Adducts of ArSCl with vinyl ethers or esters as synthones in geminal alkylation

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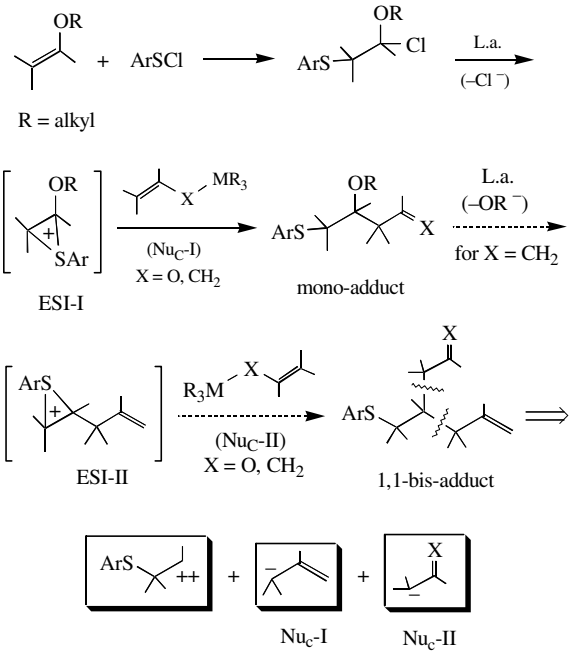
The *in situ*-prepared adducts of arylsulfenyl chloride and vinyl ethers (esters) were employed as synthetic equivalents of 1,1-bis-electrophiles in the Lewis acid-promoted reaction sequence with two different carbon nucleophiles resulting in the formation of geminal bisalkylation products.

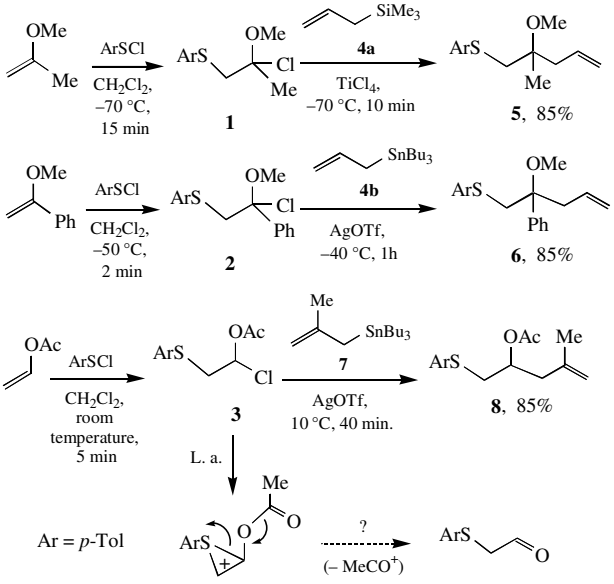
The synthetic merits of controlled geminal alkylation, which might secure an opportunity to introduce two different groups at the same carbon atom, are obvious. Most typically, this result is achieved using bifunctional reagents such as malonic ester or 1,3-dithiane, which are employed as synthetic equivalents of 1,1-bisnucleophiles in sequential transformations which involve the generation of a carbanion and reactions with carbon electrophiles (E_C).[1] At the same time, an opportunity to employ for this purpose an alternative (in a way, an inverse polarity) approach using synthetic equivalents of 1,1-biselectrophiles in sequential reactions with two different carbon nucleophiles (Nu_C) seems promising. To the best of our knowledge, no systematic attempts have been undertaken to explore the viability of this option.

Our interest in this problem is based on the reactivity of easily preparable adducts of vinyl ethers with arylsulfenyl chloride. Thus, we found that under the action of Lewis acids (L.a.) these adducts are converted into the episulfonium ion (ESI-I)-like electrophiles capable of reacting with π-donors such as vinyl silyl ethers, silyl ketene acetals and allylsilanes (stannanes) (Nu_C-I) to give the respective products of ternary coupling in preparative yields (mono-adduct, Scheme 1).[2] It was tempting to speculate that, due to the presence of a β-methoxyalkylaryl sulfide moiety in the adducts thus prepared, the latter can be used as the precursors of electrophiles (ESI-II). Hence, the second alkylation at the same carbon is considered as a feasible reaction.† This pathway, which leads eventually to the 1,1-bisadduct, is shown in Scheme 1. Retrosynthetically, it corresponds to the sequential coupling of a β-arylthio biscationic synthone with two nucleophilic synthones.

