Hexamethyldisilazanes mediated one-pot intramolecular Michael addition–olefination reactions leading to *exo*-olefinated bicyclo[6.4.0]dodecanes

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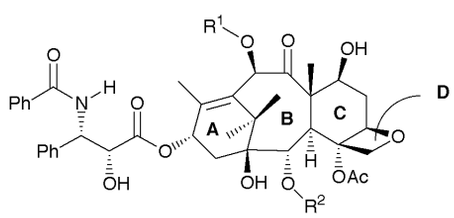
A novel one-pot reaction for the synthesis of *exo*-olefinated bicyclo[6.4.0]dodecanes **23** has been developed on the basis of an intramolecular Michael reaction of phenylsulfonyl compounds **4** with potassium hexamethyldisilazide (KHMDS) and a sequential reaction with an excess of methoxymethyl chloride (MOMCl). By this reaction, an *exo*-olefin group was regioselectively introduced at the α-position to the carbonyl group in the 6-membered ring in high yield. The regioselective introduction of the olefin moiety could be envisaged to proceed through a Mannich-type reaction involving the aminomethylating agent **24**, which, in turn, is generated *in situ* by the action of HMDS on MOMCl.

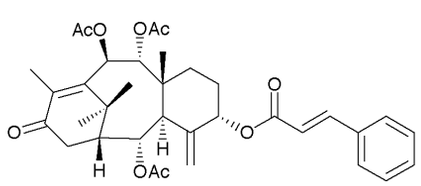
Introduction

Taxol **1** was isolated from the extracts of bark of the yew trees (*Taxus brevifolia*) and its stereostructure was disclosed by Wani *et al.* in 1971.[1] Pharmacological researchers revealed that **1** possesses significant antitumor activities against important human cancers.[2] In addition the structurally related compounds taxotere **2** and taxinine **3** were also found to show potent activities.[3,4] Due to their remarkable novel cytotoxity and unique 6-8-6 condensed structural feature, the taxane diterpenes have attracted the synthetic interests of several groups, and some of these groups have achieved total synthesis of taxol **1**.[5] In particular, an important step in the synthesis of the taxane skeleton is the assembly of the 8-membered ring, and there has been extensive research to achieve this goal.[6a,b] With the intention to develop a simple route for the construction of this framework, we have studied intramolecular cyclisation reactions using the sulfonyl group due to its flexibilities to be transformed to other functional groups.[7] Recently, we have achieved a highly efficient intramolecular Michael addition of the sulfonyl carbanion of compounds **4** formed with potassium hexamethyldisilazide (KHMDS) to provide the bicyclo[6.4.0]dodecanes **6**, BC ring precursor of taxanes (Scheme 1).[8] The high degree of success encountered in this cyclisation prompted us to investigate suitable reaction conditions for the convenient introduction of a C-1 unit at the α-position of the carbonyl group in the 6-membered ring which could be elaborated to deliver the D-ring of the taxane skeleton.

In the course of our investigations, we were delighted to find that cyclisation reactions carried out in the presence of an excess of MOMCl at 40 °C caused an unexpected regioselective olefination at the target position and directly furnished the 8-6 condensed-ring compounds possessing the *exo*-olefin moiety. Although one-pot reactions involving Michael addition and subsequent treatment with various electrophiles have been known to effect simultaneous introduction of substituents at both α- and β-positions of α,β-unsaturated carbonyl derivatives,[9] there are few examples in which an olefin group is directly assembled at the α–position. In this paper we describe details of the formation of bicyclo[6.4.0]dodecanes and their sequential *exo*-olefination.



1 taxol R^1 = Ac, R^2 = Bz
2 taxotere R^1 = H, R^2 = *t* - BuOOC

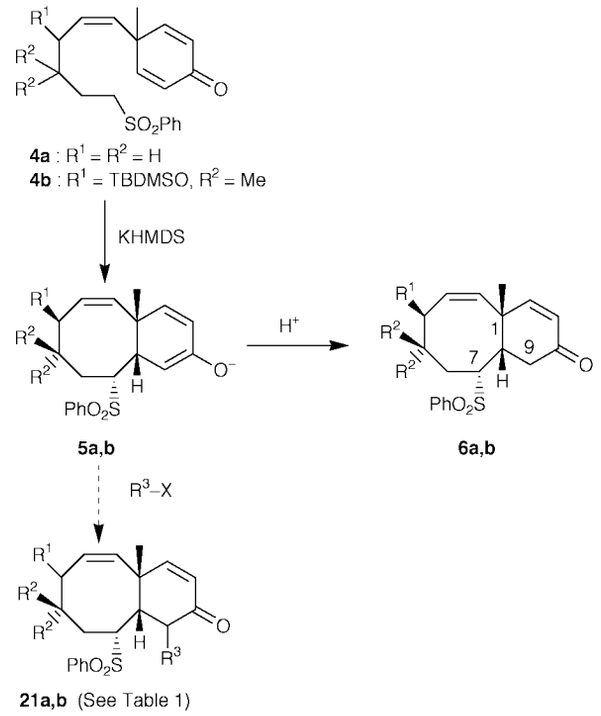


3 taxinine

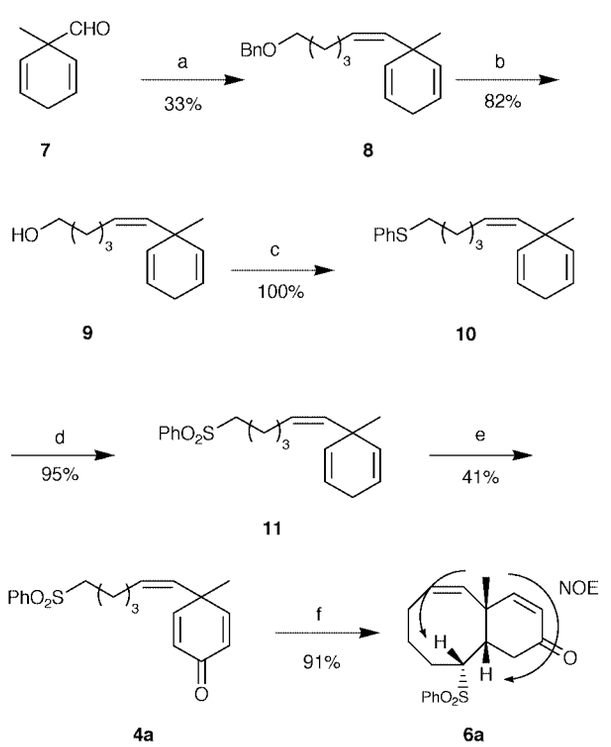
Results and discussion

Synthesis of substrates 4

Details of synthetic routes for **4a** are outlined in Scheme 2. Condensation of the aldehyde **7**[10] with non-stabilised Wittig reagent (5-benzyloxypentyl)triphenylphosphonium bromide[11] gave the (*Z*)-olefin derivative **8**, and subsequent deprotection of the benzyl ether under Birch reduction conditions provided the alcohol **9** in 27% overall yield for two steps. Transformation of the hydroxy group to a phenylthio group with diphenyl disulfide and tributylphosphine[12] gave **10** in quantitative yield. Oxidation of the sulfenyl moiety of **10** with Oxone afforded the sulfonyl derivative **11** in 95% yield. Successive oxidation of the allylic position in the cyclohexadienone ring of **11** was not an easy task. After considerable experimentation, a ruthenium catalyst was found to be ideal for the task. Thus, treatment of **11** with 20 mol% of tetrapropylammonium perruthenate

