

Vinyl Sulfoxides as Stereochemical Controllers in Intermolecular Pauson–Khand Reactions: Applications to the Enantioselective Synthesis of Natural Cyclopentanoids

Marta Rodríguez Rivero, Inés Alonso, and Juan C. Carretero*^[a]

Abstract: The use of sulfoxides as chiral auxiliaries in asymmetric intermolecular Pauson–Khand reactions is described. After screening a wide variety of substituents on the sulfur atom in α,β -unsaturated sulfoxides, the readily available *o*-(*N,N*-dimethylamino)-phenyl vinyl sulfoxide (**1i**) has proved to be highly reactive with substituted terminal alkynes under *N*-oxide-promoted conditions (CH_3CN , 0°C). In addition, these Pauson–Khand reactions occurred with complete regioselectivity and very high diastereoselectivity ($de = 86\text{--}>96\%$, (*S,R_S*) diastereomer). Experimental studies suggest that the high reactivity exhibited by the vinyl

sulfoxide **1i** relies on the ability of the amine group to act as a soft ligand on the alkyne dicobalt complex prior to the generation of the cobaltacycle intermediate. On the other hand, both theoretical and experimental studies show that the high stereoselectivity of the process is due to the easy thermodynamic epimerization at the C^5 center in the resulting 5-sulfinyl-2-cyclopentenone adducts. When it is taken into ac-

Keywords: asymmetric synthesis • cyclopentenones • natural products • Pauson–Khand reactions • vinyl sulfoxides

count that the known asymmetric intermolecular Pauson–Khand reactions are limited to the use of highly reactive bicyclic alkenes, mainly norbornene and norbornadiene, this novel procedure constitutes the first asymmetric version with unstrained acyclic alkenes. As a demonstration of the synthetic interest of this sulfoxide-based methodology in the enantioselective preparation of stereochemically complex cyclopentanoids, we have developed very short and efficient syntheses of the antibiotic (–)-pentenomycin I and the (–)-aminocyclopentitol moiety of a hopane triterpenoid.

Introduction

Over the last two decades, transition-metal-mediated reactions have acquired a prominent and ever-increasing role in improving organic synthesis efficiency.^[1] One such emblematic reaction is the cobalt-mediated formal [2+2+1] cycloaddition of an alkyne, an alkene, and CO, known as the Pauson–Khand (PK) reaction, which involves the formation of three C–C bonds in a single step. Due to this inherent synthetic efficiency, it is hardly surprising that the PK reaction has become one of the most powerful tools in current cyclopentenone synthesis.^[2] Since the first PK reactions

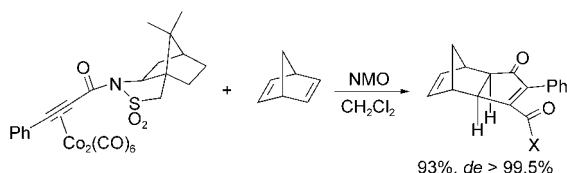
were described in the early 1970s as involving heating stoichiometric amounts of dicobaltoctacarbonyl, alkyne, and alkene,^[3] huge progress has been made. Among the key advances in this reaction, those worthy of notice are the discovery of efficient promoters that allow the process to be performed under mild conditions (for instance, tertiary amine *N*-oxides,^[4] secondary amines,^[5] thioethers,^[6] silica gel,^[7] and molecular sieves^[8]), the development of catalytic cobalt procedures,^[9] the extension of the reaction to other metal mediators, such as rhodium,^[10] ruthenium,^[11] titanium^[12] and iridium,^[13] the application of the reaction to the synthesis of complex natural products,^[2,14] the deep theoretical study of the mechanistic aspects of the reaction,^[15] and the development of highly efficient diastereoselective and asymmetric versions of PK reactions.^[16]

Despite this impressive progress, however, some important limitations still remain. One is that these improvements deal mainly with the intramolecular version of the PK reaction, essentially the cyclization of 1,6- and 1,7-enynes to provide bicyclic [3.3.0]- and [4.3.0]-fused cyclopentenones, while the thermodynamically less favorable intermolecular process has been left out of most of these advances. If we focus on the asymmetric version of the PK reaction,^[2,16] as far as we

[a] M. Rodríguez Rivero, I. Alonso, Prof. J. C. Carretero
Departamento de Química Orgánica
Facultad de Ciencias
Universidad Autónoma de Madrid, 28049 Madrid (Spain)
Fax: (+34) 914-973-966
E-mail: juancarlos.carretero@uam.es

Supporting information for this article (containing experimental procedures and characterization data of all starting vinyl sulfoxides, NMR spectra (PDF) and Cartesian coordinates of all optimized structures described in the article) is available on the WWW under <http://www.chemeurj.org/> or from the author.

