# *endo*-Selective Intramolecular Pauson – Khand Reactions of $\gamma$-Oxygenated-$\alpha$,$\beta$-unsaturated Phenylsulfones

**Javier Adrio, Marta Rodríguez Rivero, and Juan C. Carretero***[a]

**Abstract:** A wide variety of 1,6-enynes and 1,7-enynes incorporating $\gamma$-oxygenated-$\alpha$,$\beta$-unsaturated phenylsulfone moieties have readily been prepared by piperidine-promoted condensation of the corresponding alkynyl aldehyde with phenylsulfonyl-(*p*-tolylsulfinyl)methane and further protection of the hydroxyl group. Despite the enduring claim concerning the unsuitability of electronically deficient olefins in Pauson – Khand reactions, we report that these 1-sulfonylated enynes are excellent substrates in intramolecular Pauson – Khand reactions under both thermal and amine *N*-oxide-promoted conditions. Moreover, in contrast with the usual *exo*-selective Pauson – Khand cyclization of allylic substituted enynes, the reactions of these 1-sulfonylated-3-oxygenated enynes occur with a moderate or high *endo* selectivity. The evaluation of the chemical and stereochemical scope of the process in comparison with the Pauson – Khand cyclization of non-sulfonylated enynes, its application to the stereoselective preparation of optically pure C6-substituted bicyclo[3.3.0]oct-1-en-3-ones, and the interpretation of the stereochemical outcome are also discussed.

**Keywords:** allylic compounds • enynes • Pauson – Khand reaction • stereoselectivity • sulfones

## Introduction

During the last decade, the progress achieved in the application of transition metal mediated reactions in the field of organic synthesis has been impressive. One such reaction is the cobalt-mediated carbonylative co-cyclization of an alkyne and an alkene, known as the Pauson – Khand (PK) reaction, which is nowadays one of the most efficient and convergent methods of synthesis of cyclopentenones.[1] In particular, intramolecular PK reactions of 1,6-enynes and 1,7-enynes have been by far the most studied, and the resulting bicyclo[3.3.0]octenones and bicyclo[4.3.0]nonenones have been widely applied to the synthesis of structurally complex natural and non-natural compounds.[2]

As far as the stereoselectivity of the intramolecular PK reaction is concerned, it has been known since the pioneering studies of Magnus[3] that enynes possessing substituents at the allylic or propargylic positions give rise predominantly to the *exo* adducts.[4] This usual *exo* selectivity in the intramolecular PK reaction was attributed to unfavorable steric interactions between the *endo* allylic or propargylic groups and the substituent at the alkyne terminus in the *endo*-cobaltacycle intermediate.[3, 4]

Despite the general assumption that electron-deficient alkenes are unsuitable substrates in PK reactions,[5] recent publications have shown that this is not always the case.[6] For instance, Cazes et al. have reported several examples of *N*-oxide-promoted intermolecular PK reactions of methyl acrylate and phenyl vinyl sulfone.[7] On the other hand, we have reported that 1-sulfinyl-1,6-enynes can undergo intramolecular PK reaction in an efficient and stereoselective manner.[8] In the context of our current interest in the use of $\gamma$-oxygenated-$\alpha$,$\beta$-unsaturated sulfones as versatile starting materials in stereoselective synthesis,[9] we wish to report that 1,6-enynes and 1,7-enynes with $\gamma$-oxygenated-$\alpha$,$\beta$-unsaturated phenylsulfones as olefinic partners are not only excellent substrates in PK reactions, but also that their cyclizations tend to be *endo*-selective[10] rather than *exo*-selective, especially in the case of the 1,6-enynes. As these sulfonylated enynes are readily available in both racemic and enantiopure forms, and as the sulfonyl group can easily be removed in the cyclopentenone products, this methodology constitutes an efficient, stereocomplementary Pauson – Khand approach to the asymmetric synthesis of C6-substituted bicyclo[3.3.0]oct-1-en-3-ones.[11]

## Results and Discussion

**PK reactions of 1-phenylsulfonylhept-1-en-6-yn-3-ol and derivatives**: To check the viability of $\gamma$-oxygenated-$\alpha$,$\beta$-unsaturated sulfones in intramolecular PK reactions, the

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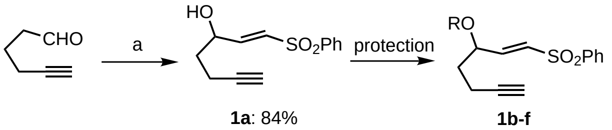
Supporting information (characterization data of the non-sulfonylated enynes and their PK products) for this article is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author.

model 1,6-enyne **1a** was readily prepared, in 84% yield, by condensation of 5-hexynal with phenylsulfonyl-(*p*-tolylsulfinyl)methane in the presence of piperidine.[12] To complement this, in order to study the effect of the electronic and steric nature of the $\gamma$-oxygenated substituent in the chemical efficiency and stereoselectivity of the cyclization, the hydroxyl group of **1a** was derivatized to give the ethoxymethyl ketal (**1b**), the TIPS and TBDMS silyl ethers (**1c** and **1d**), the acetate (**1e**), and the methyl ether (**1f**), following straightforward procedures[13] (Scheme 1). With this series of 1-sulfonylated enynes **1** in hand, we proceeded to study their reactivity under typical PK reaction conditions.

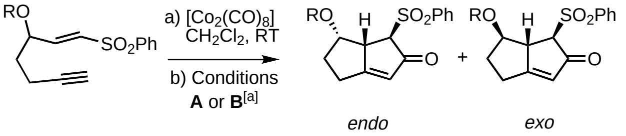


**1b**: R = $CH_2OEt$ ($ClCH_2OEt$, DIPEA, $CH_2Cl_2$, RT), 90%
**1c**: R = TIPS (TIPSOTf, 2,6-lutidine, $CH_2Cl_2$, RT), 98%
**1d**: R = TBDMS (TBDMSCl, imidazole, $CH_2Cl_2$, RT), 97%
**1e**: R = Ac ($Ac_2O$, pyridine, RT), 95%
**1f**: R = Me ($Me_3O^+BF_4^-$, 1,8-bis(dimethylamino)naphthalene, $CH_2Cl_2$, RT), 70%

Scheme 1. Synthesis of model enynes **1**. a) $PhSO_2CH_2SO$*p*Tol, piperidine, $CH_3CN$, 0 °C.

A solution of the corresponding enyne **1** in $CH_2Cl_2$ was treated with a slight excess of $[Co_2(CO)_8]$ at RT until disappearance (by TLC) of the starting material, and the resulting hexacarbonyldicobalt complex was treated under either thermal ($CH_3CN$, 80°C; conditions **A**) or trimethylamine *N*-oxide-promoted conditions (7 equiv $Me_3NO \cdot 2H_2O$, $CH_2Cl_2$, RT; conditions **B**). The results of these cobalt-mediated reactions are summarized in Table 1.

Table 1. Pauson–Khand reactions of model 1,6-enynes **1**.



| Entry | Enyne | R | Product | Condition | Yield[b] [%] | *endo*/*exo*[c] |
|---|---|---|---|---|---|---|
| 1 | **1a** | H | **9a** | **A** or **B** | – | – |
| 2 | **1b** | $CH_2OEt$ | **9b** | **A** | 76 | > 98/ < 2 |
| 3 | **1b** | $CH_2OEt$ | **9b** | **B** | 74 | > 98/ < 2 |
| 4 | **1c** | TIPS | **9c** | **A** | 75 | 90/10 |
| 5 | **1c** | TIPS | **9c** | **B** | 74 | 92/8 |
| 6 | **1d** | TBDMS | **9d** | **B** | 79 | 91/9 |
| 7 | **1e** | Ac | **9e** | **A** | 68 | 54/46 |
| 8 | **1e** | Ac | **9e** | **B** | 65 | 57/43 |
| 9 | **1f** | Me | **9f** | **B** | 70 | 60/40 |

[a] Conditions **A**: $CH_3CN$, 80°C, conditions **B**: $Me_3NO \cdot 2H_2O$ (7 equiv), $CH_2Cl_2$, RT. [b] Overall yield *endo*+*exo*. Both isomers were separated by flash chromatography. [c] Determined by $^1H$ NMR after removal of the cobalt by-products by filtration through Celite.

With the exception of the alcohol **1a**, which was recovered unaltered under both sets of experimental conditions, in the rest of the cases complete reaction was observed after 2–3 h. Interestingly, despite the electron-poor character of the double bond in the enynes **1**, the possible formation of 1,3-dienes[5] was not detected and only the PK cyclopentenones were observed by $^1H$ NMR after Celite filtration of the cobalt by-products. Good yields of the pure bicyclo[3.3.0]octenones **9** were uniformly obtained, regardless of the activation method and the nature of the $\gamma$-substituent (65–76% yield after flash chromatography). However, the most outstanding feature concerns the stereoselectivity of the PK reaction: In contrast to the usual behavior of allylic substituted 1,6-enynes, the cyclization proved in all cases to be *endo*-selective rather than *exo*-selective. In particular, very high *endo* selectivities were observed in the case of the enynes **1c** (Table 1, entries 4 and 5), **1d** (Table 1, entry 6) and, especially, **1b** which effectively afforded a single isomer (*endo*/*exo* = > 98/ < 2, Table 1, entries 2 and 3). In contrast with the significant dependence of the stereoselectivity on the substitution at the $\gamma$-position, the course of the cyclization was hardly affected by the reaction conditions and almost identical results were obtained under both thermal and *N*-oxide-promoted conditions (see the pairs of entries 2/3, 4/5, and 7/8). From a practical point of view, it is important to note that, with the exception of the acetate derivatives **9e**, the *endo*+*exo* mixtures of PK products **9** were readily separable by simple flash chromatography.

The *endo*/*exo* configuration of the bicyclo[3.3.0]octenones **9** was unequivocally established by a combination of NMR studies and chemical correlations. In the $^1H$ NMR spectra of compounds **9**, the values of $J_{5,6}$ and $\delta_6$ were particularly useful diagnostic criteria (Figure 1). Thus, as in other reported 6-substituted bicyclo[3.3.0]octenones,[3, 4] $J_{5,6}$ is significantly lower in the *endo* isomer ($J_{5,6} = 2.9-4.6$ Hz, $H_5/H_6$ in *cis* arrangement) than in the *exo* isomer ($J_{5,6} = 7.5-7.7$ Hz, $H_5/H_6$ in *trans* arrangement), and $\delta_6$ is higher in the *endo* isomer than in the *exo* isomer ($\delta_{6,endo} - \delta_{6,exo} = 0.33-0.65$ ppm). Concerning the configuration at C4/C5, the stereospecificity of the PK reaction with regard to substitution at the double bond and

**Abstract in Spanish:** *Una amplia variedad de 1,6-eninos y 1,7-eninos con estructura de fenilsulfona α,β-insaturada-γ-oxigenada han sido fácilmente sintetizados mediante condensación del correspondiente alquinil-aldehído con p-tolilsulfinil-fenilsulfonil-metano en presencia de piperidina y posterior protección del grupo hidroxilo. En contra de la extendida creencia acerca de la escasa reactividad de olefinas pobres en electrones en reacciones de Pauson–Khand, en este artículo se describe que estos eninos 1-sulfonilados se comportan como excelentes sustratos en reacciones intramoleculares de Pauson–Khand tanto en condiciones térmicas como catalizadas por N-óxidos de aminas. Por otra parte, a diferencia de la habitual selectividad exo exhibida en las ciclaciones de Pauson–Khand de eninos sustituidos en posición alílica, las reacciones de estos eninos 1-sulfonilados-3-oxigenados tienen lugar con moderada o elevada selectividad endo. Se aborda, igualmente, la determinación del alcance químico y estereoquímico del proceso en comparación con la ciclación de Pauson–Khand de eninos no sulfonilados, la aplicación a la síntesis estereoselectiva de biciclo[3.3.0]octenonas C6-sustituidas enantiopuras y la interpretación mecanística de los resultados obtenidos.*

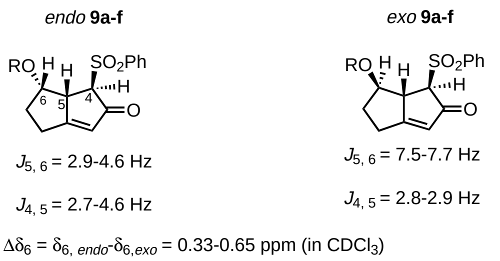


Figure 1. Relevant $^1H$ NMR data for the stereochemical *endo*/*exo* assignment.

the uniform values of $J_{4,5}$ (2.7–4.6 Hz) prove the *trans* relationship of $H_4$ and $H_5$. At the same time, the NOESY spectra of *endo*-**9c** and *exo*-**9c** corroborated these stereochemical assignments. Thus, important NOE correlations were observed between $H_5$, $H_6$ and the *ortho* protons of the phenylsulfonyl group in *endo*-**9c**, whereas a strong cross-peak between $H_4$ and $H_6$ was present in *exo*-**9c** (Figure 2).

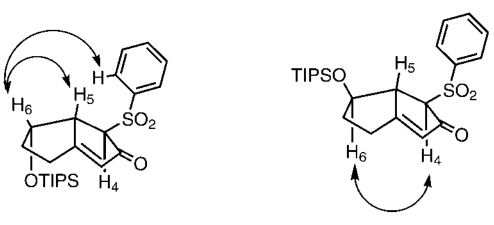
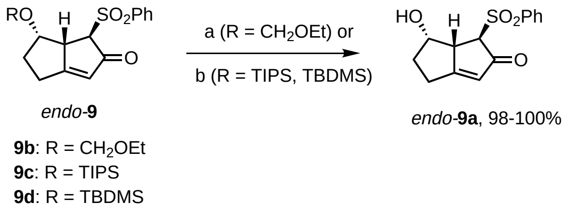


Figure 2. Relevant NOESY correlations in stereoisomers **9c**.

As chemical correlations, the nearly quantitative deprotection of the hydroxyl group in the ketal *endo*-**9b** (HCl, THF, $H_2O$) and in the silyl ethers *endo*-**9c** and *endo*-**9d** ($Bu_4NF$, THF) afforded the same alcohol *endo*-**9a** (which could not be obtained by PK reaction of **1a**), proving the structural homogeneity of all these compounds (Scheme 2). Finally, the X-ray crystal structure analysis of *endo*-**9c** (Figure 3) unambiguously proved all these stereochemical assignments.[14]



Scheme 2. Deprotection of derivatives *endo*-**9**. a) 3 M HCl, THF, RT; b) $nBu_4NF$, THF, RT.

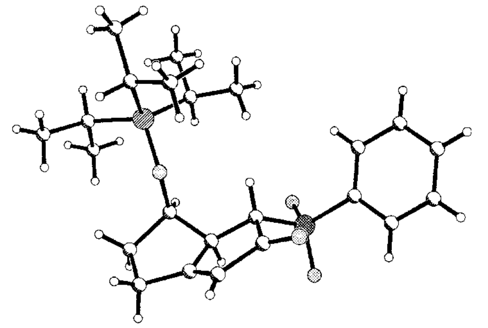
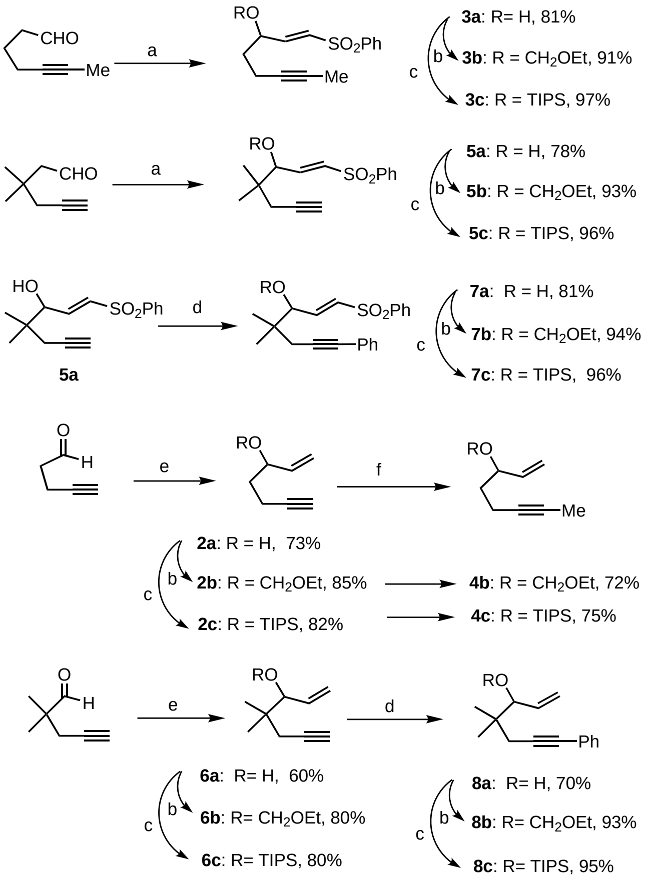


Figure 3. Structure of *endo*-**9c** in the crystal.