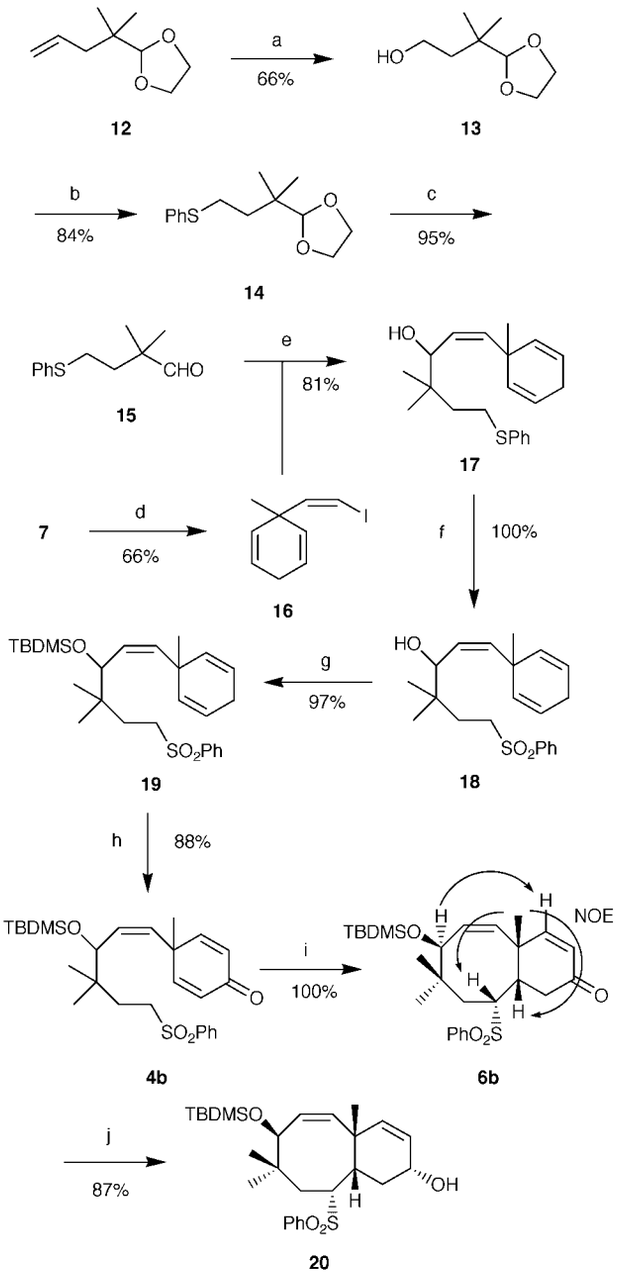


Scheme 1



Scheme 2 *Reagents and conditions*: (a) $\overset{+}{P}Ph_3(CH_2)_5OBn\ Br^-$, BuLi, THF, −78 °C; (b) Na, Bu′OH, THF–NH_3, −78 °C; (c) $(PhS)_2$, Bu_3P, Py, rt; (d) Oxone; THF–MeOH–H_2O, 50 °C; (e) TPAP, NMO, 4Å molecular sieves, MeCN, rt, (f) KHMDS, THF–toluene 0 °C.

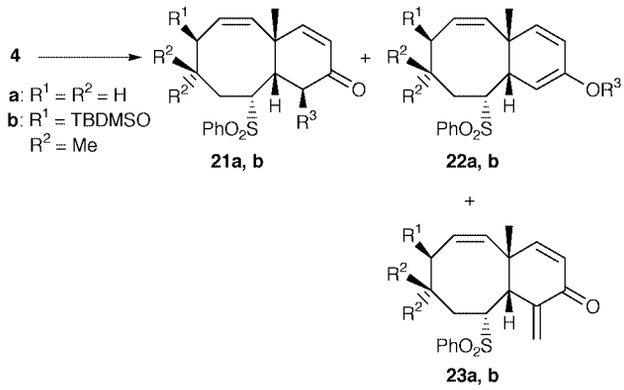
(TPAP), 4 equiv. of 4-methylmorpholine *N*-oxide (NMO), and 4Å molecular sieves in acetonitrile gave the desired dienone derivative **4a**. Although TPAP-catalyzed oxidation is a well known procedure,[13] there is no precedent in the literature in which an allylic site is efficiently oxidised to a carbonyl group under mild conditions. After extensive investigation into the cyclisation of **4a** under various conditions, a slight excess of KHMDS at 0 °C was found to be the best method, and the reaction was complete within 0.5 h to provide **6a** in 91% yield as a single stereoisomer. The stereochemistry of **6a** was determined to be *cis*-fusion by NOE measurements.



Scheme 3 *Reagents and conditions*: (a) (i) OsO_4, $NaIO_4$, Et_2O–H_2O, rt; (ii) $NaBH_4$, MeOH, 0 °C; (b) $(PhS)_2$, Bu_3P, Py, rt; (c) AcOH–H_2O, 50 °C; (d) $PPh_3CH_2\ I^-$, NaHMDS, THF, −78 °C ⟶ rt; (e) Bu^{t}Li, THF, −78 °C; (f) MCPBA, $CHCl_3$, 0 °C ⟶ rt; (g) TBDMSOTf, 2,6-lutidine, CH_2Cl_2, rt; (h) TPAP, NMO, 4 Å molecular sieves, CH_2Cl_2, rt, (i) KHMDS, THF–toluene, 0 °C, (j) L-Selectride, THF, 0 °C.

Preparation of **4b** was carried out as depicted in Scheme 3. The acetal **12** was synthesised from allyl alcohol and isobutylraldehyde in a two-step sequence involving 3,3-sigmatropic rearrangement and acetalisation.[14] Oxidation of **12** under Lemieux–Johnson oxidation conditions[15] followed by reduction with $NaBH_4$ furnished the alcohol **13** in 66% overall yield for two steps. Transformation of the hydroxy group of **13** in the same manner as above gave the phenylthio compound **14** and deprotection of the acetal group provided the aldehyde **15**. Coupling of **15** in the presence of the (*Z*)-vinyl iodide **16**,[16] which was prepared by Wittig reaction of **7** in 66% yield using (iodomethyl)triphenylphosphonium iodide,[17] gave the addition product **17** in 81% yield. Oxidation of the sulfenyl group with 3 equiv. of *m*-chloroperbenzoic acid (MCPBA, 75% purity) in $CHCl_3$ at 0 °C smoothly proceeded without formation of over-

Table 1 Treatment of 4 with KHMDS and various electrophiles[a]



Entry	Substrate	Electrophiles[b] (R^3X)	Temp. (T/°C)	Time (t/h)	Yield (%)[c] 6	21	22	23
1[d]	**4a**	$ClCO_2Me$ (2.0)	0 ⟶ rt	1.0	0	0	81	0
2	**4b**	$ClCO_2Et$ (1.5)	0	2.5	0	0	56	0
3	**4a**	$NCCO_2Me$ (2.0)	0	1.0	0	0	70	0
4	**4b**	MeI (1.5)	0 ⟶ rt	5.5	0	22	62	0
5	**4a**	$MeOCH_2Cl$ (1.5)	0 ⟶ rt	0.2	0	17	74	0
6	**4a**	$MeOCH_2Cl$ (5.0)	0 ⟶ 40	12	33	0	0	62[e]
7	**4b**	$MeOCH_2Cl$ (5.0)	0 ⟶ 40	12	8	0	0	76
8	**4b**	$MeOCH_2Cl$ (1.2)	0 ⟶ rt	0.2	0	0	94	0
9	**4b**	$MeOCH_2Cl$ (5.0)	0 ⟶ rt	0.5	0	18	59	0
10	**4b**	$MeOCH_2Cl$ (2.5)	0 ⟶ 40	1.5	92	0	0	<5
11	**4b**	$MeOCH_2Br$ (5.0)	rt ⟶ 40	12	0	0	0	59
12[f]	**4b**	$MeOCH_2Cl$ (5.0)	0 ⟶ 40	12	0	0	0	92

[a] All reactions except for entry 12 were carried out with 1.2 equiv. of KHMDS in THF. [b] Values in parentheses represent molecular equivalent of electrophiles. [c] Isolated yield. [d] 5.0 Equiv. of HMPA was added. [e] Yield was calculated from integration of ^1H NMR spectrum of the crude product. [f] Reaction was performed using DME as the solvent, and 1.2 equiv. of KHMDS.