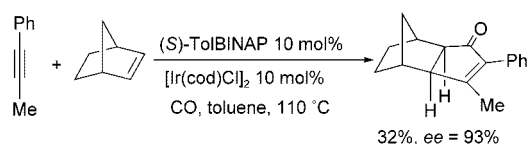
are aware, all the reported studies on intermolecular processes are limited to the use of a few highly reactive strained bicyclic alkenes, specifically norbornene, norbornadiene, and bicyclo[3.2.0]hept-6-ene. This important drawback can be easily understood by considering the low reactivity and regioselectivity usually displayed by simple unstrained alkenes. For instance, the reaction of 1-octene with the dicobalthexacarbonyl complex of phenylacetylene in refluxing toluene gives a 1:1 mixture of the 2,4- and 2,5-disubstituted cyclopentenone PK adducts in a poor yield of 18%.^[17] Among the most remarkable results described up to now in asymmetric intermolecular PK reactions are the studies of Pericàs and co-workers with either a chiral auxiliary bonded to the alkyne^[18] (for example, the Oppolzer's sultam^[18a] in Scheme 1) or a chiral ligand on the cobalt,^[19] and with norbornadiene or norbornene as the reactive alkene. By also using norbornene, Shibata et al. have recently reported the first example of a catalytic asymmetric intermolecular PK



Scheme 1. Relevant example of an asymmetric intermolecular PK reaction with a chiral auxiliary bonded to the alkyne, reported by Pericàs et al.

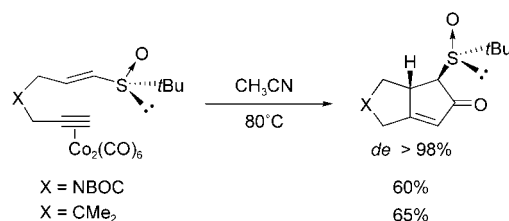
Abstract in Spanish: Se ha estudiado la utilización de sulfóxidos como auxiliares quirales en reacciones de Pauson–Khand intermoleculares. Tras considerar una amplia variedad de vinil sulfóxidos diferentemente sustituidos en el átomo de azufre, se ha encontrado que el α -(*N,N*-dimetilamino)fenil sulfóxido (**1i**) presenta una elevada reactividad frente a alquinos terminales en reacciones de Pauson–Khand. Además, estas reacciones transcurren con regioselectividades completas y diastereoselectividades muy elevadas ($ed=86$ – $>96\%$). Estudios teóricos y experimentales sugieren que la gran reactividad mostrada por el vinil sulfóxido **1i** se debe a la capacidad del grupo amino para coordinarse al complejo de dicobalto del alquino, favoreciendo así la posterior formación del cobaltaciclo intermedio. Por otro lado, estudios tanto teóricos como experimentales han demostrado que la elevada diastereoselectividad del proceso es consecuencia de la fácil epimerización termodinámica en la posición C-5 de las 5-sulfinil-2-ciclopentenonas finales. Teniendo en cuenta que hasta el momento la reacción de Pauson–Khand intermolecular estaba limitada al empleo de alquenos bíclicos muy reactivos, principalmente norborneno y norbornadieno, este nuevo procedimiento constituye la primera versión asimétrica con alquenos acíclicos no tensionados. Como demostración de la utilidad sintética de esta nueva metodología en la preparación enantioselectiva de sistemas ciclopentánicos complejos, se han desarrollado síntesis muy eficaces del antibiótico (–)-pentenomicina I y de la unidad de aminociclopentitol de un triperpenoide.

reaction, with an iridium-promoted procedure applied in this case^[13a] (Scheme 2).

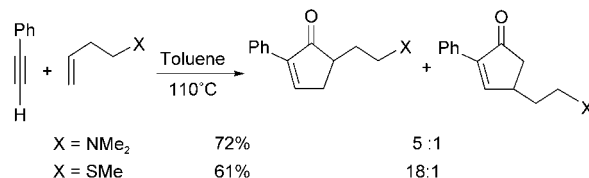


Scheme 2. Catalytic iridium-promoted asymmetric intermolecular PK reactions reported by Shibata et al.