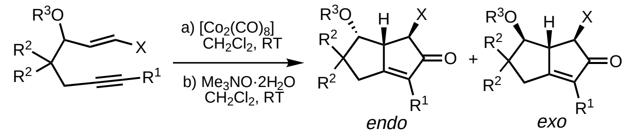
**Synthetic scope**: In order to ascertain the scope of the *endo* selectivity in the PK reactions of $\gamma$-oxygenated-$\alpha,\beta$-unsaturated phenylsulfones, three additional series of 1,6-enynes, with varying substitution at the chain and alkyne terminus (compounds **3**, **5** and **7**), were prepared. The parent alcohols **3a** and **5a** were prepared, as in the case of **1a**, by the one-step, piperidine-promoted condensation of the corresponding aldehydes[15] with phenylsulfonyl-($p$-tolylsulfinyl)methane (81% and 78% yields, respectively). On the other hand, the enyne **7a**, with a phenyl group at the alkyne terminus, was synthesized in 81% yield by means of a Sonogashira reaction between **5a** and iodobenzene [$Pd(OAc)_2$, CuI, $PPh_3$, $Et_3N$, $C_6H_6$, 80 °C]. Furthermore, in order to evaluate the precise effect of the sulfonyl group in the reactivity and stereoselectivity of the PK reaction, the corresponding substituted 3-oxygenated-1,6-enynes, but without the phenylsulfonyl group at C-1 (enynes **2**, **4**, **6** and **8**), were readily prepared by addition of vinylmagnesium bromide to the appropriate aldehyde[15] and further simple methylation or phenylation of the alkyne moiety (Scheme 3).



Scheme 3. Synthesis of 1,6-enynes **2**–**8**. a) $PhSO_2CH_2SOp$Tol, piperidine, $CH_3CN$, 0 °C; b) $ClCH_2OEt$, DIPEA, $CH_2Cl_2$, RT; c) TIPSOTf, 2,6-lutidine, $CH_2Cl_2$, RT; d) 10 mol% $Pd(OAc)_2$, 10 mol% CuI, 20 mol% $PPh_3$, $Et_3N$, PhI, benzene, RT; e) vinylmagnesium bromide, THF, −78 °C; f) 1) $n$BuLi, THF, −78 °C; 2) MeI, −78 °C.

Finally, in view of the fact that in the model series **1** the best stereoselectivities were obtained when the hydroxyl group was protected as ethoxymethyl ketal and TIPS derivatives, the alcohols **2a**–**8a** were also converted into these derivatives (substrates **b** and **c**, respectively). With the 1,6-enynes **2**–**8** in hand, we undertook the study of their PK reactions under *N*-oxide-promoted conditions. For comparatives purposes, the results obtained from **1b** and **1c** are shown again in Table 2.

Table 2. Pauson–Khand reactions of 1,6-enynes **1**–**8**.



| Entry | Enyne | X | $R^1$ | $R^2$ | $R^3$ | Product | *endo*/*exo*[a] | Yield[b] [%] (*endo*[c] [%]) |
|---|---|---|---|---|---|---|---|---|
| 1 | **1b** | $SO_2Ph$ | H | H | $CH_2OEt$ | **9b** | **>98/<2** | 76 (76) |
| 2 | **2b** | H | H | H | $CH_2OEt$ | **10b** | 28/72 | 72 (20) |
| 3 | **1c** | $SO_2Ph$ | H | H | TIPS | **9c** | **92/8** | 74 (66) |
| 4 | **2c** | H | H | H | TIPS | **10c** | 46/54 | 54 (25) |
| 5 | **3b** | $SO_2Ph$ | Me | H | $CH_2OEt$ | **11b** | **93/7** | 77 (71) |
| 6 | **4b** | H | Me | H | $CH_2OEt$ | **12b** | 25/75 | 38 (9) |
| 7 | **3c** | $SO_2Ph$ | Me | H | TIPS | **11c** | **91/9** | 73 (63) |
| 8 | **4c** | H | Me | H | TIPS | **12c** | 32/68 | 46 (15) |
| 9[e] | **5a** | $SO_2Ph$ | H | Me | H | **13a** | **80/20** | 60[d] |
| 10 | **6a** | H | H | Me | H | **14a** | 36/64 | 50[d] |
| 11 | **5b** | $SO_2Ph$ | H | Me | $CH_2OEt$ | **13b** | **67/33** | 74 (47) |
| 12 | **6b** | H | H | Me | $CH_2OEt$ | **14b** | 20/80 | 79 (16) |
| 13 | **5c** | $SO_2Ph$ | H | Me | TIPS | **13c** | **39/61** | 71 (25) |
| 14 | **6c** | H | H | Me | TIPS | **14c** | 10/90 | 63 (6) |
| 15[e] | **7a** | $SO_2Ph$ | Ph | Me | H | **15a** | **76/24** | 75[d] |
| 16 | **8a** | H | Ph | Me | H | **16a** | 17/83 | 42 (7) |
| 17[e] | **7b** | $SO_2Ph$ | Ph | Me | $CH_2OEt$ | **15b** | **87/13** | 79[d] |
| 18 | **8b** | H | Ph | Me | $CH_2OEt$ | **16b** | 16/84 | 46 (7) |
| 19[e] | **7c** | $SO_2Ph$ | Ph | Me | TIPS | **15c** | **94/6** | 78[d] |
| 20 | **8c** | H | Ph | Me | TIPS | **16c** | <2/>98 | 45 |

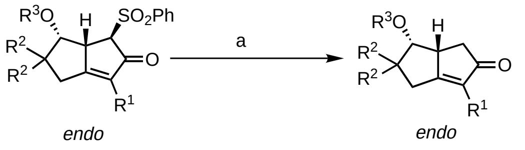
[a] Determined by $^1H$ NMR after filtration of the cobalt by-products. [b] Overall yield (*endo*+*exo*) after flash chromatographic separation. [c] Yield of pure *endo* product after chromatography in brackets. [d] The *endo* and *exo* adducts could not be separated. [e] Reaction conditions: $Me_3NO \cdot 2H_2O$ (7 equiv), molecular sieves (4 Å), toluene, RT.

Good yields of PK products were obtained from the 1-sulfonylated enynes **1**, **3**, **5** and **7** (70–80% yields), somewhat higher even than those usually obtained from the corresponding non-sulfonylated enynes **2**, **4**, **6** and **8** (45–75% yields). This result clearly shows that the phenylsulfonyl group has no significant deleterious effect on the efficiency of the process. However, in the cases of the reactions of the enynes **5a** and **7a**–**c** we required the use of a combination of $Me_3NO$ and molecular sieves[16] as promoter in order to ensure the complete conversion of the starting material.

As regards the diastereoselectivity of the process, as expected for enynes substituted at the allylic position, the PK reaction of the enynes **2** and **6** was moderately *exo*-selective,[4] and, in accordance with Magnus' model[3] (which predicts a higher *exo* selectivity with increasing steric bulk of the substituent at the alkyne terminus), the PK reactions of the alkyne-substituted series **4** and **8** proved to be somewhat more *exo*-selective (especially in the case of enynes **8**) than those of the corresponding terminal alkynes **2** and **6**, respectively.

Notably, the opposite behavior was generally observed from the 1-sulfonylated enynes: with the exception of **5c**, the PK reactions of the enynes **1**, **3**, **5** and **7** were *endo*-selective in all cases (values in bold in Table 2), even in the alkyne-substituted series **3** (entries 5 and 7) and **7** (entries 15, 17 and 19), revealing the strong capability of the phenylsulfonyl group to reverse the "natural" *exo* selectivity of the process. In the four series, therefore, complete (Table 2, entry 1) or high (entries 5, 9 and 19) levels of *endo* diastereoselectivity were achieved, this reversal of stereoselectivity being especially pronounced in the case of the pairs of enynes **1b**/**2b** (Table 2, entries 1 and 2), **3b**/**4b** (entries 5 and 6) and **7c**/**8c** (entries 19 and 20).

From an experimental point of view, it is to be noted that the *endo*+*exo* mixtures of C-4 sulfonylated bicyclo[3.3.0]octenones can usually be separated by simple flash chromatography. Interestingly enough, the resulting major *endo* adduct can be efficiently desulfonylated by simple treatment with activated zinc ($NH_4Cl$, THF, $H_2O$).[17] For instance, reductive desulfonylation of *endo*-**9b**, *endo*-**9c**, *endo*-**13b** and *endo*-**13c** furnished excellent yields of *endo*-**10b** (94%), *endo*-**10c** (93%), *endo*-**14b** (89%) and *endo*-**14c** (91%), respectively (Scheme 4). Furthermore, this chemical correlation between the sulfonylated and the non-sulfonylated series enabled us to confirm the stereochemical assignments previously established on the basis of NMR criteria, and makes evident the role of the phenylsulfonyl group as a temporary *endo* stereochemical controller of the intramolecular PK reactions of 3-oxygenated-1,6-enynes (sequential PK reaction and desulfonylation).



**9b**: $R^1$ = H, $R^2$ = H, $R^3$ = $CH_2OEt$ **10b**: 94%

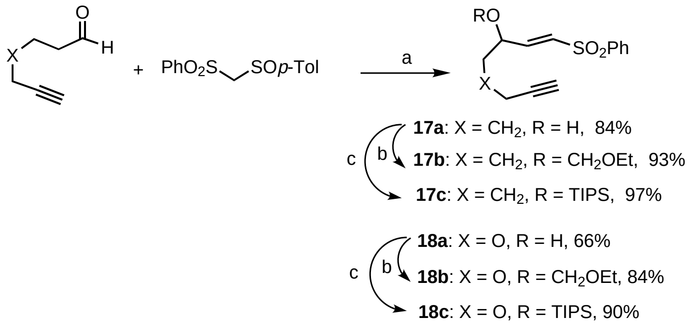
**9c**: $R^1$ = H, $R^2$ = H, $R^3$ = TIPS **10c**: 93%

**13b**: $R^1$ = H, $R^2$ = Me, $R^3$ = $CH_2OEt$ **14b**: 89%

**13c**: $R^1$ = H, $R^2$ = Me, $R^3$ = TIPS **14c**: 91%

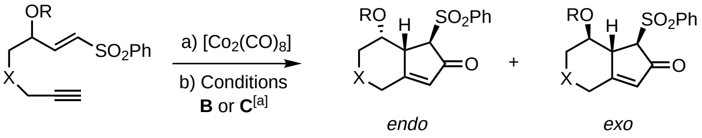
Scheme 4. Desulfonylation of *endo* 4-phenylsulfonylbicyclo[3.3.0]octenones. a) Zn, sat. $NH_4Cl$, THF/$H_2O$ 1:1, RT.

Staying with our goal of establishing the scope of the intramolecular PK reaction of $\gamma$-oxygenated-$\alpha,\beta$-unsaturated phenyl sulfones, we extended the study to the case of 1-sulfonylated 1,7-enynes. Again, the new parent alcohols **17a** and **18a** were synthesized by condensation of the corresponding aldehyde[15] with phenylsulfonyl-(*p*-tolylsulfinyl)methane in the presence of a secondary amine (piperidine or morpholine). Further protection of alcohols **17a** and **18a** as ethoxymethyl and TIPS derivatives afforded 1,7-enynes **17b**, **17c**, **18b** and **18c**, respectively (Scheme 5). The results obtained in their *N*-oxide-promoted PK reactions are collected in Table 3.



Scheme 5. Synthesis of 1,7-enynes **17** and **18**. a) piperidine ($X = CH_2$) or morpholine (X = O), $CH_3CN$, 0 °C; b) $ClCH_2OEt$, DIPEA, $CH_2Cl_2$, RT; c) TIPSOTf, 2,6-lutidine, $CH_2Cl_2$, RT.

Table 3. Pauson–Khand reactions of 1,7-enynes **17**–**18**.

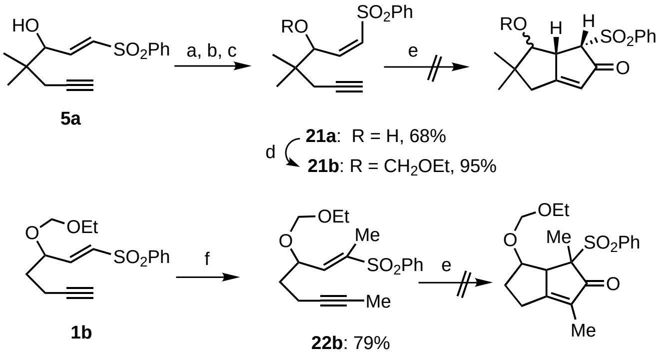


| Entry | Enyne | X | R | Conditions | Product | *endo*/*exo*[b] | Yield[c] [%] (*endo*[d] [%]) |
|---|---|---|---|---|---|---|---|
| 1 | **17a** | $CH_2$ | H | **B** | **19a** | 59/41 | 49 (29) |
| 2 | **17a** | $CH_2$ | H | **C** | **19a** | 59/41 | 48 (28) |
| 3 | **17b** | $CH_2$ | $CH_2OEt$ | **B** | **19b** | 52/48 | 49 (25) |
| 4 | **17c** | $CH_2$ | TIPS | **B** | **19c** | 34/66 | 62 (21) |
| 5 | **18a** | O | H | **B** | **20a** | – | – |
| 6 | **18a** | O | H | **C** | **20a** | 79/21 | 14 (11) |
| 7 | **18b** | O | $CH_2OEt$ | **B** | **20b** | – | – |
| 8 | **18b** | O | $CH_2OEt$ | **C** | **20b** | 66/34 | 50 (33) |
| 9 | **18c** | O | TIPS | **B** | **20c** | 58/42 | 50[e] |

[a] Conditions **B**: $Me_3NO \cdot 2H_2O$ (7 equiv), $CH_2Cl_2$, RT; conditions **C**: $Me_3NO \cdot 2H_2O$ (7 equiv), molecular sieves, toluene, RT. [b] Determined by $^1H$ NMR after filtration of the cobalt by-products. [c] Overall yield (*endo*+*exo*) after flash chromatography. [d] Yield of pure *endo* product after flash chromatographic separation in brackets. [e] The *endo* and *exo* products could not be separated by chromatography.

Two main differences may be deduced from comparison of the data collected in Table 2 and Table 3. Firstly, the PK reactions of the 1,7-enynes **17** and **18** are less favorable than those of the 1,6-enynes **1**, **3**, **5** and **7**, as is shown by the lower isolated yields obtained from the former (40–50 % instead of 70–80 % from the 1,6-enynes) and the necessity in several cases of using the combination of $Me_3NO$ and molecular sieves as promoter (see Table 3, entries 5/6 and 7/8). Secondly, although the *endo* isomer is again the major isolated diastereomer (Table 3, except entry 4), the *endo* selectivity of the cyclization of the 1,7-enynes is much lower ($de = 4$–58 %) than that observed from the 1,6-enynes (Table 2). In fact, nearly equimolecular mixtures of *endo*- and *exo*-bicyclo[4.3.0]nonenones **19**–**20** were obtained in many cases (Table 3, entries 1, 2, 3 and 9). These diastereomeric *endo*+*exo* mixtures were separated by flash chromatography and their stereochemical assignments established by NMR analysis as previously outlined for the case of the *endo*/*exo* bicyclo[3.3.0]octenones [as shown in Figure 1, for instance, $J_{5,6}$ is much higher in the *exo* isomers (9.1–10.2 Hz) than it is in the *endo* isomers (3.2–3.6 Hz)].

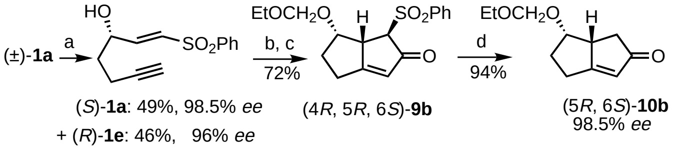
Finally, we examined the effect of substitution at the double bond. The *cis* $\gamma$-oxygenated-$\alpha,\beta$-unsaturated sulfones **21a** and **21b** were prepared from the *trans* $\gamma$-hydroxy-$\alpha,\beta$-unsaturated sulfone **5a** by oxidation to the enone (PCC, $CH_2Cl_2$; 77 % yield), quantitative photochemical *trans*/*cis* isomerization[18] (150 W Hg lamp, 24 h) and Luche carbonyl reduction ($NaBH_4$, $CeCl_3$; 89 % yield). As a second type of substrate, the trisubstituted $\alpha,\beta$-unsaturated sulfone **22b** was prepared in one step from **1b** by double deprotonation (2 equiv *n*BuLi) and further methylation (MeI, 79 % yield) (Scheme 6).



Scheme 6. Synthesis of substituted 1,6-enynes **21** and **22**. a) PCC, $CH_2Cl_2$, Celite, RT; b) $h\tilde{\nu}$ (Hg, 150 W), RT; c) $NaBH_4$, $CeCl_3$, MeOH, RT; d) $ClCH_2OEt$, DIPEA, $CH_2Cl_2$, RT; e) 1) $[Co_2(CO)_8]$, $CH_2Cl_2$, RT, 2) $Me_3NO \cdot 2H_2O$, RT; f) 1) *n*BuLi (2 equiv), THF, −78 °C; 2) MeI (2 equiv), −78 °C.