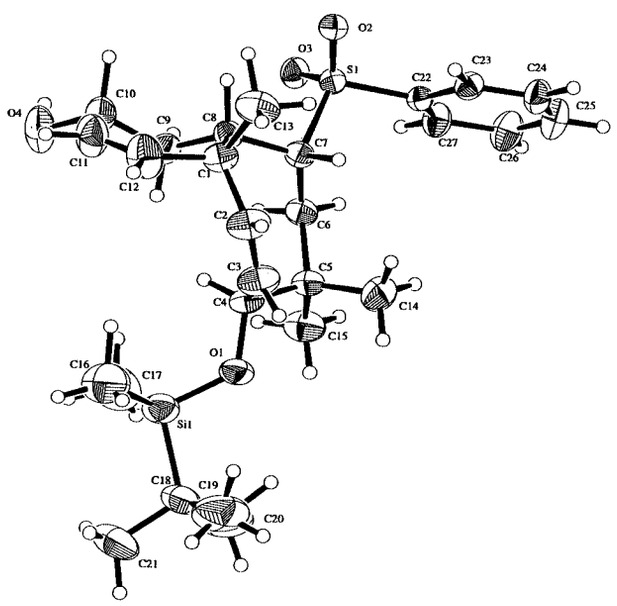


Fig. 1 Molecular structure of **20**, with crystallographic numbering scheme.

oxidised products[18] to provide the sulfone **18** in quantitative yield. Protection of the allyl alcohol **18** as its *tert*-butyldimethylsilyl (TBDMS) ether **19** and subsequent regioselective oxidation under similar conditions as above (in this case, 6 equiv. of NMO were used) provided the dienone derivative **4b** in 88% overall yield for two steps. Cyclisation reaction of **4b** with KHMDS gave the bicyclo[6.4.0]dodecane **6b** in quantitative yield. For the purpose of ascertaining the stereochemistry of **6b**, X-ray crystallographic analysis was carried out. To obtain suitable crystals, **6b** was converted to the corresponding

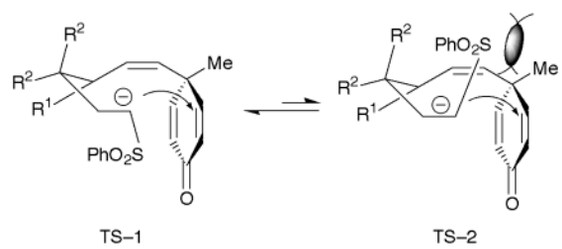


Fig. 2 Possible transition states in the KHDMS-promoted cyclisation of dienenes **4a,b** to the bicyclo[6.4.0]dodecadienones **6a,b**.

alcohol **20** by L-Selectride reduction. It was remarkable that reduction of **6b** proceeded with high diastereoselectivity (> 94/6). The X-ray analysis confirmed the stereostructure supported by NMR spectroscopy as shown in Fig. 1.

The stereochemical features observed on the cyclisation reactions suggest that the orientation of the phenylsulfonyl group should be *anti* to the angular methyl group in TS-1, presumably due to the steric repulsion in TS-2 as shown in Fig. 2.

Sequential reactions of 4 using KHMDS and electrophiles

Since effective reaction conditions for the intramolecular Michael reaction had been established, we next studied a one-pot reaction to introduce a substituent at the α-position to the carbonyl group in the 6-membered ring with various electrophiles and the results are summarised in Table 1.

Initially, **4a** was treated with chloroformates or methyl cyanoformate to yield the *O*-alkylated products **22a** (entries 1–3). On the other hand, reaction with methyl iodide afforded a mixture of **21b** and **22b** in favor of *O*-alkylation (entry 4), but the production ratio was not improved under various conditions. Treatment of **4a** with methoxymethyl chloride (MOMCl) at 0 °C gave a similar result as above, in which **21a** and **22a** were

produced in 17 and 74% isolated yield, respectively (entry 5). With the intention to enhance *C*-alkylation, **4a** was treated with an excess of MOMCl (5.0 equiv.) at various temperatures. However, to our surprise, it was found that the reaction carried out at 40 °C for 12 h gave an unexpected *exo*-olefinated analogue **23a** in moderate yield together with **6a**, products inseparable by silica gel chromatography (entry 6). Since the *exo*-olefin moiety is a suitable substituent for the assembly of the D ring of the taxane skeleton, we investigated the reaction of the functionalised substrate **4b**.

Accordingly, treatment of **4b** with 5.0 equiv. of MOMCl at 40 °C for 12 h in THF as the solvent provided the *exo*-olefinated compound **23b** in 76% yield along with 8% of dienone **6b** (entry 7). Fortunately, **23b** could be purified by column chromatography. The *exo*-olefination reaction did not take place when an equimolar amount of MOMCl was utilised even when the reaction was prolonged for 24 h at 40 °C. Based upon the observed experimental results, we presumed that the quantity of MOMCl and the temperature could drastically influence the *exo*-olefination reaction. To confirm our speculations, we examined reactions of **4b** with various quantities of MOMCl and at different temperatures.

While reaction of **4b** with 1.2 equiv. of MOMCl at 0 °C afforded **22b** in 94% yield within a very short time (*ca*. 0.2 h, entry 8), treatment with an excess of MOMCl (5.0 equiv.) at 0 °C gave a mixture of **21b** and **22b** in favor of *O*-alkylation (entry 9). Interestingly, exposure to 2.5 equiv. of MOMCl at 40 °C furnished **6b** together with a small amount of **23b** after 1.5 h (entry 10). The outcome of our study revealed that addition of an excess of MOMCl and a rise of temperature to 40 °C led to decomposition of **22b**, resulting in the formation of **6b**. Furthermore, the reaction in which MOMBr was employed under similar conditions furnished **23b** in 59% yield (entry 11). On the other hand, interestingly, the reaction performed in DME in place of THF accelerated the olefination reaction to furnish **23b** in 92% yield (entry 12). However, reactions under higher temperature (> 50 °C) in THF or DME solution resulted in poor yield of **23b**, leading to a mixture of polar products which could not be purified.

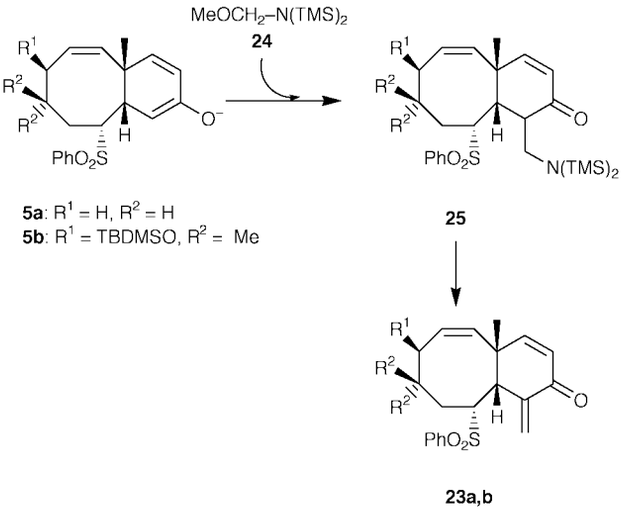
From these experiments under various conditions, it was made clear that employment of an excess of MOMCl and a slight higher than normal temperature (≈ 40 °C) were indispensable for the *exo*-olefination reaction. Moreover, DME is the best choice for the solvent.

Mechanistic aspects

It is well known that MOMCl dissociates to chloride ion, Cl^-, and methoxymethyl cation, $CH_3OCH_2^+$, in which the latter cation comprises carbenium and oxonium forms, $CH_3OCH_2^+ \leftrightarrow CH_3O^+ = CH_2$, serving as a synthon of formaldehyde.[19] For this reason, we envisaged that *exo*-olefination, after KHMDS-mediated cyclisation, was the result of a Mannich-type reaction[20] promoted by the action of hexamethyldisilazane (HMDS) on methoxymethyl cation. Namely, $CH_3OCH_2^+$ cation would be captured by hexamethyldisilazane *in situ* to form an aminomethylating reagent $[CH_3OCH_2N(TMS)_2]$ **24**[21] which could be readily converted into the corresponding iminium salt. The active species would react with enone **6** to form the Mannich base **25** (Scheme 4). The subsequent elimination of an aminomethyl group could provide the olefinated compounds **23**. Thus, it is plausible to propose that one-pot synthesis of *exo*-olefinated bicyclo[6.4.0]dodecane compounds results from an addition–elimination reaction involving the aminomethylating agent **24**.

