Trimethylsilyl derivatives as final nucleophiles in the tandem sequence of an ArSCl–initiated Ad_E reaction resulting in the synthesis of polyfunctional compounds

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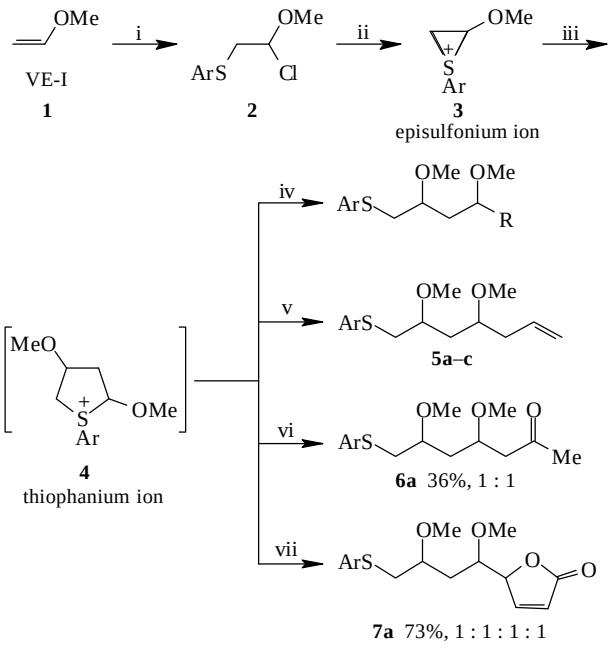
The use of allyl silanes and silyl vinyl ethers in the final step of a Lewis acid-mediated sequence involving reaction of ArSCl, two vinyl ether units and a *C*-nucleophile has been studied, thereby allowing introduction of functional groups into the four-component adduct.

Stepwise electrophilic addition reactions, in particular those where the cationoid intermediate (episulfonium ion, ESI) formed by the addition of aryl sulfenyl chloride to a double bond reacts with various *C*-nucleophiles to yield polyfunctional compounds, have been studied for some time by our group.[1] *C*-Nucleophiles included π-donors like aromatic and heteroaromatic compounds,[2] trimethylsilyl vinyl ethers,[3] allylsilanes[4] and alkyl vinyl ethers.[5] The last case was of special interest to us, since the ESI **3** formed by interaction of ArSCl with vinyl ether-I (VE-I) (see Scheme 1) reacts with a second vinyl ether (VE-II) to form another electrophilic intermediate, presumably the five-membered cyclic thiophanium ion **4** (TPI). Formation of TPI suggested an interesting synthetic opportunity of its utilisation as electrophile in the reactions with various carbon nucleophiles. Earlier[6] we described the reactions of TPI intermediates with organomagnesium reagents as one-pot, four-component coupling with the formation of two new C–C bonds (Scheme 1, path iv). It is necessary to note that the usage of Grignard reagents as final nucleophiles limits the nature of the substituents R in the product to alkyl, alkenyl and aryl groups.

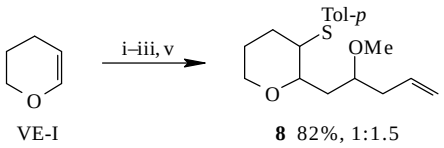
Thus, in order to broaden the list of functional groups introduced to a molecule, it was desirable to involve well-known π-donors like trimethylsilyl vinyl ethers, allylsilanes, as well as trimethylsilyl ketene acetals[7] in the final step of the reaction sequence. A preliminary study of this question showed that no significant reaction takes place at low (–78 to –20 °C) temperatures, while room temperature causes rapid decomposition of the reaction components resulting in a complex mixture of products which, however, contained trace amounts of the desired compounds.[8]

However, careful monitoring of the reaction in the temperature interval –20 to 20 °C showed that the TPI intermediate **4** formed by the reaction of 2 equiv. of the methyl vinyl ether **1** with *p*-TolSCl in CH_2Cl_2 at –78 °C is reasonably stable up to a temperature of 0 °C. The reaction of **4** with allyltrimethylsilane (path v) at this temperature proceeds slowly but eventually leads to the complete conversion of **4** into the product **5a** in the course of 5h, with a ratio 1 : 1.2 of the two expected diastereoisomers. 2-(Trimethylsilyloxy)propene and 2-(trimethylsilyloxy)furan also react with **4** under these conditions to yield products **6a** and **7a**, thus showing the possibility for carbonyl and lactone group introduction into a target molecule (paths vi and vii). In general, the products formed in the reaction are a mixture of all possible diastereoisomers.

The reaction of ArSCl with 2 equiv. of methyl vinyl ether and then with allyltrimethylsilane was chosen as a model for a preliminary study of the possible effects of factors such as the nature of the Lewis acid[9] and aryl group on the stereochemistry of the reaction. The change of the Lewis acid in some cases



	Ar	ratio of isomers for **5**	yield/%
a	*p*-Tol	1 : 1.2 ($TiCl_4$)	66
		1 : 1.6 ($SnCl_4$)	63
		1 : 1.1 ($ZnBr_2$)	65
b	*p*-ClC_6H_4	1 : 1.5 ($TiCl_4$)	77
c	2,4,6-$Me_3C_6H_2$	1 : 1.7 ($TiCl_4$)	40



Scheme 1 *Reagents and conditions:* i, ArSCl, CH_2Cl_2, –78 °C; ii, $TiCl_4$; iii, **1** (VE-II); iv, RMgX,[8] –78°C; v, allyltrimethylsilane, 0 °C, 5h; vi, 2-(trimethylsilyloxy)propene, 0 °C, 2 h; vii, 2-(trimethylsilyloxy)furan, 0 °C, 8 h.