Unfortunately, all attempts to perform PK reactions on the enynes **21a**, **21b** and **22b**, under a variety of conditions (thermal activation, or *N*-oxide and *N*-oxide and molecular sieves as promoters), were unsuccessful. We did not observe the formation of any bicyclic product and we recovered the starting enynes in all cases. These results strongly suggest that, probably as a result of the great sensitivity of the PK reaction to steric hindrance around the double bond, the intramolecular PK reaction of $\alpha,\beta$-unsaturated phenylsulfones is limited to the case of the *trans*-disubstituted alkenes.

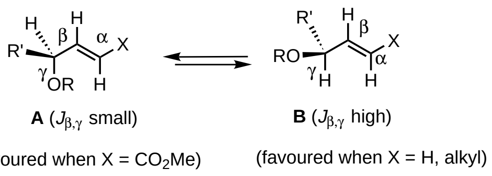
**Application to the synthesis of enantiopure *endo* 6-substituted bicyclo[3.3.0]octenones**: As a final synthetic point of interest, the application of the results shown in Table 1, Table 2 and Table 3 to the synthesis of enantiopure 6-oxygenated *endo*-bicycloalkenones would only require the preparation of the starting enynes in enantiomerically pure form. Some years ago, we described a practical, lipase-mediated kinetic resolution of a structurally wide variety of (±)-$\gamma$-hydroxy-$\alpha,\beta$-unsaturated sulfones on the basis of their highly *R*-enantioselective acetylation catalyzed by lipase PS (*Pseudomonas cepacia* lipase) in an organic solvent.[19] Pleasingly, under these conditions the reaction of (±)-**1a** stopped at 50 % conversion (48 h in toluene as solvent), affording 49 % of the alcohol (*S*)-**1a** and 46 % of the acetate (*R*)-**1e** after flash chromatography, both in very high degrees of optical purity [98.5 % *ee* for (*S*)-**1a** (HPLC, Chiralpak AS) and > 96 % *ee* for (*R*)-**1e** [$^1H$ NMR, $Pr(hfc)_3$]]. Protection of (*S*)-**1a** as ketal (*S*)-**1b** and subsequent PK cyclization afforded (4*R*,5*R*,6*S*)-**9b** as the only isolated product (72 % yield). Finally, the zinc-mediated reductive desulfonylation furnished the *endo*-substituted cyclopentenone (5*R*, 6*S*)-**10b** in 94% yield and in very high optical purity (98.5% *ee*, HPLC, Chiralcel OD) (Scheme 7).



Scheme 7. Application to the enantioselective synthesis of *endo* 6-oxygenated bicyclo[3.3.0]octenones. a) Lipase PS, vinyl acetate, molecular sieves (4 Å), toluene, RT; b) $ClCH_2OEt$, DIPEA, $CH_2Cl_2$, RT; c) 1) $[Co_2(CO)_8]$, $CH_2Cl_2$, RT; 2) $Me_3NO \cdot 2H_2O$, RT; d) Zn, $NH_4Cl$, $THF/H_2O$, RT.

**Mechanistic interpretation of the diastereoselectivity of the PK reactions**: Although the generally assumed multistep mechanism of the PK reaction, involving at least five reaction intermediates, makes any attempt to rationalize the stereochemical outcome rather difficult, there are usually two main factors invoked to explain diastereoselective intramolecular PK reactions: the conformational preferences of the starting enyne prior to metallacycle formation[10a,b] and the presumed thermodynamic stability of the putative key intermediates, the diastereomeric *cis*-cobaltacycles.[3, 20] We postulate that, in the case of the *trans* 3-oxygenated 1-sulfonylated enynes, both effects might operate in the same direction, providing a reasonable explanation for the unusual *endo* selectivity exhibited in the PK reactions of these substrates.

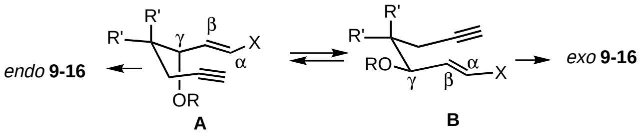
If the conformational ground state arguments are analyzed first, it is well established that in unsubstituted or *trans*-substituted allylic alcohols (and derivatives) the two most stable conformations around the $C_{\beta,\gamma}$-bond are the conformations **A** ($H_\alpha$ and OR in a 1,3-parallel arrangement) and **B** ($H_\alpha$ and $H_\gamma$ in a 1,3-parallel arrangement). Conformation **A** is usually the most stable in the case of *trans*-allylic alcohols substituted with electron-withdrawing groups, such as *trans* $\gamma$-oxygenated $\alpha,\beta$-unsaturated esters[21] (Scheme 8).



Scheme 8. Conformational analysis of allylic alcohols.

On the other hand, the relative degree of participation of each conformation can be qualitatively deduced from the value of $J_{\beta,\gamma}$, since $J_{\beta,\gamma}$ should be low in **A** ($H_\beta$ and $H_\gamma$ in *gauche* configuration) and high in **B** ($H_\beta$ and $H_\gamma$ in *anti* configuration). In view of the fact that, in the case of the enynes **1**–**8**, the formation of the *endo* product would require the participation of a conformation type **A**, and that the conformation **B** would be involved in the formation of the *exo* product, the values (in $CDCl_3$) of $J_{\beta,\gamma}$ in the enynes **1**, **2**, **5** and **6** and their observed *endo*/*exo* diastereomeric ratios are listed in Table 4, to identify any possible correlation between conformational preferences in the starting enynes and the product ratio.

Table 4. Correlation between $J_{\beta,\gamma}$ in the starting enynes and *endo*/*exo* ratios in the Pauson–Khand products.

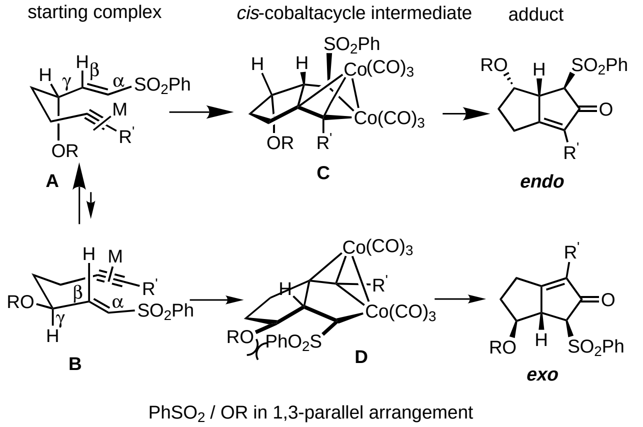


| Entry | Enyne | R | R′ | X | $J_{\beta,\gamma}$(Hz)[a] | Prod. | *endo*/*exo*[b] |
|---|---|---|---|---|---|---|---|
| 1 | **1a** | H | H | $SO_2Ph$ | 3.5 | **9a** | –[c] |
| 2 | **1b** | $CH_2OEt$ | H | $SO_2Ph$ | 3.9 | **9b** | > 98/< 2 |
| 3 | **1c** | TIPS | H | $SO_2Ph$ | 3.7 | **9c** | 92/8 |
| 4 | **1d** | TBDMS | H | $SO_2Ph$ | 4.3 | **9d** | 91/9 |
| 5 | **1e** | Ac | H | $SO_2Ph$ | 5.7 | **9e** | 57/43 |
| 6 | **1f** | Me | H | $SO_2Ph$ | 5.1 | **9f** | 60/40 |
| 7 | **2b** | $CH_2OEt$ | H | H | 7.0 | **10b** | 28/72 |
| 8 | **2c** | TIPS | H | H | 6.5 | **10c** | 46/54 |
| 9 | **5a** | H | Me | $SO_2Ph$ | 3.9 | **13a** | 80/20 |
| 10 | **5b** | $CH_2OEt$ | Me | $SO_2Ph$ | 6.6 | **13b** | 67/33 |
| 11 | **5c** | TIPS | Me | $SO_2Ph$ | 7.5 | **13c** | 39/61 |
| 12 | **6a** | H | Me | H | 7.0 | **14a** | 36/64 |
| 13 | **6b** | $CH_2OEt$ | Me | H | 8.1 | **14b** | 20/80 |
| 14 | **6c** | TIPS | Me | H | 8.6 | **14c** | 10/90 |

[a] Values in $CDCl_3$. [b] Under $Me_3NO \cdot 2H_2O$-promoted conditions. [c] No reaction was observed.

As can be observed, there is a pleasing qualitative correlation between $J_{\beta,\gamma}$ in the enynes and the *endo*/*exo* product ratio. Thus, the enynes with the lowest $J_{\beta,\gamma}$ values (Table 4, entries 2, 3, 4 and 9), and hence the highest **A** populations, gave rise to the best *endo* selectivities, while the PK reactions of the enynes with the highest $J_{\beta,\gamma}$ values (Table 4, entries 7 and 11–14), and thus a predominance of conformer **B**, afforded the highest *exo* selectivities. It should be noted that this simple conformational argument provides a reasonable explanation for the fact that any 1-sulfonylated enyne (**1**, **3**, **5** and **7**) always gives a higher amount of the *endo* adduct than the corresponding non-sulfonylated enyne (**2**, **4**, **6** and **8**, respectively) does, in accordance with the lower value of $J_{\beta,\gamma}$ in the former (compare, for instance, the pairs of entries 2/7, 3/8, 9/12, 10/13 and 11/14). If the same conformational principles were applied, it would be possible to explain why the PK cyclizations of the acetate **1e** ($J_{\beta,\gamma} = 5.7$ Hz; Table 4, entry 5) and the methyl ether **1f** ($J_{\beta,\gamma} = 5.1$ Hz; entry 6) are less *endo*-selective than those of the close derivative ketal **1b** ($J_{\beta,\gamma} = 3.9$ Hz; entry 2) and the silyl ethers **1c** and **1d** ($J_{\beta,\gamma} = 3.7$ Hz and $J_{\beta,\gamma} = 4.3$ Hz; entries 3 and 4). Similarly, the lower *endo*/*exo* ratios obtained from the C-4 *gem*-dimethyl-substituted enynes **5** and **6**, in comparison with the corresponding C-4-unsubstituted enynes **1** and **2**, are in agreement with the higher populations of the conformer **B** in the enynes **5** and **6**, as may be deduced from their much higher $J_{\beta,\gamma}$ values (compare, for instance, the pairs of entries 2/10, 3/11, 7/13 and 8/14).

If the accepted mechanism of the PK reaction is now taken into account, the stereochemically decisive step (and presumably the rate-determining step, too) would be the formation of the putative *cis*-cobaltacycle after insertion of the C–Co bond of the hexacarbonyldicobalt complex into the C=C double bond. If we now consider the presumed stability of both plausible diastereomeric *cis*-cobaltacycles **C** and **D**, then the intermediate **D**, which would lead to the *exo* product, might present a serious steric interaction between the OR and $SO_2Ph$ groups, due to their 1,3-parallel arrangement. Such interaction would not appear in the intermediate **C**, involved in the formation of the *endo* adduct, in which the OR and $SO_2Ph$ groups are located on opposite sides of the bicyclic structure (Scheme 9). This kind of steric effect would reinforce the *endo* selectivity based on the previously discussed conformational preferences about the allylic position in the sulfonylated enynes **1**, **3**, **5** and **7**.



Scheme 9. Mechanistic hypothesis for the observed *endo* selectivity.

On the other hand, the relative stability of the diastereomeric *cis*-cobaltacycle intermediates could also explain the drop in *endo* diastereoselectivity observed in the PK cyclizations of the 1-sulfonyl-1,7-enynes (**17** and **18**), compared with the behavior of the 1-sulfonyl-1,6-enynes (**1**, **3**, **5** and **7**), since in the case of the 1,7-enynes the *cis*-cobaltacycle intermediates would be less rigid and, therefore, the steric interaction between both OR and $SO_2Ph$ groups in the cobaltacycle type **D** could be partly relieved.

## Conclusion

In summary, despite the presence of a strongly electron-poor alkene, the readily available *trans* $\gamma$-oxygenated-$\alpha$,$\beta$-unsaturated phenylsulfones are excellent substrates in intramolecular PK reactions. Yields of around 70–80% were obtained in the case of 1,6-enynes and of 50–60% in that of 1,7-enynes. Interestingly, in contrast with the well known stereochemical behavior of allylic substituted enynes, which undergo *exo*-selective PK reactions, the PK cyclizations of differently substituted *trans*-3-oxygenated-1-phenylsulfonylenynes occur with moderate to high *endo* selectivity, especially in the case of the 1,6-enynes. As the *endo* isomers may readily be separated by column chromatography and the sulfonyl groups can be efficiently removed by reductive cleavage with zinc, this two-step process (PK reaction and desulfonylation) demonstrates the role of the phenylsulfonyl group as a temporary stereochemical *endo*-director of the cyclization. From a synthetic point of view, this procedure constitutes a novel, stereocomplementary Pauson–Khand approach to the synthesis of C6-substituted bicyclo[3.3.0]octenones and bicyclo[4.3.0]nonenones. Moreover, the procedure can equally well be applied to the synthesis of enantiomerically pure compounds, since the starting $\gamma$-hydroxy-$\alpha$,$\beta$-unsaturated sulfones can readily be resolved by lipase-mediated methods.

## Experimental Section

**General**: All reagents were obtained from commercial suppliers and were used without further purification. THF was distilled from sodium/benzophenone, dichloromethane was distilled from $P_2O_5$. All reactions involving the use of *n*BuLi, LDA and $[Co_2(CO)_8]$ (Fluka or Strem) were carried out in flame-dried or oven-dried glassware under inert argon atmospheres, using anhydrous solvents. Reactions were monitored by thin-layer chromatography, carried out on 0.25 mm Merck silica gel coated aluminum plates (Merck-60 230–400 mesh). Merck-60 230–400 mesh silica gel was used for flash column chromatography. NMR spectra were recorded on Bruker AC-200 or AC-300 instruments and calibrated using residual undeuterated solvent as internal reference. Optical rotations were recorded on a Perkin–Elmer 241C polarimeter. Mass spectra (MS) were recorded on a Hewlett–Packard HP-5985 mass spectrometer at 70 eV ionising voltage or under fast atom bombardment (FAB) conditions. Elemental analyses were performed with a Perkin–Elmer II 2400 CNH instrument by the "Servicio Interdepartamental de Investigación" (Universidad Autónoma de Madrid). Melting points were determined in open-end capillary tubes on a GallemKamp apparatus. HPLC analyses were performed on a HPLC Perkin–Elmer Integral 400 instrument, using Daicel Chiralpak AS and Chiralcel OD columns. Phenylsulfonyl-(*p*-tolylsulfinyl)methane[12b] and 3,3-dimethyl-5-hexynal[15] were prepared as described in the literature.

**Preparation of (*E*)-$\gamma$-hydroxy-$\alpha$,$\beta$-unsaturated phenyl sulfones**

**(*E*)-1-(Phenylsulfonyl)hept-1-en-6-yn-3-ol (1a)**: Piperidine (0.33 mL, 3.42 mmol) and 5-hexynal(252 mg, 2.62 mmol) were added sequentially to a solution of phenylsulfonyl-(*p*-tolylsulfinyl)methane (503 mg, 1.71 mmol) in $CH_3CN$ (10 mL), cooled at 0 °C. After having been stirred for 5 h at 0 °C, the reaction mixture was quenched by the addition of 5% HCl (10 mL). The mixture was extracted with $CH_2Cl_2$ (15 mL), and the organic layer was washed with saturated aqueous $NH_4Cl$ (2 × 15 mL), dried ($Na_2SO_4$) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 4:1) to afford **1a** (359 mg, 84%, white solid). M.p. 136–137 °C; $^1H$ NMR (200 MHz, $CDCl_3$): $\delta = 7.91-7.85$ (m, 2H, ArH), 7.65–7.49 (m, 3H, ArH), 7.03 (dd, $J = 3.5$, 14.9 Hz, 1H, H2), 6.65 (dd, $J = 1.9$, 14.9 Hz, 1H, H1), 4.51 (m, 1H, H3), 2.41 (m, 2H, H5), 2.01 (t, $J = 2.7$ Hz, 1H, H7), 1.95–1.63 (m, 2H, H4); $^{13}C$ NMR (50 MHz, $CD_3OD$): $\delta = 150.2$, 142.1, 134.7, 130.9, 130.5, 128.6, 84.0, 70.2, 69.4, 35.9, 15.2; elemental analysis calcd (%) for $C_{13}H_{14}O_3S$ (250.3): C 62.38, H 5.64, S 12.87; found: C 62.39, H 5.46, S 13.02.

