Additive Pummerer Reactions of Vinylic Sulphoxides. Synthesis of 2-(Phenylsulphenyl) Aldehydes and Primary Alcohols

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Abstract: Reaction in acetic anhydride solution of α , β -unsaturated sulphoxides 1 with sodium acetate and triflic anhydride gives 2-(phenylsulphenyl) acylals 4. Basic methanolysis of 4 gives 2-(phenylsulphenyl) aldehydes 8, whilst reduction gives directly 2-(phenylsulphenyl) primary alcohols 9.

Reaction of vinylic sulphoxides 1 at oxygen with electrophiles gives highly reactive species which are electrophilic at the β -position of the carbon-carbon double bond because of the strongly polarizing effect of the positively-charged sulphur atom. These intermediates may suffer β -nucleophilic attack followed by α -nucleophilic addition to the resulting sulphenium ion. We have been exploring the synthetic utility of such additive Pummerer reactions,¹ in which sulphoxides 1 are synthetically equivalent to the thioether α , β -dication synthese 2. In particular, we are assessing the viability of this approach for the synthesis of heterocycles *via* sequential carbon-carbon and carbon-heteroatom bond-forming reactions.



We recently reported² the additive Pummerer reaction of substrates 1 with trifluoroacetic anhydride to give labile α,β -bis(trifluoroacetoxy)thioethers 3. These were elaborated further by basic methanolysis into dimeric and oligomeric α -hydroxyaldehydes (R = alkyl), or into α -hydroxyketones (R = aryl). In contrast with these findings, we now report that in the presence of triflic anhydride and sodium acetate in acetic anhydride solution, vinylic sulphoxides 1 derived³ from aromatic aldehydes and aliphatic ketones undergo additive Pummerer reaction with concomitant migration of the phenylsulphenyl group to give 2-(phenylsulphenyl) acylals⁴ 4 (Scheme 1). The reaction conditions and yields of 4 are summarized in Table 1.⁵



R ¹	R ²	E: 2 °	eq. NaOAc	eq. Tf ₂ O	T (℃)	t (min)	Yield of 4 (%) ⁷
Ph	н	0:100	3	1.5	0	15 ⁸	85
<i>p</i> -Tol	н	23:77	3	1.5	0	15 ⁸	80
p-CIC ₆ H₄	н	0:100	2	1.5	0	15 ⁸	85
<i>p</i> -MeOC ₆ H₄	н	75:25	3	1	-40	20	18
<i>m</i> -MeOC ₆ H₄	н	10:90	2	1.5	0	15 ^e	28
Me	Me	-	2	2	25	15 ⁹	60
-(CH ₂)5-		-	2	2	0	15°	66
-(CH ₂) ₆ -		-	2	1	0	5	79
Et	Me	52:48	2	1.25	25	5	62

Table 1

Mechanistically, it seems likely that acetate ion attacks the O-triflylated species 5 initially at the β -position, generating the anchimerically-stabilized species 6. Rearrangement occurs with migration of the phenylsulphenyl group¹⁰ to give the O-acetyloxonium ion 7, which suffers further nucleophilic attack by acetate ion to give 4 (Scheme 2).



The presence of **6c** in the equilibrium mixture represented by the structures **6** depicted above may explain in part the failure of the reaction with substrates **1** having $\mathbb{R}^1 = \operatorname{alkyl}$, $\mathbb{R}^2 = \mathbb{H}$, and the low yields of **4** obtained from **1** derived from aromatic aldehydes possessing strongly electron-donating substituents. In the former case, the carbocationic centre in **6c** may be insufficiently stabilized to favour acetoxy migration in the transformation **6b** - **6c**, whereas in the latter, **6c** may be so stable as to inhibit migration of the phenylsulphenyl group, effectively precluding the subsequent intermediacy of **6d**. We have investigated some derivatization reactions of 2-(phenylsulphenyl) acylals 4 (Scheme 3). Basic methanolysis¹¹ in the presence of potassium carbonate followed by careful neutralization with saturated aqueous ammonium chloride gave 2-(phenylsulphenyl) aldehydes 8. The consistently lower yields obtained from acylals 4 possessing an aromatic substituent R¹ reflects the instability of the product 2-aryl-2-(phenylsulphenyl) aldehydes. Alternatively, treatment of 1,2-dimethoxyethane (DME)-isopropanol solutions of 4 with sodium borohydride gave 2-(phenylsulphenyl) primary alcohols 9 in high yield. This choice of solvent allowed the optimal combination of solubility of sodium borohydride and the rate of its decomposition by alcoholysis. The use of neat methanol as solvent necessitated the addition of large excesses of sodium borohydride because of competing methanolysis thereof. The reaction conditions and yields for these transformations are summarized in Table 2.



Scheme 3

R ¹	R ²	T (°C)	t (min)	Yield of 8 (%)	Yield of 9 (%)
Ph	н	25	15	65	82 ¹²
<i>p</i> -Tol	н	0	45	65	85
p-CIC ₆ H ₄	н	0	45	64	94
Me	Ме	0	20	75	78
-(CH ₂)5-		25	20	85	94
-(CH ₂)6-		25	10	85	100



82

20

95

In summary, the additive Pummerer reaction-rearrangement of vinylic sulphoxides 1 giving 2-(phenylsulphenyl) acylals 4 is an efficient process. Elaboration of 4 via methanolysis or reduction gives respectively synthetically useful 2-(phenylsulphenyl) aldehydes¹³ and primary alcohols.¹⁴ We are currently applying these and related reaction sequences to enantiomerically pure 1 in order to assess the extent of any asymmetric induction¹⁵ in the formation of 4 and the previously reported² additive Pummerer products 3.

