Tandem sequence of ArSCl initiated Ad_E reactions resulting in formation of two C–C bonds

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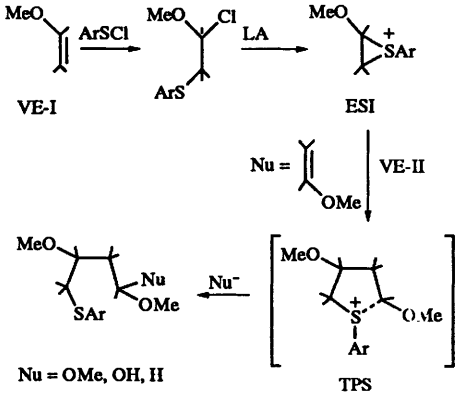
A one-pot procedure for the sequence of reactions between arylsulfanyl chloride, vinyl ether-I, vinyl ether-II and organomagnesium reagents has been developed for assembling polyfunctional compounds from simple precursors. 2,3-Dihydropyran and various vinyl ethers have been used as VE-I and/or VE-II. The dependence of the stereochemical course of the carbon–carbon bond formation step upon the Lewis acid has been studied. In the case of the sequence *p*-tolylsulfanyl chloride, 2,3-dihydropyran, 1-methoxy-2-methylpropene and Grignard reagent the reaction initiated with $TiCl_4$ takes place with a very high diastereoselectivity (> 95%).

As reported earlier, various β-arylsulfanylalkyl chlorides (adducts of alkenes with arylsulfanyl chlorides) are able to react with π-donors such as aromatic compounds,[1a] trimethylsilyl vinyl ethers,[1b] allylsilanes[1c] or trimethylsilylketene acetals[1d] in the presence of Lewis acids (LA) with the formation of the corresponding γ-arylsulfanylalkylated products. The intermediate formation of episulfonium ions (ESIs) as electrophilic species was substantiated by the exclusive Markovnikov regioselectivity of the reaction and its *trans* stereospecificity.[1e] Especially promising preparative results were obtained when vinyl ethers (VE) were used both as alkenes for the generation of ESIs and then as the π-donors at the alkylation step (VE-I and VE-II, respectively, see Scheme 1).[2a–c] This reaction led to the formation of γ-arylsulfanyl-substituted aldol-like products, useful intermediates in the synthesis of polyfunctional compounds. Surprisingly, no oligomerization was noticed in this reaction, although formation of higher oligomers is a typical complication in the course of many Ad_E (electrophilic addition) alkylations of vinyl ethers.[3] It was also discovered that the final outcome of the reaction may vary depending on the nature of the nucleophile (Nu) used for the quenching of the reaction mixture. Thus, carbonyl compounds can be obtained upon the usual aqueous work-up, while acetals or ethers are formed if alcohols or hydride donors are used as the quenchers, respectively. These data suggested a stepwise mechanism for the whole sequence that envisaged: (i) formation of the first cationoid intermediate, ESI (upon the interaction of the preformed adduct ArSCl–VE-I with LA), (ii) alkylation of VE-II with ESI as an electrophile, leading to the formation of the second cationoid intermediate, presumably the tetrahydrothiophenium salt (TPS)[4] and (iii) interaction of the latter with Nu upon the final quenching of the reaction mixture.

These data also offered a challenging synthetic opportunity to be realized if carbon nucleophiles (Nu_C) are used as the final quenchers at step (iii). Here we present results,[5] which demonstrate the viability of this option, at least for certain types of Nu_C.

Results and discussion

Initial attempts were aimed at the utilization of π-donors like trimethylsilyl vinyl ethers or allylsilanes as Nu_C. However, trial experiments performed with the reaction complex obtained upon the coupling of adduct **2** (formed *in situ* by the reaction



Scheme 1

of **1** with ArSCl)[6] with **3** in the presence of $TiCl_4$ revealed that no reaction with these π-donors occurred at low temperature (−78–20 °C),[7] while an extensive decomposition occurred at elevated temperatures. The complex mixture of the products thus formed contained only trace amounts of the desired products, corresponding to the quenching of TPS **4** with these nucleophiles (MS data).

