SULFOXIDE-MODIFIED JULIA–LYTHGOE OLEFINATION: HIGHLY STEREOSELECTIVE DI-, TRI-, AND TETRASUBSTITUTED DOUBLE BOND FORMATION

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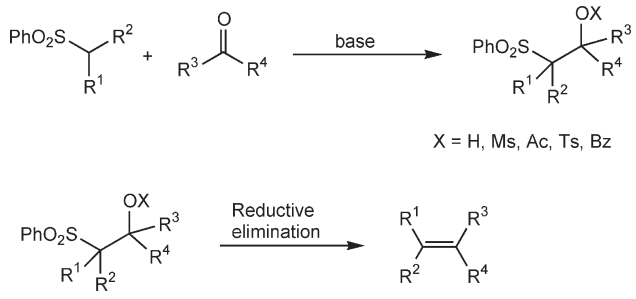
A novel modification of the classical Julia–Lythgoe olefination, using sulfoxides instead of sulfones, affords, after in situ benzoylation and SmI_2/HMPA or SmI_2/DMPU-mediated reductive elimination, 1,2-di-, tri- and tetrasubstituted olefins in moderate to good yields and *E*/*Z* selectivity. The conditions are mild and the procedure is widely applicable. The reaction mechanism was studied and a general model, describing the reaction selectivity, is proposed.
Keywords: Olefinations; Samarium; Reaction mechanisms; Additions; Synthetic methods; Julia–Lythgoe olefination; Sulfoxides; Alkenes; Reductive elimination.

The Julia olefination ranks among most powerful methods for the formation of C–C double bonds in modern organic chemistry. Originally, this procedure was based on the reaction of sulfones with carbonyl compounds. In the first step, an anion in α-position to sulfone group was added to a carbonyl compound, furnishing the corresponding β-hydroxysulfone[1] (Scheme 1). In the second step, this β-hydroxysulfone was treated with Na–Hg and underwent reductive elimination to give the desired olefin. Later on, it was observed that the transformation of the alcohol function of the β-hydroxysulfone into a better leaving group led to increased yields in the reductive-elimination step. Therefore, β-mesyloxy- or (acyloxy)sulfones are preferentially used nowadays as the intermediates subjected to the reductive elimination. As an additional advantage, acylating or mesylating reagents can be employed as trapping agents during the addition of the sulfonyl anion to the carbonyl function. The in situ capture of the β-alkoxysulfone anion intermediate further increases the yields of the addition step. Gradually, the original reductive-elimination method using Na–Hg amalgam has been superseded by mild, more selective and less toxic reducing agents such as SmI_2 (ref.[2]) or Mg (ref.[3]).

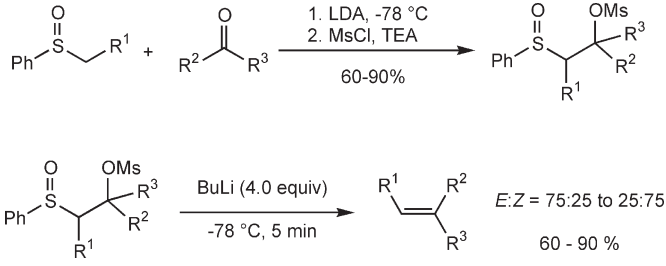


SCHEME 1

Disappointingly, this widely used method still suffers from several drawbacks. One of them is the relatively high stability of the sulfonyl anion which limits its reactivity. For example, if an additional electron-withdrawing substituent is present on the anion-bearing carbon, this negatively charged organometallic species becomes so stable that it does not add even to activated aldehydes[2c]. Moreover, in the case of the reaction of unstabilized sulfones with hindered aldehydes and with ketones, the position of the equilibrium between the starting carbonyl compounds and the sulfone anion is shifted towards the reactants. The desired adduct (tertiary alkoxide) is therefore present in the reaction mixture as a minor component. Trapping this intermediate in situ with some electrophiles, such as benzoyl chloride, mesyl chloride or acyl chloride, is a common trick employed to shift the equilibrium towards the products. However, in the case of highly crowded sulfones and/or ketones, even if the electrophile-trapping protocol is employed, the addition reaction does not proceed at all or only in a very low yield.

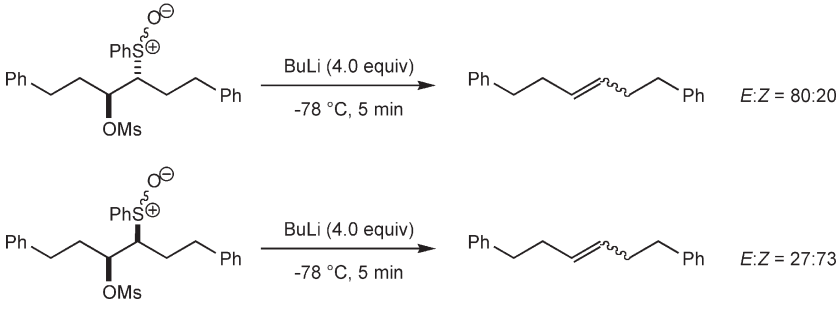
Moreover, this in situ capture method is not useful if the anion α to the sulfone is so stable that it does not add even to highly activated aldehydes. This problem occurs when the anion is present on the sulfonyl carbon bearing also phenyl or an electron-withdrawing group. To overcome this disadvantage, Satoh et al. reintroduced[4] recently sulfoxides as sulfone equivalents in the Julia–Lythgoe olefination[5]. To advantage, the carbanion generated (to the sulfoxide group is far less stabilized[6] than in the case of the corresponding sulfone and the addition reaction, leading to the formation of the C–C bond, is favored even in the case of ketones. The β-hydroxysulfoxides were then mesylated and subjected to BuLi (4 equivalents) mediated reductive elimination to give the desired olefins (Scheme 2). Using this modification, styrene and stilbene derivatives were prepared by the Julia olefination method for the first time. Disappointingly, the *E*/*Z* stereoselectivity was rather low. For example, 1,2-disubstituted olefins were gen-

erally prepared in 60–90% yields, with *E*/*Z* ratios varying, in the best cases, between 75:25 and 25:75. Trisubstituted alkenes were obtained from various α-branched sulfoxides and cyclohexanone in 60–90% yields. Unsymmetrical ketones were not studied. It was reported, though, that tetrasubstituted olefins could not be generated using this method.