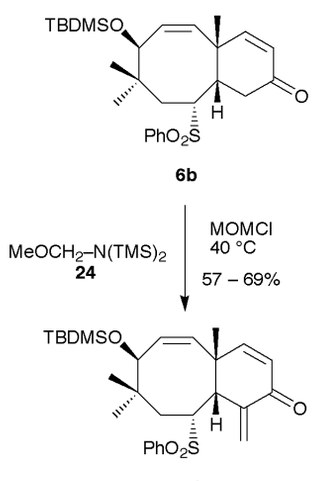
Reaction of 6b with aminomethylating reagent 24

Based upon the proposed reaction pathway, we envisaged that the direct treatment of **6** with **24** would give an aminomethylated compound **25**, which could undergo deaminomethylation



Scheme 4 A plausible mechanism for *exo*-olefination.

promoted by MOMCl. Therefore, the possible transformation of **6b** to **23b** using the reagent **24** in the presence or absence of MOMCl was examined (Scheme 5). Although reactions carried



Scheme 5

out in the absence of MOMCl or using 1.0 equiv. of MOMCl at 40 °C did not afford **23b**, the use of 5 equiv. of MOMCl promoted the olefination to provide the desired compound **23** in 57% isolated yield after 12 h at 40 °C together with 37% of recovered starting material **6b**. Furthermore, reaction with 10 equiv. of MOMCl in DME under the same conditions yielded 69% of **23b** and 13% of recovered **6b**.

Conclusions

An efficient synthetic method for *exo*-olefinated bicyclo-[6.4.0]dodecane compounds has been developed. The key step of the synthesis involved the KHMDS-mediated intramolecular cyclisation and *in situ* olefination promoted by the addition of an excess of MOMCl. The intramolecular Michael addition between a carbanion stabilised by a phenylsulfonyl group and a symmetrical dienone led to the formation of the BC ring skeleton of taxanes as a single stereoisomer. The regiospecific introduction of the one-carbon unit in the 6-membered ring was accomplished by a Mannich-type reaction promoted by **24**. The olefination reaction was highly dependent on temperature, and 5.0 equiv. of MOMCl in DME at 40 °C provided ideal conditions for the reaction. Further studies on the modification of this synthetic methodology for the con-

struction of various olefin derivatives utilising the reagent **24** and MOMCl are currently in progress in our laboratory.

Experimental

General

All moisture- or air-sensitive reactions were carried out under an atmosphere of nitrogen or argon. All reagents and solvents were used as obtained from commercial suppliers except for the following: THF and diethyl ether (hereafter referred to as ether) were distilled from benzophenone ketyl under argon. CH_2Cl_2, $CHCl_3$, DME, benzene, toluene, acetonitrile, diisopropylamine, and triethylamine were freshly distilled from calcium hydride prior to use. 2,6-Lutidine (2,6-dimethylpyridine) was distilled from calcium hydride and stored over KOH pellets. DMF, TMEDA and HMPA were distilled from calcium hydride and stored over 4 Å molecular sieves. Mps were measured on a Yanaco melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded using a JEOL GX-500 at 500 MHz, an Hitachi R-3000 or a Varian Gemini-2000 at 300 MHz for samples in $CDCl_3$ using tetramethylsilane as the internal standard. Column chromatography was carried out on silica gel (230–400 mesh). IR spectra were recorded with a JASCO IR Report-100 spectrophotometer. ^{1}H NMR data are described in the following order: chemical shift, multiplicity [s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broadened)], coupling constant(s) (*J*/Hz) and integration. ^{13}C NMR spectra were recorded using a Varian Gemini-2000 at 75 MHz for samples in $CDCl_3$. Mass spectra were taken on JEOL-DX-300 spectrometer.

(*Z*)-6-Benzyloxy-1-(1-methylcyclohexa-2,5-dienyl)hex-1-ene 8

To a suspension of (5-benzyloxypentyl)triphenylphosphonium bromide (9.5 g, 18.0 mmol) in THF (35 cm^3) was added BuLi (1.56 M solution in hexane; 10.2 cm^3, 15.9 mmol) at −78 °C. After being stirred for 1 h at −78 °C, the reaction mixture was warmed to room temperature and stirred for an additional 15 min. The solution was recooled to −78 °C and then **7** (1.5 g, 12.0 mmol) in THF (10 cm^3) was added to the reaction mixture. After being stirred for 1 h at 0 °C, the reaction mixture was diluted with ether (20 cm^3) and the phases were separated. The organic layer was washed successively with H_2O (15 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (100 : 1 hexanes–ether) to afford **8** (1.79 g, 33%) as an oil (Found: M$^+$, 282.1982. $C_{20}H_{26}O$ requires *M*, 282.1982); ν_{max} (neat)/cm^{-1} 3380; δ_H (300 MHz) 1.14 (s, 3H), 1.28–1.43 (m, 3H), 1.4–1.60 (m, 2H), 2.02–2.14 (m, 2H), 2.52–2.72 (m, 2H), 3.61 (t, *J* 6.6, 2H), 5.28–5.40 (m, 2H), 5.52–5.66 (m, 4H); *m*/*z* (M$^+$) 282.

(*Z*)-6-(1-Methylcyclohexa-2,5-dienyl)hex-5-en-1-ol 9

A mixture of **8** (1.1 g, 4.0 mmol) in THF–Bu′OH (11 cm^3; 10/1 v/v) was cooled to −78 °C, and then liq. NH_3 (≈ 75 cm^3) was introduced. To the reaction mixture was added Na metal (292 mg, 12.7 mmol) portion by portion, and the resultant mixture was stirred for 30 min. After removal of ammonia, the reaction mixture was then poured into H_2O (20 cm^3) and extracted with ether (3 × 15 cm^3). The combined extracts were washed with brine (20 cm^3), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (5 : 1 hexanes–ether) to give **9** (636 mg, 82%) as a colorless oil (Found: M$^+$, 192.1550. $C_{13}H_{20}O$ requires *M*, 192.1514); ν_{max} (neat)/cm^{-1} 3380; δ_H (300 MHz) 1.14 (s, 3H), 1.28–1.43 (m, 3H), 1.48–1.60 (m, 2H), 2.02–2.14 (m, 2H), 2.52–2.72 (m, 2H), 3.61 (t, *J* 6.6, 2H), 5.28–5.40 (m, 2H), 5.52–5.66 (m, 4H); *m*/*z* (M$^+$) 192.

3-Methyl-3-[(*Z*)-6-(phenylsulfenyl)hex-1-enyl]cyclohexa-1,4-diene 10

To a mixture of **9** (636 mg, 3.31 mmol), tributylphosphine (2.50 cm^3, 10.0 mmol), and pyridine (2.70 cm^3, 33 mmol) was added diphenyl disulfide (2.20 g, 10.0 mmol) over 15 min at ambient temperature. The reaction mixture was stirred for 7 h, and then diluted with ether (30 cm^3). To the mixture was added 10% aq. NaOH (25 cm^3), and the mixture was stirred vigorously for 30 min. The phases were separated, and the organic phase was washed with brine (15 cm^3), dried ($MgSO_4$), and concentrated. Column chromatography of the residue (20 : 1 hexanes–ether) provided **10** (940 mg, 100%) as an oil (Found: M$^+$, 284.1615. $C_{19}H_{24}S$ requires *M*, 284.1598); ν_{max} (neat)/cm^{-1} 1580; δ_H (300 MHz) 1.13 (s, 3H), 1.37–1.50 (m, 2H), 1.56–1.68 (m, 2H), 2.03–2.14 (m, 2H), 2.48–2.70 (m, 2H), 2.84–2.94 (m, 2H), 5.26–5.39 (m, 2H), 5.46–5.65 (m, 4H), 7.12–7.38 (m, 5H); δ_C 25.8, 26.6, 28.7, 28.8, 31.6, 33.4, 37.1, 120.8, 125.8, 128.9, 129.0, 132.9, 133.7, 137.2, 137.6; *m*/*z* (M$^+$) 284.

