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Preliminary Communication

Studies of the zinc(II) catalysed addition of silyl enol ethers to cyclic enol ethers

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Abstract

The addition of silyl enol ethers to cyclic enol ethers by zinc dibromide catalysed electrophilic addition of a phenylsulphenyl group has been shown to give exclusively the *trans*-diastereoisomer when the silyl enol ether of acetophenone is used. The same reaction was catalysed by a zinc(II) alkoxyamine complex, but the use of the chiral ligand (+)-cinchonine in this reaction did not result in any asymmetric induction.

1. Introduction

Electrophilic addition of phenylsulphenyl chloride to a cyclic enol ether followed by trapping with a silyl enol ether [1] results in formation of the addition product **1**. Other synthetically useful transformations of this compound include the removal of the sulphur group by reduction [2] or oxidation to the sulphoxide followed by elimination [3]. The reaction is believed to proceed *via* an intermediate episulphonium ion and the *trans*-addition product usually predominates [1,4–6].

2. Results and Discussion

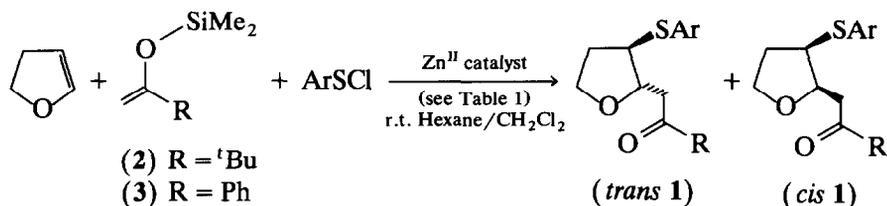
The initial addition reaction of the phenylsulphenyl chloride across an enol ether double bond is known to be very rapid [6]. Loss of chloride anion to give an oxonium cation is followed by trapping by a silyl enol ether. As part of a programme aimed at the development of an asymmetric version of this reaction we wished to see whether a chiral, non-racemic, catalyst was capable of asymmetric induction in the reaction. This might be achieved during the initial addition stage by assisting removal of chloride from phenylsulphenyl chloride or in a kinetic resolution process during the

second step. However, in order to maximise the resulting utility of the process it was essential to find conditions under which one diastereoisomer was formed exclusively. We have studied the effects of modifications of the arylsulphenyl group and the attacking nucleophile, and the results are given below (Scheme 1, Table 1).

Initially we employed silyl enol ether **2**, derived from pinacolone, as the nucleophile, since this has been previously reported [1a]. Variation of the electron richness of the arylsulphenium group was first examined to see whether this had any bearing on the selectivity of the reaction (entries 1–3) [1b]. However no improvement in the 4:1 ratio with phenylsulphenyl chloride was observed, and in the case of the *para*-methoxy group a lower selectivity was observed (entry 2). This was surprising, since it was expected that a more electron rich, and therefore less reactive, group would give a higher selectivity in the addition step. In view of these disappointing results we turned our attention to the structure of the silyl enol ether used in the reaction. Remarkably the silyl enol ether **3** derived from acetophenone gave a product **1** that appeared to be a single diastereoisomer, as assessed by 270 MHz ^1H -NMR spectroscopy (entry 4) [7,8]. This may be due to the lower reactivity of the conjugated silyl ether compared with that of the alkyl compound. Alternatively, in the case of **3** these may be some form of π -stacking interaction between the electrophilic and nucleophilic reagents that cannot occur with **2**. In the absence of zinc dibromide less than 10% of impure product was formed (entry 5).