($SnCl_4$, $ZnBr_2$) showed little or no effect on the diastereoisomeric ratio of the products (Scheme 1), while other

Lewis acids ($AgSbF_6$, $BF_3{\cdot}OEt_2$, $ZnCl_2{\cdot}OEt_2$, TMSOTf) turned out to be rather inefficient in promoting reaction of the TPI with allylsilane, even at room temperature. When the Ar group was changed from *p*-Tol to *p*-ClC_6H_4 and 2,4,6-$Me_3C_6H_2$ only a slight increase in the formation of one of the diastereoisomers was observed. Our previous observations[8] showed that when 2,3-dihydropyran was used as VE-I and RMgX as a nucleophile, the diastereoselectivity was very high (> 95%). But in our case the sequence *p*-TolSCl, 2,3-dihydropyran (VE-I), $TiCl_4$, methyl vinyl ether **1** (VE-II), allyltrimethylsilane, in CH_2Cl_2 (–78 °C, 5 h) again resulted in a mixture of diastereoisomeric *trans*-2-(2-methoxypent-4-enyl)-3-(*p*-tolylthio)tetrahydropyrans **8** in no better than a 1 : 1.5 ratio and 82% yield.†

Our current experiments include application of a wider selection of components in the sequence (VE-I, VE-II, Nu_C), as well as a search for other parameters (Lewis acid, solvent) which can enhance the stereoselectivity of novel C–C bond formation.

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† All new compounds synthesized were isolated using preparative column chromatography and had satisfactory elemental analysis data. Their structures were confirmed by ^1H, ^{13}C NMR and mass spectroscopic data.

8 (upper isomer), yield 33%, R_f =0.37 (hexane–EtOAc = 1 0 : 1); ^1H NMR ($CDCl_3$, TMS) δ 1.31–1.70 (m, 4H, CH_2CH_2-ring), 2.31 (s, 3H, MePh), 2.00–2.42 (m, 4H, C*H*$_2$CHOMeC*H*$_2$), 2.71 (dt, 1H, CHS; J_1 =3.9Hz, J_2 = 10.6Hz), 3.35 (s, 3H, MeO), 3.23–3.55 (m, 3H, CH_aOCH-ring, C*H*OMe), 3.89 (m, 1H, CH_eO-ring), 5.01 (m, 2H, CH_2=), 5.78 (m, 1H, CH=), 7.07 and 7.32 (2d, 4H-arom, J =8.0Hz); ^{13}C NMR ($CDCl_3$) δ 20.92 (*Me*Ph), 27.07 and 31.65 (CH_2CH_2-ring), 38.43 and 38.76 (*C*H$_2$CHOMe*C*H$_2$), 49.49 (CHS), 56.83 (MeO), 67.58 (CH_2O), 76.50 (*C*HOMe), 78.02 (CHO-ring), 116.83 (CH_2=), 129.39 (2CH-arom), 129.66 (CH=), 133.65 (2CH-arom), 134.68 and 137.32 (2C-arom); MS *m*/*z* 306 (M^+, 8%), 274 (7), 265 (12), 233 (3), 215 (4), 207 (100), 189 (57), 161 (37), 123 (22), 85 (50); HRMS: found *m*/*z* 306.1651; calc. for $C_{18}H_{26}O_2S$ (M^+) *m*/*z* 306.1654; elemental analysis: found C, 70.63; H, 8.49; S, 10.35%; calc. for $C_{18}H_{26}O_2S$: C, 70.54; H, 8.55; S, 10.46%.

8 (lower isomer), yield 49%, R_f =0.27 (hexane–EtOAc = 1 0 : 1); ^1H NMR ($CDCl_3$, TMS) δ 1.43–1.83 (m, 4H, CH_2CH_2-ring), 2.32 (s, 3H, MePh), 2.03-2.47 (m, 4H, C*H*$_2$CHOMeC*H*$_2$), 2.81 (dt, 1H, CHS; J_1 =4.0Hz, J_2 = 10.6Hz), 3.34 (s, 3H, MeO), 3.19–3.55 (m, 3H, CH_aOCH-ring, C*H*OMe), 3.90 (m, 1H, CH_eO-ring), 5.10 (m, 2H, CH_2=), 5.88 (m, 1H, CH=), 7.09 and 7.31 (2d, 4H-arom, J =8.0Hz); ^{13}C NMR ($CDCl_3$) δ 21.06 (*Me*Ph), 27.02 and 31.92 (CH_2CH_2-ring), 36.98 and 37.55 (*C*H$_2$CHOMe*C*H$_2$), 49.82 (CHS), 56.32 (MeO), 67.71 (CH_2O), 77.64 (*C*HOMe), 78.63 (CHO-ring), 116.75 (CH_2=), 129.60 (2CH-arom), 129.87 (CH=), 133.49 (2CH-arom), 135.01 and 137.47 (2C-arom); MS *m*/*z* 306 (M^+, 12%), 274 (5), 265 (15), 233 (4), 215 (10), 207 (100), 189 (67), 161 (17), 123 (32), 85 (97); HRMS: found *m*/*z* 306.1657; calc. for $C_{18}H_{26}O_2S$ (M^+) *m*/*z* 306.1654; elemental analysis: found C, 70.55; H, 8.63; S, 10.37%; calc. for $C_{18}H_{26}O_2S$: C, 70.54; H, 8.55; S, 10.46%.

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