3-Methyl-3-[(*Z*)-6-(phenylsulfonyl)hex-1-enyl]cyclohexa-1,4-diene 11

To a mixture of **10** (160 mg, 0.563 mmol) in THF–MeOH–H_2O (8 cm^3; 3/1/1 v/v/v) was added Oxone (1.0 g, 1.6 mmol) portion by portion at 0 °C. The reaction mixture was stirred for 3 h at room temperature and quenched by H_2O (5 cm^3). The organic phase was extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with brine (7 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (1 : 5 hexanes–ethyl acetate) to provide **11** (169 mg, 95%) as a solid (Found: C, 71.85; H, 7.55. $C_{19}H_{24}O_2S$ requires C, 72.1; H, 7.6%); ν_{max} (neat)/cm^{-1} 1310, 1150; δ_H (300 MHz) 1.12 (s, 3H), 1.28–1.42 (m, 2H), 1.60–1.73 (m, 2H), 1.98–2.09 (m, 2H), 2.45–2.70 (m, 2H), 3.00–3.12 (m, 2H), 5.23 (dt, *J* 11.3 and 7.0, 1H), 5.34 (dt, *J* 11.3 and 1.4, 1H), 5.46–5.63 (m, 4H), 7.53–7.72 (m, 3H), 7.87–7.95 (m, 2H); δ_C 22.2, 25.7, 26.2, 28.0, 31.6, 37.0, 56.1, 120.8, 128.1, 129.3, 132.1, 133.5, 133.7, 138.1, 139.3; *m*/*z* (M$^+$) 316.

4-Methyl-4-[(*Z*)-6-(phenylsulfonyl)hex-1-enyl]cyclohexa-2,5-dienone 4a

To a suspension of diene **11** (330 mg, 1.04 mmol), NMO (730 mg, 6.24 mmol), and 4Å molecular sieves (400 mg) in acetonitrile (7 cm^3) was added TPAP (362 mg, 0.1 mmol) at room temperature. After being stirred for 18 h, the reaction mixture was diluted with ether (15 cm^3) and filtered through Celite. After concentration of the filtrate, flash chromatography of the residue (1 : 2 hexanes–ethyl acetate) gave **4a** (141 mg, 41%) as a solid (Found: M$^+$, 330.1306. $C_{19}H_{22}O_3S$ requires *M*, 330.1290); ν_{max} (neat)/cm^{-1} 1670, 1310, 1160; δ_H (300 MHz) 1.30–1.42 (m, 2H), 1.34 (s, 3H), 1.55–1.68 (m, 2H), 1.82–1.92 (m, 2H), 2.96–3.05 (m, 2H), 5.31–5.43 (m, 2H), 6.17–6.24 (m, 2H), 6.82–6.89 (m, 2H), 7.54–7.71 (m, 3H), 7.86–7.93 (m, 2H); δ_C 21.9, 26.6, 27.7, 28.1, 42.3, 55.9, 126.9, 128.0, 129.4, 129.8, 133.8, 134.9, 139.2, 154.9, 185.8; *m*/*z* (M$^+$) 330.

(±)-(1*R**,7*R**,8*S**)-1-Methyl-7–(phenylsulfonyl)bicyclo[6.4.0]-dodeca-2,11-dien-10-one 6a

To a solution of **4a** (20 mg, 61 μmol) in THF (0.6 cm^3) was added KHMDS (0.5 M solution in toluene; 0.133 cm^3, 67 μmol) at 0 °C. The solution was stirred for 15 min and quenched with saturated aq. NH_4Cl (3 cm^3). The mixture was extracted with ethyl acetate, and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (3 : 1 hexanes–ethyl acetate) to give **6a** (18 mg, 91%) as a solid (Found: C, 68.85; H, 6.65. $C_{19}H_{22}O_3S$ requires C, 69.05; H, 6.7%); mp 182.0–183.0 °C; ν_{max} (neat)/cm^{-1} 1690, 1315, 1160; δ_H (500 MHz; C_6D_6) 0.95 (s, 3H), 1.11–1.29 (m, 2H), 1.61–1.71 (m, 1H), 1.73–1.81 (m, 1H), 1.82–1.92 (m, 1H), 2.19–2.27 (m, 1H), 2.70 (dd, *J* 16.5 and 11.6, 1H), 2.83–2.89 (m, 1H), 3.04 (dd, *J* 16.5 and 3.7, 1H), 3.37–3.43 (m, 1H), 5.11 (d, *J* 11.6, 1H), 5.31 (ddd,

J 11.6, 10.4 and 7.9, 1H), 5.82 (d, *J* 9.8, 1H), 6.03 (d, *J* 9.8, 1H), 6.94–7.06 (m, 3H), 7.78–7.88 (m, 2H); δ_C 20.0, 25.0, 25.6, 26.5, 36.4, 40.9, 42.3, 63.1, 128.8, 129.5, 133.0, 133.6, 134.0, 138.2, 159.1, 198.5; *m/z* (M^+) 330.

4,4-Ethylenedioxy-3,3-dimethylbutan-1-ol 13

To a solution of **12** (2.00 g, 12.8 mmol) in ether–water (1:1 v/v; 160 cm^3) was added osmium tetraoxide (160 mg, 640 mmol) at 20 °C. Sodium periodate (16.4 g, 76.8 mmol) was added portionwise under vigorous stirring to the resulting mixture over 50 min at room temperature. After being stirred for 1 h, the mixture was diluted with ether (30 cm^3), and phases were separated. The aqueous phase was extracted with ether (3 × 30 cm^3), and the combined organic phases were washed successively with water (40 cm^3) and brine (40 cm^3), dried ($MgSO_4$), and concentrated. The residue was dissolved in methanol (40 cm^3). To the crude aldehyde was added sodium borohydride (480 mg, 12.7 mmol) portion by portion at 0 °C, and the mixture was allowed to warm to ambient temperature and stirred for 1 h. The solvent was removed *in vacuo* and the residue was poured into water (25 cm^3), and then the mixture was extracted with ether (3 × 30 cm^3). The combined extracts were washed with brine (20 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (2:1 hexanes–ethyl acetate) to afford **13** (1.45 g, 66%) as an oil (Found: $M^+ - 1$, 159.1038. $C_8H_{15}O_3$ requires $M - 1$, 159.1021); ν_{max} (neat)/cm^{-1} 3380; δ_H (300 MHz) 0.96 (s, 6H), 1.63 (t, *J* 6.4, 2H), 2.60–2.71 (m, 1H), 3.62–3.76 (m, 1H), 3.82–4.02 (m, 4H), 4.58 (s, 1H); δ_C 22.5, 36.5, 41.1, 59.2, 65.2, 109.7; *m/z* ($M^+ - 1$) 159.

1,1-Ethylenedioxy-2,2-dimethyl-4-(phenylthio)butane 14

To a mixture of **13** (800 mg, 5.00 mmol), tributylphosphine (3.74 cm^3, 15.0 mmol), and pyridine (4.04 cm^3, 50 mmol) was added diphenyl disulfide (3.28 g, 15.0 mmol) over 15 min at room temperature. The mixture was stirred for 12 h, and then diluted with ether (30 cm^3). To the resultant mixture was added 10% aq. NaOH (25 cm^3), and the mixture was stirred vigorously for 30 min. The phases were separated, and the organic phase was washed with brine (15 cm^3), dried ($MgSO_4$), and concentrated. Column chromatography of the residue (20:1 hexanes–ether) provided sulfide **14** (1.06 g, 84%) as an oil (Found: C, 66.65; H, 7.95. $C_{14}H_{20}O_2S$ requires C, 66.60; H, 8.0%); ν_{max} (neat)/cm^{-1} 1110; δ_H (300 MHz) 0.94 (s, 6H), 1.63–1.75 (m, 2H), 2.91–3.02 (m, 2H), 3.79–3.97 (m, 4H), 4.54 (s, 1H), 7.10–7.36 (m, 5H); δ_C 21.7, 28.5, 37.2, 37.5, 65.3, 109.7, 125.7, 128.7, 129.0, 137.2; *m/z* (M^+) 252.

2,2-Dimethyl-4-(phenylthio)butanal 15

A mixture of **14** (827 mg, 3.29 mmol), acetic acid (24 cm^3), and water (6 cm^3) was stirred for 5 h at 50 °C and then the solvents were removed by azeotropic distillation with toluene (30 cm^3) under reduced pressure. The residue was purified by column chromatography (20:1 hexanes–ether) to give aldehyde **15** (652 mg, 95%) as an oil (Found: M^+, 208.0916, $C_{12}H_{16}O_5$ requires *M*, 208.0922); ν_{max} (neat)/cm^{-1} 1728; δ_H (300 MHz) 1.09 (s, 6H), 1.78–1.87 (m, 2H), 2.79–2.87 (m, 2H), 7.16–7.35 (m, 5H), 9.45 (s, 1H); δ_C 21.3, 28.7, 36.6, 45.9, 126.3, 129.1, 129.3, 136.1, 205.5; *m/z* (M^+) 208.