Having established that a stereoselective addition reaction could be achieved we turned our attention to the nature of the zinc catalyst employed. Homochiral amino alcohols have found extensive use in asymmetric catalysis and have been used in reactions involving zinc(II) organometallics [9] and tin(II) species [10]. The use of 4.4 mol% of the adduct of 2-dimethylaminoethanol with zinc dibromide that was formed in the presence of triethylamine proved to be an effective catalyst, but a low yield of product was obtained (entry 6). A more effective way of forming the catalyst was by the reaction between the ethanolamine and diethyl zinc, since this leads to irreversible formation of alkoxide with release of ethane. The use of 4.4 mol% of a catalyst formed in this way proved to be effective for

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Scheme 1.

catalysis of the reaction but the use of 50 mol% gave mostly products from competing side reactions, such as acetophenone and α -phenylthioacetophenone (**4**) (entries 7–9). Although the yields were low a reaction was attempted using a complex of (+)-cinchonine and diethyl zinc. At the 4.4 mol% level this complex was effective in the catalysis of the reaction but no asymmetric induction was observed in the product **1** (entry 10). In all the reactions shown in entries 7–10 a 1:1 complex had been formed between the zinc organometallic reagent and the amino alcohol.

Although no evidence of ethyl group transfer or reduction was observed in any of the products from these reactions we were concerned that this might influence the title reaction. The incorporation of an easily-displaced group such as trifluoromethanesulphonyl into a tin complex has been reported to improve its effectiveness at the catalysis of a nucleophilic addition reaction [10]. In view of this we argued that a more effective catalyst for our reaction could be produced by this expedient. Hence reaction of one equivalent of diethylzinc with one equivalent of trifluoromethanesul-

phonic acid and (+)-cinchonine gave a complex that, at the 4.4 mol% level, gave the addition product in similar yield (entries 11 and 12). It is important to note that it is essential to add the trimethylsilyl enol ether **3** slowly to the preformed mixture of zinc(II) catalyst, dihydrofuran and phenylsulphenyl chloride to obtain the optimum yield. If **3** is not the last reagent to be added, or if it is added too rapidly, a significant amount of **4** is formed. However, as was previously observed, no asymmetric induction was achieved by use of this strategy.

A typical experiment procedure is as follows:

Preparation of catalyst from (+)-cinchonine, diethyl zinc and trifluoromethane sulphonic acid: A hexane solution of diethylzinc (1 M, 2ml, 2 mmol) was added to 2ml of dry hexane in a flame-dried Schlenk tube under nitrogen. The solution was cooled to 0°C and trifluoromethane sulphonic acid (0.3 g, 0.177 ml, 2 mmol) was added dropwise. The mixture became cloudy and evolution of gas was observed. After 5 min stirring solid (+)-cinchonine (0.56 g, 2 mmol) was added. The solution was stirred for 1 h at 0°C during which the

TABLE 1

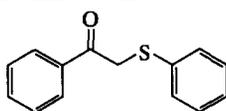
Entry	Silyl ether	Ar in ArSCl	Zn catalyst	Yield of 1	<i>trans</i> : <i>cis</i>
1	2	Ph	ZnBr ₂ (5 mol%)	72%	4 : 1
2	2	<i>p</i> -(MeO)C ₆ H ₄	ZnBr ₂ (5 mol%)	45%	3 : 2
3	2	<i>p</i> -(NO ₂)C ₆ H ₄	ZnBr ₂ (5 mol%)	40%	4 : 1
4	3	Ph	ZnBr ₂ (5 mol%)	73%	only <i>trans</i>
5	3	Ph	none	< 10%	NA
6	3	Ph	^a (4.4 mol%)	30%	only <i>trans</i>
7	3	Ph	^b (4.4 mol%)	38%	only <i>trans</i>
8	3	Ph	^b (4.4 mol%)	32%	only <i>trans</i>
9	3	Ph	^b (50 mol%)	< 5%	only <i>trans</i>
10	3	Ph	^c (4.4 mol%)	48%	only <i>trans</i> (0% e.e.)
11	3	Ph	^d (4.4 mol%)	45%	only <i>trans</i> (0% e.e.)
12	3	Ph	^d (4.4 mol%)	49%	only <i>trans</i> (0% e.e.)

