1). A strong acid such as *p*-toluenesulfonic acid was found to accelerate the Pummerer reaction of these sulfoxides markedly. Meanwhile, the reduction of aryl cyanomethyl sulfoxide with trimethylsilyl chloride in the presence of pyridine is known to be extremely sluggish as compared to other sulfoxides¹⁵⁾ due mainly to the difficulty of the initial trimethylsilylation of the sulfinyl function of which the basicity is very low.

The kinetic data of the Pummerer reactions of a few cyanomethyl (*p*-substituted phenyl) sulfoxides **1a–e** are summarized in Table 1. The rate was found to decrease with the increase of electron-withdrawing effect of substituent and the Hammett plot of the logarithms of rates against σ -values gave ρ -value of

TABLE 1. KINETIC DATA FOR THE PUMMERER REACTION OF ARYL CYANOMETHYL SULFOXIDES (**1a–e**) WITH ACETIC ANHYDRIDE CONTAINING ACETIC ACID

<i>p</i> -YC ₆ H ₄ S(O)CH ₂ CN Y	λ^a nm	[AcOH] M	<i>T</i> °C	10 ⁴ <i>k</i> s ⁻¹	
CH ₃ 1b	247	0	120	0.31±0.04	
H 1c	246	0	120	0.29±0.04	
CH ₃ O 1a	251	6.92	120	11.9 ±0.3	
CH ₃ 1b	247	6.92	120	8.18±0.11	$\rho = -0.70 \pm 0.1$ (vs. σ , $\gamma = 0.9803$)
H 1c	246	6.92	120	9.13±0.24	
Cl 1d	249	6.92	120	5.08±0.18	
NO ₂ 1e	282	6.92	120	2.20±0.06	
CH ₃ 1b	247	3.50	120	4.52±0.22	$k_H/k_D = 1.01$
<i>p</i> -CH ₃ C ₆ H ₄ S(O)CD ₂ CN	247	3.50	120	4.47±0.18	
CH ₃ O 1a	251	3.50	120	4.97±0.28	
Cl 1d	249	3.50	120	2.42±0.18	
H 1c	246	3.50	120	4.73±0.20	$E_a = 70.3 \pm 1.7 \text{ kJ mol}^{-1}$
H 1c	246	3.50	110	2.76±0.13	$\Delta H^\ddagger = 66.9 \pm 1.7 \text{ kJ mol}^{-1}$
H 1c	246	3.50	100	1.50±0.10	$\Delta S^\ddagger = -141 \pm 4 \text{ J K}^{-1} \text{ mol}^{-1}$ (120 °C)

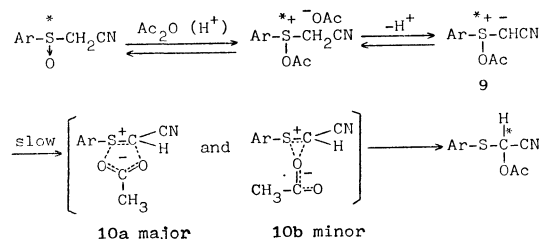
a) Wavelength of UV absorption at which the rate was followed.

Fig. 1. Time course of the Pummerer reaction of cyanomethyl phenyl sulfoxide (**1c**) with acetic anhydride containing acetic acid.

a): [AcOH]=0 M, b): 0.83 M, c): 1.75 M, d): 3.50 M, e): 6.92 M. A: UV Absorption intensity.

-0.7 ± 0.1 ($\gamma = 0.9803$). The negative ρ -value also supports the rate-determining heterolysis of the S–O bond of the ylide intermediate **9**. The values of activation parameters at 120 °C $E_a = (70.3 \pm 1.7) \text{ kJ mol}^{-1}$, $\Delta H^\ddagger = (66.9 \pm 1.7) \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = (-141 \pm 4) \text{ J K}^{-1} \text{ mol}^{-1}$, are quite different from those of the intermolecular Pummerer reaction of methyl phenyl sulfoxide at 120 °C ($E_a = 88.7 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -86.6 \text{ J K}^{-1} \text{ mol}^{-1}$)¹⁶ and also those of the Pummerer reaction of arylmethylsulfonium bis(methoxycarbonyl)methylide with acetic anhydride ($\Delta H^\ddagger = 89.5 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -92.9 \text{ J K}^{-1} \text{ mol}^{-1}$) in which the rate-determining step is believed to be the S–C linkage cleavage.¹⁷ The large

negative value of entropy of activation ($\Delta S^\ddagger = -141 \text{ J K}^{-1} \text{ mol}^{-1}$) seems to suggest the transition state to be very tight, as in a similar intramolecular tosyloxy migration in the reaction of isoquinoline *N*-oxide with *p*-toluenesulfonyl chloride, *i.e.*, $\Delta H^\ddagger = 40.2 \text{ kJ mol}^{-1}$, $\Delta S^\ddagger = -168 \text{ J K}^{-1} \text{ mol}^{-1}$.¹⁸ Based on all these observations and related data, the scheme of the Pummerer reaction of cyanomethyl aryl sulfoxides leading to the asymmetric induction may be illustrated as shown below. The initial acetylation is an acid-catalyzed equilibrium reaction and the second step of proton-removal is also fast and reversible in view of the lack of kinetic isotope effect, $k_H/k_D = 1.01$, and the loss of α -deuterium during the reaction. The rate-determining S–O bond heterolysis is considered to be followed by



very rapid recombination of acetate with α -carbon atom intramolecularly. The asymmetric induction cannot be caused by the stereoselective proton removal from the acetoxysulfonium salt, as was suggested by Allenmark in their stereoselective Pummerer reaction,⁹ since the resulting α -cyano carbanion, the ylide **9**, is known to be a coplanar resonance-stabilized carbanion. The dual pathways for the acetoxyl migration in which the five-membered cyclic path predominates over the three-membered sliding path is not particularly strange. Similar dual paths for acyloxy migration have been known in several rearrangements of tertiary amine oxides with acylating agents.¹⁸ Then what factor is important in inducing the chirality from the chiral sulfur atom to prochiral α -carbon in this Pummerer reaction? The preferential structural difference between