3-[(*Z*)-2-Iodovinyl]-3-methylcyclohexa-1,4-diene 16

To a suspension of (iodomethyl)triphenylphosphonium iodide (2.60 g, 4.90 mmol) in THF (7 cm^3) was added NaHMDS (1.0 M solution in THF; 4.90 cm^3, 4.90 mmol) at room temperature, and the reaction mixture was stirred for 5 min. The solution was cooled to −78 °C and aldehyde **7** (0.50 g, 4.10 mmol) in 3 cm^3 of THF was added. The reaction was allowed to proceed for 1.5 h at room temperature and the mixture was diluted with ether–H_2O (50:50 v/v; 25 cm^3), and then filtered through Celite. The filtrate was washed with brine (10 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by distillation to give **16** (690 mg, 66%) as an oil, bp 120–122 °C/5 mmHg (Found: C, 43.70; H, 4.6; I, 51.5. $C_9H_{11}I$ requires C, 43.9; H, 4.5; I, 51.5%); ν_{max} (neat)/cm^{-1} 1635; δ_H (300 MHz) 1.27 (s, 3H), 2.64–2.72 (m, 2H), 5.42–5.52 (m, 2H), 5.69–5.79 (m, 2H), 6.39 (d, *J* 8.1, 1H), 6.47 (d, *J* 8.1, 1H); *m/z* (M^+) 246.

(*Z*)-4,4-Dimethyl-1-(1-methylcyclohexa-2,5-dienyl)-6-(phenylthio)hex-1-en-3-ol 17

To a mixture of **16** (485 mg, 1.97 mmol) and **15** (408 mg, 1.96 mmol) in THF (20 cm^3) was added dropwise *tert*-butyllithium (1.6 M solution in pentane; 2.69 cm^3, 4.30 mmol) at −78 °C. After being stirred at −78 °C for 30 min, the mixture was treated with saturated aq. $NaHCO_3$ (5 cm^3), and then the resulting solution was extracted with ethyl acetate (3 × 5 cm^3). The combined extracts were washed with brine (7 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (25:1 hexanes–ethyl acetate) to afford **17** (520 mg, 81%) as an oil [Found: $M^+ - 18$, 310.1740. $C_{21}H_{26}S$ ($M - 18$) requires *m/z* 310.1755]; ν_{max} (neat)/cm^{-1} 3480; δ_H (300 MHz) 0.85 (s, 3H), 0.89 (s, 3H), 1.17 (s, 3H), 1.36–1.80 (m, 3H), 2.55–2.75 (m, 2H), 2.79–2.99 (m, 2H), 4.56 (br d, *J* 9.6, 1H), 5.44–5.77 (m, 6H), 7.11–7.35 (m, 5H); δ_C 22.2, 22.4, 25.8, 28.4, 31.9, 37.2, 37.4, 38.6, 70.8, 121.0, 121.7, 125.6, 128.5, 128.9, 131.4, 134.0, 134.5, 137.3, 141.6; *m/z* ($M^+ - H_2O$) 310.

(*Z*)-4,4-Dimethyl-1-(1-methylcyclohexa-2,5-dienyl)-6-(phenylsulfonyl)-hex-1-en-3-ol 18

To a mixture of **17** (810 mg, 2.47 mmol) in chloroform (20 cm^3) was added MCPBA (1.29 g, 7.50 mmol) at 0 °C. After being stirred at 0 °C for 15 min, the reaction mixture was warmed to room temperature and stirred for an additional 25 min. To the resultant mixture was added 10% aq. $NaHCO_3$ (15 cm^3) and the layers were separated. The aqueous layer was extracted with chloroform (3 × 10 cm^3). The combined organic phases were washed with brine (10 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (4:1 hexanes–ethyl acetate) to give 890 mg (100%) of **18** as a colorless oil (Found: M^+, 360.1737. $C_{21}H_{28}O_3S$ requires *M*, 360.1759); ν_{max} (neat)/cm^{-1} 3530, 1310, 1150; δ_H (300 MHz) 0.77 (s, 3H), 0.81 (s, 3H), 1.15 (s, 3H), 1.50–1.82 (m, 3H), 2.48–2.65 (m, 2H), 3.06–3.22 (m, 2H), 4.43 (d, *J* 9.8, 1H), 5.37–5.73 (m, 6H), 7.51–7.70 (m, 3H), 7.85–7.95 (m, 2H); δ_C 22.2, 22.7, 25.8, 31.4, 31.8, 36.4, 37.4, 52.6, 70.9, 121.0, 121.8, 128.2, 129.4, 131.0, 133.7, 134.0, 134.4, 139.4, 142.1; *m/z* (M^+) 360.

3-[(*Z*)-3-*tert*-Butyldimethylsiloxy-4,4-dimethyl-6-(phenylsulfonyl)hex-1-enyl]-3-methylcyclohexa-1,4-diene 19

To a mixture of **18** (616.1 mg, 1.71 mmol) and 2,6-lutidine (0.70 cm^3, 6.00 mmol) in CH_2Cl_2 (15 cm^3) was added dropwise TBDMSOTf (0.79 cm^3, 3.42 mmol) at 20 °C. After being stirred for 1 h, the reaction mixture was quenched with 10% aq. $KHSO_4$ (10 cm^3). After separation, the aqueous phase was extracted with CH_2Cl_2 (3 × 10 cm^3), and the combined extracts were washed with brine (10 cm^3), dried ($MgSO_4$), and concentrated. Flash chromatography of the residue (10:1 hexanes–ethyl acetate) provided **19** (790 mg, 97%) as an oil (Found: C, 68.25; H, 8.90; S, 6.80. $C_{27}H_{42}O_3SSi$ requires C, 68.30; H, 8.90; S, 6.75%); ν_{max} (neat)/cm^{-1} 1305, 1150; δ_H (300 MHz) −0.05 (s, 3H), −0.03 (s, 3H), 0.73 (s, 3H), 0.74 (s, 3H), 0.75 (s, 9H), 1.13 (s, 3H), 1.46–1.76 (m, 2H), 2.48–2.71 (m, 2H), 2.95–3.20 (m, 2H), 4.52 (br d, *J* 9.9, 1H), 5.10 (dd, *J* 12.3 and 9.9, 1H), 5.25 (br d, *J* 12.3, 1H), 5.45–5.71 (m, 4H), 7.53–7.67 (m, 3H), 7.87–7.91 (m, 2H); δ_C −4.9, −3.8, 18.1, 22.85, 22.90, 25.8, 26.0,

30.7, 31.9, 38.2, 38.8, 52.8, 73.1, 121.5, 122.3, 128.2, 128.9, 129.4, 133.20, 133.24, 133.7, 137.8, 139.3; *m/z* ($M^+ - Bu^t$) 417.

4-[(*Z*)-3-*tert*-Butyldimethylsiloxy-4,4-dimethyl-6-(phenylsulfonyl)hex-1-enyl]-4-methylcyclohexa-2,5-dienone 4b

Obtained from **19** (1.44 g, 3.05 mmol) (in the same way as **4a** was prepared from **11**) in 88% yield (from **18**) (1.31 g) as an oil (Found: C, 66.45; H, 7.85. $C_{27}H_{40}O_4SSi$ requires C, 66.35; H, 8.25%); ν_{max} (neat)/cm^{-1} 1670, 1310; δ_H (300 MHz) −0.05 (s, 3H), −0.04 (s, 3H), 0.66 (s, 3H), 0.68 (s, 3H), 0.77 (s, 9H), 1.36 (s, 3H), 1.46–1.75 (m, 2H), 2.91–3.17 (m, 2H), 4.10 (d, *J* 8.8, 1H), 5.29–5.43 (m, 2H), 6.21 (dd, *J* 9.9 and 1.9, 1H), 6.30 (dd, *J* 9.9 and 1.9, 1H), 6.87 (dd, *J* 9.9 and 3.0, 1H), 6.95 (dd, *J* 9.9 and 3.0, 1H), 7.52–7.69 (m, 3H), 7.84–7.92 (m, 2H); δ_C −4.8, −3.7, 18.1, 23.10, 23.14, 25.7, 28.5, 30.0, 38.6, 43.6, 52.6, 74.7, 127.2, 128.1, 129.4, 133.10, 132.9, 133.8, 139.3, 153.5, 153.7, 185.5; *m/z* ($M^+ - Bu^t$) 431.