Rewardingly, the desired coupling was realized with stronger nucleophiles, namely Grignard reagents. Thus, treatment of the same complex **4** with allylmagnesium chloride led to the formation of the corresponding allylation product **5** in good yield (Scheme 2).† In a similar way, complex **6**, formed with the use of **1** as both VE-I and VE-II, reacted with 2-methylallylmagnesium chloride giving adduct **7**. The utilization of **8** as VE-I, **1** as VE-II, and phenylmagnesium bromide as the Nu_C for quenching of complex **9** gave phenyl derivative **10** (Scheme 2).

Attempts to use methyl- or vinyl-magnesium halides as nucleophiles failed. Thus, no reaction of **4** with these reagents occurred at −78 °C, and intensive decomposition was observed upon temperature increase.

Compounds **5**, **7** and **10** were isolated as mixtures of diastereoisomers (**a**, **b**). Ratios given were determined by ^1H

† The yields given refer to the isolated products. No special attempts were made to optimize the reaction conditions.

NMR and/or GC–MS data. The stereochemistry of the reaction was shown to be sensitive to variations in the nature of the Lewis acid (see respective data for **5** in Scheme 2). The best ratio of **5a**:**5b** = 9:1 was achieved with $AgBF_4$, while slightly reverse selectivity was observed for TMSOTf. Analysis of available NMR data did not permit configurational assignments in this series. Therefore it is premature to discuss the observed pattern of the reaction diastereoselectivity. Nevertheless, one may safely claim that further studies of this aspect are most certainly warranted, especially in view of plethora of published data referring to the opportunity to control the stereochemical outcome of related reactions by the proper choice of reaction parameters.[8]

Variability in the stereochemistry of the coupling was also observed for the cases when dihydropyran **11** was employed as VE-I. In fact, interaction of adduct **12** (prepared *in situ* by an addition of *p*-TolSCl to **11**) with **3** in the presence of $TiCl_4$ gave a complex, which was quenched with 2-methylallylmagnesium chloride with the formation of adduct **13a** (Scheme 3) as virtually the only stereoisomer (purity 95%, ^1H NMR and GC–MS data). A similar reaction carried out in the presence of $SnCl_4$ produced the same adduct but as a 1:1 mixture of isomers **13a**, **b**. These stereoisomers were separated by HPLC and the structure of the sulfone of one of them [**13a**, with relative configuration (2*S*,2′*S*,3*R*)-(2′-methoxy-1′,1′,4′-trimethylpent-4′-enyl)-3-(*p*-tolylsulfanyl)pyran (rel. config.)] was determined by X-ray crystallography (see Fig. 1). Interestingly the use of $AgBF_4$ instead of $TiCl_4$ led to a reversal of the stereoselectivity and isomer **13b**, (2*S*,2′*R*,3*R*)-(2′-methoxy-1′,1′,4′-trimethylpent-4′-enyl)-3-(*p*-tolylsulfanyl)pyran, became the predominate component in the mixture, the ratio of isomers being also dependent on the nature of the ArSCl electrophile (see data in Scheme 3). We cannot presently explain the rather significant changes in stereoselectivity that are observed upon changing the Lewis acid.

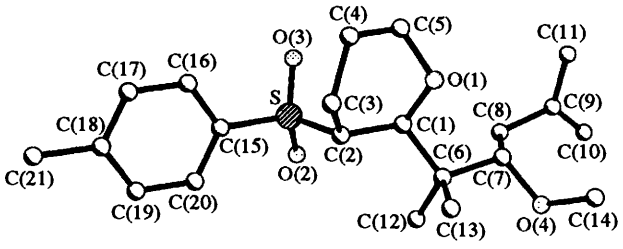
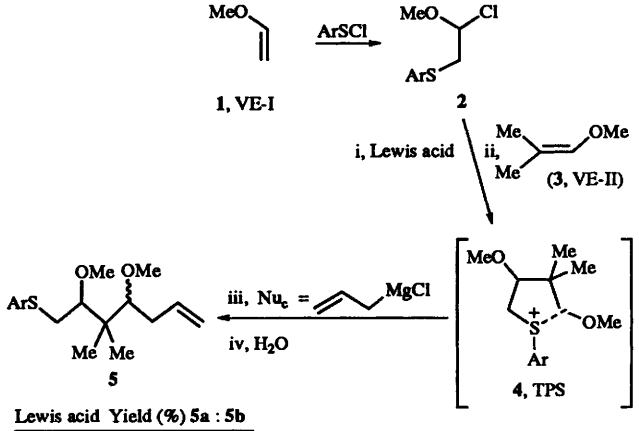
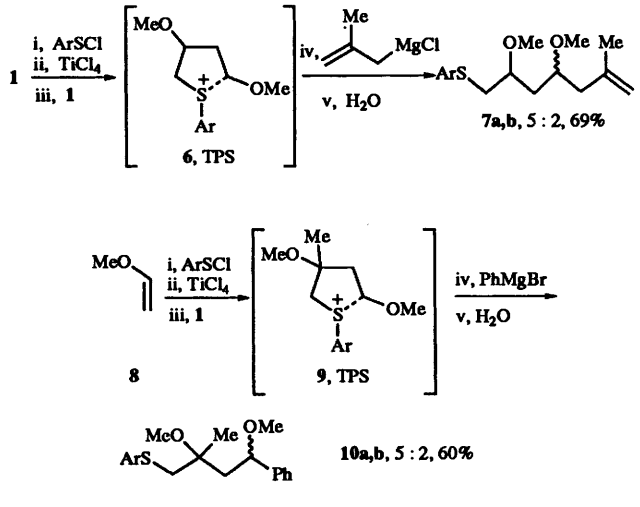