Acknowledgements

Et

Me

25

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References and notes

- 1. See reference 2, footnote 4 for examples.
- 2. Craig, D.; Daniels, K.; MacKenzie, A. R. Tetrahedron Lett. 1990, 31, 6441.
- Sulphoxides 1 were synthesized according to a modified one-pot Wadsworth-Emmons procedure: Craig, D.; Daniels, K.; Marsh, A.; Rainford, D.; Smith, A. M. Synlett 1990, 531.
- 4. Acylals are gem-diacetates; for leading references, see: March, J. Advanced Organic Chemistry, 3rd ed.; Wiley: New York, 1985; pp 686, 861, 1076, 1079.
- 5. Typical procedure for the preparation of 4. A 5-ml round-bottomed flask containing (\pm) -(Z)-2-phenyl-1-(phenylsulphinyl)ethene (30.9 mg, 0.14 mmol) and anhydrous sodium acetate (33 mg, 0.42 mmol, 3 eq.), and equipped with a magnetic stirrer bar was degassed, and acetic anhydride (677 µl, 0.2M solution) added *via* syringe. The heterogeneous mixture was cooled to 0°C and triflic anhydride (23 µl, 38.6 mg, 0.14 mmol, 1 eq.) added dropwise *via* syringe with stirring. After 10 min at 0°C further triflic anhydride (11 µl, 18.4 mg, 0.07 mmol, 0.5 eq.) was added *via* syringe. The reaction mixture was stirred for a further 5 min and then quenched by the addition of saturated aqueous sodium hydrogencarbonate (5 ml). The mixture was extracted with dichloromethane and the combined extracts were washed with saturated aqueous sodium hydrogencarbonate, and dried (MgSO₄). Removal of the solvent under reduced pressure and chromatography (20% diethyl ether-petroleum ether; silica gel) of the resulting yellow oil gave (\pm)-1,1-diacetoxy-2-phenyl-2-(phenylsulphenyl)ethane 4 (R¹ = Ph, R² = H) (38 mg, 85%) as a colourless oil. For larger-scale reactions, solid sodium hydrogencarbonate was used to quench acetic anhydride.
- 6. Measured by ¹H nmr.
- All yields cited herein are for isolated (flash chromatography on silica gel), pure materials, characterized by ¹H nmr, ir, ms, and elemental combustion analysis.
- 8. 1 Eq. Tf₂O, 10 min, followed by 0.5 eq. Tf₂O, 5 min, then work-up.
- 9. 1 Eq. Tf₂O, 10 min, followed by 1 eq. Tf₂O, 5 min, then work-up.
- For related rearrangements of hemithioacetals possessing 2-oxy substituents, see: (i) Sato, T.; Otera, J.; Nozaki, H. J. Org. Chem. 1990, 55, 6116; (ii) Otera, J. Synthesis, 1988, 95 (review); (iii) Sato, T.; Okazaki, H.; Otera, J.; Nozaki, H. J. Am. Chem. Soc. 1988, 110, 5209; (iv) Mandai, T.; Hara, K.; Nakajima, T.; Kawada, M.; Otera, J. Tetrahedron Lett. 1983, 24, 4993; (v) De Groot, Ae.; Jansen, B. J. M. Tetrahedron Lett. 1981, 22, 887.
- 11. Tufariello, J. J.; Kissel, W. J. Tetrahedron Lett. 1966, 6145.
- 12. 3 Eq. of sodium borohydride was used.
- For a recent application of the aldol products derived from 2-(phenylsulphenyl)aldehydes in the synthesis of oxygen and nitrogen heterocycles, see: (i) Aggarwal, V. K.; Coldham, I.; McIntyre, S.; Warren, S. J. Chem. Soc., Perkin Trans. 1 1991, 451, and references cited therein; (ii) Coldham, I.; Warren, S. Tetrahedron Lett. 1989, 30, 5937.
- 14. For example, treatment of enantiomerically enriched 1-(phenylsulphenyl)-2-alkanols (prepared *via* diastereospecific reduction of enantiomerically pure β-ketosulphoxides, followed by conversion of the sulphoxide to the sulphide function) with trimethyloxonium tetrafluoroborate followed by base gives epoxides in high e.e.: Solladié, G.; Demailly, G.; Greck, C. *Tetrahedron Lett.* **1985**, *26*, 435.
- Additive Pummerer reactions of enantiomerically pure 1 (R = alkyl) with dichloroketene have been reported to proceed with high levels of asymmetric induction from sulphur to carbon. See: (i) Marino, J. P.; Perez, A. D. J. Am. Chem. Soc. 1984, 106, 7643; (ii) Marino, J. P.; de la Pradilla, R. F. Tetrahedron Lett. 1985, 26, 5381; (iii) Posner, G. II.; Asirvatham, E.; Ali, S. F. J. Chem. Soc., Chem. Commun. 1985, 542; (iv) Kosugi, K.; Tagami, A.; Takahashi, H.; Kanna, H.; Uda, H. J. Chem. Soc., Perkin Trans. 1 1989, 935.

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