(±)-(1*R,4*S**,7*R**,8*S**)-[4-*tert*-Butyldimethylsiloxy-1,5,5-trimethyl-7-(phenylsulfonyl)bicyclo[6.4.0]dodeca-2,11-dien-10-one 6b**

Obtained from **4b** (16 mg, 33 μmol) (in the same way as **6a** was prepared from **4a**) in 100% yield (16 mg) as a solid; mp 140–142 °C (Found: 66.35; H, 8.25. $C_{27}H_{40}O_4SSi$ requires C, 66.35; H, 8.25%); ν_{max} (neat)/cm^{-1} 1680, 1300, 1150; δ_H (500 MHz) −0.06 (s, 3H), −0.05 (s, 3H), −0.01 (s, 3H), 0.71 (s, 3H), 0.81 (s, 9H), 1.44 (s, 3H), 1.71 (dd, *J* 16.5 and 6.1, 1H), 1.74–1.81 (m, 1H), 2.80 (dd, *J* 18.3 and 7.3, 1H), 3.20–3.28 (m, 1H), 3.42 (br d, *J* 18.3, 1H), 3.55–3.62 (m, 1H), 4.28 (dd, *J* 7.3 and 1.8, 1H), 5.36 (dd, *J* 12.2 and 1.8, 1H), 5.51 (dd, *J* 12.2 and 7.3, 1H), 6.10 (d, *J* 10.4, 1H), 6.62 (dd, *J* 10.4 and 1.2, 1H), 7.50–7.56 (m, 2H), 7.58–7.64 (m, 1H), 7.79–7.87 (m, 2H); δ_C −4.9, −4.1, 16.4, 17.9, 25.7, 29.2, 30.2, 34.3, 34.9, 39.2, 40.3, 42.0, 62.7, 73.5, 128.1, 129.39, 129.42, 133.2, 134.0, 138.4, 140.4, 156.4, 197.1; *m/z* (M^+) 488.

(±)-(1*S,4*R**,7*S**,8*R**,10*S**)-4-*tert*-Butyldimethylsiloxy-1,5,5-trimethyl-7-(phenylsulfonyl)bicyclo[6.4.0]dodeca-2,11-dien-10-ol 20**

L-Selectride (1.0 M solution in THF; 0.74 cm^3, 74 μmol) was added to a solution of **6b** (24 mg, 49 μmol) in THF (1 cm^3) at 0 °C. The reaction mixture was allowed to react for 14 h, and saturated aq. NH_4Cl (2 cm^3) and ether (5 cm^3) were added. After separation, the aqueous phase was extracted with ether (3 × 2 cm^3). The combined organic phases were dried ($MgSO_4$) and concentrated, and the residue was purified by column chromatography (5:1 hexanes–ethyl acetate) to afford **20** (21 mg, 87%) as a solid, recrystallisation of which from methanol provided needles, mp 167–169 °C (Found: C, 65.80; H, 8.70. $C_{27}H_{42}O_4SSi$ requires C, 66.0; H, 8.65%); ν_{max} (neat)/cm^{-1} 3450, 1290, 1150; δ_H (300 MHz) −0.05 (s, 3H), −0.03 (s, 3H), 0.17 (s, 3H), 0.80 (s, 3H), 0.83 (s, 9H), 1.14 (s, 3H), 1.67 (d, *J* 15.9, 1H), 2.05–2.13 (br s, 1H), 2.26 (br t, *J* 5.8, 2H), 2.48 (br dd *J* 15.9 and 8.2, 1H), 2.72–2.81 (br s, 1H), 3.43–3.54 (br s, 1H), 4.21 (d, *J* 6.6, 1H), 4.26–4.36 (br s, 1H), 5.24 (d, *J* 12.4, 1H), 5.33 (dd, *J* 12.4 and 6.6, 1H), 5.62 (dd, *J* 10.2 and 1.4, 1H), 5.80 (dd, *J* 10.2 and 3.5, 1H), 7.52–7.68 (m, 3H), 7.84–7.91 (m, 2H); δ_C −5.0, −4.2, 17.6, 18.0, 25.8, 29.2, 31.4, 32.3, 34.9, 37.7, 38.7, 40.2, 61.7, 63.9, 74.1, 128.0, 129.3, 129.33, 133.8, 134.2, 136.2, 137.2, 138.3; *m/z* (M^+) 490.

Crystal data for 20. Monoclinic, space group $P2_1/a$, $a = 15.048(4)$, $b = 11.327((3))$, $c = 16.988(4)$ Å, $\beta = 97.02(2)°$, $V = 2873(1)$ Å^3, $Z = 4$, $\mu = 16.17$ cm^{-1}, $D_c = 1.134$ g cm^{-3}, $F(000) = 1064$, $T = 290$ K, R, $R_w = 0.063$, 0.063 for 2964 absorption-corrected reflections with $I > 3.00\ \sigma(I)$. CCDC reference number 207/349. See http://www.rsc.org/suppdata/p1/1999/2609 for crystallographic files in .cif format.

(±)-(1*R,4*S**, 7*R**,*8S**,9*R**)-4-*tert*-Butyldimethylsiloxy-9-methoxymethyl-1,5,5-trimethyl-7-(phenylsulfonyl)bicyclo-[6.4.0]dodeca-2,11-dien-10-one 21b ($R^3 = CH_2OMe$) and (±)-(1*R**,4*S**,7*R**,8*S**)-4-*tert*-butyldimethylsiloxy-10-methoxymethoxy-1,5,5-trimethyl-7-(phenylsulfonyl)bicyclo[6.4.0]-dodeca-2,9,11-triene 22b ($R^3 = CH_2OMe$) (entry 9, Table 1)**

To a solution of **4b** (210 mg, 0.431 mmol) in THF (5 cm^3) was added KHMDS (0.5 M solution in toluene; 1.11 cm^3, 0.560 mmol) at 0 °C. After this mixture had been stirred for 10 min at 0 °C, MOMCl (0.16 cm^3, 2.160 mmol) was added *via* syringe. The reaction mixture was then warmed to ambient temperature, stirred for 30 min, and treated with saturated aq. NH_4Cl (10 cm^3), and the resulting mixture was extracted with ethyl acetate (3 × 10 cm^3). The combined organic layers were dried ($MgSO_4$) and concentrated, and the residue was purified by column chromatography (10:1 hexanes–ethyl acetate) to afford **21b** ($R^3 = CH_2OMe$) (41 mg, 18%) as a solid, mp 156–157 °C, and **22b** ($R^3 = CH_2OMe$) (131 mg, 59%) as a solid, mp 111–112 °C.

Spectral data for 21b. (Found: M^+, 532.2715. $C_{29}H_{44}O_5SSi$ requires *M*, 532.2679); ν_{max} (neat)/cm^{-1} 1670, 1300, 1155; δ_H (300 MHz) −0.06 (s, 6H), 0.06 (s, 3H), 0.73 (s, 3H), 0.82 (s, 9H), 1.46 (s, 3H), 1.64 (d, *J* 16.5, 1H), 1.83 (d, *J* 16.5, 1H), 3.33 (br s, 1H), 3.36 (s, 3H), 3.37–3.44 (m, 1H), 3.65–3.75 (m, 2H), 3.97 (ddd, *J* 9.6, 5.5 and 0.8, 1H), 4.20 (d, *J* 7.1, 1H), 5.35 (d, *J* 12.1, 1H), 5.52 (dd, *J* 12.1 and 7.1, 1H), 6.12 (d, *J* 10.4, 1H), 6.64 (d, *J* 10.4 and 1.8, 1H), 7.49–7.68 (m, 3H), 7.80–7.90 (m, 2H); δ_C −5.0, −4.1, 16.6, 17.9, 25.7, 29.2, 33.3, 35.3, 38.7, 39.6, 44.0, 46.3, 58.9, 63.1, 73.7, 74.7, 127.4, 129.3, 129.4, 134.0, 134.8, 138.4, 140.4, 156.8, 198.0; *m/z* (M^+) 532.