The adducts of p-TolSCl with 2-methoxypropene **1**, α-methoxystyrene **2** and vinyl acetate **3** were chosen as model compounds.‡ The reaction of **1** with allyltrimethylsilane **4a** in the presence of $TiCl_4$ (or another Lewis acid) proceeded uneventfully to give adduct **5** in a good yield (Scheme 2).[3] Unexpectedly, the reaction of adduct **2** with **4a** proceeded very slowly in the presence of Lewis acids ($TiCl_4$, $EtAlCl_2$, TMSOTf and $AgSbF_6$).§ Required product **6** was prepared by the reaction of **2** with more reactive tributylallylstannane **4b** in the presence of $AgSbF_6$ or AgOTf. The possibility to generate episulfonium ion-like electrophilic species from adduct **3** seemed questionable because of the deactivating effect of the acetoxy group. Moreover, it is believed that in this case the ESI-like intermediate once formed would immediately undergo fragmentation, as shown in Scheme 2. Much to our reward, we found that the generation of the cationoid intermediate from **3** and its reaction with tributylmethallylstannane **7** could be carried out under the action of AgOTf to form required adduct **8** in a nearly quantitative yield.¶



Scheme 1

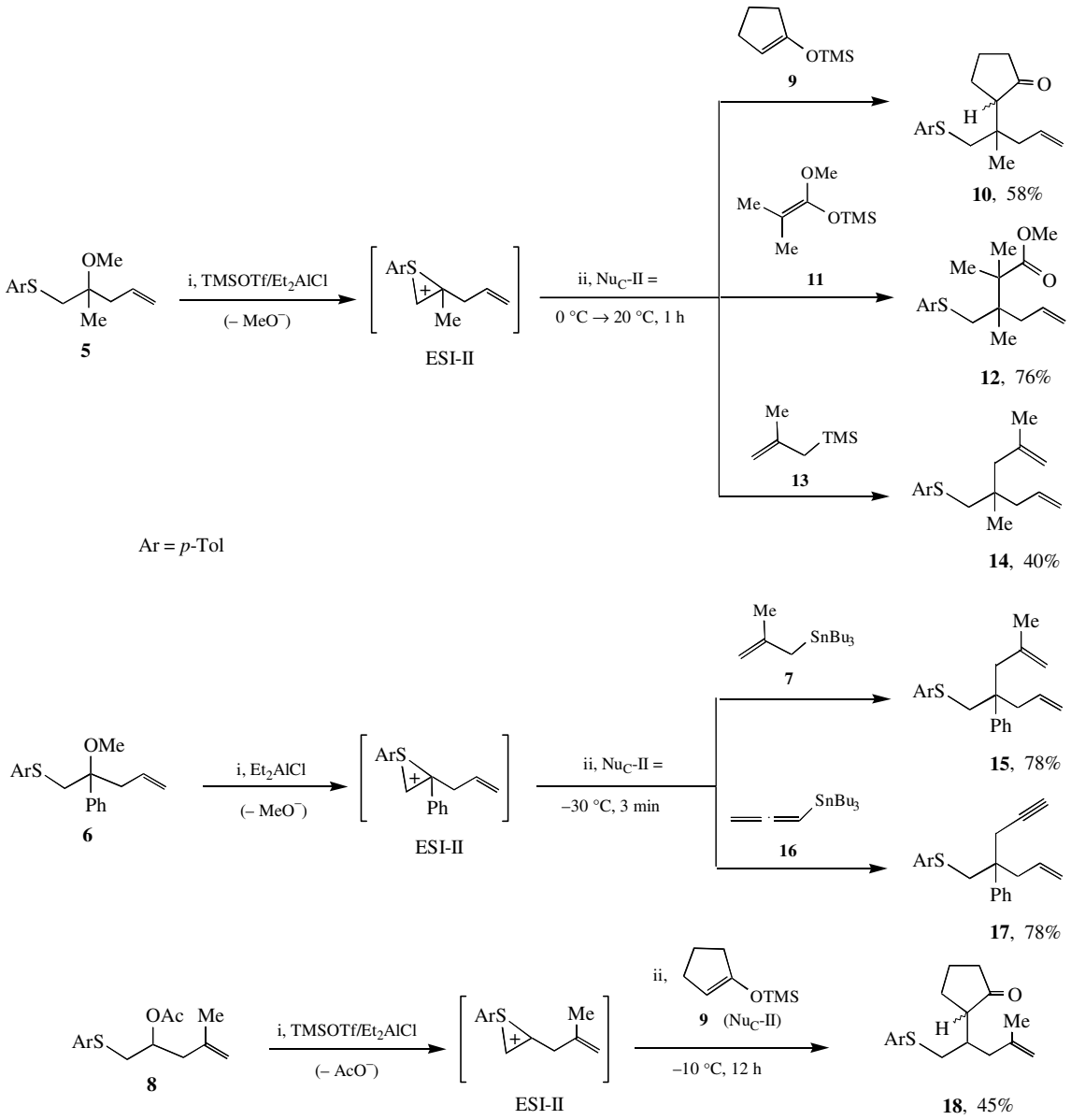


Scheme 2

† It seems obvious that this assumption could be considered as plausible only for the adducts formed with the use of allylsilanes (stannanes) as Nu_C (X = CH_2, see Scheme 1), since the carbonyl-containing adducts (X = O) most certainly would undergo methoxy group elimination under the action of a Lewis acid, leading to the formation of α,β-unsaturated carbonyl derivatives.

‡ Adducts **1**–**3** were prepared using the equimolar quantities of the reactants in a CH_2Cl_2 solution under the conditions specified in Scheme 2. The identity of **1**–**3** was ascertained by ^{1}H NMR data. The *in situ*-prepared solutions of these adducts were used in further reactions.

§ TLC-monitored experiments ascertained the easiness of the formation of an ESI intermediate upon the treatment of **2** with a Lewis acid. Thus, it seems likely that the sluggishness of the overall transformation **2** → **6** could be explained by the 'hyperstabilization effect' of the intermediately formed electrophile due to the presence of the phenyl group at the reacting carbocationic centre.