TABLE 2. REACTION OF OPTICALLY ACTIVE SULFOXIDES WITH ACETIC ANHYDRIDE IN THE PRESENCE OF DCC

Sulfoxide	DCC ^{a)}	T °C	t h	Product	Yield %	$[\alpha]_D$ °	e.e. ^{b)} %	Recovered	
								Yield %	Retention %
1b	—	60	3.5	2b	81	+26.8	29	—	—
3	—	120	4	4	51	−18.8	(29) ^{c)}	—	—
3	2	110	6	4	35	−44.0	65	63	77.7
3	4	120	8	4	57	−36.4	57	—	—
5	—	110	4	6	26	−24.5	29	68	96
5	2	110	6	6	10	−52.5	70	—	—
5	4	120	8	6	43	−40.2	(50) ^{c)}	47	87
7a	—	110	1	8a	88	−0.5	(0.5) ^{c)}	—	—
7a	2	110	2	8a	58	−5.5	(6) ^{c)}	—	—
7a	4	110	1.25	8a	32	−35.9	(38) ^{c)}	—	—
7a	4	130	1	8a	88	−9.0	10	—	—

a) Equivalent to the sulfoxide. b) e.e. values were determined on the basis of NMR spectra using the chiral shift reagent, Eu(hfc)₃. c) e.e. value was calculated on the basis of the other e.e. value determined with the shift reagent.

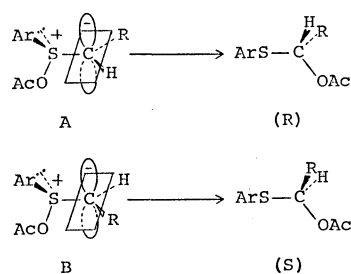


Fig. 2.

the two sulfonium ylides (A) and (B) would reflect on the preferential formation of one enantiomeric ester to the other. Then which one of the conformers (A) and (B) would be the more favored would be solved when the absolute configuration of the resulted ester is determined. From the X-ray crystallographic analysis of (−)-**4**,²⁵⁾ which is also product we obtained as optically active form and was recrystallized to optically pure crystals as described in the next section, (−)-**4** was found to have *R*-configuration, suggesting that the sterically more favored structure (A) is predominant among the acetoxysulfonium intermediates (A) and (B).

*Reaction of Optically Active Carbonyl-substituted Methyl *p*-Tolyl Sulfoxides 3, 5, and 7a with Acetic Anhydride.* In the intramolecular Pummerer reactions of optically active sulfoxides to afford the corresponding optically active α -acetoxy sulfides **4**, **6**, and **8a** under the usual conditions, the extent of asymmetric induction has never exceeded 30% e.e. The low percents of e.e. are considered to be due to the formation of acetic acid which assists the dissociation of the intimate ion-pair during the migration of acetoxyl group. Since the Pummerer reaction of optically active carbonyl-substituted methyl *p*-tolyl sulfoxides with acetic anhydride were found to proceed slowly but quite well in the presence of DCC, unlike the cyanomethyl analog, we have carried out the Pummerer reactions of a few optically active carbonyl-substituted methyl *p*-tolyl sul-

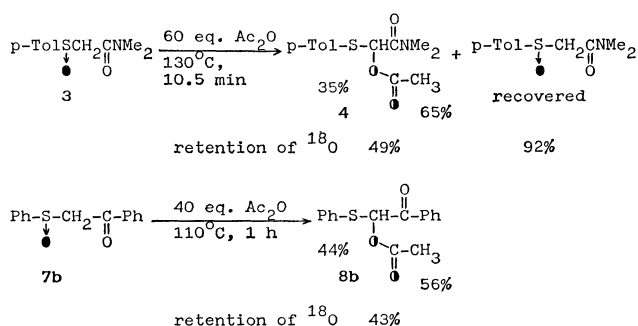
foxides **3**, **5**, and **7a** in a large excess of acetic anhydride with two equivalent amounts of DCC in the temperature range of 110–130 °C for a few hours and found a remarkable increase of up to 70% e.e. of asymmetric induction at the α -carbon of the resulted esters.