Fig. 1 Schematic drawing of sulfone of **13a** from crystal structure determination

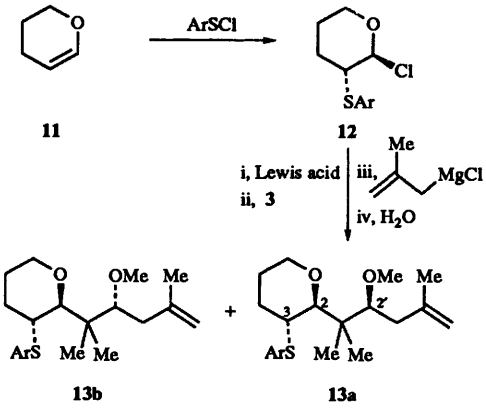


Lewis acid	Yield (%)	5a : 5b
$TiCl_4$	67	3 : 2
$SnCl_4$	73	4 : 3
$ZnCl_2$	50	3 : 1
$AgBF_4$	68	9 : 1
BF_3•Et_2O	78	7 : 1
TMSOTf	50	3 : 4

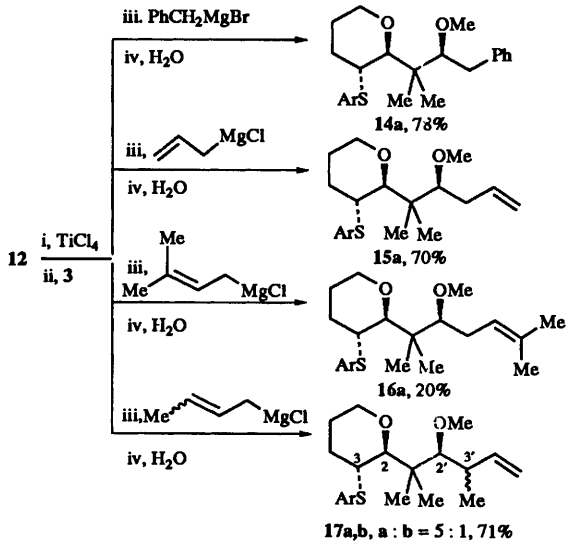


Ar = *p*-MeC_6H_4 in all cases, except those specified

Scheme 2



Lewis acid	Yield (%)	13a : 13b
$TiCl_4$	62	> 19 : 1
$SnCl_4$	60	1 : 1
$AgBF_4$	56	1 : 3
$AgBF_4$	52	2 : 3 (Ar = *p*-ClC_6H_4)

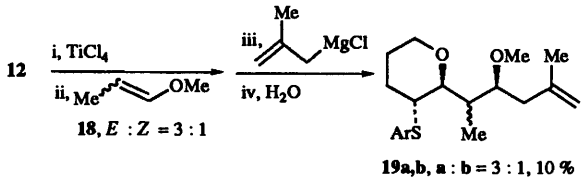


Scheme 3

Table 1 Characteristic ^{1}H NMR data for compounds **13a**, **13b** and **14a–16a**[a]

Compound	δ, CMe_2	$\Delta\delta$, CMe_2	J, $CHOCH_3$	ΔJ, $CHOCH_3$	$J_{1,2}$
13a	1.11, 1.16	0.05	J_1 2.75 J_2 8.5	5.75	8.6
13b	0.94, 1.095	0.155	J_1 5.0 J_2 7.2	2.2	7.6
14a	1.18, 1.21	0.03	J_1 2.1 J_2 9.6	7.5	8.6
15a	1.12, 1.15	0.03	J_1 3.2 J_2 8.7	5.5	8.5
16a	1.11, 1.14	0.03	J_1 3 J_2 9	6	8.2

[a] J Values are given in Hz.