SCHEME 2

Mechanistic studies of this reaction by Satoh showed that this elimination was highly stereospecific and that the geometry of the newly formed olefin depended on the relative configuration of the β-hydroxysulfoxide. Thus, if the *anti*-diastereoisomer was subjected to BuLi-mediated reductive elimination, the *E* isomer was preferentially formed. In contrast, if the *syn*-diastereoisomer was used, the *Z* isomer was generated as the major product. The influence of additional stereogenic centres present on sulfur atoms, on the stereoselectivity of the reaction was not studied (Scheme 3).



SCHEME 3

For some time now, we have been interested in the modification and development of various Julia–Lythgoe olefination methods[2c,7]. Recently, we have introduced the SmI_2/HMPA-mediated reductive elimination of β-(benzoyloxy)sulfones, formed by the addition of α-sulfone anions to ketones, as an efficient and stereoselective route to trisubstituted olefins. Based upon our previous results, we envisaged that the SmI_2-mediated

reductive elimination of β-(benzoyloxy)sulfoxides might produce the desired olefins in high yields and with good *E*/*Z* selectivity. Moreover, we envisioned that the trapping of the β-oxysulfoxide anion intermediate by the benzoyl group would increase the yield of the addition product. The resulting β-(benzoyloxy)sulfoxides, if properly substituted, might lead, for the first time, to tetrasubstituted olefins.

In this article, we wish to report in detail the results of our investigation in the development of a sulfoxide version of the Julia–Lythgoe olefination based on the concepts described above[8].

RESULTS AND DISCUSSION

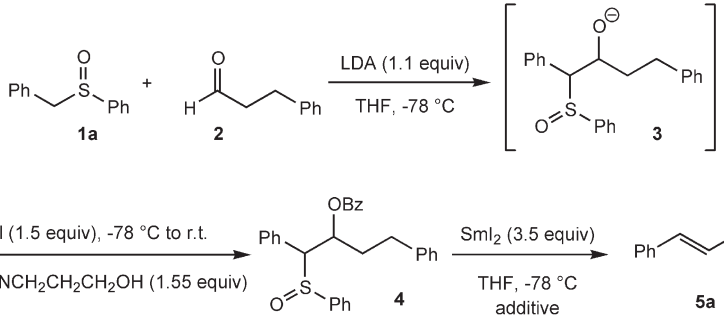
At the onset of our work, it was crucial to assess the feasibility of the SmI_2-mediated reductive elimination. Therefore, sulfoxide **1a**[9] was reacted with aldehyde **2** and the in situ generated β-hydroxysulfoxide **3** was trapped with benzoyl chloride to give the β-(benzoyloxy)sulfoxide **4**. During the addition of the sulfoxide anion to aldehyde **2**, two new stereogenic centres are formed and intermediate **4** is thus obtained as a mixture of all four possible diastereoisomers. To avoid their tedious separation, it was decided to use the mixture of adducts **4** in the subsequent reductive-elimination step[10]. Some pertinent results are collected in Table I[11].

As can be seen from Table I, SmI_2 itself does not promote the reductive elimination, not even at room temperature (Table I, entries 1 and 2). Therefore, HMPA and DMPU were added as additives[12] to increase the reduction potential of SmI_2 (–1.33 V)[13]. It was found that the presence of only small quantities of HMPA (0.25 equivalent) promoted the reductive elimination and furnished the desired olefin **5a** in 25% yield (Table I, entry 3). Further optimization of the reaction conditions showed that addition of one equivalent of HMPA was optimal (Table I, entry 6). Further increase in the HMPA loading did not give better results (Table I, entry 7). This observation suggests that a reduction potential of –1.43 V (HMPA/SmI_2 = 1:1) is the optimum potential required for the reductive-elimination. If the potential is increased (Table I, entry 7) to –1.46 V (HMPA/SmI_2 = 2:1), the reaction does not proceed faster or with better yields.

DMPU was next employed as an alternative, non-toxic HMPA equivalent. However, under all the reaction conditions tested, the yields remained lower than with HMPA (Table I, entries 8–15). Moreover, a large excess of DMPU and higher temperatures (0 °C to room temperature) had to be employed (Table I, entries 11–15). Using this additive, as for HMPA, the best results were obtained when a reduction potential of –1.42 V was reached[14].

TABLE I

Optimization of the reductive elimination step



Entry	Additive	Equiv. to SmI_2	Temp. (°C)	Yield[a] (%)	*E* /*Z* [b]
1	-	-	-78	-	n/a
2	-	-	25	-	n/a
3	HMPA[c]	0.25	-78	25	>95:1
4	HMPA	0.5	-78	34	>95:1
5	HMPA	0.75	-78	43	>95:1
6	HMPA	1.0	-78	67	>95:1
7	HMPA	2.0	-78	64	>95:1
8	DMPU[d]	15.0	-78	2	n/a
9	DMPU	15.0	-50	12	n/a
10	DMPU	15.0	-25	32	>95:1
11	DMPU	15.0	0	48	>95:1
12	DMPU	15.0	25	10	n/a
13	DMPU	5.0	0	-	n/a
14	DMPU	10.0	0	11	>95:1
15	DMPU	20.0	0	41	>95:1