**(*E*)-1-(Phenylsulfonyl)oct-1-en-6-yn-3-ol (3a)**: Through the same procedure, treatment of phenylsulfonyl-(*p*-tolylsulfinyl)methane (450 mg, 1.53 mmol) with 5-heptynal (218 mg, 1.98 mmol) and piperidine (302 µL, 3.06 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 4:1), **3a** (327 mg, 81%, colourless oil). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 7.97-7.85$ (m, 2H, ArH), 7.70–7.40 (m, 3H, ArH), 6.99 (dd, $J = 4.1$, 14.9, 1H, H2), 6.63 (dd, $J = 2.1$, 14.8, 1H, H1), 4.56 (m, 1H, H3), 2.31 (m, 2H, H5), 1.77 (t, $J = 1.8$ Hz, 3H, H8), 1.76–1.59 (m, 2H, H4); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta = 147.8$, 140.0, 133.3, 129.6, 129.2, 127.5, 77.6, 69.5, 69.3, 34.7, 14.9, 4.8; HRMS (EI+): calcd for: 264.0820; found: 264.0813 $[M]^+$.

**(*E*)-4,4-Dimethyl-1-(phenylsulfonyl)hept-1-en-6-yn-3-ol (5a)**: Through the same procedure, treatment of phenylsulfonyl-(*p*-tolylsulfinyl)methane (1.37 g, 4.66 mmol) with 3,3-dimethyl-5-hexyn-1-al (754 mg, 6.08 mmol) and piperidine (0.92 mL, 9.37 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 4:1), **5a** (0.99 g, 78%, white solid). M.p. 78–79 °C; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta = 7.88-7.84$ (m, 2H, ArH), 7.63–7.49 (m, 3H, ArH), 7.05 (dd, $J = 4.1$, 15.0 Hz, 1H, H2), 6.62 (dd, $J = 1.6$, 14.9 Hz, 1H, H1), 4.30 (m, 1H, H3), 2.24 (dd, $J = 1.9$, 13.8 Hz, 1H, H5), 2.09

(dd, *J* = 1.8, 13.8 Hz, 1 H, H5), 2.02 (t, *J* = 1.9 Hz, 1 H, H7), 1.01 (s, 3 H, $CH_3$), 0.92 (s, 3 H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 145.5, 140.1, 133.4, 131.6, 129.3, 127.5, 81.3, 75.5, 71.2, 38.6, 28.9, 23.5, 22.2; elemental analysis calcd (%) for $C_{15}H_{18}O_3S$ (278.3): C 64.72, H 6.52, S 11.52; found: C 64.34, H 6.37, S 11.01.

**(*E*)-1-(Phenylsulfonyl)oct-1-en-7-yn-3-ol (17 a)**: Through the same procedure, treatment of phenylsulfonyl-(*p*-tolylsulfinyl)methane (430 mg, 1.46 mmol) with 6-heptynal (209 mg, 1.90 mmol) and piperidine (0.29 mL, 2.92 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 4:1), **17 a** (324 mg, 84 %, white solid). M.p. 72 – 75 °C; $^1H$ NMR (200 MHz, $CDCl_3$): δ = 7.89 – 7.83 (m, 2 H, ArH), 7.63 – 7.52 (m, 3 H, ArH), 6.98 (dd, *J* = 3.8, 15.1 Hz, 1 H, H2), 6.61 (dd, *J* = 1.6, 15.1 Hz, 1 H, H1), 4.43 (m, 1 H, H3), 2.46 (m, 1 H, OH), 2.31 – 2.21 (m, 2 H, H6), 1.97 (t, *J* = 2.7 Hz, 1 H, H8), 1.79 – 1.57 (m, 4 H, H4, H5); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 148.4, 139.8, 133.3, 129.3, 129.2, 127.3, 83.6, 69.3, 68.9, 34.7, 23.7, 17.8; elemental analysis calcd (%) for $C_{14}H_{16}O_3S$ (264.3): C 63.61, H 6.10, S 12.13; found: C 63.10, H 6.19, S 12.21.

**(*E*)-1-Phenylsulfonyl-5-oxa-oct-1-en-7-yn-3-ol (18 a)**: Through the same procedure, treatment of phenylsulfonyl-(*p*-tolylsulfinyl)methane (808 mg, 2.74 mmol) with 3-(2-propynyloxy)propanal (400 mg, 3.57 mmol) and morpholine (0.48 mL, 5.49 mmol) afforded, after chromatographic purification (hexane/diethyl ether 1:1), **18 a** (482 mg, 66 %, colourless oil). $^1H$ NMR (200 MHz, $CDCl_3$): δ = 7.91 – 7.87 (m, 2 H, ArH), 7.67 – 7.50 (m, 3 H, ArH), 6.96 (dd, *J* = 3.2, 15.1 Hz, 1 H, H3), 6.73 (dd, *J* = 1.1, 15.1 Hz, 1 H, H4), 4.59 (m, 1 H, H2), 4.20 (t, *J* = 2.7 Hz, 2 H, $OCH_2CCH$), 3.73 (dd, *J* = 3.5, 9.5 Hz, 1 H, H1), 3.46 (dd, *J* = 7.3, 9.4 Hz, 1 H, H1), 2.61 (d, *J* = 4.3 Hz, 1 H, OH), 2.48 (t, *J* = 2.7 Hz, 1 H, $OCH_2CCH$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 144.0, 139.8, 133.4, 131.2, 129.2, 127.5, 78.8, 75.3, 72.0, 69.0, 58.4; HRMS (FAB + ): calcd for: 267.0691; found: 267.0700 $[M+H]^+$.

**(*E*)-4,4-Dimethyl-7-phenyl-1-(phenylsulfonyl)hept-1-en-6-yn-3-ol (7 a)**: $Pd(OAc)_2$ (3 mg, 0.015 mmol), $PPh_3$ (19 mg, 0.3 mmol), CuI (2 mg, 0.015 mmol) and iodobenzene (33 mg, 0.16 mmol) were added sequentially to a solution of the sulfone **5 a** (41 mg, 0.15 mmol) in benzene (6 mL). The resulting mixture was stirred for 2 h at RT, filtered through Celite and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 4:1) to afford **7 a** (52 mg, 81 %, colourless oil). $^1H$ NMR (200 MHz, $CDCl_3$): δ = 7.96 – 7.85 (m, 2 H, $SO_2ArH$), 7.71 (m, 3 H, $SO_2ArH$), 7.60 – 7.36 (m, 5 H, ArH), 7.25 (dd, *J* = 4.0, 14.9, 1 H, H2), 6.69 (dd, *J* = 2.0, 39.0 Hz, 1 H, H1), 4.40 (m, 1 H, H3), 2.55/2.34 (AB system, *J* = 16.9 Hz, 2 H, H5), 2.16 (d, *J* = 5.2 Hz, 1 H, OH), 1.10 (s, 3 H, $CH_3$), 1.00 (s, 3 H, $CH_3$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 145.5, 140.3, 133.3, 131.6, 131.4, 129.2, 128.2, 127.8, 127.5, 123.2, 86.7, 83.4, 75.7, 39.1, 30.0, 23.7, 22.3; HRMS (FAB + ): calcd for: 355.1367; found: 355.1357 $[M+H]^+$.

**(*Z*)-4,4-Dimethyl-1-(phenylsulfonyl)hept-1-en-6-yn-3-ol (21 a)**: The sulfone **5 a** (311 mg, 1.12 mmol) was added to a suspension of PCC (365 mg, 1.70 mmol) and Celite (365 mg) in $CH_2Cl_2$ (10 mL) at RT, and the resulting mixture was stirred for 4 h. The solvent was removed under reduced pressure, and the residue was diluted with $Et_2O$ (50 mL), filtered over Celite and concentrated to afford (*E*)-4,4-dimethyl-1-(phenylsulfonyl)-hept-1-en-6-yn-3-one (238 mg, 77 %). The residue was used directly in the next reaction. $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.96 – 7.91 (m, 2 H, ArH), 7.75 (m, 1 H, ArH), 7.66 – 7.55 (m, 2 H, ArH), 7.18/7.05 (AB system, *J* = 15.3 Hz, 2 H, H1, H2), 2.59 (m, 2 H, H5), 1.95 (t, *J* = 2.7 Hz, 1 H, H7), 1.29 (s, 6 H, $C(CH_3)_2$).

A solution of (*E*)-4,4-dimethyl-1-(phenylsulfonyl)hept-1-en-6-yn-3-one (276 mg, 1.0 mmol) in $CH_2Cl_2$ (7 mL) was irradiated (Hg lamp, 150 W) for 2 d. The reaction mixture was concentrated to afford (*Z*)-4,4-dimethyl-1-(phenylsulfonyl)hept-1-en-6-yn-3-one (274 mg, 99 %). The residue was used directly in the next reaction. $^1H$ NMR (300 MHz, $CDCl_3$): δ = 8.02 – 7.96 (m, 2 H, ArH), 7.68 – 7.56 (m, 3 H, ArH), 6.88/6.45 (AB system, *J* = 10.1 Hz, 2 H, H1, H2), 2.56 (m, 2 H, H5), 1.99 (t, *J* = 2.7 Hz, 1 H, H7), 1.40 (s, 3 H, $CH_3$), 1.11 (s, 3 H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 206.8, 140.3, 133.9, 133.7, 129.5, 128.4, 127.3, 80.8, 71.3, 47.1, 29.1, 23.9.

$NaBH_4$ (12 mg, 0.31 mmol) and $CeCl_3$ (372 mg, 0.31 mmol) in MeOH (5 mL) were added to a solution of (*Z*)-4,4-dimethyl-1-(phenylsulfonyl)-hept-1-en-6-yn-3-one (71 mg, 0.26 mmol) in MeOH (3 mL). After having been stirred for 10 min, the reaction mixture was quenched with water and extracted with $CH_2Cl_2$ (2 × 15 mL). The combined organic layers were washed with saturated aqueous $NH_4Cl$ (2 × 15 mL), dried ($Na_2SO_4$) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 1:1) to afford **21 a** (65 mg, 89 %, colourless oil). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.96 – 7.93 (m, 2 H, ArH), 7.67 – 7.53 (m, 3 H, ArH), 6.44 – 6.36 (m, 2 H, H1, H2), 5.10 (m, 1 H, H3), 2.77 (m, 1 H, OH), 2.33 (dt, *J* = 2.4, 7.1 Hz, 2 H, H5), 2.03 (t, *J* = 2.2 Hz, 1 H, H7), 1.01 (s, 3 H, $CH_3$), 0.96 (s, 3 H, $CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): 143.7, 140.7, 133.7, 132.5, 129.3, 127.5, 81.8, 70.7, 70.6, 37.6, 28.5, 23.0, 21.3; HRMS (EI + ): calcd for: 278.0976; found: 278.0977 $[M]^+$.

**Preparation of (ethoxymethoxy)enynes (enynes b)**

**(*E*)-3-Ethoxymethoxy-1-(phenylsulfonyl)hept-1-en-6-yne (1 b)**: *N*,*N*-Diisopropylethylamine (0.22 mL, 1.30 mmol) and chloromethyl ethyl ether (0.23 mL, 2.60 mmol) were added sequentially to a solution of **1 a** (163 mg, 0.65 mmol) in dry $CH_2Cl_2$ (12 mL). The solution was stirred for 12 h at RT, and saturated aqueous $NH_4Cl$ (10 mL) was then added. The organic layer was separated, washed with saturated aqueous $Na_2CO_3$ (2 × 10 mL), dried ($Na_2SO_4$) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 8:1) to afford **1 b** (180 mg, 90 %, colourless oil). $^1H$ NMR (200 MHz, $CDCl_3$): δ = 7.92 – 7.89 (m, 2 H, ArH), 7.71 – 7.49 (m, 3 H, ArH), 6.92 (dd, *J* = 3.9, 15.0 Hz, 1 H, H2), 6.55 (dd, *J* = 1.4, 14.9 Hz, 1 H, H1), 4.64 (m, 2 H, $OCH_2O$), 4.48 (m, 1 H, H3), 3.60 (m, 2 H, $CH_3CH_2O$), 2.30 (m, 2 H, H5), 1.93 (t, *J* = 2.0 Hz, 1 H, H7), 1.82 (m, 2 H, H4), 1.19 (t, *J* = 6.9 Hz, 3 H, $CH_3CH_2O$); $^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 145.4, 140.1, 133.4, 131.2, 129.3, 127.5, 93.8, 82.7, 73.2, 69.4, 63.8, 33.2, 14.8, 14.2; HRMS (FAB + ): calcd for: 309.1160; found: 309.1157 $[M+H]^+$.

When alcohol (*S*)-**1 a** was used instead of (±)-**1 a**, (S)-**1 b** was obtained, $[\alpha]_D = -3.5$ ($c = 1.8$, $CHCl_3$).

**(*E*)-3-Ethoxymethoxy-1-(phenylsulfonyl)oct-1-en-6-yne (3 b)**: Through the same procedure, treatment of **3 a** (74 mg, 0.28 mmol) with *N*,*N*-diisopropylethylamine (95 μL, 0.56 mmol) and chloromethyl ethyl ether (106 μL, 1.10 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), **3 b** (82 mg, 91 %, colourless oil). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.89 – 7.86 (m, 2 H, ArH), 7.62 – 7.51 (m, 3 H, ArH), 6.94 (dd, *J* = 4.3, 14.9 Hz, 1 H, H2), 6.55 (dd, *J* = 1.2, 15.2 Hz, 1 H, H1), 4.61 (q, *J* = 7.7 Hz, 2 H, $OCH_2O$), 4.44 (m, 1 H, H3), 3.60 (m, 2 H, $OCH_2CH_3$), 2.35 (m, 2 H, H5), 1.75 (s, 3 H, H8), 1.73 (m, 2 H, H4), 1.12 (t, *J* = 7.7 Hz, 3 H, $OCH_2CH_3$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 145.8, 140.2, 133.4, 130.9, 129.3, 127.6, 93.9, 76.8, 74.1, 73.3, 63.8, 33.8, 14.9, 14.6, 3.4; MS (70 eV, EI): *m*/*z* (%): 319 (1), 197 (6), 125 (35), 107(14), 91 (17), 77(36), 59 (100); HRMS (FAB + ): calcd for: 323.1317; found: 323.1303 $[M+H]^+$.

**(*E*)-4,4-Dimethyl-3-ethoxymethoxy-1-(phenylsulfonyl)hept-1-en-6-yne (5 b)**: Through the same procedure, treatment of **5 a** (100 mg, 0.30 mmol) with *N*,*N*-diisopropylethylamine (0.10 mL, 0.60 mmol) and chloromethyl ethyl ether (0.14 mL, 1.50 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), **5 b** (92 mg, 93 %, colourless oil). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.89 – 7.86 (m, 2 H, ArH), 7.64 – 7.50 (m, 3 H, ArH), 6.93 (dd, *J* = 6.3, 15.1 Hz, 1 H, H2), 6.55 (dd, *J* = 1.2, 15.2 Hz, 1 H, H1), 4.57 (q, *J* = 7.1 Hz, 2 H, $OCH_2O$), 4.16 (m, 1 H, H3), 3.61 (m, 2 H, $CH_3CH_2O$), 2.28 (dd, *J* = 2.5, 16.4 Hz, 1 H, H5), 2.07 (dd, *J* = 2.7, 16.6 Hz, 1 H, H5), 1.93 (t, *J* = 2.3 Hz, 1 H, H7), 1.12 (t, *J* = 7.1 Hz, 3 H, $CH_3CH_2O$), 0.95 (s, 6 H, $C(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 143.6, 140.4, 133.4, 133.0, 129.3, 127.5, 94.3, 81.1, 80.0, 71.0, 64.0, 38.4, 29.0, 23.4, 22.4, 14.8; elemental analysis calcd (%) for $C_{18}H_{24}O_4S$ (336.1): C 64.26, H 7.19, S 9.53; found: C 63.90, H 6.91, S 10.07.

**(*E*)-4,4-Dimethyl-3-ethoxymethoxy-7-phenyl-1-(phenylsulfonyl)hept-1-en-6-yne (7 b)**: Through the same procedure, treatment of **7 a** (100 mg, 0.30 mmol) with *N*,*N*-diisopropylethylamine (95 μL, 0.56 mmol) and chloromethyl ethyl ether (105 μL, 1.12 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), **7 b** (109 mg, 94 %, colourless oil). $^1H$ NMR (300 MHz, $CDCl_3$): δ = 7.88 – 7.85 (m, 2 H, ArH), 7.61 – 7.48 (m, 3 H, ArH), 7.39 (m, 2 H, ArH), 7.33 (m, 3 H, ArH), 6.94 (dd, *J* = 6.2, 15.1 Hz, 1 H, H2), 6.55 (dd, *J* = 1.2, 15.2 Hz, 1 H, H1), 4.55 (q, *J* = 7.7 Hz, 2 H, $OCH_2O$), 4.21 (d, *J* = 6.3 Hz, 1 H, H3), 3.55 (m, 2 H, $OCH_2CH_3$), 2.51/2.28 (AB system, *J* = 17.1 Hz, 2 H, H5), 1.06 (t, *J* = 7.7 Hz, 3 H, $OCH_2CH_3$), 0.99 (s, 6 H, $C(CH_3)_2$); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 143.7, 140.3, 133.4, 133.0, 131.5, 129.3, 128.2, 127.7, 127.5, 123.5, 94.3, 86.8, 83.2, 80.3, 64.1, 39.0, 30.0, 23.6, 22.5, 14.8; HRMS (FAB + ): calcd for: 412.1708; found: 412.1721 $[M+H]^+$.