Scheme 3

Previously,[4] it was found that the cleavage of a methoxy group from β-methoxyalkylaryl sulfides leading to the formation of ESI-like intermediates can be achieved under the action of Lewis acids.[4] The substrates employed in all these cases contained the properly positioned double bond or aromatic residue. Hence, the cationic species formed *in situ* were able to undergo an intramolecular reaction with these π-donors to give cyclization products. One might have anticipated that a similar ESI-like intermediate generated from **5** (ESI-II, Scheme 3) would also be useful as a carbon electrophile (E_C) in intermolecular reactions with various π-donors. However, the initial results of our experiments to employ adduct **5** as the precursor of electrophilic species were discouraging since in the presence of Lewis acids ($TiCl_4$, Et_2AlCl, TMSOTf and $SnCl_4$) no desired reaction occurred under mild conditions (at –70 to –20 °C) with even such a reactive carbon nucleophile as trimethylsiloxy cyclopent-1-ene **9** and only trace amounts of expected product **10** were formed under more severe conditions. We found that the desired transformation can be carried out under the action of an excess of the mixed Lewis acid TMSOTf–Et_2AlCl at 0–20 °C to give product **10** in a satisfactory yield (Scheme 3). The same reaction conditions are applicable to the Lewis acid-induced coupling of **5** with other π-donors like trimethylsilylketene acetal **11** or methallylsilane **13**, which furnished respective adducts **12** and **14**.†† As would be expected, the conversion of **6** into ESI-like electrophilic species and interaction of the latter with methallylstannane **7** or allenylstannane **16** proceeded under milder conditions (–30 °C, Et_2AlCl) and resulted in the formation of products **15** or **17** in good yields.

The above examples referred to the generation of ESI-II intermediates *via* the Lewis acid-induced removal of the methoxy group from the tertiary carbon atom. This approach was found

¶ The identity of all the mono- and 1,1-bisadducts was unambiguously established by ^1H and ^{13}C NMR spectroscopy and microanalysis. Yields refer to the isolated and purified products.