[a] Overall yields refer to pure, isolated products

[b] Determined by capillary GC

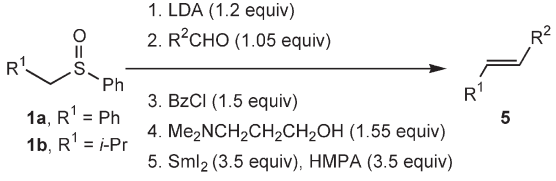
[c] HMPA - hexamethylphosphoramide

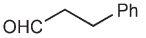
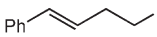
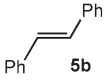
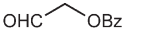
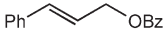
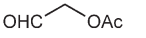
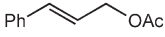
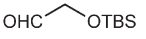
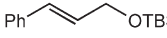
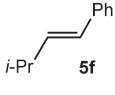
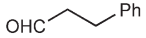
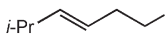
[d] DMPU - 1,3-dimethyl-3,4,5,6-tetrahydro-2-(1H)-pyrimidinone

Having designed suitable reaction conditions to successfully effect this sulfoxide variant of the Julia–Lythgoe olefination, the scope and limitations of this protocol were next investigated.

Initially, our attention focused on the formation of 1,2-disubstituted olefins. Thus, sulfoxide **1a** was reacted with aliphatic and aromatic aldehydes, affording the corresponding 1,2-disubstituted olefins **5a**–**5e** in good yields and with excellent stereoselectivities (Table II, entries 1–5). It is noteworthy that some of the most commonly used OH-protecting groups are perfectly tolerated in this transformation (Table II, entries 3–5).

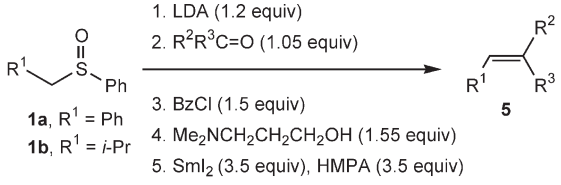
TABLE II
Preparation of 1,2-disubstituted olefins

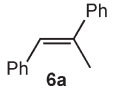
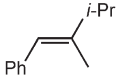
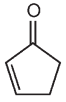
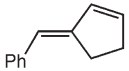
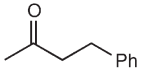
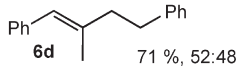
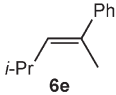
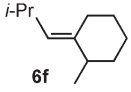
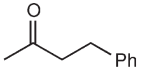
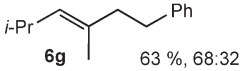
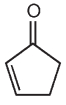
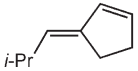
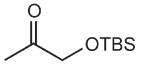
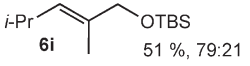


Entry	1	R^2CHO	Product	Yield[a] *E* / *Z*[b]
1	**1a**		 **5a**	67 %, >95:1
2	**1a**		 **5b**	75 % >95:1
3	**1a**		 **5c**	71 %, >95:1
4	**1a**		 **5d**	68 %, >95:1
5	**1a**		 **5e**	70 %, >95:1
6	**1b**		 **5f**	70 % 76:24
7	**1b**		 **5g**	69 %, 94:6

[a] Overall yields refer to pure, isolated products
[b] Determined by ^{1}H NMR spectroscopy

TABLE III
Preparation of trisubstituted olefins



Entry	1	$R^2R^3C=O$	Product	Yield[a] *E* / *Z*[b]
1	**1a**		 **6a**	51 % 76:24
2	**1a**		 **6b**	57 % 91:9
3	**1a**		 **6c**	68 % 65:35
4	**1a**		 **6d**	71 %, 52:48
5	**1b**		 **6e**	64 % 74:26
6	**1b**		 **6f**	64 % 88:12
7	**1b**		 **6g**	63 %, 68:32
8	**1b**		 **6h**	63 % 75:25
9	**1b**		 **6i**	51 %, 79:21

[a] Overall yields refer to pure, isolated products
[b] Determined by ^{1}H NMR spectroscopy

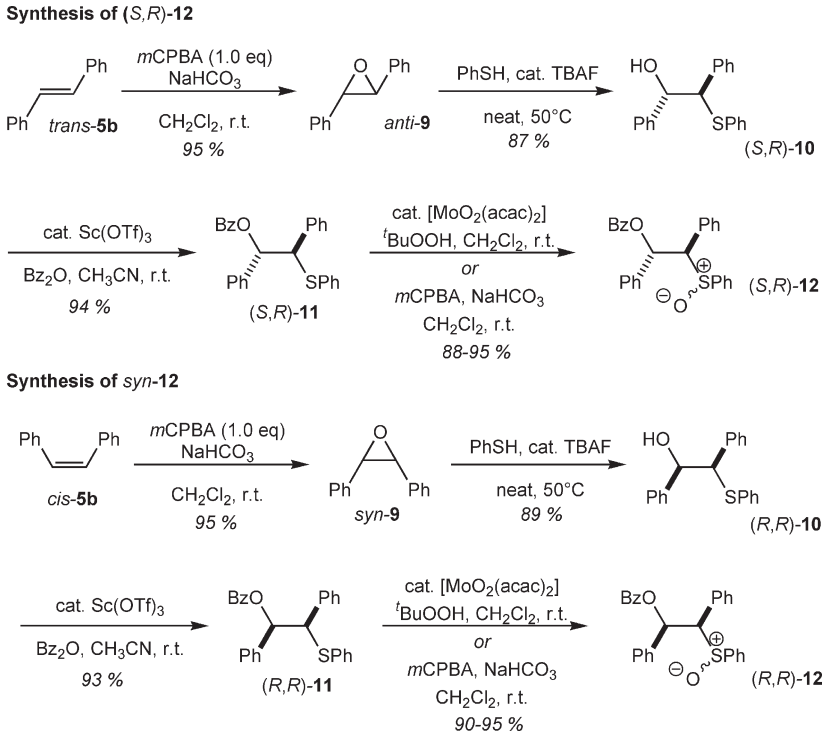
Next, the coupling of the more hindered sulfoxide **1b** was examined under these reaction conditions. It was found that if **1b** was reacted with aliphatic aldehydes (Table II, entry 7), the desired olefin **5g** was formed in good yield and with very high selectivity (*E*/*Z* = 94:6). Surprisingly, when **1b** was reacted with benzaldehyde, the desired alkene **5f** was formed with only moderate selectivity *E*/*Z* = 76:24, though in a similar yield (Table II, entry 6).