^a ZnBr₂/Me₂NCH₂CH₂OH/Et₃N; 1 : 2 : 2

^b ZnEt₂/Me₂NCH₂CH₂OH; 1 : 1

^c ZnEt₂/(+)-cinchonine; 1 : 1

^d ZnEt₂/(+)-cinchonine/TfOH; 1 : 1 : 1



(4)

thick suspension dissolved to yield a cloudy solution. The resulting catalyst solution was assumed to be ca. 0.5 M in strength.

Addition of trimethylsilylenol ether **3** to 2,3-dihydrofuran: A portion (0.176 ml, 0.088 mmol) of the above solution was added to dichloromethane (2 ml) in a flame-dried Schlenk tube under nitrogen. The cloudy solution was cooled to -78°C and 2,3-dihydrofuran was added (0.147 g, 0.159 ml, 2.1 mmol), followed by phenylsulphenyl chloride [11] (1 M solution, 2 ml, 2 mmol), which was added dropwise during 30 min. After this time the cloudy solution was warmed to room temperature and the trimethylsilylenol ether **3** [12] (0.386 g, 0.41 ml, 2 mmol) in dichloromethane (2 ml) was added dropwise during 30 min. The mixture was stirred overnight and then quenched by addition of saturated aqueous sodium bicarbonate (10 ml). The product was extracted with dichloromethane (2×5 ml), washed with water (10 ml), and dried (magnesium sulphate) and the solvent removed to leave an oil. The product (**1**, R = Ar = Ph) [7] was isolated by flash chromatography as a white solid (0.291 g, 48%).

3. Conclusions

It has been shown that the diastereoselectivity of the zinc(II) catalysed reaction of phenylsulphenyl chloride and a silyl enol ether with dihydrofuran can be significantly improved by the use of an appropriately substituted silyl enol ether. Ethanolamine-substituted zinc (II) complexes are also effective in catalysis of the reaction but the incorporation of a chiral ligand does not induce asymmetry in the product. This suggests that either the rate of reaction of phenylsulphenyl chloride with the enol ether, which is known to be fast [6] is not influenced by the catalyst or that the catalyst assists in the generation of an essentially "free" phenylsulphenyl cation. We believe that the results of these investigations will be of considerable interest to those concerned with syntheses involving enol ether chemistry and asymmetric catalysis. We are currently investigating this reaction further.

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- Data for **1** (R = Ar = Ph); $[\alpha]_{\text{D}}^{20} = 0^{\circ}$, ν_{max} 3078, 1688, 1588 cm^{-1} ; δ_{H} (270 MHz, CDCl_3) 7.87–7.93 (2H, m, aryl H), 7.24–7.55 (5H, m, aryl H), 7.19–7.23 (3H, m, aryl H), 4.30 (1H, m, 2-H), 3.82–3.97 (2H, m, 5-H), 3.46–3.54 (1H, q, J 8 Hz, 3-H), 3.16 (2H, d, J 6 Hz, $\text{CH}_2\text{C}=\text{O}$), 2.31–2.44 (1H, m, 4-H), 1.90–2.02 (1H, m, 4-H); δ_{C} (60 MHz, CDCl_3) 133.11 (d), 132.04 (d), 129.06 (d), 128.54 (d), 128.28 (d), 127.34 (d), 80.24 (d), 67.04 (t), 50.01 (d), 43.04 (t) 33.54 (t); m/z (CI) 299 ($\text{M}+1^+$, 100), 189 (40), 179 (65), 161 (10), 121 (10), 105 (30) (found C; 72.40, H; 6.12, $\text{C}_{18}\text{H}_{18}\text{O}_2\text{S}$ requires C; 72.48, H; 6.04%).
- We thank Dr. I. Paterson for spectral details for *trans*-**1** (R = ^tBu, Ar = Ph) for comparison with those for our products.
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