**(*E*)-3-Ethoxymethoxy-1-(phenylsulfonyl)oct-1-en-7-yne (17 b)**: Through the same procedure, treatment of **17 a** (61 mg, 0.23 mmol) with *N*,*N*-diisopropylethylamine (80 μL, 0.46 mmol) and chloromethyl ethyl ether (0.11 mL, 1.15 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), **17b** (69 mg, 93 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.91–7.86 (m, 2H, ArH), 7.67–7.49 (m, 3H, ArH), 6.91 (dd, $J$ = 5.4, 15.0 Hz, 1H, H2), 6.52 (dd, $J$ = 1.1, 15.0 Hz, 1H, H1), 4.64/4.58 (AB system, $J$ = 7.0 Hz, 2H, OC$H_2$O), 4.29 (m, 1H, H3), 3.56 (m, 2H, OC$H_2$CH$_3$), 2.22 (td, $J$ = 2.7, 7.0 Hz, 2H, H6), 1.95 (t, $J$ = 2.5 Hz, 1H, H8), 1.66 (m, 4H, H4, H5), 1.13 (t, $J$ = 7.3 Hz, 2H, OCH$_2$C$H_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 145.8, 140.2, 133.4, 130.9, 129.2, 127.5, 93.6, 83.4, 74.1, 68.9, 63.7, 33.2, 23.6, 18.1, 14.8; HRMS (FAB+): calcd for: 323.1317; found: 323.1306 [$M$+H]$^+$.

**(*E*)-3-Ethoxymethoxy-1-phenylsulfonyl-5-oxa-oct-1-en-7-yne (18b)**: Through the same procedure, treatment of **18a** (99 mg, 0.37 mmol) with *N*,*N*-diisopropylethylamine (0.13 mL, 0.74 mmol) and chloromethyl ethyl ether (0.17 mL, 1.86 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 3:1), **18b** (101 mg, 84 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.90–7.87 (m, 2H, ArH), 7.65–7.49 (m, 3H, ArH), 6.98 (dd, $J$ = 4.3, 15.1 Hz, 1H, H3), 6.64 (dd, $J$ = 2.1, 15.1 Hz, 1H, H4), 4.73/4.64 (AB system, $J$ = 7.0 Hz, 2H, OC$H_2$O), 4.49 (m, 1H, H2), 4.16 (d, $J$ = 2.7 Hz, 2H, OC$H_2$CCH), 3.69–3.43 (m, 4H, H1, OC$H_2$CH$_3$), 2.44 (t, $J$ = 2.2 Hz, 1H, OCH$_2$CC$H$), 1.12 (t, $J$ = 7.3 Hz, 3H, OCH$_2$C$H_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 143.2, 140.0, 133.3, 131.6, 129.1, 127.4, 94.0, 78.8, 75.0, 73.4, 70.6, 63.6, 58.3, 14.7; HRMS (FAB+): calcd for: 325.1110; found: 325.1110 [$M$+H]$^+$.

**(*Z*)-4,4-Dimethyl-3-ethoxymethoxy-1-(phenylsulfonyl)hept-1-en-6-yne (21b)**: Through the same procedure, treatment of **21a** (50 mg, 0.15 mmol) with *N*,*N*-diisopropylethylamine (52 µL, 0.30 mmol) and chloromethyl ethyl ether (70 µL, 0.75 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), **21b** (48 mg, 95 %, colourless oil). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.98–7.95 (m, 2H, ArH), 7.63–7.48 (m, 3H, ArH), 6.91 (m, 1H, H2), 6.55 (m, 1H, H1), 5.45 (d, $J$ = 11.1 Hz, 1H, H3), 4.63 (q, $J$ = 7.1 Hz, 2H, OC$H_2$O), 3.60 (m, 2H, OC$H_2$CH$_3$), 2.32 (m, 2H, H5), 1.94 (t, $J$ = 2.1 Hz, 1H, H7), 1.14 (t, $J$ = 7.7 Hz, 2H, OCH$_2$C$H_3$), 1.05 (s, 3H, C$H_3$), 0.99 (s, 3H, C$H_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 142.5, 140.9, 134.7, 132.5, 129.2, 128.1, 94.6, 81.8, 70.7, 63.8, 38.0, 28.7, 23.5, 22.1, 15.1; HRMS (FAB+): calcd for: 291.1054; found: 291.1048 [$M$ − C$_2$H$_5$O]$^+$.

**(*E*)-5-Ethoxymethoxy-7-(phenylsulfonyl)oct-6-en-1-yne (22b)**: *n*BuLi (0.44 mL, 1.07 mmol, 2.4 M in hexane) was added under argon atmosphere to a solution of **1b** (163 mg, 0.53 mmol) in THF (9 mL), cooled to −78 °C. The resulting mixture was stirred for 30 min and MeI (107 µL, 1.07 mmol) was added. After having been stirred for 1 h at −78 °C, the reaction mixture was quenched with saturated aqueous NH$_4$Cl (10 mL). The mixture was extracted with CH$_2$Cl$_2$ (2 × 15 mL) and the combined organic layers were dried (Na$_2$SO$_4$) and evaporated. The residue was purified by chromatography (hexane/ethyl acetate 5:1) to afford **22b** (141 mg, 79 %, colourless oil). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.87–7.84 (m, 2H, ArH), 7.62–7.50 (m, 3H, ArH), 6.59 (dq, $J$ = 1.1, 8.0 Hz, 1H, H2), 4.59 (q, $J$ = 6.4 Hz, 2H, OC$H_2$O), 4.55 (m, 1H, H3), 3.59 (m, 2H, OC$H_2$CH$_3$), 2.31 (m, 2H, H5), 1.91 (d, $J$ = 1.2 Hz, 3H, H1), 1.81 (m, 1H, H5), 1.74 (t, $J$ = 2.4 Hz, 3H, H7), 1.71 (m, 1H, H5), 1.60 (t, $J$ = 6.5 Hz, 3H, OCH$_2$C$H_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 140.1, 139.8, 133.3, 129.7, 128.1, 126.4, 93.3, 77.6, 75.9, 70.8, 63.5, 33.7, 15.0, 14.7, 11.9, 3.3; HRMS (FAB+): calcd for 291.1054; found: 291.1049 [$M$ − C$_2$H$_5$O]$^+$.

**Preparation of the (triisopropylsiloxy)enynes (enynes c)**

**(*E*)-1-Phenylsulfonyl-3-(triisopropylsiloxy)hept-1-en-6-yne (1c)**: 2,6-Lutidine (82 µL, 0.60 mmol) and TIPSOTf (0.13 mL, 0.48 mmol) were added sequentially to a solution of **1a** (100 mg, 0.40 mmol) in dry CH$_2$Cl$_2$ (5 mL). After having been stirred for 6 h at RT, the reaction mixture was quenched with a saturated aqueous solution of NH$_4$Cl (5 mL). The organic layer was separated, the aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 10 mL) and the combined organic layers were dried (Na$_2$SO$_4$) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 9:1) to afford **1c** (159 mg, 98 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.91–7.83 (m, 2H, ArH), 7.65–7.49 (m, 3H, ArH), 7.03 (dd, $J$ = 3.5, 14.9 Hz, 1H, H2), 6.65 (dd, $J$ = 1.8, 14.9 Hz, 1H, H1), 4.71 (m, 1H, H3), 2.41 (m, 2H, H5), 2.01 (t, $J$ = 2.7 Hz, 1H, H7), 1.95–1.63 (m, 2H, H4), 1.10 (m, 21H, TIPS); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 147.5, 140.1, 133.2, 130.4, 129.0, 127.3, 83.0, 69.6, 69.2, 35.5, 17.7, 17.5, 13.2, 12.2, 12.1; elemental analysis calcd (%) for C$_{22}$H$_{34}$O$_3$SSi (406.6): C 64.98, H 8.43, S 7.89; found: C 65.24, H 8.81, S 7.72.

**(*E*)-1-Phenylsulfonyl-3-(triisopropylsiloxy)oct-1-en-6-yne (3c)**: Through the same procedure, treatment of **3a** (137 mg, 0.52 mmol) with 2,6-lutidine (75 µL, 0.63 mmol) and TIPSOTf (0.28 mL, 1.04 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), **3c** (212 mg, 97 %, colourless oil). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.88–7.86 (m, 2H, ArH), 7.63–7.50 (m, 3H, ArH), 7.04 (dd, $J$ = 5.0, 13.8 Hz, 1H, H2), 6.55 (dd, $J$ = 1.9, 13.8 Hz, 1H, H1), 4.65 (m, 1H, H3), 2.33 (m, 2H, H5), 1.86 (m, 2H, H4), 1.79 (s, 3H, H8), 0.65 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 148.9, 140.5, 133.3, 130.2, 129.2, 127.5, 77.9, 71.5, 70.1, 36.5, 17.9, 13.9, 12.2, 3.4; HRMS (FAB+): calcd for: 377.1606; found: 377.1611 [$M$ − C$_3$H$_7$]$^+$.

**(*E*)-4,4-Dimethyl-1-phenylsulfonyl-3-(triisopropylsiloxy)hept-1-en-6-yne (5c)**: Through the same procedure, treatment of **5a** (53 mg, 0.19 mmol) with 2,6-lutidine (33 µL, 0.28 mmol) and TIPSOTf (100 µL, 0.38 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), **5c** (79 mg, 96 %, colourless oil). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.89–7.86 (m, 2H, ArH), 7.65–7.52 (m, 3H, ArH), 7.04 (dd, $J$ = 7.4, 15.3 Hz, 1H, H2), 6.55 (dd, $J$ = 1.5, 13.8 Hz, 1H, H1), 4.30 (d, $J$ = 7.2 Hz, 1H, H3), 2.23 (m, 2H, H5), 1.96 (t, $J$ = 2.7 Hz, 1H, H7), 0.95 (s, 27H, C(C$H_3$)$_2$, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 146.1, 140.5, 136.8, 133.7, 132.5, 129.7, 128.0, 81.1, 70.8, 39.6, 30.1, 28.9, 23.6, 22.6, 18.1, 12.2; MS (70 eV, EI): $m/z$ (%): 391 (40) [$M$ − *i*Pr]$^+$, 354 (34), 255 (100), 249 (55), 191 (54), 149 (70), 103 (45), 75 (78); HRMS (FAB+): calcd for: 435.2389; found: 435.2382 [$M$+H]$^+$.

**(*E*)-4,4-Dimethyl-7-phenyl-1-phenylsulfonyl-3-(triisopropylsiloxy)hept-1-en-6-yne (7c)**: Through the same procedure, treatment of **7a** (46 mg, 0.13 mmol) with 2,6-lutidine (20 µL, 0.17 mmol) and TIPSOTf (70 µL, 0.26 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), **7c** (64 mg, 96 %, colourless oil). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.88–7.86 (m, 2H, ArH), 7.63–7.50 (m, 3H, ArH), 7.40–7.12 (m, 5H, ArH), 6.95 (dd, $J$ = 6.7, 15.1 Hz, 1H, H2), 6.55 (dd, $J$ = 1.5, 15.1 Hz, 1H, H1), 4.42 (d, $J$ = 6.0 Hz, 1H, H3), 2.51/2.30 (AB system, $J$ = 16.0 Hz, 2H, H5), 0.95 (m, 27H, C(C$H_3$)$_2$, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 145.8, 140.3, 137.4, 133.4, 131.9, 130.2, 129.2, 128.2, 127.4, 123.2, 87.2, 83.2, 76.5, 40.1, 29.5, 23.3, 22.5, 18.0, 14.2; HRMS (FAB+): calcd for: 467.2076; found: 467.2071 [$M$ − C$_3$H$_7$]$^+$.

**(*E*)-1-Phenylsulfonyl-3-(triisopropylsiloxy)oct-1-en-7-yne (17c)**: Through the same procedure, treatment of **17a** (137 mg, 0.52 mmol) with 2,6-lutidine (91 µL, 0.78 mmol) and TIPSOTf (0.42 mL, 1.55 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), **17c** (212 mg, 97 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.90–7.85 (m, 2H, ArH), 7.61–7.48 (m, 3H, ArH), 6.96 (dd, $J$ = 4.3, 15.1 Hz, 1H, H2), 6.53 (dd, $J$ = 1.1, 15.1 Hz, 1H, H1), 4.57 (m, 1H, H3), 2.18 (td, $J$ = 2.7, 7.0 Hz, 2H, H6), 1.94 (t, $J$ = 2.7 Hz, 1H, H8), 1.82–1.25 (m, 4H, H4, H5), 0.96 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 148.3, 140.3, 133.1, 130.1, 129.0, 127.3, 83.4, 70.3, 68.7, 35.6, 22.4, 18.2, 17.7, 11.9; HRMS (FAB+): calcd for: 421.2233; found: 421.2227 [$M$+H]$^+$.

**(*E*)-1-Phenylsulfonyl-3-triisopropylsiloxy-5-oxa-oct-1-en-7-yne (18c)**: Through the same procedure, treatment of **18a** (33 mg, 0.12 mmol) with 2,6-lutidine (22 µL, 0.19 mmol) and TIPSOTf (100 µL, 0.37 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 20:1), **18c** (47 mg, 90 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.89–7.86 (m, 2H, ArH), 7.61–7.47 (m, 3H, ArH), 7.08 (dd, $J$ = 3.8, 15.1 Hz, 1H, H3), 6.62 (dd, $J$ = 1.6, 15.1 Hz, 1H, H4), 4.62 (m, 1H, H2), 4.13 (d, $J$ = 2.7 Hz, 2H, OC$H_2$CCH), 3.62 (dd, $J$ = 5.4, 9.1 Hz, 1H, H1), 3.46 (dd, $J$ = 6.5, 9.1 Hz, 1H, H1), 2.42 (t, $J$ = 2.5 Hz, 1H, OCH$_2$CC$H$), 0.97 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ = 146.7, 140.4, 133.3, 130.9, 129.2, 127.6, 79.1, 75.0, 73.1, 70.3, 58.5, 17.8, 12.1; HRMS (FAB+): calcd for: 379.1399; found: 379.1392 [$M$ − C$_3$H$_7$]$^+$.

**(*E*)-3-*tert*-Butyldimethylsiloxy-1-(phenylsulfonyl)hept-1-en-6-yne (1d)**: Imidazole (43 mg, 0.63 mmol) and TBDMSCl (63 mg, 0.42 mmol) were added sequentially to a solution of **1a** (53 mg, 0.21 mmol) in CH$_2$Cl$_2$ (8 mL), cooled at 0 °C under argon atmosphere. After having been stirred for 4 h at RT, the reaction mixture was quenched with saturated aqueous NH$_4$Cl (5 mL). The mixture was extracted with CH$_2$Cl$_2$ (2 × 15 mL) and the combined organic layers were dried (Na$_2$SO$_4$) and evaporated. The residue was purified by chromatography (hexane/ethyl acetate 10:1) to afford **1d** (74 mg, 97 %, colourless oil). $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ = 7.93–7.88 (m, 2H, ArH), 7.66–7.46 (m, 3H, ArH), 6.97 (dd, $J$ = 4.3, 15.1 Hz, 1H, H2), 6.52 (dd, $J$ = 1.7, 15.0 Hz, 1H, H1), 4.49 (m, 1H, H3), 2.33 (m, 2H, H5), 1.91 (t, $J$ = 2.4 Hz, 1H, H7), 1.77 (m, 2H, H4), 0.81 (s, 9H, *t*Bu), 0.05 (s, 3H, SiCH$_3$), −0.08 (s, 3H, SiCH$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ = 147.9, 140.5, 133.2, 130.1, 129.4, 127.3, 83.1, 69.3, 35.4, 25.5, 18.1, 14.0, −4.7, −5.1;

elemental analysis calcd (%) for $C_{19}H_{28}O_3SSi$ (364.5): C 62.59, H 7.74, S 8.80; found: C 62.81, H 8.06, S 9.12.

**(*E*)-3-Acetoxy-1-phenylsulfonyl-hept-1-en-6-yne (1e)**: $Ac_2O$ (228 μL, 2.4 mmol) was added at RT to a solution of **1a** (61 mg, 0.24 mmol) in pyridine (3 mL). After the solution was stirred for 5 h, the reaction mixture was diluted with $CH_2Cl_2$ (10 mL) and cooled to 0 °C, and saturated aqueous $NaHCO_3$ was then slowly added until a basic pH value was reached. The organic layer was separated, dried ($Na_2SO_4$) and evaporated. The residue was purified by chromatography (hexane/ethyl acetate 2:1) to afford **1e** (66 mg, 95%, colourless oil). $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.90-7.85$ (m, 2H, ArH), 7.65–7.51 (m, 3H, ArH), 6.92 (dd, $J = 5.7$, 16.1 Hz, 1H, H2), 6.55 (dd, $J = 1.6$, 15.1 Hz, 1H, H1), 5.59 (m, 3H, H3), 2.25 (m, 2H), 2.08 (s, 3H), 1.93 (m, 2H); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 169.5$, 142.6, 139.7, 133.6, 131.3, 129.3, 127.6, 82.1, 70.2, 69.8, 32.1, 20.7, 14.2; elemental analysis calcd (%) for $C_{15}H_{16}O_4S$ (292.3): C 61.62, H 5.52, S 10.97; found: C 61.57, H 5.70, S 11.26.