The formation of trisubstituted olefins also proceeded smoothly (Table III). Sulfoxides **1a** and **1b** were reacted with various ketones furnishing the desired adducts **6a**–**6i** in unoptimized yields ranging from 51 to 71%. The stereoselectivity of the C–C bond linkage was lower with trisubstituted olefins than in the case of 1,2-disubstituted ones. Generally, aryl-substituted alkenes formed by the reaction of **1a** with ketones, gave slightly higher *E*/*Z* ratios than those bearing an isopropyl side chain. Additionally, it was observed that the *E*/*Z* selectivity depended upon the steric discrimination between the groups present in the ketone molecule. When the carbonyl function was bonded to a methyl group on one side and a linear alkyl on the other side, the newly formed double bond was generated with low selectivity (Table III, entries 4 and 7). In the case of bulkier alkyl, the *E* isomer was formed preferentially (Table III, entries 2, 6 and 9). Remarkably, this modified Julia–Lythgoe olefination proceeds smoothly when enones are employed as substrates though the highly conjugated, thermodynamically more favored olefin was formed only in a moderate *E*/*Z* ratio (Table III, entries 3 and 8).

Based on these results, it can be concluded that, during the reductive elimination step, the steric requirements of the substrate are overruling the conjugative effect present in the final adduct.

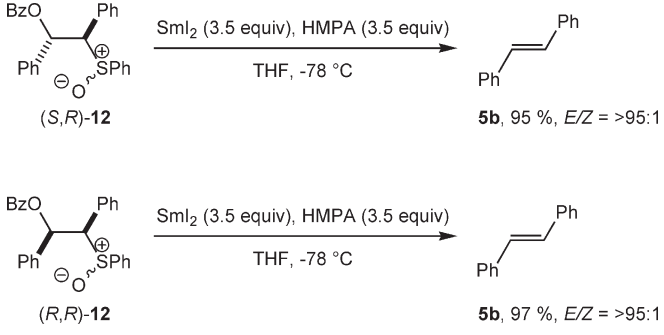
Finally, the formation of tetrasubstituted olefins was examined under our standard conditions. Accordingly, sulfoxide **7** [15] was reacted with various ketones to give tetrasubstituted olefins **8** in low yield but excellent *E*/*Z* selectivity (Table IV). To the best of our knowledge, this is the first report describing the successful preparation of tetrasubstituted alkenes, using this sulfoxide variant of the Julia–Lythgoe olefination, with such high selectivity levels.

At this stage, it was deemed important to find out whether the reductive elimination, mediated by the SmI_2/HMPA system, was a stereoselective or a stereospecific process. Therefore, the *syn*- and *anti*-β-(benzoyloxy)sulfoxides **12** were prepared[16] (Scheme 4) and independently subjected to the reductive elimination conditions.



SCHEME 4

In both cases, olefin **5b** was obtained in an excellent *E*/*Z* ratio of >95:1, indicating that the reductive-elimination step proceeded via a stereoselective process (Scheme 5).

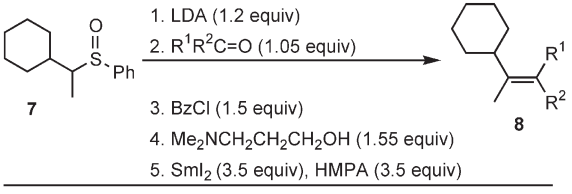


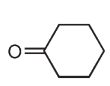
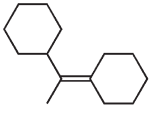
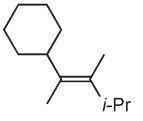
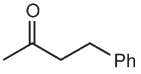
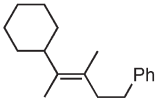
SCHEME 5

To generalize our observation, the *syn*- and *anti*-sulfoxides **13** were prepared and their reductive elimination was examined (Scheme 6). Since direct access to each individual diastereoisomers of **13** would have been prohibitive, **13** was synthesized according to our standard Julia olefination procedure, as a mixture of isomers. The desired four diastereoisomers (a pair of *syn*-**13** and a pair of *anti*-**13**) were then separated via tedious column chromatography (7 columns required). The relative stereochemistry of more and less polar (*R*,*R*)-**13** and more and less polar (*S*,*R*)-**13** was established by their conversion to the corresponding sulfone derivatives, (*R*,*R*)-**14** and (*S*,*R*)-**14**, respectively, and by comparison with their reported literature data.