When optically active *N,N*-dimethyl-*p*-tolylsulfinylacetamide (**3**) with $[\alpha]_D +188^\circ$ was heated with a large excess of acetic anhydride in the presence of two equivalent amounts of DCC at 100 °C for 6 h, the recovered sulfoxide and the corresponding α -acetoxy sulfide **4** formed were obtained in 63% and 35% yields, respectively and the Pummerer product **4** was found to be optically active, $[\alpha]_D -44.0^\circ$, to the extent of 66% e.e. A similar reaction of ethyl *p*-tolylsulfinylacetate (**5**) with $[\alpha]_D +188^\circ$ and *o*-(*p*-tolylsulfinyl)acetophenone (**7a**) with $[\alpha]_D +272^\circ$ under the same conditions gave the corresponding highly optically active α -acetoxy sulfides **6** and **8a** in the early stage of the reaction (before a half completion). The asymmetric induction was found to be rather low, *i.e.*, below 30% e.e., when the Pummerer reaction of these optically active sulfoxides **3**, **5** and **7a** were carried out without DCC, the scavenger of acetic acid. All the stereochemical results of the reactions are tabulated in Table 2. The usual ¹⁸O-tracer experiments were carried out using ¹⁸O-labeled sulfoxides **3** and **7b** and the esters formed were also allowed to react with 2 equivalent amounts of phenylhydrazine to convert acetyl group to 1-acetyl-2-phenylhydrazine in order to determine the distribution of ¹⁸O in the two oxygens of the ester function of the migrated esters **4** and **8b**. The results are summarized in Table 3 and illustrated in the equations shown below. When the Pummerer reaction was carried out with the sulfoxide **3** labeled with 0.607 ex. atom% of ¹⁸O in 60 equiv. amounts of acetic acid at 130 °C for 10.5 h without DCC, the corresponding Pummerer reaction product **4**, obtained in 50% yield was found to have 0.198 ex. atom% of ¹⁸O while the sulfoxide recovered in 50% yield retained 92% (0.558 ex. atom%) of ¹⁸O of the original

TABLE 3. ^{18}O EXPERIMENTAL DATA IN THE PUMMERER REACTION OF ^{18}O -LABELED ARYL (SUBSTITUTED METHYL) SULFOXIDES WITH ACETIC ANHYDRIDE

ArSCH ₂ X ^{18}O	^{18}O -Content (ex. atom%)	Yield %	Pummer product		^{18}O -Distribution(%)			Recovered sulfoxide		
			^{18}O -Content (ex. atom%)	Incorporation(%)	Carbonyl ^{18}O -Content (ex. atom%)	(Ether)		Yield %	^{18}O -Content (ex. atom%)	Retention %
1d	0.680	2d 35	0.290	85	0.366	63	(37)	55	0.655	96
3	0.607	4 50	0.198	49	0.386	65	(35)	50	0.558	92
3^a	0.607	4 76	0.267	66	0.480	60	(40)	20	0.522	86
7b	0.840	8b 74	0.243	43	0.411	56	(44)	—	—	—

a) The reaction was carried out in the presence of 4 equiv. of DCC.



^{18}O -label of the sulfoxide **3**. The uneven distribution of ^{18}O rich in favor for the carbonyl oxygen in the resulting Pummerer product **4** is also in keeping with the result observed in the Pummerer product **2d**. All these observations together with other pertinent data clearly indicate that these stereoselective intramolecular acetoxyl migrations proceed *via* intimate ion-pairs formed by concurrent electron-transfer within the acetoxysulfonium ylide and S-O bond heterolysis, and the subsequent recombination of the sulfenyl carbenium ion and acetate is so rapid that there is not enough time to achieve complete racemization and complete ^{18}O -scrambling in the resulted esters.

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. UV absorptions were measured using a JASCO UNIDEC-1 spectrophotometer. 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 distilled under reduced pressure, bp $47\text{--}48^\circ\text{C}/20 \text{ mmHg}$.**

^{18}O -Analysis. ^{18}O -Analysis was carried out by the method developed by Rittenberg and Ponticorvo,¹⁹ with a modification which involves the use of $\text{Pb}(\text{OAc})_2$ 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 $\text{Hg}(\text{CN})_2$, 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 $\text{C}^{16}\text{O}^{18}\text{O}$,

respectively, were recorded on a mass spectrometer.

Materials. **Aryl Cyanomethyl Sulfides:** Chloroacetonitrile was treated with respective sodium arenethiolates in ethanol at room temperature. The sulfides thus obtained in 70–80% yields have the following physical properties. **R-S-CH₂CN:** R, bp (or mp), NMR (CDCl_3) δ ; Ph, 107–109 $^\circ\text{C}/3 \text{ mmHg}$, 3.52 (2H, s), 7.6 (5H, s broad); *p*-tolyl, 114–116 $^\circ\text{C}/3 \text{ mmHg}$, 2.38 (3H, s), 3.52 (2H, s), 7.1–7.6 (4H, m); *p*-ClC₆H₄, mp 85–87 $^\circ\text{C}$, 3.52 (2H, s), 7.3–7.6 (4H, m); *p*-MeOC₆H₄, liquid (bp not determined), 3.46 (2H, s), 3.83 (3H, s), 6.8–7.6 (4H, m).

Cyanomethyl *p*-Nitrophenyl Sulfide: Chloroacetonitrile was treated with *p*-nitrobenzenethiol in the presence of triethylamine in chloroform at room temperature to give cyanomethyl *p*-nitrophenyl sulfide in 75% yield, mp 84–85 $^\circ\text{C}$, 3.78 (2H, s), 7.5–8.3 (4H, m).

