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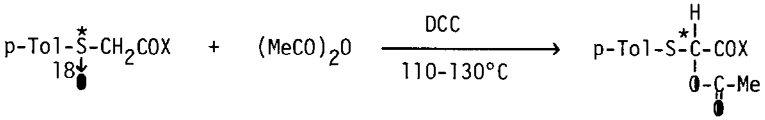
UNUSUALLY HIGH ASYMMETRIC INDUCTION IN THE PUMMERER REACTION OF OPTICALLY ACTIVE SULFOXIDES

Tatsuo Numata, Osamu Itoh and Shigeru Oae*
Department of Chemistry, University of Tsukuba, Sakura-mura, Ibaraki, 300-31 Japan

Summary: The Pummerer reaction of optically active β-carbonyl substituted alkyl sulfoxides with acetic anhydride in the presence of dicyclohexylcarbodiimide was found to be of highly stereoselective affording the corresponding α-acetoxysulfides with nearly 70% e.e.

Among several examples of stereoselective Pummerer reaction of sulfoxides,$^{1)}$ a few reported examples of asymmetric induction at α-carbon during the reaction$^{2)}$ are quite interesting, however, the extent of asymmetric induction was never more than 30% e.e. The low yield of e.e. could be due to the formation of acetic acid which assists the dissociation of the intimate ion pair during the acyloxy migration. Thus we run the Pummerer reaction of optically active β-carbonyl substituted sulfoxides with acetic anhydride in the presence of dicyclohexylcarbodiimide (DCC), since we found recently that DCC is an effective scavenger of acetic acid formed during the Pummerer reaction of sulfoxides with acetic anhydride,$^{3)}$ and found a remarkable increase of up to 70% e.e. of asymmetric induction at the α-carbon in the Pummerer reaction.

When optically active N,N-dimethyl p-toluenesulfinylacetamide (1) with $[\alpha]_D$ +188° was heated with a large excess of acetic anhydride in the presence of two equivalent amounts of DCC at 110°C for 6 hr, the recovered starting sulfoxide and the corresponding α-acetoxysulfide (4) produced were obtained in 63% and 35% yields, respectively, and the Pummerer product (4) was found to be of optically active ($[\alpha]_D$ -44.0°, 65% e.e.). Other β-carbonyl substituted alkyl sulfoxides such as ethyl p-toluenesulfinylacetate (2) with $[\alpha]_D$ +188° and ω-(p-toluenesulfinyl)-acetophenone (3) with $[\alpha]_D$ +272°, also gave the corresponding highly optically active Pummerer products such as (5) and (6) in the early stage of the reaction (before a half completion) by the treatment with acetic anhydride/DCC system. Meanwhile, the asymmetric induction was found to be below 30% e.e. in the absence of DCC.$^{4)}$ These results are listed in Table.



$$\text{p-Tol-}\underset{18\downarrow\mathbf{O}}{\overset{*}{\text{S}}}\text{-CH}_2\text{COX} + (\text{MeCO})_2\text{O} \xrightarrow[110\text{-}130^{\circ}\text{C}]{\text{DCC}} \text{p-Tol-S-}\underset{\text{O-}\underset{\mathbf{O}}{\underset{\|}{\text{C}}}\text{-Me}}{\overset{\overset{\text{H}}{*|}}{\text{C}}}\text{-COX}$$

X = NMe_2 (1), OEt (2), Ph (3)

X = NMe_2 (4), OEt (5), Ph (6)

Thus the Pummerer reaction with acetic anhydride/DCC system was found to proceed highly stereoselectively, while the markedly high asymmetric induction was due to the intramolecular acetoxy migration during the reaction in view of the following ^{18}O tracer experiments. The sulfoxide (1) which contains 0.709 ex. ^{18}O atom% labeled at sulfinyl oxygen gave the correspond-

Table

Reaction of Sulfoxides with Acetic Anhydride in the Presence of DCC [a]

Sulfoxide	DCC (eq. to sulfoxide)	Temp. (°C)	Time (hr)	Product	Yield (%)	$[\alpha]_D$	e.e.(%)[b]
1	-	120	4	4	51	-18.8°	(29)[c]
1	2	110	6	4	35[d]	-44.0°	65
1	4	120	8	4	57	-36.4°	57
2	-	110	4	5	26[e]	-24.5°	29
2	2	110	6	5	10	-52.5°	70
2	4	120	8	5	43	-40.2°	(50)[c]
3	-	110	1	6	80	-0.5°	(0.5)[c]
3	2	110	2	6	58	-5.5°	(6)[c]
3	4	110	1.25	6	32	-35.9°	(38)[c]
3	4	130	1	6	88	-9.0°	10

a) general reaction condition: sulfoxide (0.2-0.4 mmole) was heated with acetic acid free acetic anhydride (1-2 ml) at 110°-130°C. 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. d) the starting sulfoxide was recovered in 63% yield. e) the starting sulfoxide was recovered in 68% yield.

ing Pummerer product (4) with 0.312 ex.atom% of ^{18}O in 76% yield after heating with a large excess of acetic anhydride in the presence of DCC (4 eq.) at 130°C for 8 hr, suggesting that the reaction proceeded through at least 66% of intramolecular acetoxy migration route.[5] ^{18}O-Distribution in the ester was found to be uneven, i.e., 60% of ^{18}O in the carbonyl oxygen [determined after conversion with $PhNHNH_2$ into PhNHNHCOMe (0.564 ex.atom%)] and 40% of ^{18}O in the ether oxygen, indicating that intramolecular acetoxy migration underwent via an intimate ion pair.[1,2b]

References and Notes

1. see review: S. Oae, in "Topics in Organic Sulfur Chemistry", ed. by M. Tisler, pp 289-336, University Press, Ljubljana, Yugoslavia (1978).
2. a) B. Stridsberg and S. Allenmark, Acta Chem. Scand., 30, 219 (1976). b) T. Numata and S. Oae, Tetrahedron Lett., 1337 (1977). c) T. Numata, O. Itoh and S. Oae, Chem. Lett., 909 (1977). d) M. Mikołajczyk, et al., J. Org. Chem., 43, 2518 (1978).
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4. When the sulfoxides were heated with acetic anhydride at 110°C until completion of the reaction, the corresponding α-acetoxysulfides were obtained in high yields. (4 in 92% for 4 hr, 5 in 84% for 2 hr, and 6 in 80% in 1 hr)
5. Calculated ^{18}O-content in the ester (4) in the case of 100% of intramolecular acetoxy migration becomes 0.512 ex.atom% for involving the non-labeled carbamoyl oxygen atom.

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