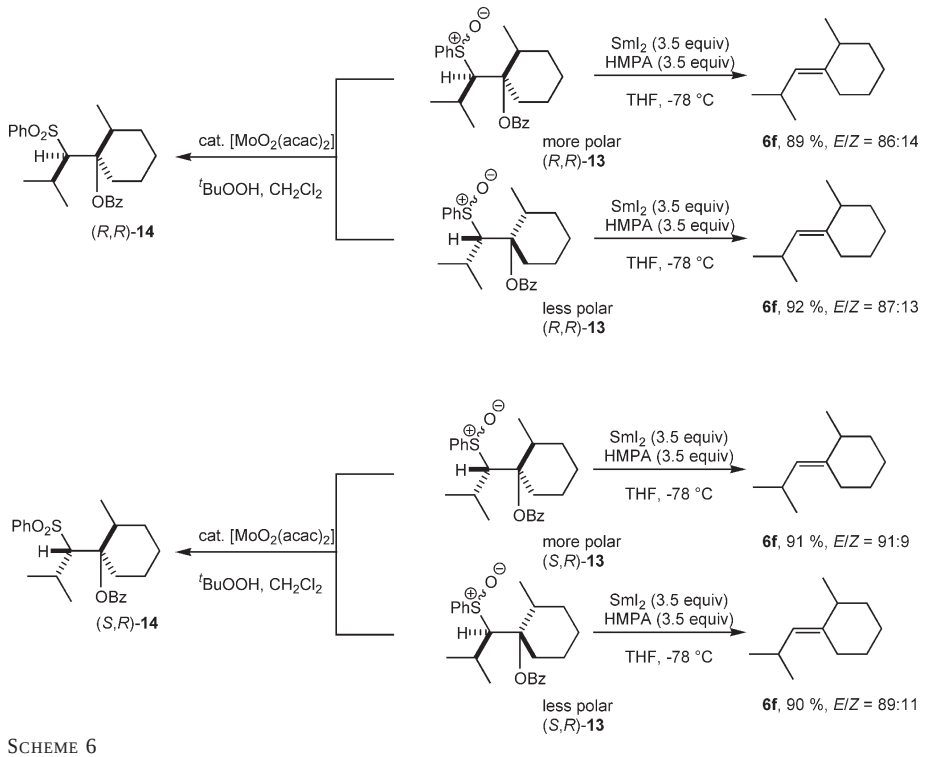
Interestingly, the reductive elimination of pure more and less polar (*R*,*R*)- and (*S*,*R*)-sulfoxides **13** gave essentially the same *E*/*Z* ratio, ranging from 86:14 to 91:9. When the reaction was performed with a mixture of all four diastereoisomers, the 88:12 *E*/*Z* ratio was obtained, which is a good average of the individually measured stereoselectivities. This observation clearly

TABLE IV
Preparation of tetrasubstituted olefins



Entry	$R^2R^3C=O$	Product	Yield[a] *E* / *Z*[b]
1		 **8a**	33 %
2		 **8b**	29 % 97:3
3		 **8c**	32 % 91:9

[a] Overall yields refer to pure, isolated products
[b] Determined by ^{1}H NMR spectroscopy

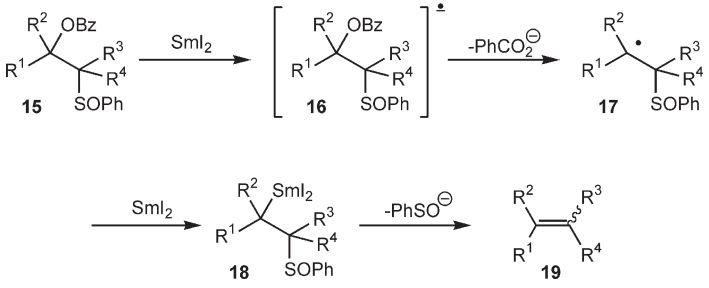


SCHEME 6

suggests that the double bond geometry of the final alkene **6f** is independent of the relative stereochemistry of the sulfoxide adduct **13**.

Based on these results, a plausible mechanism for the reductive elimination, and a mnemonic model generalizing the observed *E*/*Z* selectivities, can be proposed. We believe that the reductive elimination of β-(benzoyloxy)-sulfoxides proceeds in the same way as in the case of the β-(benzoyloxy)-sulfones[17] (Scheme 7). Thus, transfer of a single electron to the benzoate moiety, which appears to be the lowest energy pathway, leads to the radical anion **16**. Subsequent collapse of this intermediate liberates the benzoate anion and produces radical **17**[18]. Further transformation of **17** to the organosamarium intermediate **18**, followed by elimination of the phenylsulfinyl group, eventually affords the olefin **19**.

It is plausible that the formation of the organosamarium species **18** is a slower process than epimerization of the radical-bearing centre. Moreover, the samarium derivative **18** might not be configurationally stable and inversion might occur faster than elimination to **19**. The elimination of the phenylsulfinyl group is believed to proceed through an E_2 type process,



SCHEME 7

leading to the general model for the stereoselectivity of the double bond formation depicted in Fig. 1. Based on this model, steric hindrance of the substituents present on the sulfoxide and on the carbonyl substrate play a crucial role in final *E*/*Z* stereoselectivity.

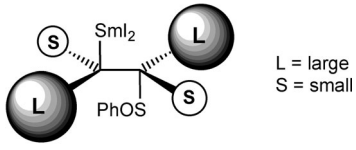


FIG. 1
General model for the stereoselectivity of the double bond formation

CONCLUSIONS

In summary, we have developed a novel, highly stereoselective version of the Julia–Lythgoe olefination. This method embraces a wider scope than the classical Julia olefination protocol. For the first time, tetrasubstituted olefins were prepared in a highly stereoselective manner. We have also shed some light on the reaction mechanism and proposed a mnemonic model that predicts the stereochemical outcome of the olefination process. The use of this method in natural product synthesis and in the assembly of products previously impossible to prepare via the classical Julia procedure, is currently in progress in our laboratory.

EXPERIMENTAL

General

IR spectra (ν, cm^{-1}) were recorded on a FTIR ATI Mattson spectrophotometer in NaCl cell or KBr tablets. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini-2000 (300 and 75 MHz, respectively) or on a Bruker AC-250 (250 and 62.5 MHz, respectively) at ambient

temperature in $CDCl_3$ (Aldrich or Rocc). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Mass spectra were recorded on a Finigan TSQ 7000. All compounds (Acros, Aldrich and Fluka) were used as received. THF was distilled under argon from sodium benzophenone ketyl. Flash chromatography was performed on silica gel 60 (40–63 μm) (Rocc).