Aryl Cyanomethyl Sulfoxides (1a–e): The corresponding sulfides were allowed to react with *m*-chloroperbenzoic acid in chloroform at room temperature. The sulfoxides obtained in nearly quantitative yields were recrystallized from either benzene or acetonitrile. Physical properties are the followings. **R-S(O)-CH₂CN:** R, mp, NMR (CDCl_3) δ , anal; *p*-MeOC₆H₄, **1a**, 65–66 $^\circ\text{C}$, 3.70 (2H, s), 3.87 (3H, s), 7.0–7.8 (4H, m), Found: C, 55.35; H, 4.72; N, 7.41%. Calcd for $\text{C}_9\text{H}_9\text{NO}_2\text{S}$: C, 55.38; H, 4.65; N, 7.18%. *p*-tolyl, **1b**, 72–3 $^\circ\text{C}$, 2.47 (3H, s), 3.70 (2H, s), 7.3–7.8 (4H, m), Found: C, 60.33; H, 5.10; N, 7.66%. Calcd for $\text{C}_9\text{H}_9\text{NOS}$: C, 60.33; H, 5.06; N, 7.82%. Ph, **1c**, 65–66 $^\circ\text{C}$, 3.70 (2H, s), 7.4–7.8 (5H, m), Found: C, 58.04; H, 4.29; N, 8.68%. Calcd for $\text{C}_8\text{H}_7\text{NOS}$: C, 58.18; H, 4.27; N, 8.48%. *p*-ClC₆H₄, **1d**, 87–88 $^\circ\text{C}$, 3.73 (2H, s), 7.5–7.8 (4H, m), Found: C, 48.00; H, 3.03; N, 6.86%. Calcd for $\text{C}_8\text{H}_6\text{ClNOS}$: C, 48.09; H, 3.01; N, 7.01%. *p*-NO₂C₆H₄, **1e**, 153–154 $^\circ\text{C}$, (DMSO-*d*₆) 4.50 (2H, AB quartet), 7.9–8.5 (4H, m), Found: C, 45.73; H, 2.96; N, 13.18%. Calcd for $\text{C}_8\text{H}_6\text{N}_2\text{O}_3\text{S}$: C, 45.72; H, 2.88; N, 13.33%.

Optically Active Cyanomethyl *p*-Tolyl Sulfoxide (1b): The optically active **1b** was synthesized by either one of the following two procedures.

1): HMPT solution (50 ml) of (+)-bromomethyl *p*-tolyl sulfoxide (2.0 g), synthesized according to the reported procedure,²⁰ was mixed with aqueous solution (2 ml) of potassium cyanide (1 g), and heated at 50°C for 1 d. The HMPT solution was diluted with 100 ml of chloroform, and the whole solution was washed three times with 1000 ml portion of water. Then the resultant chloroform solution was dried and concentrated to afford a dark red oily product which was separated through silica-gel chromatography with chloroform as an eluent, giving crystalline optically active cyanomethyl *p*-tolyl sulfoxide which was recrystallized from benzene–hexane. Thus, (+)-cyanomethyl *p*-tolyl sulfoxide (**1b**) obtained (300 mg, 15% yield) has $[\alpha]_D^{25} +252^\circ$ (*c* 1,

** 1 mmHg $\approx$ 133.3 Pa.

EtOH), mp 72 °C. Upon measurement of NMR contact shift using chiral lanthanoid shift reagent, Eu(hfc)₃, the sulfoxide was found to be more than 90% optically pure. (*vide infra*)

2): Optically active bromomethyl *p*-tolyl sulfoxide (220 mg), prepared by usual α -bromination of optically active methyl *p*-tolyl sulfoxide,²⁰ was treated with 1.2 equiv. amount of KCN (68 mg) in the presence of 18-crown-6 (23 mg) in CHCl₃ (10 ml) under reflux for 4 h. The crude optically active cyanomethyl *p*-tolyl sulfoxide (**1b**) (125 mg) obtained in 72% yield was recrystallized from benzene-hexane giving 100 mg of the partially optically active title compound with $[\alpha]_D +145^\circ$ (*c* 1.5, acetone).

Optically Active N,N-Dimethyl-*p*-tolylsulfinylacetamide (3): A solution of 6.4 ml of butyllithium (15 wt% in hexane) was added to a solution containing optically active (+)-(*R*)-methyl *p*-tolyl sulfoxide (1.54 g, 10 mmol) in 20 ml of a freshly distilled THF at -70 °C in an acetone-Dry Ice bath and then the mixture was stirred for 30 min. After dimethylcarbamoyl chloride (537.5 mg, 5 mmol) was added to the THF solution with a syringe at -70 °C, the reaction mixture was allowed to stir at room temperature for 1 h. Into this mixture 20 ml of cold water was added, then the solution was acidified with aqueous solution of ammonium chloride (*ca.* pH 3) and extracted with chloroform. The combined orange layer was washed twice, and then dried over Na₂SO₄. Evaporation of the solvent gave an oily residue which was separated through silica-gel column chromatography with benzene-acetone (4:1) as an eluent. Then the product was distilled to give a colorless oil (584 mg, 40% yield): bp 130 °C/1 mmHg (Kugelrohr), $[\alpha]_D +188^\circ$ (acetone).