Scheme 4

Similarly, the exclusive formation (within the limits of detection by ^{1}H NMR) of single diastereoisomers (among the four possible) **14a**, **15a** and **16a** was observed in $TiCl_4$ mediated reactions of **12** with **3** when allyl-, 1,1-dimethylallyl- and benzylmagnesium derivatives were used as Nu_C, respectively. The structures of these compounds were assigned on the basis of NMR data and comparison with the adduct **13a** with established stereochemistry (see Table 1).

The utilization of crotylmagnesium chloride (as a mixture of *Z*- and *E*-isomers, *ca.* 1:3) in this sequence gave nearly exclusively the product of S_N2' attack **17a**, **b** as a mixture of diastereoisomers at C-3′ in a ratio of 5:1 (see Scheme 4). Thus, a high diastereoselectivity can be also achieved even in the case when four chiral centres are formed from achiral precursors.

Attempts to utilize methyl propenyl ethers **18** as VE-II in this sequence were not especially successful preparatively since the yield of the target adduct **19** did not exceed 10% (in this case the major complications were due to the ease of polymerization of this VE). However, preliminary data suggest that the coupling proceeded with a high stereoselectivity since the ratio **19a**:**19b** determined roughly reflects the ratio of isomers (3:1) in the starting mixture of *E*,*Z*-isomers of **18**.

Conclusions

The reactions shown in Schemes 2–4 were carried out as a one pot four component coupling resulting in the formation of two novel C–C bonds. The viability of these one pot reactions is based on the sequential formation of two discrete cationoid intermediates, ESI and TPS (see Scheme 1). In this way the starting electrophile ArS^+ is employed as a sewing tool for consecutive stitching of three nucleophilic components. The promise of this coupling for the elaboration of a convergent and general protocol for the assembly of polyfunctional molecules from simple precurors seems to be obvious, especially in view of the existing data attesting to the opportunity to control the stereochemical outcome of the reaction. Its application for the synthesis of chiral intermediates from chiral vinyl ethers, like protected glucals, is now under intensive study.

It is also appropriate to note that the results of this study in conjunction with the previously reported data referring to the peculiarities of Ad_E reactions across double bond of dicobalt hexacarbonyl complexes of conjugated enynes may serve as a convincing illustration of the generality and fruitfulness of the novel approach based on the idea of the channelling Ad_E reactions *via* a truly stepwise mode.[9]

Experimental

General

^{1}H and ^{13}C NMR spectra were recorded on Bruker WM-250 and Bruker MA-300 spectrometers and chemical shifts are given in ppm relative to $CHCl_3$. Coupling constants, J, are reported in Hz. Mass spectrometric data were obtained on Varian MAT CH-6 and GC–MS on a Hewlett-Packard 5790 GS with a Hewlett-Packard 5970 mass selective detector (70 eV). The column was a 30 m × 0.25 mm ID J&W Scientific, Inc. DB5 coated capillary. Elemental analyses were performed by the microanalysis laboratory of the Zelinsky Institute of Organic Chemistry. Preparative TLC was carried out by using glass plates, 200 × 250 mm, with an unfixed layer of Merck silica gel 60, 230–400 mesh. Analytical TLC was performed on Merck precoated 0.2 mm plates of silica gel 60 F_{254}. All reactions were carried out under an atmosphere of dry argon using oven-dried or flame-dried glassware and freshly distilled and dried solvents. Ether refers to diethyl ether.

Arylsulfanyl chlorides were obtained *via* a reaction of the corresponding benzenethiols with SO_2Cl_2 in CCl_4 at −10 °C. Methyl vinyl ether was synthesized from butyl vinyl ether in the presence of $Hg(OAc)_2$.[10] 1-Methoxyprop-1-ene and 1-methoxy-2-methylprop-1-ene were obtained by pyrolysis of the corresponding methyl acetals in the presence of toluene-*p*-sulfonic acid.[11] Other chemicals are commercially available. Adducts of alkenes with ArSCl were obtained at −78 °C by adding a solution of the corresponding vinyl ether to ArSCl in CH_2Cl_2 until the orange colour disappeared and were used *in situ* without purification.