The identity of every product was confirmed by comparison with literature data. The structure determination of new compounds was made using 2D-COSY, HSQC, HMBC, 2D-NOESY and NOEdiff experiments. The following compounds have been previously described: **5a** [19], **5b** [20], **5c** [21], **5d** [22], **5e** [23], **5f** [24], **5g** [25], **6a** [26], **6b** [27], **6e** [28], **6d**, **6e** [8] and **8a**–**8c** [8]. The corresponding sulfoxides **7** [29], (*R*,*R*)-**12** and (*S*,*R*)-**12** [16] were prepared according to the literature.

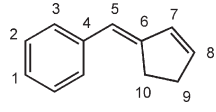
Coupling Step

A solution of a sulfoxide (1.0 mmol) in dry THF (10 ml, 0.1 mol/l) was cooled to –78 °C and LDA (550 μl, 1.1 mmol) was added dropwise. The colour of the mixture changed from slightly yellow to orange-red. After stirring at –78 °C for 30 min, an aldehyde/ketone (1.05 mmol), dissolved in dry THF (0.5 ml), was added dropwise and the mixture was stirred at –78 °C for an additional 2 h. Benzoyl chloride (1.5 mmol) in dry THF (0.5 ml) was then added. The resulting mixture was stirred for 30 min at –78 °C and then allowed to warm to room temperature over 1 h. After an additional 30 min at room temperature, $Me_2N(CH_2)_3OH$ (1.55 mmol) was added and the resulting suspension was stirred at room temperature for 10 min. The suspension was then diluted with Et_2O–H_2O, 1:1 (10 ml) and the layers were separated. The aqueous layer was extracted with Et_2O (3 × 10 ml) and the combined organic layers were washed with aqueous 1.0 M HCl (10 ml), H_2O (10 ml) and brine (10 ml), dried over anhydrous $MgSO_4$ and evaporated under reduced pressure to give the crude product, which was used without additional purification in the subsequent step.

Reductive Elimination

To a solution of SmI_2 (35 ml, 0.1 mol/l in THF, 3.5 equivalents), HMPA (613 μl, 3.5 equivalents) was added and the mixture was cooled to –78 °C. The crude coupled product (1.0 mmol) in dry THF (0.5 ml) was added dropwise and the resulting mixture was stirred at –78 °C for an additional 30 min. Then, aqueous NH_4Cl (20 ml) was added and the whole was allowed to warm to room temperature The layers were separated and the aqueous phase was extracted with Et_2O (3 × 20 ml). The combined organic layers were washed with 10% aqueous $Na_2S_2O_3$ (20 ml), H_2O (20 ml), brine (20 ml), dried over anhydrous $MgSO_4$ and evaporated under reduced pressure. The crude product was then purified by chromatography on silica gel.

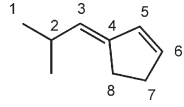
Compound **6c** (Table III, entry 3): purified by column chromatography (2.5 cm × 11 cm, SiO_2, 5 ml fractions; *n*-pentane) to give 106 mg (68%, *E*/*Z* = 65:35) of **6c** as a colourless oil.



IR (NaCl, neat): 3084 (w), 3072 (w), 3021 (w), 2954 (m), 2923 (m), 2868 (w), 1602 (w), 1495 (w), 1454 (w), 742 (m), 699 (m). ^{1}H NMR (250 MHz, $CDCl_3$): 1.71–1.83 (m, 2 H, H-9); 2.20–2.31 (m, 2 H, H-10); 6.19 (broad s, 1 H, H-5^{cis}); 6.22 (m, 1 H, H-7^{trans}); 6.49–6.52 (m,

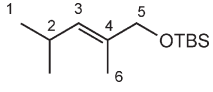
1 H, H-8); 6.52 (broad s, 1 H, H-5^{trans}); 7.25 (broad s, H-7^{cis}); 7.02–7.68 (m, 5 H, arom. CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): 28.3 (C-10^{trans}); 30.4 and 30.5 (C-9); 37.2 (C-10^{cis}); 117.2 (C-5^{cis}); 132.4 (C-5^{trans}); 27.3 (C-2^{trans}); 29.9 (C-2^{cis}); 34.4 (C-5^{cis}); 35.0 (C-6); 41.8 (C-5^{trans}); 123.5–137.2 (arom. CH and C_q); 132.7 (C-7^{trans}); 134.5 (C-7^{cis}); 143.2 (C-8). MS (CI, CH_4/N_2O), *m/z* (%): 156.11 (100) [M^+], 157.25 [M^+ + 1] (23), 79.2 (26), 77.5 (16). For $C_{12}H_{12}$ (156.2) calculated: 92.26% C, 7.74% H; found: 92.34% C, 7.66% H.

Compound **6h** (Table III, entry 7): purified by column chromatography (2.5 cm × 11 cm, SiO_2, 5 ml fractions; *n*-pentane) to give 77 mg (63%, *E*/*Z* = 68:32) of **6h** as a colourless oil.



IR (NaCl, neat): 3058 (w), 2957 (m), 2862 (w), 1604 (w), 1494 (w), 1453 (w). ^{1}H NMR (250 MHz, $CDCl_3$): 0.92 (dd, 6 H, $^3J_{1,2}$ = 6.7, $^3J_{1,1'}$ = 1.4, H-1^{cis}); 0.95 (dd, 6 H, $^3J_{1,2}$ = 6.7, $^3J_{1,1'}$ = 1.4, H-1^{trans}); 1.52–1.74 (m, 2 H, H-7); 1.98–2.09 (m, 2 H, H-8); 2.36 (m, 1 H, H-2^{cis}); 2.61 (m, 1 H, H-2^{trans}); 5.17 (d, 1 H, $^3J_{3,2}$ = 9.1, H-3^{trans}); 5.44 (d, 1 H, $^3J_{3,2}$ = 10.1, H-3^{cis}); 6.28 (broad s, 1 H, H-5^{trans}); 6.78 (m, 1 H, H-6); 7.35 (m, 1 H, H-5^{cis}). ^{13}C NMR (62.5 MHz, $CDCl_3$): 21.4 (C-1^{cis}); 23.2 (C-1^{trans}); 28.3 (C-2^{trans}); 29.2 (C-8^{trans}); 30.3 (C-2^{cis}); 31.9 (C-7); 36.2 (C-8^{cis}); 134.2 (C-5^{trans}); 134.3 (C-4^{cis}); 134.5 (C-5^{cis}); 135.9 (C-4^{trans}); 137.2 (C-3^{cis}); 138.2 (C-3^{trans}); 140.6 (C-6). MS (CI, CH_4/N_2O), *m/z* (%): 122.19 (100) [M^+], 95.7 (15), 79.7 (39), 51.3 (8). For C_9H_{14} (122.2) calculated: 88.45% C, 11.55% H; found: 88.51% C, 11.49% H.