**(*E*)-3-Methoxy-1-(phenylsulfonyl)hept-1-en-6-yne (1f)**: $Me_3OBF_4$ (47 mg, 0.31 mmol) and 1,8-bis(dimethylamino)naphthalene (89 mg, 0.42 mmol) were added sequentially to a solution of **1a** (53 mg, 0.21 mmol) in $CH_3CN$ (3 mL). After the solution was stirred for 4 d at RT, the reaction mixture was quenched with saturated aqueous $NH_4Cl$ (5 mL). The mixture was extracted with $CH_2Cl_2$ (2 × 15 mL) and the combined organic layers were dried ($Na_2SO_4$) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 6:1) to afford **1f** (39 mg, 70%, white solid). M.p. 127–129 °C; $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.90-7.88$ (m, 2H, ArH), 7.66–7.52 (m, 3H, ArH), 6.90 (dd, $J = 5.1$, 15.1 Hz, 1H, H2), 6.55 (dd, $J = 1.3$, 15.1 Hz, 1H, H1), 4.02 (m, 1H, H3), 3.31 (s, 3H, OMe), 2.30 (m, 2H, H5), 1.96 (t, $J = 2.6$ Hz, 1H, H7), 1.72 (m, 2H, H4); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 145.2$, 140.1, 133.4, 131.3, 129.2, 127.6, 82.9, 69.3, 57.7, 32.9, 17.7, 14.2.

**Enantioselective acetylation of $\gamma$-hydroxy-$\alpha,\beta$-unsaturated phenyl sulfones**

**(1*E*,3*S*)-1-(Phenylsulfonyl)hept-1-en-6-yn-3-ol [(*S*)-1a] and (1*E*,3*R*)-3-(acetoxy)-1-(phenylsulfonyl)hept-1-en-6-yne [(*R*)-1e]**: Vinyl acetate (774 mg, 9.01 mmol), Lipase PS (*Pseudomonas cepacia*, Amano company, 25 mg mL$^{-1}$) and molecular sieves (4 Å, 50 mg mL$^{-1}$) were added sequentially to a solution of the racemic alcohol **1a** (450 mg, 1.80 mmol) in toluene. After having been stirred vigorously at RT for 48 h (50% of conversion by $^1$H NMR) the resulting mixture was filtered and evaporated. The residue was purified by chromatography (hexane/ethyl acetate 4:1) to afford (*S*)-**1a** (225 mg, 49%) and (*R*)-**1e** (242 mg, 46%).

(*S*)-**1a**: $[\alpha]_D = +28$ ($c = 1$, $CHCl_3$); *ee* = 98.5% (HPLC, Daicel Chiralpak AS column, hexane/isopropanol 85:15, 0.5 mL min$^{-1}$, $t_R = 52.9$ and 58.0). The spectral data were identical to those described for (±)-**1a**. (*R*)-**1e**: $[\alpha]_D = +5.1$ ($c = 1$, $CHCl_3$); *ee* > 96% [$^1$H NMR, Pr(hfc)$_3$, 0.4 equiv). The spectral data were identical to those described for (±)-**1e**.

**Typical Pauson–Khand reactions**

***6-Ethoxymethoxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (9b)***

*Thermal reaction in acetonitrile* (*method A*): A solution of the enyne **1b** (98 mg, 0.32 mmol) in dry $CH_2Cl_2$ (5 mL) was added to a flask containing solid $[Co_2(CO)_8]$ (136 mg, 0.40 mmol). The resulting solution was stirred until TLC analysis showed that formation of the complex was complete, and the solvent was then removed under reduced pressure. The residue was diluted with $CH_3CN$ (7 mL) and the resulting solution was heated at reflux until complete disappearance of the complex. The reaction mixture was filtered through a pad of Celite, which was washed with diethyl ether (30 mL). The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 5:1) to afford *endo*-**9b** (68 mg, 76%, white solid). M.p. 73–74 °C; $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.99-7.96$ (m, 2H, ArH), 7.70–7.55 (m, 3H, ArH), 5.92 (m, 1H, H2), 4.69/4.59 (AB system, $J = 7.1$, 27.9 Hz, 2H, $OCH_2O$), 4.28 (t, $J = 4.1$ Hz, 1H, H6), 4.23 (d, $J = 4.4$ Hz, 1H, H4), 3.59 (m, 1H, H5), 3.51 (m, 2H, $OCH_2CH_3$), 2.71 (m, 2H, H8), 2.24 (m, 2H, H7), 1.21 (t, $J = 7.0$ Hz, 3H, $OCH_2CH_3$); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 198.1$, 185.0, 138.6, 134.0, 129.2, 129.1, 125.0, 93.8, 76.3, 68.3, 63.7, 53.2, 32.5, 24.3, 15.1; elemental analysis calcd (%) for $C_{17}H_{20}O_5S$ (336.4): C 60.70, H 5.99, S 9.53; found: C 60.46, H 6.42, S 9.92. Compound (4*R*,5*R*,6*S*)-**9b** was obtained from (*S*)-**1b**, $[\alpha]_D = +241$ ($c = 0.4$ in $CHCl_3$).

*Amine N-oxide-promoted reaction* (*method B*): A solution of enyne (*S*)-**1b** (187 mg, 0.61 mmol) in $CH_2Cl_2$ (5 mL) was added dropwise, under argon atmosphere at RT, to a stirred solution of $[Co_2(CO)_8]$ (250 mg, 0.73 mmol) in $CH_2Cl_2$ (5 mL). The solution was stirred for 10 min and $Me_3NO \cdot 2H_2O$ (407 mg, 3.66 mmol) was added in one portion. The resulting solution was stirred for 3 h at RT and filtered through a pad of Celite, which was washed with diethyl ether (30 mL). The combined solvents were evaporated and the residue was purified by flash chromatography (hexane/ethyl acetate 5:1) to afford *endo*-**9b** (151 mg, 74%).

*Reaction promoted by amine N-oxide and molecular sieves* (*method C*): The procedure was identical to method B but with the addition of molecular sieves (4 Å, 800% of the weight of the starting enyne) to the initial solution of $[Co_2(CO)_8]$ in toluene.

**4-Phenylsulfonyl-6-(triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (9c)**: When method A was used, treatment of **1c** (111 mg, 0.27 mmol) with $[Co_2(CO)_8]$ (116 mg, 0.34 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), *endo*-**9c** (77 mg, 67%, white solid) and *exo*-**9c** (7 mg, 7%, colourless oil). When method B was used, treatment of **1c** (130 mg, 0.32 mmol) with $[Co_2(CO)_8]$ (120 mg, 0.35 mmol) and $Me_3NO \cdot 2H_2O$ (249 mg, 2.24 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), *endo*-**9c** (91 mg, 66%) and *exo*-**9c** (9 mg, 7%).

*endo*-**9c**: M.p. 109–110 °C; $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.96-7.90$ (m, 2H, ArH), 7.69–7.54 (m, 3H, ArH), 5.90 (m, 1H, H2), 4.62 (t, $J = 3.6$ Hz, 1H, H6), 4.11 (d, $J = 4.1$ Hz, 1H, H4), 3.61 (m, 1H, H5), 2.71 (m, 2H, H8), 2.39 (m, 1H, H7), 2.15 (m, 1H, H7), 1.15 (s, 21H, TIPS); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 197.6$, 184.9, 138.9, 134.1, 128.7, 127.9, 126.5, 71.8, 68.2, 54.1, 36.1, 23.9, 17.8, 12.5; elemental analysis calcd (%) for $C_{23}H_{34}O_4SSi$ (434.6): C 63.55, H 7.88, S 7.38; found: C 63.23, H 7.98, S 7.80.

*exo*-**9c**: $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.94-7.90$ (m, 2H, ArH), 7.66–7.51 (m, 3H, ArH), 5.87 (m, 1H, H2), 3.97 (q, $J = 7.5$ Hz, 1H, H6), 3.85 (d, $J = 2.8$ Hz, 1H, H4), 2.84 (m, 1H, H5), 2.61 (m, 2H, H8), 2.30 (m, 2H, H7), 1.15 (s, 21H, TIPS); $^{13}$C NMR (50 MHz, $CDCl_3$): $\delta = 197.5$, 185.2, 138.5, 133.9, 128.2, 127.8, 75.4, 71.5, 54.8, 35.1, 25.3, 18.1, 12.5.

**6-*tert*-Butyldimethylsiloxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (9d)**: When method B was used, treatment of **1d** (33 mg, 0.09 mmol) with $[Co_2(CO)_8]$ (37 mg, 0.10 mmol) and $Me_3NO \cdot 2H_2O$ (148 mg, 1.33 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), *endo*-**9d** (25 mg, 72%, white solid) and *exo*-**9d** (2 mg, 6%, colourless oil).

*endo*-**9d**: M.p. 139–140 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 7.96-7.88$ (m, 2H, ArH), 7.70–7.55 (m, 3H, ArH), 5.91 (m, 1H, H2), 4.40 (t, $J = 3.4$ Hz, 1H, H6), 3.99 (d, $J = 4.6$ Hz, 1H, H4), 3.55 (m, 1H, H5), 2.69 (m, 2H, H8), 2.31 (m, 1H, H7), 2.05 (m, 1H, H7), 0.80 (s, 9H, *t*Bu), 0.31 (s, 6H, $Si(CH_3)_2$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 198.2$, 187.3, 138.7, 133.9, 129.1, 129.0, 125.1, 76.5, 70.1, 68.6, 54.4, 35.9, 25.6, 24.3, 17.9; elemental analysis calcd (%) for $C_{20}H_{28}O_4SSi$ (392.6): C 61.19, H 7.19, S 8.17; found: C 61.06, H 7.07, S 8.50.

*exo*-**9d**: $^1$H NMR (300 MHz, $CDCl_3$): $\delta = 7.95-7.92$ (m, 2H, ArH), 7.67–7.55 (m, 3H, ArH), 5.87 (m, 1H, H2), 3.85 (q, $J = 7.7$ Hz, 1H, H6), 3.77 (d, $J = 2.8$ Hz, 1H, H4), 3.67 (m, 1H, H5), 2.85 (m, 1H, H8), 2.59 (m, 1H, H8), 2.20 (m, 2H, H7), 0.81 (s, 9H, *t*Bu), 0.30 (s, 3H, $SiCH_3$), 0.21 (s, 3H, $SiCH_3$).

**6-Acetoxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (9e)**: When method A was used, treatment of **1e** (65 mg, 0.22 mmol) with $[Co_2(CO)_8]$ (94 mg, 0.27 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 2:1), *endo*-**9e** and *exo*-**9e** (48 mg, 68%) as an inseparable *endo*/*exo* mixture (54:46). When method B was used, treatment of **1e** (53 mg, 0.18 mmol) with $[Co_2(CO)_8]$ (80 mg, 0.23 mmol) and $Me_3NO \cdot 2H_2O$ (140 mg, 1.26 mmol) afforded *endo*-**9e** and *exo*-**9e** (38 mg, 65%) as an inseparable diastereoisomeric mixture (57:43). $^1$H NMR (200 MHz, $CDCl_3$): $\delta = 7.99-7.91$ (m, 4H, ArH, *endo*+*exo*), 7.75–7.47 (m, 6H, ArH, *endo*+*exo*), 5.71 (m, 1H, H2 *endo*), 5.69 (m, 1H, H2 *exo*), 5.19 (t, $J = 2.1$ Hz, 1H, H6 *endo*), 4.98 (m, 1H, H6 *exo*), 4.35 (d, $J = 2.2$ Hz, 1H, H4 *exo*), 3.95 (d, $J = 2.2$ Hz, 1H, H4 *endo*), 3.70 (m, 1H, H5 *endo*), 3.50 (m, 1H, H5 *exo*), 2.73–2.20 (m, 8H, *endo*+*exo*), 2.01 (s, 6H, *endo*+*exo*); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 197.4$, 185.3, 182.6, 171.5, 169.8, 138.6, 138.2, 134.2, 133.9, 129.1, 126.6, 125.5, 74.3, 72.3, 72.0, 68.2, 52.3, 51.8, 33.3, 31.5, 30.1, 24.7, 24.3, 20.9; HRMS (FAB+): calcd for: 321.0796; found: 321.0785 $[M+H]^+$.

**6-Methoxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (9f)**: When method B was used, treatment of **1f** (119 mg, 0.45 mmol) with $[Co_2(CO)_8]$ (184 mg, 0.54 mmol) and $Me_3NO \cdot 2H_2O$ (299 mg, 2.70 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 6:1), *endo*-**9f** (55 mg, 42%, colourless oil) and *exo*-**9f** (37 mg, 28%, colourless oil).

*endo*-**9f** : $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.03-7.95$ (m, 2H, ArH), 7.77–7.52 (m, 3H, ArH), 5.88 (m, 1H, H2), 4.22 (d, $J = 2.9$ Hz, 1H, H6), 3.80 (t, $J = 2.7$ Hz, 1H, H4), 3.55 (m, 1H, H5), 3.25 (s, 3H, OMe), 2.63 (m, 2H, H8), 2.28 (m, 1H, H7), 2.13 (m, 1H, H7); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 198.1$, 186.6, 138.5, 133.9, 129.1, 129.0, 124.8, 77.8, 67.9, 56.4, 53.2, 30.4, 24.3.

*exo*-**9f**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 7.99-7.91$ (m, 2H, ArH), 7.77–7.55 (m, 3H, ArH), 5.90 (m, 1H, H2), 3.92 (d, $J = 2.8$ Hz, 1H, H6), 3.50 (m, 2H, H4, H5), 3.38 (s, 3H, OMe), 2.83 (m, 1H, H8), 2.60 (m, 1H, H8), 2.36 (m, 1H, H7), 2.14 (m, 1H, H7); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 197.0$, 185.1, 138.1, 134.0, 129.3, 128.8, 125.8, 83.0, 72.1, 57.5, 52.7, 31.3, 25.0.

**6-Ethoxymethoxy-2-methyl-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (11b)**: When method B was used, treatment of **3b** (69 mg, 0.21 mmol) with [Co$_2$(CO)$_8$] (81 mg, 0.24 mmol) and Me$_3$NO·2H$_2$O (162 mg, 1.47 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 5:1), *endo*-**11b** (54 mg, 71%, colourless oil) and *exo*-**11b** (3 mg, 5%, colourless oil).

*endo*-**11b**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.00-7.94$ (m, 2H, ArH), 7.75 (m, 3H, ArH), 4.70/4.61 (AB system, $J = 6.9$ Hz, 2H, OC$H_2$O), 4.31 (m, 1H, H6), 4.19 (d, $J = 4.0$ Hz, 1H, H4), 3.52 (m, 3H, H5, OC$H_2$CH$_3$), 2.48 (m, 2H, H8), 2.26 (m, 2H, H7), 1.68 (s, 3H, CH$_3$), 1.24 (t, $J = 7.0$ Hz, 3H, OCH$_2$C$H_3$); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 198.3$, 179.2, 138.7, 133.9, 132.9, 132.7, 129.1, 128.9, 93.7, 74.5, 67.7, 63.6, 50.8, 32.3, 23.2, 15.0.

*exo*-**11b**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.02-7.94$ (m, 2H, ArH), 7.75 (m, 3H, ArH), 4.80/4.66 (AB system, $J = 7.2$ Hz, 2H, OC$H_2$O), 3.86 (d, $J = 3.0$ Hz, 1H, H4), 3.79 (m, 1H, H6), 3.50 (m, 3H, H5, OC$H_2$CH$_3$), 2.70 (m, 1H, H5), 2.55 (m, 1H, H8), 2.33 (m, 1H, H8), 2.26 (m, 1H, H7), 1.55 (s, 3H, CH$_3$), 1.21 (t, $J = 7.0$ Hz, 3H, OCH$_2$C$H_3$); HRMS (FAB+): calcd for: 351.1266; found: 351.1254 [$M$+H]$^+$.

**2-Methyl-4-phenylsulfonyl-6-(triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (11c)**: When method B was used, treatment of **3c** (59 mg, 0.14 mmol) with [Co$_2$(CO)$_8$] (55 mg, 0.16 mmol) and Me$_3$NO·2H$_2$O (108 mg, 0.98 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 10:1), *endo*-**11c** (39 mg, 63%, colourless oil) and *exo*-**11c** (4 mg, 7%, colourless oil).