†† The typical experimental procedure is described for the conversion of adduct **5** into 1,1-bisadduct **12**: TMSOTf (0.4 ml, 2.2 mmol) was added to a stirred solution of Et_2AlCl (1.2 ml, 1.8 M solution, 2.2 mmol) in CH_2Cl_2 (5 ml) at 0 °C. After 5 min, a solution of ketene acetal **11** (150 mg, 0.86 mmol) and adduct **5** (110 mg, 0.43 mmol) in CH_2Cl_2 (5 ml) was added. After stirring for 30 min at room temperature, TLC data revealed the complete disappearance of the starting compound. The reaction mixture was quenched with $NaHCO_3$–H_2O–Et_2O; the organic layer was separated and dried over $MgSO_4$; the solvent was evaporated in a vacuum; the residue was subjected to preparative TLC to give analytically pure product **12** in 76% yield. ^1H NMR (250 MHz, $CDCl_3$) δ: 7.42 (d, 2H, *J* 8.3 Hz), 7.23 (d, 2H, *J* 8.3 Hz), 6.08–5.92 (m, 1H), 5.33–5.19 (m, 2H), 3.82 (s, 3H), 3.25 (s, 2H), 2.62–2.42 (m, 2H), 2.47 (s, 3H), 1.43 (s, 6H), 1.22 (s, 3H). Found (%): C, 70.38; H, 8.52; S, 10.40. Calc. for $C_{18}H_{26}O_2S$ (%): C, 70.54; H, 8.55; S, 10.46.

ineffective when we used an analogue of adduct **5** bearing a methoxy group at the secondary carbon atom (easily preparable from the ArSCl adducts with methyl vinyl ether following the general sequence shown in Scheme 2). Therefore, it was rather rewarding to find out that this goal could be achieved for acetoxy adduct **8** containing a better leaving group. The mixed Lewis acid TMSOTf–Et_2AlCl was found to be a preferable agent for the generation of ESI-II species. The reaction of the latter formed *in situ* with model carbon nucleophile **9** afforded expected adduct **18**.¶

Finally, we found that the transformations tentatively outlined in Scheme 1 could be carried out as a one-pot four-component coupling. Thus adduct **10** was formed in 36% yield as a result of the consecutive Lewis acid-induced reactions of *in situ* formed adduct **1** with silane **4** (Nu_C-I) followed by the treatment of arising adduct **5** with silyl enol ether **9** (Nu_C-II). Similarly, a one-pot procedure was also effective for the preparation of adducts **15** and **17** directly from α-methoxystyrene (*via* intermediate adducts **2** and **6**) in 65–70% overall yields.#

The typical experimental procedure is described for the one-pot preparation of **17**: β-methoxystyrene (45 mg, 0.33 mmol), allyltributyltin **4b** (120 mg, 0.37 mmol) and AgOTf (103 mg, 0.44 mmol) were added to a stirred solution of *p*-TlSCl (53 mg, 0.33 mmol) in CH_2Cl_2 (3 ml) at –50 °C. The reaction mixture was stirred for 1 h at –40 °C and additionally for 30 min at room temperature. After that the mixture was cooled down to –30 °C and tributylallenyltin **16** (91 mg, 0.26 mmol) and Et_2AlCl (0.56 ml, 1.8 M solution, 1 mmol) were added. TLC data revealed the complete conversion of adduct **6** into target compound **17**. The reaction mixture was quenched with $NaHCO_3$–H_2O–Et_2O; the organic layer was separated and dried over $MgSO_4$ and the solvent was evaporated in a vacuum. The residue was subjected to preparative TLC to give analytically pure product **17** in 60% yield. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 7.40–7.00 (m, 9H), 5.55–5.40 (m, 1H), 5.15–5.00 (m, 2H), 3.45 (s, 2H), 2.92 (dd, 1H, *J* 16.1 Hz, *J* 2.4 Hz), 2.79 (dd, 1H, *J* 16.1 Hz, *J* 2.4 Hz), 2.65–2.75 (m, 2H), 2.30 (s, 3H), 2.05 (t, 1H, *J* 2.4 Hz). Found (%): C, 82.37; H, 7.24; S, 10.41. Calc. for $C_{21}H_{22}S$ (%): C, 82.30; H, 7.24; S, 10.46.

The above results, preliminary as they are, nevertheless represent a 'proof-of-principle' evidence attesting to the promise of further studies in this area. Our current research efforts are aimed at the condition optimization and broadening the scope of the preparative application of the suggested novel 1,1-bisalkylation protocol with the help of cationic reactions as a potentially promising method of the multi-component coupling. It is also noteworthy that the described approach might be especially useful for the ready preparation of the polyfunctional adducts capable of serving as substrates for a number of intramolecular transformations such as Pauson–Khand alkyne–alkene–carbonyl cycloaddition (*e.g.* adduct **17**), ene reaction (adducts **10** or **18**) or cationic cyclization (adducts **14** or **15**).

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