X-Ray crystallography of sulfone of 13a

$C_{21}H_{32}O_4S$, M = 380.53, orthorhombic, space group *Pbca*, a = 23.98(1), b = 7.000(3), c = 24.926(8) Å, V = 4184(3) Å^3, λ = 0.710 73 Å, Z = 8, D_c = 1.208 g cm^{-3}, $F(000)$ = 1648.0, μ = 0.177 mm^{-1}, Enraf-Nonius diffractometer, room temperature, crystal size 0.40 × 0.35 × 0.10 mm^3, 2748 total reflections ($3 < 2\theta < 45°$). Data reduction and solution refinement were carried out using standard crystallographic programs NRCVAX-PC and SHELXL-93.[12] The structure was solved by direct methods and subsequent difference Fourier synthesis. All nonhydrogen atoms were refined anisotropically with refinement on F_o^2. Hydrogen atoms were calculated on idealized positions and included in the final refinement with fixed thermal parameters. Final residual values for refinement on F_o^2 for 1142 reflections with $I > 2\sigma(I)$ were R_1 and wR_2 0.0494 and 0.1063, respectively; $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma w(F_o^2)^2\}^{0.5}$. Atomic coordinates,

thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.‡

General procedure

A solution of vinyl ether **1** (1.00 mmol) (VE-1) in CH_2Cl_2 (1 cm^3) was added to a solution of ArSCl (1.00 mmol) in CH_2Cl_2 (10 cm^3) at −78 °C (colour changed from yellow to colourless). A solution of vinyl ether **3** (1.20 mmol) (VE-II) in CH_2Cl_2 (2 cm^3) was added over 5 min. A solution of Lewis acid (1.20 mmol) in CH_2Cl_2 (2 cm^3) was then added. The mixture was stirred for 30 min at −78 °C and then a solution of Grignard reagent in ether (1 mol dm^{-3}; 2.00 mmol) was added. After stirring for 1 h at −78 °C, the mixture was quenched with saturated aqueous $NaHCO_3$, extracted with ether and then dried over Na_2SO_4. Preparative TLC (ether–hexane, 1:4) of the crude material, after removing the solvent under reduced pressure, afforded the pure substance.

4,6-Dimethoxy-5,5-dimethyl-7-(*p*-tolylsulfanyl)heptene 5. Yield 78% (using $BF_3{\cdot}Et_2O$, for other Lewis acids see Scheme 2), R_f (ether–hexane, 1:1) 0.81; n_D^{20} 1.5257; ν_{max}(neat)/cm^{-1} 1640 (C=C); δ_H 0.86 and 0.97 [2 × s, 6 H, $C(CH_3)_2$], 2.15 (1 H, m, $J_{3,3'}$ 15.5, CHCH=), 2.35 (1 H, m, CHCH=), 2.33 (3 H, s, CH_3), 2.92 (1 H, A-part ABX-system, J_{AB} 14, J_{AX} 9.4, SCH^A), 3.10 (1 H, X-part of A'B'X'-system, $J_{A'X'}$ 8.25, $J_{B'X'}$ 3.5, 4-H), 3.24 (1 H, B-part of ABX-system, J_{AB} 14, J_{BX} 2.4, SCH^B), 3.25 (1 H, X-part of ABX-system, J_{AX} 9.4, J_{BX} 2.4, 6-H), 3.35, 3.52 (6 H, 2 × s, 2 × OCH_3), 5.06 and 5.92 (3 H, m, $J_{1,2}$ 17.5, $J_{2,3}$ 14.5, $J_{1',2}$ 10.5, $J_{2,3'}$ 7.3, $CH{=}CH_2$) and 7.21 (4 H, m, ArH); δ_C 20.00, 21.07 (3 × CH_3), 35.62 ($CH_2C{=}$), 37.52 (CS), 44.35 [$C(CH_3)_2$], 59.97, 61.32 (2 × OCH_3), 85.79, 86.06 (2 × OCH), 116.19 (=CH_2), 129.80, 130.25, 133.75 (ArC) and 137.34 (=CH); *m/z* 308 (M^+) (Found: C, 70.1; H, 9.0; S, 10.4. Calc. for $C_{18}H_{28}O_2S$: C, 70.08; H, 9.15; S, 10.39%).