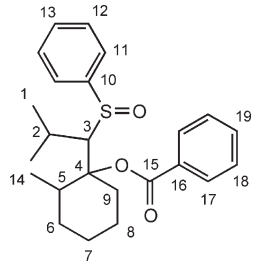
Compound **6i** (Table III, entry 9): purified by column chromatography (2.5 cm × 11 cm, SiO_2, 5 ml fractions; 100% *n*-pentane) to give 117 mg (51%, *E*/*Z* = 79:21) of **6i** as a colourless oil.



^{1}H NMR (250 MHz, $CDCl_3$): 0.03 (s, 6 H, Si**Me**$_2$Bu^t); 0.91 (s, 9 H, SiMe$_2$**Bu**^{t}); 0.92 (dd, 6 H, $^3J_{1,2}$ = 6.7, $^3J_{1,1'}$ = 1.5, H-1^{cis}); 0.96 (dd, 6 H, $^3J_{1,2}$ = 6.7, $^3J_{1,1'}$ = 1.4, H-1^{trans}); 1.67 (m, 1 H, H-6^{trans}); 1.89 (m, 1 H, H-6^{cis}); 2.49 (m, 1 H, H-2^{trans}); 2.75 (m, 1 H, H-2^{cis}); 4.01–4.12 (m, 2 H, H-5); 4.76 (d, 1 H, $^3J_{3,2}$ = 9.5, H-3^{trans}); 5.11 (d, 1 H, $^3J_{3,2}$ = 9.3, H-3^{cis}). ^{13}C NMR (62.5 MHz, $CDCl_3$): –3.2 (Si**Me**$_2$Bu^t); 14.0 (C-6^{trans}); 18.7, 21.4 (C-6^{cis}); 22.9 (C-1^{cis}); 23.2 (C-1^{trans}); 24.1 (C-2^{trans}); 26.2 (SiMe$_2$**Bu**^{t}); 28.1 (C-2^{cis}); 64.2 (C-5^{trans}); 70.2 (C-5^{cis}); 132.1 (C-4^{cis}); 132.3 (C-4^{trans}); 138.9 (C-3^{trans}); 148.8 (C-3^{cis}). MS (CI, CH_4/N_2O), *m/z* (%): 128.45 (67) [M^+], 114.6 (100), 97.9 (65), 77.2 (15), 55.2 (12). For $C_{13}H_{28}OSi$ (228.5) calculated: 68.35% C, 12.35% H, 12.29% Si; found: 68.51% C, 12.23% H, 12.24% Si.

Sulfoxides **13**

Compounds **13** were prepared according to the standard coupling procedure. The crude mixture was purified by repeated (7×) column chromatography (2.5 cm × 11 cm, SiO_2, 5 ml fractions; petroleum ether–Et_2O, 20:1) to give four diastereoisomers more polar (*R*,*R*)-**13** (11 mg), less polar (*R*,*R*)-**13** (15 mg), more polar (*S*,*R*)-**13** (25 mg) and less polar (*S*,*R*)-**13** (28 mg).



More polar (*R*,*R*)-**13**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.86 (dd, 3 H, $^3J_{1,2}$ = 6.5, $^2J_{1,1'}$ = 1.4, one of H-1); 1.06 (d, 3 H, $^3J_{14,5}$ = 7.2, H-14); 1.21 (dd, 3 H, $^3J_{1,2}$ = 6.8, $^2J_{1,1'}$ = 1.3, the other H-1); 1.17–2.27 (m, 10 H, H-2, 5–9); 3.89 (d, 1 H, $^3J_{3,2}$ = 7.0, H-3); 7.11–8.24 (m, 10 H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.5, 20.3, 21.8, 22.9, 24.3, 29.2, 31.8, 32.8, 36.2, 71.9 (C-3); 76.8 (C-4); 124.3–147.9 (arom. CH and C_q); 166.2 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 586.46 (67) [M^+], 587.67 [M^+ + 1] (34), 121 (100), 181.3 (43), 96.9 (15), 77.3 (20). HR CI MS calculated: 398.1916; found: 398.1924.

Less polar (*R*,*R*)-**13**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.86 (dd, 3 H, $^3J_{1,2}$ = 6.5, $^2J_{1,1'}$ = 1.4, one of H-1); 1.07 (d, 3 H, $^3J_{14,5}$ = 7.2, H-14); 1.20 (dd, 3 H, $^3J_{1,2}$ = 6.8, $^2J_{1,1'}$ = 1.2, the other H-1); 1.17–2.28 (m, 10 H, H-2, 5–9); 4.12 (d, 1 H, $^3J_{3,2}$ = 7.1, H-3); 7.10–8.25 (m, 10 H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.6, 20.3, 21.8, 22.9, 24.4, 29.3, 31.8, 32.8, 36.2, 71.4 (C-3); 76.5 (C-4); 124.1–147.9 (arom. CH and C_q); 166.1 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 586.4 (63) [M^+], 587.6 [M^+ + 1] (33), 121.4 (100), 181.3 (38), 96.9 (19), 77.3 (21). HR CI MS calculated: 398.1916; found: 398.1918.