*endo*-**11c**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 7.98-7.95$ (m, 2H, ArH), 7.69–7.55 (m, 3H, ArH), 4.61 (m, 1H, H6), 4.05 (d, $J = 4.2$ Hz, 1H, H4), 3.50 (m, 1H, H5), 2.50 (m, 2H, H8), 2.21 (m, 2H, H7), 1.69 (s, 3H, CH$_3$), 0.99 (s, 21H, TIPS); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 198.7$, 180.2, 138.8, 133.8, 132.9, 129.2, 128.8, 70.8, 67.8, 52.2, 35.9, 23.1, 17.9, 12.3; MS (70 eV, EI): $m/z$ (%): 405 (100), 265 (2), 255 (2), 191 (3), 125 (8), 91 (4), 77 (9); HRMS (FAB+): calcd for: 449.2181; found: 449.2182 [$M$+H]$^+$.

*exo*-**11c**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 7.99-7.94$ (m, 2H, ArH), 7.67–7.54 (m, 3H, ArH), 4.61 (m, 1H, H6), 4.11 (m, 1H, H4), 3.55 (m, 1H, H5), 2.64 (m, 2H, H8), 2.22 (m, 2H, H7), 1.66 (s, 3H, CH$_3$), 1.01 (s, 21H, TIPS); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 199.0$, 180.2, 138.5, 133.9, 131.9, 129.2, 128.9, 70.9, 67.9, 52.3, 35.7, 23.2, 18.0, 12.3; MS (70 eV, EI): $m/z$ (%): 405 (100), 391 (48), 265 (3), 255 (3), 191 (4), 91 (6), 77 (14); HRMS (FAB+): calcd for: 449.2181; found: 449.2175 [$M$+H]$^+$.

**7,7-Dimethyl-6-hydroxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (13a)**: When method C was used, treatment of **5a** (50 mg, 0.18 mmol) with [Co$_2$(CO)$_8$] (68 mg, 0.20 mmol), Me$_3$NO·2H$_2$O (140 mg, 1.26 mmol) and 4 Å molecular sieves (400 mg) afforded *endo*-**13a** and *exo*-**13a** (33 mg, 60%) as an inseparable *endo*/*exo* mixture (80/20). $^{1}$H NMR (200 MHz, C$_6$D$_6$): $\delta = 8.23$ (m, 2H, ArH), 8.17 (m, 2H, ArH), 7.00 (m, 6H, ArH), 5.56 (m, 1H, H2 *endo*), 5.44 (m, 1H, H2 *exo*), 4.38 (d, $J = 4.5$ Hz, 1H, H6 *endo*), 4.04 (m, 1H, H5 *endo*), 3.66 (m, 1H, H6 *exo*), 3.51 (m, 1H, H4 *endo*), 3.46 (d, $J = 5.0$ Hz, 1H, H5 *exo*), 3.10 (m, 1H, H4 *exo*), 1.75 (m, 4H, H8 *endo*+*exo*), 0.90 (s, 3H, CH$_3$), 0.85 (s, 3H, CH$_3$), 0.71 (s, 3H, CH$_3$), 0.69 (s, 3H, CH$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta = 197.8$, 196.5, 186.6, 182.1, 138.5, 137.6, 134.4, 134.0, 129.5, 129.2, 129.0, 125.8, 125.2, 82.0, 77.1, 73.9, 78.5, 53.0, 52.2, 46.1, 43.5, 41.7, 39.8, 29.6, 28.1, 23.6, 23.3; HRMS (FAB+): calcd for: 307.1004; found: 307.1014 [$M$+H]$^+$.

**7,7-Dimethyl-6-ethoxymethoxy-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (13b)**: When method B was used, treatment of **5b** (67 mg, 0.20 mmol) with [Co$_2$(CO)$_8$] (75 mg, 0.22 mmol) and Me$_3$NO·2H$_2$O (155 mg, 1.40 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 6:1), *endo*-**13b** (34 mg, 47%, colourless oil) and *exo*-**13b** (18 mg, 25%, colourless oil).

*endo*-**13b**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.01-7.95$ (m, 2H, ArH), 7.71–7.55 (m, 3H, ArH), 5.85 (m, 1H, H2), 4.72/4.63 (AB system, $J = 6.6$ Hz, 2H, OC$H_2$O), 4.24 (d, $J = 4.2$ Hz, 1H, H6), 3.93 (m, 1H, H5), 3.71 (d, $J = 4.5$ Hz, 1H, H4), 3.56 (q, $J = 6.9$ Hz, 2H, OC$H_2$CH$_3$), 2.49 (m, 2H, H8), 1.24 (s, 3H, CH$_3$), 1.19 (t, $J = 6.9$ Hz, 3H, OCH$_2$C$H_3$), 1.15 (s, 3H, CH$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 197.7$, 186.2, 138.7, 133.9, 129.2, 125.2, 96.8, 85.4, 69.1, 64.4, 51.7, 46.4, 40.3, 29.4, 24.3, 15.0.

*exo*-**13b**: $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.05-7.99$ (m, 2H, ArH), 7.71–7.57 (m, 3H, ArH), 5.88 (m, 1H, H2), 4.96/4.69 (AB system, $J = 7.6$ Hz, 2H, OC$H_2$O), 3.96 (d, $J = 3.1$ Hz, 1H, H6), 3.79 (m, 1H, H5), 3.68 (m, 1H, OC$H_2$CH$_3$), 3.47 (d, $J = 9.7$ Hz, 1H, H4), 2.67/2.45 (AB system, $J = 18.2$ Hz, 2H, H8), 1.26 (s, 3H, C$H_3$), 1.25 (t, $J = 6.9$ Hz, 3H, OCH$_2$C$H_3$), 1.12 (s, 3H, C$H_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 196.9$, 182.6, 139.2, 134.0, 129.3, 126.2, 94.3, 85.2, 63.6, 51.2, 41.8, 28.8, 24.7, 15.0.

**7,7-Dimethyl-4-phenylsulfonyl-6-(triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (13c)**: When method B was used, treatment of **5c** (48 mg, 0.11 mmol) with [Co$_2$(CO)$_8$] (51 mg, 0.15 mmol) and Me$_3$NO·2H$_2$O (85 mg, 0.77 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 10:1), *endo*-**13c** (15 mg, 25%, colourless oil) and *exo*-**13c** (22 mg, 43%, colourless oil).

*endo*-**13c**: $^{1}$H NMR (200 MHz, CDCl$_3$): $\delta = 8.00-7.94$ (m, 2H, ArH), 7.78–7.54 (m, 3H, ArH), 5.85 (m, 1H, H2), 4.25 (m, 1H, H6), 3.99 (m, 2H, H4, H5), 2.48 (m, 2H, H8), 1.08 (m, 27H, C(CH$_3$)$_2$, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 197.2$, 184.5, 138.1, 134.0, 129.3, 126.0, 82.2, 71.3, 52.9, 44.2, 41.8, 28.7, 24.5, 18.3, 13.5; MS (70 eV, EI): $m/z$ (%): 419 (100), 321 (6), 277 (4), 219 (2), 149 (15), 121, (12), 77 (22), 57 (34).

*exo*-**13c**: $^{1}$H NMR (200 MHz, CDCl$_3$): $\delta = 7.97-7.81$ (m, 2H, ArH), 7.76–7.55 (m, 3H, ArH), 5.89 (m, 1H, H2), 3.86 (m, 1H, H6), 3.67 (d, $J = 7.9$ Hz, 1H, H4), 3.55 (m, 1H, H5), 2.43 (m, 2H, H8), 1.13 (s, 27H, C(CH$_3$)$_2$, TIPS); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 198.1$, 184.5, 138.7, 134.5, 129.2, 128.9, 124.9, 80.0, 68.7, 52.6, 47.1, 40.0, 29.3, 24.8, 18.3, 13.8; HRMS (FAB+): calcd for: 463.2338; found: 463.2328 [$M$+H]$^+$.

**7,7-Dimethyl-6-hydroxy-2-phenyl-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (15a)**: When method C was used, treatment of **7a** (88 mg, 0.25 mmol) with [Co$_2$(CO)$_8$] (92 mg, 0.27 mmol), Me$_3$NO·2H$_2$O (194 mg, 1.75 mmol) and molecular sieves (4 Å, 704 mg) afforded, after chromatographic purification (hexane/ethyl acetate 1:1), *endo*-**15a** and *exo*-**15a** (71 mg, 75%) as an inseparable *endo*/*exo* mixture (76/24). $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.19-7.95$ (m, 4H, ArH, *endo*+*exo*), 7.87–7.21 (m, 6H, ArH, *endo*+*exo*), 4.44 (d, $J = 3.5$ Hz, 1H, H6 *endo*), 4.08 (m, 1H, H6 *exo*), 3.92 (m, 1H, H4 *endo*), 3.91 (m, 1H, H5 *endo*), 3.86 (m, 1H, H4 *endo*), 3.77 (m, 1H, H8 *exo*), 3.59 (m, 1H, H8 *endo*), 3.40 (m, 1H, H5 *exo*), 2.90 (m, 2H, H8 *exo*), 1.70 (m, 2H *endo*), 1.34–1.15 (m, *endo*+*exo*); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 196.3$, 194.9, 180.3, 176.8, 138.5, 136.1, 135.5, 132.0, 134.9, 134.3, 133.9, 130.4, 129.5, 129.0, 128.9, 128.6, 128.4, 128.2, 128.1, 127.2, 81.9, 76.7, 74.4, 68.9, 50.9, 50.1, 46.0, 44.3, 43.4, 41.1, 28.9, 28.0, 23.5, 23.4; HRMS (FAB+): calcd for: 383.1317; found: 383.1305 [$M$+H]$^+$.

**7,7-Dimethyl-6-ethoxymethoxy-2-phenyl-4-(phenylsulfonyl)bicyclo[3.3.0]oct-1-en-3-one (15b)**: When method C was used, treatment of **7b** (30 mg, 0.07 mmol) with [Co$_2$(CO)$_8$] (27 mg, 0.08 mmol), Me$_3$NO·2H$_2$O (54 mg, 0.49 mmol) and molecular sieves (4 Å, 240 mg) afforded, after chromatographic purification (hexane/ethyl acetate 4:1), *endo*-**15b** and *exo*-**15b** (25 mg, 79%) as an inseparable *endo*/*exo* mixture (87:13). $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.09-8.00$ (m, 3H, ArH *endo*+*exo*), 7.77–7.55 (m, 3H, ArH *endo*+*exo*), 7.44–7.16 (m, 5H, ArH *endo*+*exo*), 4.77 (m, 4H, OC$H_2$O *endo*+*exo*), 4.45 (d, $J = 4.1$ Hz, 1H, H6 *endo*), 4.15 (m, 1H, H6 *exo*), 4.05 (m, 1H, H5 *endo*), 3.83 (d, $J = 4.2$ Hz, 1H, H4 *endo*), 3.70 (d, $J = 4.0$ Hz, 1H, H4 *exo*), 3.66 (m, 5H, OC$H_2$CH$_3$ *endo*+*exo*, H5 *exo*), 2.85/2.83 (AB system, $J = 16.0$ Hz, 2H, H8 *endo*), 2.70 (m, 2H, H8 *exo*), 1.35–1.10 (m, 18H, *endo*+*exo*); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta = 196.3$, 195.3, 180.0, 177.1, 138.8, 134.9, 134.0, 130.1, 129.3, 128.9, 128.3, 128.1, 96.8, 95.1, 85.1, 84.5, 70.3, 69.6, 64.5, 63.2, 49.6, 48.0, 46.5, 41.7, 37.5, 29.7, 29.5, 24.4, 15.0; HRMS (FAB+): calcd for: 441.1735; found: 441.1747 [$M$+H]$^+$.

**7,7-Dimethyl-2-phenyl-4-phenylsulfonyl-6-(triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (15c)**: When method C was used, treatment of **7c** (63 mg, 0.12 mmol) with [Co$_2$(CO)$_8$] (46 mg, 0.13 mmol), Me$_3$NO·2H$_2$O (93 mg, 0.84 mmol) and molecular sieves (4 Å, 504 mg) afforded, after chromatographic purification (hexane/ethyl acetate 8:1), *endo*-**15c** and *exo*-**15c** (51 mg, 78%) as an inseparable *endo*/*exo* mixture (94/6). $^{1}$H NMR (300 MHz, CDCl$_3$): $\delta = 8.04-8.00$ (m, 4H, ArH *endo*+*exo*), 7.87–7.55 (m, 6H, ArH *endo*+*exo*), 7.48–7.20 (m, 10H, ArH *endo*+*exo*), 4.36 (d, $J$ = 3.8 Hz, 1H, H6 *endo*), 4.29 (m, 1H, H6 *exo*), 4.19 (d, $J$ = 3.7 Hz, 1H, H4 *endo*), 4.10 (m, 3H, H5 *endo*, H4/H5 *exo*), 2.79/2.84 (AB system, $J$ = 16.9 Hz, 2H, H8 *endo*), 2.31 (m, 2H, H8 *exo*), 1.27–0.99 (m, 58H, $C(CH_3)_2$, TIPS *endo*+*exo*); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 205.9$, 181.1, 140.0, 136.1, 134.0, 131.2, 129.3, 128.9, 128.3, 128.2, 128.1, 79.8, 69.0, 50.6, 47.2, 41.1, 24.9, 22.6, 18.1, 13.8; HRMS (FAB +): calcd for: 539.2651; found: 539.2644 $[M+H]^+$.

**5-Hydroxy-7-(phenylsulfonyl)bicyclo[4.3.0]non-1(9)-en-8-one (19a)**: When method B was used, treatment of **17a** (82 mg, 0.31 mmol) with $[Co_2(CO)_8]$ (138 mg, 0.40 mmol) and $Me_3NO\cdot 2H_2O$ (241 mg, 2.17 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 2:1), *endo*-**19a** (27 mg, 29 %, white solid) and *exo*-**19a** (18 mg, 20 %, white solid). When method C was used, treatment of **17a** (45 mg, 0.17 mmol) with $[Co_2(CO)_8]$ (75 mg, 0.22 mmol), $Me_3NO\cdot 2H_2O$ (131 mg, 1.18 mmol) and molecular sieves (4 Å, 360 mg) afforded, after chromatographic purification (hexane/ethyl acetate 2:1), *endo*-**19a** (14 mg, 28 %) and *exo*-**19a** (10 mg, 20 %).

*endo*-**19a**: M.p. 152–153 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.93$–7.89 (m, 2H, ArH), 7.71–7.52 (m, 3H, ArH), 5.87 (m, 1H, H9), 4.34 (m, 1H, H5), 4.16 (d, $J$ = 3.2 Hz, 1H, H7), 3.43 (m, 1H, H6), 2.80 (m, 1H, H2), 2.32 (m, 1H, H2), 2.00–1.73 (m, 4H, H3, H4); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 196.3$, 179.7, 137.8, 134.1, 129.2, 129.0, 128.2, 68.8, 68.2, 48.3, 31.9, 30.5, 19.6; HRMS (FAB +): calcd for: 293.0848; found: 293.0849 $[M+H]^+$.

*exo*-**19a**: M.p. 161–162 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.97$–7.90 (m, 2H, ArH), 7.75–7.55 (m, 3H, ArH), 5.86 (m, 1H, H9), 3.97 (d, $J$ = 2.7 Hz, 1H, H7), 3.47–3.26 (m, 2H, H5, H6), 2.80 (m, 1H, H2), 2.43–1.30 (m, 5H, H2, H3, H4); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 195.3$, 179.9, 137.2, 134.5, 129.5, 129.1, 127.6, 75.0, 71.9, 51.4, 34.1, 30.0, 23.5; HRMS (FAB +): calcd for: 293.0848; found: 293.0837 $[M+H]^+$.

**5-Ethoxymethoxy-7-(phenylsulfonyl)bicyclo[4.3.0]non-1(9)-en-8-one (19b)**: When method B was used, treatment of **17b** (78 mg, 0.24 mmol) with $[Co_2(CO)_8]$ (107 mg, 0.32 mmol) and $Me_3NO\cdot 2H_2O$ (188 mg, 1.69 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 3:1), *endo*-**19b** (21 mg, 25 %, white solid) and *exo*-**19b** (20 mg, 24 %, white solid).

*endo*-**19b**: M.p. 108–109 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.93$–7.90 (m, 2H, ArH), 7.72–7.53 (m, 3H, ArH), 5.86 (m, 1H, H9), 4.66/4.58 (AB system, $J$ = 7.0 Hz, 2H, $OCH_2O$), 4.16 (m, 1H, H5), 4.09 (d, $J$ = 3.2 Hz, 1H, H7), 3.50 (q, $J$ = 7.0 Hz, 2H, $CH_3CH_2O$), 3.45 (m, 1H, H6), 2.82 (m, 1H, H2), 2.41–1.59 (m, 5H, H2, H3, H4), 1.17 (t, $J$ = 7.0 Hz, 3H, $CH_3CH_2O$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 196.0$, 179.5, 138.1, 134.1, 129.1, 129.0, 127.9, 94.3, 74.6, 68.8, 64.0, 47.8, 30.4, 28.8, 20.0, 15.0; HRMS (FAB +): calcd for: 351.1266; found: 351.1263 $[M+H]^+$.