4,6-Dimethoxy-2-methyl-7-(*p*-tolylsulfanyl)heptene 7. Yield 69% (two diastereoisomers, ratio 3:1), R_f (ether–hexane, 1:1) 0.60; δ_H 1.76 (3 H, s, CH_3), 1.82 (2 H, t, *J* 6, $CHCH_2CH$), 2.13 (2 H, m, $CH_2CH{=}$), 3.08 (2 H, AB-part of ABX-spectrum, J_{AB} 13, $J_{AX} = J_{BX}$ = 6, SCH_2), 3.12 and 3.14 (2 H, 2 × s, OCH_3), 3.48 (2 H, m, 2 × $CHOCH_3$), 4.73 and 4.81 (2 H, 2 × s, =CH_2) and 7.20 (4 H, m, ArH). Minor diastereoisomer: δ_H 1.67 (t, $CHCH_2CH$) and 3.15, 3.18 (2 × s, 2 × OCH_3) (Found: 294.1653. Calc. for $C_{17}H_{26}O_2S$: (M^+) *m/z*, 294.1647).

2,4-Dimethoxy-2-methyl-4-phenyl-1-(*p*-tolylsulfanyl)butane 10. Yield 60% (two diastereoisomers, ratio 3:1), R_f (ether–hexane, 1:2) 0.50; δ_H 1.42 and 1.28 (3 H, 2 × s, CH_3), 1.93 (2 H, AB-part of ABX-spectrum, J_{AB} 15, J_{AX} 2.75, J_{BX} 2.5, $PhCHCH_2$), 2.31 (3 H, s, CH_3), 3.15–3.25 (8 H, 6 × s, SCH_2 and 2 × OCH_3), 4.32 (1 H, X-part of ABX-spectrum, CHPh) and 7.2 (m, 9 H, ArH) (Found: C, 72.8; H, 8.1; S, 9.75. Calc: for $C_{20}H_{26}O_2S$: C, 72.69; H, 7.93; S, 9.70%).

2-(2'-Methoxy-1',1',4'-trimethylpent-4'-enyl)-3-(*p*-tolylsulfanyl)pyran 13a, b. Yield 62% ($TiCl_4$, one isomer **13a**), 68% ($SnCl_4$, two isomers **13a** and **13b**, ratio 1:1), R_f (ether–hexane, 1:2) 0.74.

(2*S*,2'*S*,3*R*)-Isomer **13a**: δ_H 1.11 and 1.16 [6 H, 2 × s, $C(CH_3)_2$], 1.60 and 1.97 (4 H, 2 × m, CH_2CH_2), 2.14 (2 H, m, $CH_2C{=}$), 2.34 (3 H, s, CH_3), 3.12 (1 H, d, *J* 8.5, CHCHO), 3.21 [1 H, td, J_t 8.6, J_d 4 (this value was taken from spectrum in C_6D_6), SCH], 3.33 (1 H, td, J_t 11, J_d 5.25, OCH_{ax}), 3.41 (3 H, s, OCH_3), 3.53 (1 H, X-part of ABX-spectrum, $J_{AX} = J_{BX}$ = 2.75, $CHOCH_3$), 3.93 (1 H, m, OCH_{eq}), 4.79 and 4.87 (2 H, 2 × s, =CH_2) and 7.21 (4 H, m, ArH); δ_C 19.23, 19.58, 21.13 and 22.65 (4 × CH_3), 24.91 and 30.77 (CH_2CH_2), 39.34 ($CH_2C{=}$), 43.63 [$C(CH_3)_2$], 46.72 (CHS), 60.93 (OCH_3), 67.24 (OCH_2), 84.23 and 85.35 (2 × OCH), 112.32 (=CH_2), 129.74, 130.68, 133.23, 137.34 and 144.56 (ArC, =CCH_3).