Optically Active Ethyl *p*-Tolylsulfinylacetate (5): Diethyl carbonate (590 mg, 5 mmol) was treated with 2 equivalent molar amount of a *p*-tolylsulfinylmethylide ion dried from the corresponding (+)-methyl *p*-tolyl sulfoxide (1.54 g, 10 mmol) with $[\alpha]_D +154^\circ$ (in acetone) and lithium diethylamide prepared from 6.4 ml of butyllithium solution (0.1 g/ml) in hexane and diethylamine (730 mg, 10 ml) at -70 °C. The reaction mixture was then stirred at 0 °C for 1 h. After addition of 20 ml of water, the solution was acidified with aqueous ammonium chloride solution (*ca.* pH 3) and extracted with 50 ml of chloroform three times, dried over MgSO₄, and the solvent was evaporated to give an oily residue which was separated through silica-gel column chromatography with benzene-ethyl acetate (4:1) as an eluent. Then the product was distilled to give a colorless oil (531 mg, 47% yield) with bp 130 °C/1.5 mmHg (Kugelrohr) and $[\alpha]_D +188^\circ$ (*c* 1.0, acetone). IR (KBr) 1730 and 1045 cm⁻¹; NMR (CDCl₃) δ =7.36 (4H, ABq), 4.12 (2H, q), 3.67 (2H, ABq), 2.40 (3H, s), 1.21 (3H, s); Found: C, 57.92; H, 6.28%. Calcd for C₁₁H₁₄O₃S: C, 58.38; H, 6.28%.

Optically Active ω -(*p*-Tolylsulfinyl)acetophenone (7a): Reaction of ethyl benzoate with *p*-tolylsulfinylmethylide ion prepared by treating (+)-(*R*)-methyl *p*-tolyl sulfoxide ($[\alpha]_D +154^\circ$, acetone) with butyllithium in diethylamine gave the optically active **7a**: $[\alpha]_D +272^\circ$ (*c* 1, acetone), mp 87–88 °C; lit.²¹ $[\alpha]_D +264.5^\circ$ (acetone), mp 74 °C.

¹⁸O-Labeled Cyanomethyl *p*-Chlorophenyl Sulfoxide (1d): Cyanomethyl *p*-chlorophenyl sulfide (4.5 g, 24 mmol) was dissolved in a mixture of acetic acid (20 ml), pyridine (6 ml) and ¹⁸O-enriched water (1.8 ml) (1.6 atom%). To the cooled solution was added bromine (3.9 g, 24 mmol) at 0 °C.²² After keeping the solution for 2 h at 0 °C, the reaction mixture was quenched with 200 ml of water and extracted with chloroform (200 ml). The chloroform solution was washed with aqueous Na₂S₂O₃ solution, diluted aqueous HCl solu-

tion and water, and then dried (MgSO₄). After evaporation of chloroform with a rotary evaporator, an oily substance obtained was separated through silica-gel column chromatography, giving ¹⁸O-labeled cyanomethyl *p*-chlorophenyl sulfoxide (**1d**) which was recrystallized from benzene. Thus the ¹⁸O-labeled **1d** obtained (600 mg, 12% yield) was found to contain 0.680 ex. ¹⁸O atom%.

¹⁸O-Labeled N,N-Dimethyl-*p*-tolylsulfinylacetamide (3): The ¹⁸O-labeled sulfoxide **3** was obtained by the reaction of dimethylcarbamoyl chloride (613 mg, 5.7 mmol) with *p*-tolylsulfinylmethylide ion prepared by treating ¹⁸O-labeled methyl *p*-tolyl sulfoxide (1.747 g, 11.3 mmol) with lithium diethylamide (prepared from 0.1 g/ml solution of butyllithium in hexane and diethylamine in THF). Then the usual work-up as mentioned above gave the ¹⁸O-labeled **3**: mp 59–60 °C, 0.607 ex. atom% of ¹⁸O, IR (KBr) 1640, 1265, and 1045 cm⁻¹, NMR (CDCl₃) δ =7.41 (4H, ABq), 3.33 (2H, ABq), 2.93 (3H, s), 2.90 (3H, s) and 2.39 (3H, s); Found: C, 58.77; H, 6.72; N, 6.20%. Calcd for C₁₁H₁₅NO₂S: C, 58.64, H, 6.71; N, 6.21%.

¹⁸O-Labeled ω -Phenylsulfinylacetophenone (7b): The reaction of ethyl benzoate with the phenylsulfinylmethylide ion prepared by treating ¹⁸O-labeled methyl phenyl sulfoxide (1.621 ex. atom%) with butyllithium in diethylamine gave the ¹⁸O-labeled **7b**: mp 70–71 °C, (lit.²³ mp 70–71 °C), ¹⁸O-content: 0.840 ex. atom%.

Cyanomethyl-d₂ Phenyl and Cyanomethyl-d₂ *p*-Tolyl Sulfoxides: The nonlabeled sulfoxide (370 mg) was dissolved in anhydrous chloroform (10 ml) containing two drops of anhydrous pyridine. The chloroform solution was vigorously shaken with D₂O (1 ml) at room temperature in a separatory funnel, and the aqueous layer was separated out. After the chloroform solution was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure, the solid dideuterated sulfoxide was obtained. Then the partially labeled sulfoxide thus obtained was treated additionally with D₂O for H-D exchange as the same procedure mentioned above. Thus the sulfoxide obtained by the two consecutive H-D exchange was found to be completely labeled by D upon NMR measurement and recrystallized from anhydrous benzene.