Spectral data for 22b. (Found: C, 65.25; H, 8.35. $C_{29}H_{44}O_5SSi$ requires C, 65.35; H, 8.30%); ν_{max} (neat)/cm^{-1} 1660, 1300, 1140; δ_H (300 MHz) −0.02 (s, 6H), 0.04 (s, 3H), 0.76 (s, 3H), 0.84 (s, 9H), 1.24 (s, 3H), 1.65 (d, *J* 16.9, 1H), 1.89 (dd, *J* 16.9 and 6.2, 1H), 3.30–3.39 (m, 1H), 3.40–3.47 (m, 1H), 3.48 (s, 3H), 4.36 (d, *J* 7.0, 1H), 4.98 (d, *J* 5.9, 1H), 5.10 (d, *J* 5.9, 1H), 5.21 (dd, *J* 6.2 and 1.8, 1H), 5.30 (d, *J* 11.7, 1H), 5.43 (dd, *J* 11.7 and 7.0, 1H), 5.67 (d, *J* 9.9, 1H), 6.83 (dd, *J* 9.9 and 1.8, 1H), 7.45–7.62 (m, 3H), 7.79–7.86 (m, 2H); δ_C −5.0, −4.1, 16.1, 17.9, 25.7, 29.3, 29.8, 33.5, 38.4, 39.3, 42.3, 56.3, 63.2, 74.4, 94.0, 94.9, 121.4, 129.16, 129.19, 133.6, 134.4, 138.4, 138.9, 139.1, 150.5; *m/z* (M^+) 532.

(±)-(1*R,4*S**,7*R**,8*R**)-[4-*tert*-Butyldimethylsiloxy-1,5,5-trimethyl-9-methylene-7-(phenylsulfonyl)bicyclo[6.4.0]dodeca-2,11-dien-10-one 23b (entry 12, Table 1)**

To a solution of **4b** (100 mg, 205 μmol) in DME (2 cm^3) was added KHMDS (0.5 M solution in toluene; 0.492 cm^3, 246 mol) at 0 °C. The reaction mixture was stirred for 15 min at 0 °C and then treated with MOMCl (0.023 cm^3, 30 μmol). After the mixture had been stirred for 45 min at room temperature, more MOMCl (0.77 cm^3, 1.00 mmol) was added. After 12 h of stirring at 40 °C, the reaction mixture was quenched with H_2O (3 cm^3). The phases were separated, and the aqueous phase was extracted with ether (3 × 5 cm^3). The combined organic phases were washed with brine (7 cm^3), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (10:1 hexanes–ethyl acetate) to afford **23b** (94 mg, 92%) as a solid, mp 163–165 °C (Found: C, 67.15; H, 8.05. $C_{28}H_{40}O_4SSi$ requires C, 67.15; H, 8.05%); ν_{max} (neat)/cm^{-1} 1675, 1300, 1150; δ_H (300 MHz) −0.17 (s, 3H), −0.03 (s, 3H), −0.02 (s, 3H), 0.71 (s, 3H), 0.83 (s, 9H), 1.42 (s, 3H), 1.69 (d, *J* 16.5, 1H), 1.90 (dd, *J* 16.5 and 6.6, 1H), 3.61–3.72 (m, 1H), 4.06–4.15 (m, 1H), 4.36 (dd, *J* 7.0 and 1.0, 1H), 5.43 (d, *J* 11.7, 1H), 5.55 (dd, *J* 11.7 and 7.0, 1H), 5.97 (s, 1H), 6.19 (d, *J* 10.3, 1H), 6.43 (d, *J* 1.8, 1H), 6.70 (d, *J* 10.3, 1H), 7.50–7.68 (m, 3H), 7.80–7.90 (m, 2H); δ_C −4.0, −0.1, 15.0, 11.6, 17.6, 21.7, 25.7, 29.3, 30.4, 34.6, 39.4, 42.2, 55.3, 63.5, 73.6, 97.3, 128.4, 129.4, 129.5,

130.9, 132.9, 133.9, 139.3, 140.5, 146.5, 156.6, 219.2; *m*/*z* (M^+) 500.

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References and notes

1 M. C. Wani, H. L. Taylor, M. E. Wall, P. Coggon and A. T. McPhail, *J. Am. Chem. Soc.*, 1971, **93**, 2325.
2 E. K. Rowinsky, L. A. Cazenave and R. C. Donehover, *J. Natl. Cancer Inst.*, 1990, **82.** 1247.
3 I. Ringel and S. B. Horwiz, *J. Natl. Cancer Inst.*, 1991, **83**, 288.
4 J. Kobayashi, A. Ogiwara, H. Hosoyama, H. Shigemori, N. Yoshida, T. Sasaki, Y. Li, S. Iwasaki, M. Naito and T. Tsuruno, *Tetrahedron*, 1994, **50,** 7401; H. Morita, L. Wei, A. Gouda, K. Takeya, M. Itokawa, H. Fukaya, H. Shigemori and J. Kobayashi, *Tetrahedron*, 1997, **53**, 4621.
5 For a recent total synthesis: K. Morihara, R. Hara, S. Kawahara, T. Nishimori, N. Nakamura, H. Kusama and I. Kuwajima, *J. Am. Chem. Soc.*, 1998, **120**, 12980 and references therein.
6 (*a*) For reviews, see: K. C. Nicolaou, W.-M. Dai and R. K. Guy, *Angew. Chem.*, *Int. Ed. Engl.*, 1994, **33**, 15; B. Norton and N. Biother, *Drugs Fut.*, 1996, **21**(1), 95; (*b*) G. Mehta and V. Singh, *Chem. Rev*, 1999, **99**, 881.
7 N. S. Simpkins, (*a*) *Sulfones in Organic Chemistry*, Pergamon Press, Oxford, 1993, p. 100; (b) *Tetrahedron*, 1990, **46**, 6951.
8 A part of this work has been published as a preliminary communication: M. Ihara, S. Suzuki, Y. Tokunaga, H. Takeshita and K. Fukumoto, *Chem. Commun.*, 1996, 1801.
9 P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon Press, Oxford, 1992.
10 S. Arseniyadis, D. V. Yashunsky, M. M. Dorada, R. B. Alves, E. Toromanoff, L. Toupet and P. Potier, *Tetrahedron Lett.*, 1993, **34**, 4927.
11 This reagent was prepared from (5-bromopentyloxymethyl)benzene and triphenylphosphine in toluene under reflux for 10 h in 76% yield.
12 I. Nakagawa and T. Hata, *Tetrahedron Lett.*, 1975, 1409; I. Nakagawa, K. Aki and T. Hata, *J. Chem. Soc.*, *Perkin Trans. 1*, 1983, 1315.
13 For a review, see: S. V. Ley, J. Norman, W. P. Griffith and S. P. Marsden, *Synthesis*, 1994, 639.
14 D. Sternbach and C. L. Ensinger, *J. Org. Chem.*, 1990, **55,** 2725.
15 R. Rappo, D. S. Allen, R. U. Lemieux and W. S. Johnson, *J. Org. Chem.*, 1956, **21**, 478.
16 The vinyl iodide **16** was obtained as a mixture of *E*/*Z* isomers (1/15).
17 G. Stork and K. Zhao, *Tetrahedron Lett.*, 1989, **30**, 2137; D. Seyferth, J. K. Heeren, G. Singh, S. O. Grim and W. B. Hughes, *J. Organomet. Chem.*, 1966, **5**, 267.
18 MCPBA (purchased from Wako Pure Chemical Co. Ltd) had to be added to the reaction mixture in one portion at 0 °C to prevent the formation of over-oxidised products.
19 J. K. Pau, J. K. Kim and M. C. Caserio, *J. Am. Chem. Soc.*, 1978, **100**, 3831, 3838; S. Okada, Y. Abe, S. Taniguchi and S. Yamabe, *J. Am. Chem. Soc.*, 1987, **109**, 295.
20 For reviews, see: M. Arend, B. Westermann and N. Risch, *Angew. Chem.*, *Int. Ed.*, 1998, **37**, 1044; M. Tramontini, *Synthesis*, 1973, 703.
21 T. Morimoto, T. Takeshita and M. Sekiya, *J. Chem. Soc.*, *Chem Commun.*, 1984, **794**, 883.

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