(2*S*,2'*R*,3*R*)-Isomer **13b**: δ_H 0.94 and 1.095 [6 H, 2 × s, $C(CH_3)_2$], 1.55–2.0 (4 H, m, CH_2CH_2), 1.85 (3 H, s, CH_3), 2.18 (2 H, d, *J* 6.2, $CH_2CH{=}$), 2.34 (3 H, s, CH_3), 3.25 (1 H, m, SCH), 3.33 (1 H, d, *J* 7.6, OCHCHS), 3.41 (3 H, s, OCH_3), 3.45 (1 H, m, $CH_{ax}O$), 3.65 (1 H, X-part of ABX-spectrum, $J_{AX} = J_{BX}$ = 5.2, $CHOCH_3$), 4.81 and 4.88 (2 H, 2 × s, =CH_2) and 7.22 (4 H, m, ArH); δ_H 18.68, 18.75, 21.15 and 22.99 (4 × CH_3), 23.08 and 28.59 (CH_2CH_2), 39.60 ($CH_2C{=}$), 43.58 [$C(CH_3)_2$], 46.32 (CHS), 60.30 (OCH_3), 66.14 (OCH_2), 83.23 and 83.38 (OCH, CH_3OCH), 112.65 (=CH_2) and 129.79, 131.25, 133.06, 137.30 and 144.51 (ArC, =CCH_3). For the mixture of isomers: *m/z* 348 (M^+) (Found: C, 72.55; H, 9.25; S, 9.3. Calc. for $C_{21}H_{32}O_2S$: C, 72.37; H, 9.25; S, 9.20%).

2-(2-Methoxy-1,1-dimethyl-3-phenylpropyl)-3-(*p*-tolylsulfanyl)pyran 14a. Yield 78%, R_f (hexane–ether, 3:1) 0.60; mp 109–111 °C; δ_H 1.32 and 1.39 [6 H, 2 × s, $C(CH_3)_2$], 1.56 and 1.97 (4 H, 2 × m, CH_2CH_2), 2.14 (3 H, s, CH_3), 2.60 and 2.83 (2 H, AB-part of ABX-spectrum, J_{AB} 13.6, J_{AX} 9.6, J_{BX} 2.1, CH_2Ph), 3.00 (3 H, s, OCH_3), 3.12 (1 H, m, OCH_{ax}), 3.21 (1 H, d, *J* 8.6, OCHCHS), 3.30 (1 H, m, CHS), 3.66 (1 H, X-part of ABX-spectrum, H_3COCH), 3.82 (1 H, m, OCH_{eq}) and 7.25 (9 H, m, ArH); δ_C 19.23, 19.81 and 21.13 (3 × CH_3), 24.99 and 30.85 (CH_2CH_2), 37.12 ($PhCH_2$), 43.70 [$C(CH_3)_2$], 46.77 (CHS), 61.19 (OCH_3), 67.40 (OCH_2), 85.42 and 88.11 (OCHCHS, MeOCH) and 125.64, 126.01, 128.11, 129.52, 129.74, 130.63, 133.26, 133.68, 137.34 and 141.37 (ArC); *m/z* 384 (M^+) (Found: C, 74.7; H, 8.25; S, 8.6. Calc. for $C_{24}H_{32}O_2S$: C, 74.95; H, 8.39; S, 8.34%).

2-(2-Methoxy-1,1-dimethylpent-4-enyl)-3-(*p*-tolylsulfanyl)-pyran 15a. Yield 70%, R_f (hexane–ether, 3:1) 0.58; n_D^{20} 1.5380; δ_H 1.12 and 1.15 [6 H, 2 × m, $C(CH_3)_2$], 1.61 and 1.97 (4 H, 2 × m, CH_2CH_2), 2.17 (2 H, m, $CH_2C{=}$), 2.35 (3 H, s, CH_3), 3.14 (1 H, d, *J* 8.5, OCHCHS), 3.27 (1 H, m, CHS), 3.37 (1 H, m, OCH_{ax}), 3.46 (3 H, s, OCH_3), 3.49 (1 H, dd, J_1 3.2, J_2 8.7, $CHOCH_3$), 3.92 (1 H, m, OCH_{eq}), 5.06 (2 H, m, =CH) and 7.23 (4 H, m, ArH); *m/z* 334 (M^+) (Found: C, 71.61; H, 9.14; S, 9.16. Calc. for $C_{20}H_{30}O_2S$: C, 71.81; H, 9.03; S, 9.59%).