Reaction of Aryl Cyanomethyl Sulfoxides (1b–e) with Acetic Anhydride. The sulfoxides **1b–e** (*ca.* 400 mg) were heated

with 20 ml of acetic anhydride at 110–115 °C for 4–6 h until the sulfoxides were found to have disappeared upon monitoring with TLC method. After evaporation of excess acetic anhydride and any volatile product *in vacuo*, the remaining residue was separated by column chromatography through silica gel with benzene as an eluent. The corresponding α -acetoxy sulfides, the Pummerer products, were obtained in 85–90% yields. Physical properties of R-S-CH(OAc)CN (**2b–e**) were the followings: R, mp (or bp), NMR (CDCl₃) δ , Anal; *p*-tolyl **2b**: 100 °C/4 mmHg (Kugelrohr), 2.15 (3H, s), 2.39 (3H, s), 6.48 (1H, s), 7.1–7.6 (4H, m). Ph **2c**: 100 °C/4 mmHg (Kugelrohr oven), 2.17 (3H, s), 6.52 (1H, s), 7.4–7.7 (5H, m), Found: C, 57.86; H, 4.50; N, 6.76%. Calcd for C₁₀H₉NO₂S: C, 57.97; H, 4.38; N, 6.76%. *p*-ClC₆H₄ **2d**: 53–55 °C, 2.18 (3H, s), 6.49 (1H, s), 7.3–7.7 (4H, m), Found: C, 49.63; H, 3.36; N, 5.80%. Calcd for C₁₀H₈ClNO₂S: C, 49.59; H, 3.31; N, 5.79%. *p*-NO₂C₆H₄ **2e**: 92–3 °C, 2.21 (3H, s), 6.63 (1H, s), 7.7–8.3 (4H, m).

Reaction of Optically Active Cyanomethyl *p*-Tolyl Sulfoxide (1b) with Acetic Anhydride. 1): After heating of the optically active sulfoxide **1b** ($[\alpha]_D +252^\circ$ 50 mg) with 1 ml of acetic anhydride at 120 °C for 3.5 h and then evaporation of an excess acetic anhydride and any volatile product *in vacuo*,

an oily product was purified through column chromatography (silica gel, benzene as an eluent) to afford a colorless oily Pummerer product, acetoxycyanomethyl *p*-tolyl sulfide (**2b**) (50 mg, 81% yield). The oily **2b** was further purified by distillation with micro-distillation apparatus (100 °C/1 mmHg bath temp) giving the pure **2b** with $[\alpha]_D +26.8^\circ$ (*c* 5, EtOH). This optically active α -acetoxy sulfide **2b** was found to be of $29.0 \pm 0.8\%$ of enantiomer excess (e.e.) by treatment with the chiral lanthanoids shift reagent, Eu(hfc)₃, (*vide infra*). Prolonged heating (120 °C, 7 h) of the sulfoxide **1b** with acetic anhydride also gave the partially optically active Pummerer product **2b** with $[\alpha]_D +25.7^\circ$ (*c* 4.35, EtOH).

2): When the optically active **1b** (50 mg) was heated with 1 ml of acetic anhydride containing 0.2 ml of acetic acid (120 °C, 3 h), the Pummerer product **2b** obtained (52 mg) after the same work-up has only $[\alpha]_D +1.2^\circ$ (*c* 5.2, EtOH).

3): When the optically active **1b** (51 mg) was heated with acetic anhydride (1 ml) at 120 °C for 6 min, the Pummerer reaction was found to have proceeded only to 22% conversion by monitoring with NMR measurement of the reaction mixture of the sulfoxide and the α -acetoxy sulfide **2b** after evaporation of excess of acetic anhydride. The only mixture was separated through column chromatography (silica gel, benzene, and then chloroform as eluents), giving the recovered sulfoxide **1b** (42 mg) with $[\alpha]_D +234^\circ$ (*c* 4.2, EtOH), and with $[\alpha]_D +251^\circ$ (*c* 0.63, EtOH) after recrystallization from benzene-hexane.

Reaction of ¹⁸O-Labeled Cyanomethyl p-Chlorophenyl Sulfoxide (1d) with Acetic Anhydride.

1): When the ¹⁸O-labeled title sulfoxide **1d** (600 mg) (0.680 ex. atom%) was heated with 5 ml of acetic anhydride at 120 °C for 1 h, the oily residue obtained after evaporation of excess of acetic anhydride and any volatile product *in vacuo* was separated by column chromatography through silica gel with benzene and then chloroform as eluents. The sulfoxide recovered and the Pummerer product **2d** were recrystallized from benzene and hexane, respectively, to afford the sulfoxide (332 mg, 55% yield) and the Pummerer product (252 mg, 35% yield). The starting sulfoxide, the recovered sulfoxide and the Pummerer product were subjected to measurement of ¹⁸O-content by the routine ¹⁸O-analysis technique and the ¹⁸O-contents were found to be 0.680, 0.655, and 0.290 ex. atom%, respectively.

2): When the ¹⁸O-labeled **1d** (100 mg, 0.680 ex. atom%) was heated with 4 ml of acetic anhydride containing 830 mg of acetic acid at 100 °C for 16 min, the Pummerer reaction proceeded to 10% conversion, and the unreacted starting sulfoxide recovered was found to retain original ¹⁸O-label completely (0.680 ex. atom%). While the sulfoxide **1d** (102 mg, 0.680 ex. atom%) was heated with acetic anhydride (2 ml) containing acetic acid (0.4 ml) at 120 °C for 2 h, the Pummerer product **2d** recrystallized from hexane was found to contain 0.154 ex. atom% of ¹⁸O.