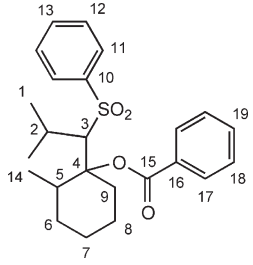
More polar (*S*,*R*)-**13**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.87 (dd, 3 H, $^3J_{1,2}$ = 6.5, $^2J_{1,1'}$ = 1.3, one of H-1); 1.07 (d, 3 H, $^3J_{14,5}$ = 7.2, H-14); 1.21 (dd, 3 H, $^3J_{1,2}$ = 6.8, $^2J_{1,1'}$ = 1.3, the other H-1); 1.17–2.25 (m, 10 H, H-2, 5–9); 4.26 (d, 1 H, $^3J_{3,2}$ = 6.9, H-3); 7.11–8.24 (m, 10 H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.4, 20.5, 21.8, 22.8, 24.8, 29.3, 31.8, 32.8, 36.3, 72.3 (C-3); 77.1 (C-4); 124.5-147.9 (arom. CH and C_q); 165.1 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 586.6 (78) [M^+], 587.9 [M^+ + 1] (40), 122.4 (100), 181.9 (43), 97.0 (17), 77.4 (21). HR CI MS calculated: 398.1916; found: 398.1910.

Less polar (*S*,*R*)-**13**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.87 (dd, 3 H, $^3J_{1,2}$ = 6.5, $^2J_{1,1'}$ = 1.3, one of H-1); 1.07 (d, 3 H, $^3J_{14,5}$ = 7.1, H-14); 1.21 (dd, 3 H, $^3J_{1,2}$ = 6.9, $^2J_{1,1'}$ = 1.3, the other H-1); 1.17–2.25 (m, 10 H, H-2, H5–H9); 4.36 (d, 1 H, $^3J_{3,2}$ = 7.1, H-3); 7.14–8.25 (m, 10 H, arom. CH). ^{13}C NMR (75 MHz, $CDCl_3$): 13.4, 20.4, 21.8, 22.9, 24.8, 29.3, 31.7, 32.8, 36.8, 72.1 (C-3); 76.7 (C-4); 124.7–147.7 (arom. CH and C_q); 164.9 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 586.4 (45) [M^+], 587.6 [M^+ + 1] (23), 121.7 (100), 182.1 (43), 96.7 (24), 77.0 (16). HR CI MS calculated: 398.1916; found: 398.1907.

Preparation of Sulfones (*R*,*R*) and (*S*,*R*)-**14**

A solution of sulfoxide **13** (5 mg, 12.5 μmol, 1.0 equivalent) in CH_2Cl_2 (1 ml) was degassed by the freeze-pump-thaw method (3×) and [$MoO_2(acac)_2$] (0.82 mg, 2.5 μmol, 0.2 equivalent) was added. The resulting mixture was cooled to 0 °C and TBHP (15 drops, 5.5 M solution in dodecane) was added dropwise. An exothermic reaction occurred and the resulting orange solution was stirred at room temperature for 4 h. A saturated solution of $Na_2S_2O_3$ (1 ml) was added and the layers were separated. The aqueous layer was extracted with EtOAc

(2 × 2 ml) and the pooled organic layers were washed with H_2O (1 ml), brine (1 ml), dried over anhydrous $MgSO_4$ and evaporated in vacuo to give 7–8 mg of a pale yellow oil (the product contains dodecane). Purification by column chromatography (1.0 cm × 10 cm, SiO_2, 2.5 ml fractions; petroleum ether–EtOAc, 1:1) gave 5.1–5.2 mg (99%) of colourless oil.



(*R*,*R*)-**14**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.87 (dd, 3 H, $^3J_{1,2}$ = 6.8, $^2J_{1,1'}$ = 1.3, one of H-1); 0.99 (d, 3 H, $^3J_{14,5}$ = 7.0, H-14); 1.20 (dd, 3 H, $^3J_{1,2}$ = 6.7, $^2J_{1,1'}$ = 1.4, the other H-1); 1.27–2.09 (m, 10 H, H-5–H9); 3.65 (m, 1 H, H-2); 3.87 (d, 1 H, $^3J_{3,2}$ = 7.1, H-3); 7.14–8.25 (m, 10 H, arom. CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): 16.4, 20.5, 23.3, 24.1, 24.9, 30.9, 34.2, 35.1, 39.2, 71.8 (C-3); 85.9 (C-4); 126.6–140.3 (arom. CH and C_q); 167.1 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 414.7 (100) [M^+], 415.6 [M^+ + 1] (22), 141.9 (34), 121.5 (56), 181.3 (28), 77.0 (15).

(*S*,*R*)-**14**. ^{1}H NMR (300 MHz, $CDCl_3$): 0.88 (dd, 3 H, $^3J_{1,2}$ = 6.8, $^2J_{1,1'}$ = 1.4, one of H-1); 1.01 (d, 3 H, $^3J_{14,5}$ = 7.0, H-14); 1.20 (dd, 3 H, $^3J_{1,2}$ = 6.7, $^2J_{1,1'}$ = 1.5, the other H-1); 1.26–2.10 (m, 10 H, H-5–H9); 3.67 (m, 1 H, H-2); 3.89 (d, 1 H, $^3J_{3,2}$ = 7.1, H-3); 7.14–8.25 (m, 10 H, arom. CH). ^{13}C NMR (62.5 MHz, $CDCl_3$): 16.3, 20.5, 23.8, 24.5, 24.9, 31.1, 34.2, 35.3, 39.2, 71.6 (C-3); 86.1 (C-4); 126.7–140.1 (arom. CH and C_q); 167.2 (C-15). MS (CI, CH_4/N_2O), *m/z* (%): 414.7 (100) [M^+], 415.6 [M^+ + 1] (21), 141.9 (34), 121.5 (48), 181.3 (23), 77.0 (16).

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