2-(2-Methoxy-1,1,5-trimethylhex-4-enyl)-3-(*p*-tolylsulfanyl)-pyran 16a. Yield 20%, R_f (hexane–ether, 3:1) 0.60; δ_H 1.11 and 1.14 [6 H, 2 × s, $C(CH_3)_2$], 1.60 and 1.97 (4 H, 2 × m, CH_2CH_2), 1.68 and 1.73 [6 H, 2 × s, $=C(CH_3)_2$], 2.09 (2 H, m, $CH_2C{=}$), 2.36 (3 H, s, CH_3), 3.14 (1 H, d, *J* 8.2, OCHCHS), 3.22 (1 H, m, CHS), 3.31 (1 H, dd, J_1 3, J_2 9, $CHOCH_3$), 3.37 (1 H, m, OCH_{ax}), 3.41 (3 H, s, OCH_3), 3.92 (1 H, m, OCH_{eq}), 5.31 (1 H, m, =CH) and 7.25 (4 H, m, ArH); *m/z* 362 (M^+) (Found: C, 72.8; H, 9.5; S, 8.7. Calc. for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84%).

2-(2-Methoxy-1,1,7-trimethylpent-4-enyl)-3-(*p*-tolylsulfanyl)-pyran 17a, b. Yield 71%, R_f (hexane–ether, 2:1) 0.75; δ_H(major isomer) 1.07 (3 H, d, CH_3), 1.10 [6 H, s, $C(CH_3)_2$], 1.59 and 1.91 (4 H, 2 × m, CH_2CH_2), 2.31 (3 H, s, CH_3), 2.45 (1 H, m, $CHCH_3$), 3.15 (1 H, m, OCH_{ax}), 3.20 (1 H, m, CHS), 3.23 (1 H, d, *J* 11.1, CHCHS), 3.40 (3 H, s, OCH_3), 3.89 (1 H, m, CH_{eq}), 4.95 (2 H, m, =CH_2), 5.95 (1 H, m, =CH) and 7.20 (4 H, m, ArH) (Found: *m/z* 348.2122. Calc. for $C_{21}H_{32}O_2S$ (M^+) *m/z* 348.2115).

2-(2-Methoxy-1,4-dimethylpent-4-enyl)-3-(*p*-tolylsulfanyl)-pyran 19a, b. Yield 10% (using $TiCl_4$), 9% ($AgBF_4$), R_f (hexane–ether, 3:1) 0.56. Isomer **19a**: δ_H 0.90 (3 H, d, *J* 6.8, CH_3CH), 1.60 (4 H, m, CH_2CH_2), 1.80 (3 H, s, $CH_3C{=}$), 2.20 (2 H, m, $CH_2C{=}$), 2.34 (3 H, s, CH_3), 2.51 (1 H, qd, $J_1 = J_2$ = 6.8, J_3 1.8, CH_3CH), 2.97 (1 H, td, $J_1 = J_2$ = 10.5, J_3 3.7, CHS), 3.30 (1 H, m, OCH_{ax}), 3.37 (3 H, s, OCH_3), 3.40 (1 H, dd, J_1 10.5, J_2 1.8, OCHCHS), 3.60 (1 H, ddd, J_1 10, J_2 6.8, J_3 3.5, $CHOCH_3$), 3.89 (1 H, m, OCH_{eq}), 4.80 (2 H, s, =CH_2) and 7.23 (4 H, m, ArH).

Isomer **19b**: δ_H 1.01 (3 H, d, *J* 6.8, CH_3CH), 1.60 (4 H, m,

‡ For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, 1995, Issue 1.

CH_2CH_2), 1.80 (3 H, s, CH_3CH=), 2.09 (1 H, dd, J_1 15, J_2 9.25, CH_2C=), 2.35 (3 H, s, CH_3), 2.44 (1 H, d, J 15, CH_2C=), 2.66 (1 H, m, J_1 7.2, J_2 4.5, J_3 3.3, $CHCH_3$), 3.11 (1 H, m, CHS), 3.25 (1 H, dd, J_1 9.8, J_2 3.3, OC*H*CHS), 3.30 (1 H, m, OCH_{ax}), 3.39 (3 H, s, OCH_3), 3.66 (1 H, ddd, J_1 9.25, J_2 4.5, J_3 2.5, $CHOCH_3$), 3.92 (1 H, m, OCH_{eq}), 4.78 (2 H, s, $=CH_2$) and 7.23 (4 H, m, ArH). MS m/z 334 (M^+) (Found: C, 71.75; H, 9.1; S, 9.5. Calc. for $C_{20}H_{30}O_2S$: C, 71.81; H, 9.04; S, 9.59%).

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