¹⁸O-Distribution in Ester Function of the Pummerer Product (2d). When the Pummerer product (400 mg, 0.290 ex atom%) was treated with three molar excess of phenylhydrazine (540 mg) in 5 ml of benzene at 60 °C for 0.5 h, 1-acetyl-2-phenylhydrazine precipitated was collected (130 mg) and recrystallized twice from benzene. The pure 1-acetyl-2-phenylhydrazine (80 mg, mp 125–128 °C) was found to contain 0.366 ex atom% of ¹⁸O by the routine ¹⁸O-analysis.

Kinetic Procedure for the Pummerer Reaction of Aryl Cyanomethyl Sulfoxide (1a–e).

The Pummerer reaction was carried out at $120.0 \pm 0.07^\circ\text{C}$ in sealed tubes, in which each sulfoxide **1a–e** (0.22–0.38 mmol) was dissolved in 2 ml of acetic

anhydride solution containing acetic acid (0–13.8 mmol). In this solution, the concentration of acetic anhydride was maintained above 50 molar excess as compared with that of the sulfoxide. A sealed tube containing 200 μl solution of the above mixture was recovered at several time intervals and was cooled in an ice-bath to stop the reaction. The aliquot portion (50–70 μl) was pipetted out and then diluted with ethanol resulting in making of 50 ml of ethanol solution, which was measured by UV spectrometer around 246–282 nm. Thus the rate of the Pummerer reaction was readily obtained by following the decrease of the band of the starting sulfoxide at 246–282 nm, since the starting sulfoxides absorb light at 246–282 nm ($\epsilon=7000\text{--}7500$) and the Pummerer products absorb light at the same range with substantially small absorption coefficient ($\epsilon=4000\text{--}6000$).

Reaction of Aryl Cyanomethyl-d₂ Sulfoxides with Acetic Anhydride.

1): After heating of cyanomethyl-d₂ phenyl sulfoxide (45 mg) with 0.4 ml of acetic anhydride at 120 °C for 40 min, and separation of product mixture through column chromatography, the starting sulfoxide recovered (29 mg, 35% conversion) was found to have lost deuterium substantially (66% H-incorporation) upon determination by NMR measurement.

2): Cyanomethyl-d₂ *p*-tolyl sulfoxide (55 mg) was heated with 2 ml of acetic anhydride solution containing acetic acid (0.416 g, 6.93 mmol) at 120 °C for 16 min, where the Pummerer reaction was found to have proceeded 51% conversion upon determination by monitoring with UV. Then after evaporation of solvent of the reaction solution and measurement of the residue redissolved in CDCl₃ with NMR instrument, both the sulfoxide and the Pummerer product were found to retain no deuterium.

Reaction of the Optically Active N,N-Dimethyl-p-tolylsulfinylacetamide with Acetic Anhydride.

1): The optically active sulfoxide **3** (74.4 mg, $[\alpha]_D +188^\circ$) was heated with 2 ml of acetic anhydride at 120 °C for 4 h. Then, after evaporation of excess acetic anhydride and any volatile product *in vacuo*, the remaining residue was separated by column chromatography through silica gel with benzene-ethyl acetate (4:1) as an eluent. The Pummerer product (**4**, 44.7 mg, 51% yield) with $[\alpha]_D -18.8^\circ$ (*c* 2.0, acetone) was obtained.

2): The sulfoxide **3** (55 mg) was heated with 2 ml of acetic anhydride in the presence of 2 equiv. molar amount of DCC to the sulfoxide at 110 °C for 6 h, the Pummerer product **4** (22.7 mg, 35% yield) with $[\alpha]_D -44^\circ$ (acetone) and the recovered sulfoxide (34 mg, 63% yield, $[\alpha]_D +146^\circ$) were obtained. The product **4** was recrystallized repeatedly from hexane to give optically pure crystals with maximum rotation $[\alpha]_D -59.2^\circ$ (*c* 0.4, acetone). Mp 65–65.5 °C.

3): When the sulfoxide **3** (50 mg) was heated with 2 ml of acetic anhydride in the presence of 4 equiv. of DCC (163 mg) to the sulfoxide at 120 °C for 8 h, the Pummerer product **4** (59.3 mg) with $[\alpha]_D -36.4^\circ$ was obtained.

Reaction of the Optically Active Ethyl p-Tolylsulfinylacetate (5) with Acetic Anhydride.

1): The sulfoxide **5** (101 mg, $[\alpha]_D +188^\circ$) was heated with 2 ml of acetic anhydride at 110 °C for 4 h. Then after evaporation of excess acetic anhydride and any volatile product *in vacuo*, the remaining residue was separated through silica-gel column chromatography with benzene-ethyl acetate (4:1) as the eluent to give the Pummerer product **6** (26 mg, 22% yield) with $[\alpha]_D -18.8^\circ$ (*c* 2.6, acetone) and the sulfoxide recovered retaining nearly the same initial optical purity ($[\alpha]_D +180^\circ$). The e.e. value of the chiral Pummerer product was found

to be 29% by measurement of the peak splitted on NMR recorder using the chiral lanthanoid shift reagent, $\text{Eu}(\text{hfc})_3$. Mp 39.5–41.0 °C; IR (KBr) 1750, 1742, and 1203 cm^{-1} ; NMR (CDCl_3) δ =7.45 (2H, d, J =8.4 Hz), 7.18 (2H, d, J =8.4 Hz), 6.16 (1H, s), 4.15 (2H, q), 2.35 (3H, s), 2.20 (3H, s), 1.20 (3H, t); Found: C, 58.43; H, 6.02%. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_4\text{S}$: C, 58.19; H, 6.01%.