*exo*-**19b**: M.p. 112–114 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.90$–7.87 (m, 2H, ArH), 7.71–7.51 (m, 3H, ArH), 5.87 (m, 1H, H9), 4.68/4.59 (AB system, $J$ = 7.0 Hz, 2H, $OCH_2O$), 3.87 (m, 1H, H7), 3.71–3.50 (m, 2H, $CH_3CH_2O$), 3.34–3.15 (m, 2H, H5, H6), 2.77 (m, 1H, H2), 2.32–2.03 (m, 3H, H2, H4), 1.66–1.35 (m, 2H, H3), 1.18 (t, $J$ = 7.0 Hz, 3H, $CH_3CH_2O$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 196.1$, 180.5, 138.0, 134.0, 129.3, 128.9, 127.6, 93.5, 80.2, 71.3, 63.7, 50.4, 31.4, 30.3, 24.0, 15.1; HRMS (FAB +): calcd for: 351.1266; found: 351.1273 $[M+H]^+$.

**7-Phenylsulfonyl-5-(triisopropylsiloxy)bicyclo[4.3.0]non-1(9)-en-8-one (19c)**: When method B was used, treatment of **17c** (67 mg, 0.16 mmol) with $[Co_2(CO)_8]$ (71 mg, 0.21 mmol) and $Me_3NO\cdot 2H_2O$ (124 mg, 1.11 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 5:1), *endo*-**19c** (15 mg, 21 %, white solid) and *exo*-**19c** (29 mg, 41 %, white solid).

*endo*-**19c**: M.p. 136–137 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.91$–7.87 (m, 2H, ArH), 7.66–7.52 (m, 3H, ArH), 5.87 (m, 1H, H9), 4.59 (m, 1H, H5), 4.03 (d, $J$ = 2.7 Hz, 1H, H7), 3.48 (m, 1H, H6), 2.82 (m, 1H, H2), 2.33 (m, 1H, H2), 2.09–1.55 (m, 4H, H3, H4), 1.01 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 196.2$, 180.4, 138.1, 134.1, 129.2, 129.0, 127.9, 70.1, 69.0, 49.2, 32.3, 30.6, 19.9, 18.1, 12.7; HRMS (FAB +): calcd for: 449.2182; found: 449.2184 $[M+H]^+$.

*exo*-**19c**: M.p. 151–153 °C; $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.88$–7.72 (m, 2H, ArH), 7.71–7.51 (m, 3H, ArH), 5.84 (m, 1H, H9), 3.92 (m, 1H, H7), 3.48–3.35 (m, 2H, H5, H6), 2.74 (m, 1H, H2), 2.36–1.20 (m, 5H, H2, H3, H4), 1.08 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 197.2$, 181.5, 138.0, 134.2, 129.6, 129.1, 127.4, 77.7, 71.4, 52.8, 35.6, 30.6, 24.6, 18.4, 13.1; elemental analysis calcd (%) for $C_{24}H_{36}O_4SSi$ (420.7): C 64.24, H 8.09, S 7.15; found: C 64.06, H 7.92, S 7.15.

**5-Hydroxy-7-phenylsulfonyl-3-oxabicyclo[4.3.0]non-1(9)-en-8-one (20a)**: When method C was used, treatment of **18a** (80 mg, 0.30 mmol) with $[Co_2(CO)_8]$ (133 mg, 0.39 mmol), $Me_3NO\cdot 2H_2O$ (234 mg, 2.10 mmol) and molecular sieves (4 Å, 640 mg) afforded, after chromatographic purification (hexane/ethyl acetate 1:1), *endo*-**20a** (10 mg, 11 %, colourless oil) and *exo*-**20a** (3 mg, 3 %, colourless oil).

*endo*-**20a**: $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.97$–7.93 (m, 2H, ArH), 7.71–7.56 (m, 3H, ArH), 6.03 (m, 1H, H9), 4.68 (d, $J$ = 13.4 Hz, 1H, H2), 4.31 (m, 1H, H5), 4.23 (d, $J$ = 3.8 Hz, 1H, H7), 4.20–4.04 (m, 2H, H2, H4), 3.83 (d, $J$ = 11.8 Hz, 1H, H4), 3.71 (m, 1H, H6); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 195.4$, 169.9, 137.8, 134.4, 129.2, 129.1, 128.8, 71.3, 68.0, 67.9, 67.0, 46.3.

*exo*-**20a**: $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 8.00$–7.96 (m, 2H, ArH), 7.74–7.59 (m, 3H, ArH), 5.97 (m, 1H, H9), 4.64 (d, $J$ = 14.0 Hz, 1H, H2), 4.20 (m, 1H, H4), 4.15 (d, $J$ = 14.5 Hz, 1H, H2), 3.99 (d, $J$ = 3.8 Hz, 1H, H7), 3.69 (m, 1H, H5), 3.48 (m, 1H, H6), 3.40 (dd, $J$ = 10.2, 11.3 Hz, 1H, H4); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 194.2$, 171.1, 136.8, 134.8, 129.6, 129.3, 127.4, 72.4, 71.7, 71.4, 66.1, 49.2.

**5-Ethoxymethoxy-7-phenylsulfonyl-3-oxabicyclo[4.3.0]non-1(9)-en-8-one (20b)**: When method C was used, treatment of **18b** (33 mg, 0.10 mmol) with $[Co_2(CO)_8]$ (45 mg, 0.13 mmol), $Me_3NO\cdot 2H_2O$ (79 mg, 0.71 mmol) and molecular sieves (4 Å, 264 mg) afforded, after chromatographic purification (hexane/ethyl acetate 4:1), *endo*-**20b** (12 mg, 33 %, colourless oil) and *exo*-**20b** (6 mg, 17 %, colourless oil).

*endo*-**20b**: $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta = 7.95$–7.92 (m, 2H, ArH), 7.70–7.57 (m, 3H, ArH), 5.96 (s, 1H, H9), 4.77/4.69 (AB system, $J$ = 7.0 Hz, 2H, $OCH_2O$), 4.69 (d, $J$ = 14.1 Hz, 1H, H2), 4.28 (d, $J$ = 13.7 Hz, 1H, H2), 4.24 (d, $J$ = 3.6 Hz, 1H, H7), 4.20 (dd, $J$ = 2.2, 12.9 Hz, 1H, H4), 4.06 (m, 1H, H5), 3.71 (m, 2H, H4, H6), 3.62–3.51 (m, 2H, $OCH_2CH_3$), 1.18 (t, $J$ = 7.0 Hz, 3H, $OCH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 195.2$, 170.9, 137.9, 134.3, 129.2, 129.1, 127.8, 94.6, 73.5, 68.5, 67.8, 66.5, 64.0, 45.1, 14.9.

*exo*-**20b**: $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta = 7.91$–7.88 (m, 2H, ArH), 7.70–7.56 (m, 3H, ArH), 6.00 (s, 1H, H9), 4.65/4.62 (AB system, $J$ = 7.3 Hz, 2H, $OCH_2O$), 4.58 (d, $J$ = 12.9 Hz, 1H, H2), 4.17 (m, 1H, H4), 4.10 (d, $J$ = 13.3 Hz, 1H, H2), 3.91 (d, $J$ = 1.6 Hz, 1H, H7), 3.68–3.41 (m, 5H, H4, H5, H6, $OCH_2CH_3$), 1.20 (t, $J$ = 7.0 Hz, 3H, $OCH_2CH_3$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 195.5$, 171.9, 137.6, 134.3, 129.3, 129.0, 128.2, 94.7, 78.1, 70.9, 70.2, 66.1, 63.9, 48.4, 15.0.

**7-Phenylsulfonyl-5-triisopropylsiloxy-3-oxabicyclo[4.3.0]non-1(9)-en-8-one (20c)**: When method B was used, treatment of **18c** (50 mg, 0.12 mmol) with $[Co_2(CO)_8]$ (53 mg, 0.15 mmol) and $Me_3NO\cdot 2H_2O$ (92 mg, 0.83 mmol) afforded, after chromatographic purification (hexane/ethyl acetate 6:1), *endo*-**20c** and *exo*-**20c** (27 mg, 50 %, white solid) as an inseparable *endo*/*exo* mixture (58/42). $^{1}$H NMR (200 MHz, $CDCl_3$): $\delta = 7.91$–7.82 (m, 4H, ArH, *endo*+*exo*), 7.71–7.54 (m, 6H, ArH, *endo*+*exo*), 5.94 (m, 2H, H9 *endo*, H9 *exo*), 4.65 (d, $J$ = 13.7 Hz, 1H, H2 *endo*), 4.53 (d, $J$ = 12.9 Hz, 1H, H2 *exo*), 4.40 (m, 1H, H5 *endo*), 4.26 (d, $J$ = 14.1 Hz, 1H, H2 *endo*), 4.16 (d, $J$ = 3.2 Hz, 1H, H7 *endo*), 4.09 (d, $J$ = 10.1 Hz, 1H, H2 *exo*), 4.07 (dd, $J$ = 4.0, 11.3 Hz, 1H, H4 *exo*), 4.01 (dd, $J$ = 2.2, 12.9 Hz, 1H, H4 *endo*), 3.90 (d, $J$ = 1.6 Hz, 1H, H7 *exo*), 3.75 (d, $J$ = 11.7 Hz, 1H, H4 *endo*), 3.69–3.61 (m, 2H, H6 *endo*, H5 *exo*), 3.55 (m, 1H, H6 *exo*), 3.43 (dd, $J$ = 9.3, 11.2 Hz, 1H, H4 *exo*), 1.08 (s, 21H, TIPS *endo*), 1.00 (s, 21H, TIPS *exo*); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 196.3$, 195.6, 172.5, 172.1, 138.0, 137.5, 134.2, 129.4, 129.2, 129.1, 129.0, 128.0, 127.6, 74.2, 72.5, 71.0, 70.7, 69.3, 68.0, 66.4, 66.1, 50.8, 46.8, 18.0, 17.9, 12.7, 12.6; HRMS (FAB +):calcd for: 451.1974; found: 451.1984 $[M+H]^+$.

### Reductive desulfonylation

***endo*-6-(Ethoxymethoxy)bicyclo[3.3.0]oct-1-en-3-one (*endo*-10b)**: Saturated aqueous $NH_4Cl$ (7 mL) and a solution of *endo*-**9b** (37 mg, 0.11 mmol) in THF (3 mL) were sequentially added to a vigorously stirred suspension of powdered activated Zn (442 mg) in THF (7 mL). The resulting mixture was stirred at RT for 1 h. The reaction mixture was filtered through Celite and washed with $CH_2Cl_2$. The combined solvents were evaporated, and the residue was purified by flash chromatography (hexane/ethyl acetate 5:1) to afford *endo*-**10b** (20 mg, 94 %, colourless oil). $^{1}$H NMR (300 MHz, $CDCl_3$): $\delta = 5.93$ (m, 1H, H2), 4.76/4.59 (AB system, $J$ = 7.1 Hz, 2H, $OCH_2O$), 4.23 (m, 1H, H6), 3.53 (m, 2H, $CH_3CH_2O$), 3.03 (m, 1H, H5), 2.65 (m, 2H, H4), 2.44 (m, 2H, H8), 2.22 (m, 2H, H7), 1.19 (t, $J$ = 7.1 Hz, 3H, $CH_3CH_2O$); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta = 211.3$, 188.6, 125.5, 93.4, 74.8, 63.4, 60.3, 51.5, 36.5, 32.7, 24.3, 15.0; HRMS (FAB +): calcd for: 197.1177; found: 197.1174 $[M+\mathrm{H}]^+$.

When (4*R*,5*R*,6*S*)-**9b** was used (instead of the racemic), (5*R*,6*S*)-**10b** was obtained. $[\alpha]_\mathrm{D} = +90.2$ ($c = 0.2$, $\mathrm{CHCl_3}$); *ee* = 98.5% (HPLC, Daicel Chiralcel OD column, hexane/isopropanol 97:3, $0.5\,\mathrm{mL\,min^{-1}}$, $t_\mathrm{R} = 20.8$ and 25.8 min).

***endo*-6-(Triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (*endo*-10c)**: Through the same procedure, treatment of *endo*-**9c** (91 mg, 0.21 mmol) with activated Zn (844 mg) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), *endo*-**10c** (57 mg, 93%, colourless oil). $^1$H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.92$ (m, 1H, H2), 4.42 (t, $J = 3.5$ Hz, 1H, H6), 2.95 (m, 1H, H5), 2.66–2.10 (m, 6H, H4, H7, H8), 1.01 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 212.1$, 189.5, 125.4, 71.1, 53.2, 36.9, 36.5, 24.4, 18.0, 12.3; HRMS (FAB +): calcd for: 295.2093; found: 295.2093 $[M+\mathrm{H}]^+$.

***endo*-7,7-Dimethyl-6-(ethoxymethoxy)bicyclo[3.3.0]oct-1-en-3-one (*endo*-14b)**: Through the same procedure, treatment of *endo*-**13b** (53 mg, 0.14 mmol) with activated Zn (570 mg) afforded, after chromatographic purification (hexane/ethyl acetate 5:1), *endo*-**14b** (29 mg, 89%, colourless). $^1$H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.87$ (m, 1H, H2), 4.66 (m, 2H, $\mathrm{OC}H_2\mathrm{O}$), 3.66 (d, $J = 4.8$ Hz, 1H, H6), 3.60 (m, 2H, $\mathrm{OC}H_2\mathrm{CH_3}$), 3.41 (m, 1H, H5), 2.42 (m, 4H, H4, H8), 1.18 (m, 9H, $\mathrm{C(CH_3)_2}$, $\mathrm{OCH_2C}H_3$); $^{13}$C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 210.9$, 188.4, 125.6, 96.0, 84.0, 64.1, 50.0, 46.2, 40.4, 37.3, 29.6, 24.4, 14.9; HRMS (FAB +): calcd for: 225.1488; found: 225.1490 $[M+\mathrm{H}]^+$.

***endo*-7,7-Dimethyl-6-(triisopropylsiloxy)bicyclo[3.3.0]oct-1-en-3-one (*endo*-14c)**: Through the same procedure, treatment of *endo*-**13c** (47 mg, 0.10 mmol) with activated Zn (408 mg) afforded, after chromatographic purification (hexane/ethyl acetate 9:1), *endo*-**14c** (30 mg, 91%). $^1$H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.85$ (m, 1H, H2), 4.04 (d, $J = 4.8$ Hz, 1H, H6), 3.36 (m, 1H, H5), 2.42 (m, 4H, H4, H8), 1.18 (s, 3H, $\mathrm{CH_3}$), 1.15 (s, 3H, $\mathrm{CH_3}$), 1.05 (s, 21H, TIPS); $^{13}$C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 211.1$, 189.4, 125.1, 80.3, 51.4, 47.0, 40.6, 37.9, 29.4, 24.7, 18.2, 13.5; HRMS (FAB +): calcd for: 323.2406; found: 323.2408 $[M+\mathrm{H}]^+$.

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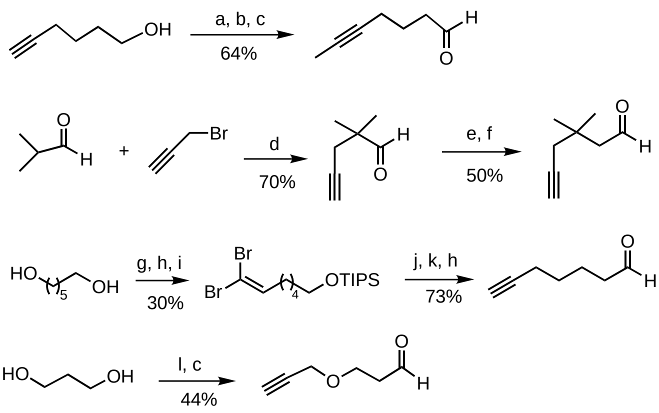
[15] The non-commercially available aldehydes 5-heptynal, 2,2-dimethyl-4-pentynal, 3,3-dimethyl-5-hexynal, 6-heptynal and 3-(2-propyniloxy)-propanal were prepared by straightforward methods as indicated in Scheme 10:



Scheme 10. a) TMSCl, imidazole, $CH_2Cl_2$, RT; b) 1) *n*BuLi, THF, −78°C, 2) MeI; c) PCC, Celite, $CH_2Cl_2$, RT; d) NaOH/$H_2O$, *n*$Bu_4N^+I^-$, $CH_2Cl_2$, DMSO, RT; e) $Ph_3P{=}CHOMe$, $Et_2O$, 0°C; f) HCl, THF, RT; g) NaH, TIPSCl, THF, RT; h) $(COCl)_2$, DMSO, $CH_2Cl_2$, −78°C; $Et_3N$, RT; i) $PPh_3$, $CBr_4$, $CH_2Cl_2$, RT; j) *n*BuLi, THF, 0°C; k) 5 M HCl, MeOH, RT; l) NaOH, propargyl bromide, RT.

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