2): The sulfoxide **5** (100 mg) was heated with 2 ml of acetic anhydride in the presence of 2 equiv. of DCC (182 mg) to the sulfoxide at 110 °C for 6 h. After the work-up as mentioned above, the Pummerer product **6** (11.8 mg, 10%) with $[\alpha]_D -52.5^\circ$ (c 1.18, acetone) was obtained. The e.e. value of this Pummerer product induced with optical activity was 69.5% by treatment as mentioned above.

3): The sulfoxide **5** (45.0 mg) was heated with 1 ml of acetic anhydride in the presence of 4 equiv. DCC (165 mg) to the sulfoxide at 120 °C for 8 h. The Pummerer product **6** (22.9 mg, 43% yield with $[\alpha]_D +163^\circ$ was obtained.

Reaction of the Optically Active ω -(p-Tolylsulfinyl)acetophenone (7a) with Acetic Anhydride. The optically active sulfoxide **7a** (200 mg) was heated with acetic anhydride (5 ml) at 110 °C for 1 h, and after evaporation of excess acetic anhydride and any volatile product an yellow oily residue

was separated by column chromatography on silica gel with benzene as an eluent. The Pummerer product **8a** (204 mg, 88% yield) with $[\alpha]_D -0.5^\circ$ (c 11, acetone) and a small amount of deoxygenated product (*p*-TolSCH₂COPh, 18 mg, 10% yield) were obtained. Both products gave the same IR and NMR spectra of the authentic samples reported.²⁴⁾

Reaction of ^{18}O -Labeled N,N-Dimethyl-p-tolylsulfinylacetamide (3) with Acetic Anhydride. 1): The ^{18}O -labeled sulfoxide **3** (400 mg, 0.607 ex. atom%) was heated with 60 equiv.

acetic anhydride at 130 °C for 10.5 min. Then after work-up as mentioned above the reaction of optically active **3** and chromatography on silica gel gave the Pummerer product **4** (237 mg, 50% yield) and the sulfoxide recovered (200 mg, 50% yield) which were recrystallized from ether-hexane and ethyl acetate-hexane, respectively, were found to have 0.198 and 0.558 ex. atom% of ^{18}O , respectively. **4**: mp 59–60 °C; IR (KBr) 1750, 1653 and 1230 cm^{-1} ; NMR (CDCl_3) δ =7.5–7.1 (9H, m), 6.20 (1H, s), 2.29 (3H, s), 2.06 (3H, s); Found: C, 58.43; H, 6.42; N, 5.90%. Calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_3\text{S}$: C, 58.40; H, 6.40; N, 5.23%.

2) After the sulfoxide **3** (400 mg) was allowed to react with 60 equiv. acetic anhydride at 120 °C for 8 h in the presence of 4 equivalent DCC, the usual work-up and chromatography on silica gel gave the Pummerer product **4** (361 mg, 76% yield). The Pummerer product **4** was found to contain 0.267 ex. atom% of ^{18}O .

^{18}O -Distribution in Ester Function of the Pummerer Product (4). After the Pummerer products **4** (134 mg, 0.198 ex. atom% of ^{18}O and 143 mg, 0.267 ex. atom% of ^{18}O) in 2 ml of benzene with 2 molar excess of phenylhydrazine were heated at 80 °C for 12 h, the reaction mixture was cooled to precipitate 1-acetyl-2-phenylhydrazine which was filtered off and washed with benzene. Then the product was recrystallized twice from benzene to give pure crystals (48 mg and 50 mg, respectively, mp 130–131 °C) which were found to contain 0.386 and 0.480 ex. atom% of ^{18}O , respectively.

Reaction of ^{18}O -Labeled ω -Phenylsulfinylacetophenone (7b) with Acetic Anhydride. ^{18}O -Labeled sulfoxide **7b** (310 mg, 0.840 ex. atom%) was heated with acetic anhydride (5 ml) at 110 °C for 1 h. After the usual work-up process, the Pummerer product **8b** obtained was recrystallized from benzene-hexane giving colorless needles (270 mg, 74% yield). The product **8b**: mp 65–67 °C; 0.243 ex. atom% of ^{18}O ; IR (KBr) 1730, 1690, and 1220 cm^{-1} ; NMR (CDCl_3) δ =

2.13 (3H, s), 6.87 (1H, s), 7.2–7.9 (10H, m); MS (20 eV), m/e (rel intensity), 286 (M^+ , 10), 181 ($\text{M}-\text{PhCO}^+$, 38), 105 (PhCO^+ , 72), 43 (Ac^+ , 100).

^{18}O -Distribution in the Ester Function of the Pummerer Product (8b). The Pummerer product **8b** (220 mg) with 0.243 ex. atom% of ^{18}O was heated with three equivalent amounts

of phenylhydrazine (250 mg) at 120 °C for 1 h. Into this red solution, benzene was added to precipitate 1-acetyl-2-phenylhydrazine which was filtered off and washed with benzene. Then the product was recrystallized from benzene giving colorless crystals (59 mg, 51% yield) with mp 129–131 °C, and 0.411 ex. atom% of ^{18}O .

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