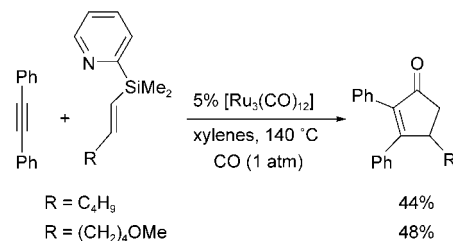
Therefore, paradoxically, the direct enantioselective synthesis of a simple chiral nonfused cyclopentenone remains a challenging target in this field. Taking into account our previous work on the behavior of the *tert*-butylsulfinyl group as an efficient chiral auxiliary in intramolecular PK reactions of 1,6-enynes (Scheme 3),^[20] and keeping in mind the results described first by Krafft et al. (Scheme 4)^[21] and more recently by Yoshida and co-workers (Scheme 5)^[11c] regarding



Scheme 3. The *tert*-butylsulfinyl group as an efficient chiral auxiliary in intramolecular PK reactions of 1,6-enynes. BOC = *tert*-butoxycarbonyl.



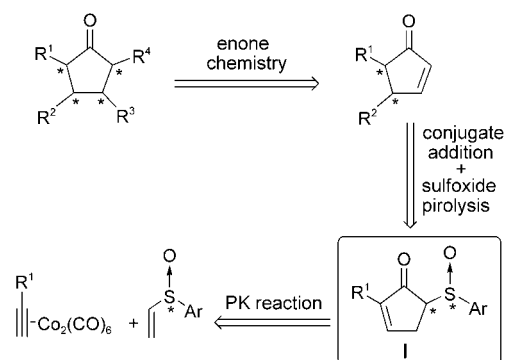
Scheme 4. Relevant examples of regioselective intermolecular PK reactions reported by Krafft et al.^[21]



Scheme 5. Relevant examples of regioselective intermolecular PK reactions reported by Yoshida et al.^[11c]

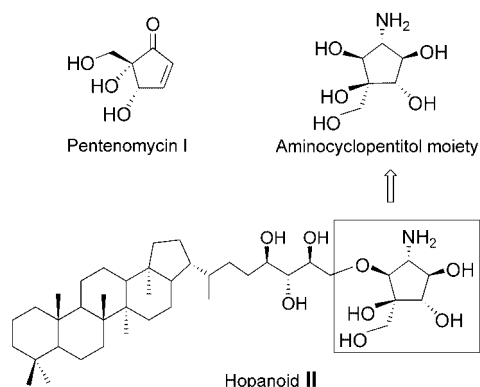
the use of achiral alkenes with nitrogen- or sulfur-tethered substituents as controlling metal-chelating groups in regioselective intermolecular PK reactions, we envisaged that a possible alternative to the asymmetric synthesis of substituted nonfused cyclopentenones could rely on the use of ap-

appropriately substituted vinyl sulfoxides as unstrained chiral alkene partners. Particularly, we thought that by using a suitable potentially cobalt-coordinating group tethered to the sulfoxide, thereby giving a pseudointramolecular character to the reaction, the sulfinyl chiral auxiliary group could simultaneously improve the reactivity and control the regioselectivity and stereoselectivity of the process. In addition, as illustrated in Scheme 6, the chemical versatility offered by



Scheme 6. Proposed enantioselective synthesis of substituted cyclopentanoids based on the intermolecular asymmetric PK reaction of vinyl sulfoxides.

the enone moiety and the sulfinyl group in the expected 5-sulfinyl-2-cyclopentenone product (**I**) turns this type of PK adduct into a very appealing synthetic intermediate for asymmetric synthesis, especially for the enantioselective synthesis of stereochemically complex cyclopentanoids. Herein, we describe in detail the scope and limitations of sulfoxides as stereochemical controllers in intermolecular PK reactions^[22] and the application of this new methodology to the efficient enantioselective synthesis of two natural cyclopentanols: the antibiotic (–)-pentenomycin I and the (–)-aminocyclopentitol moiety of the hopanoid of *Zymomonas mobilis* (**II**, Scheme 7).

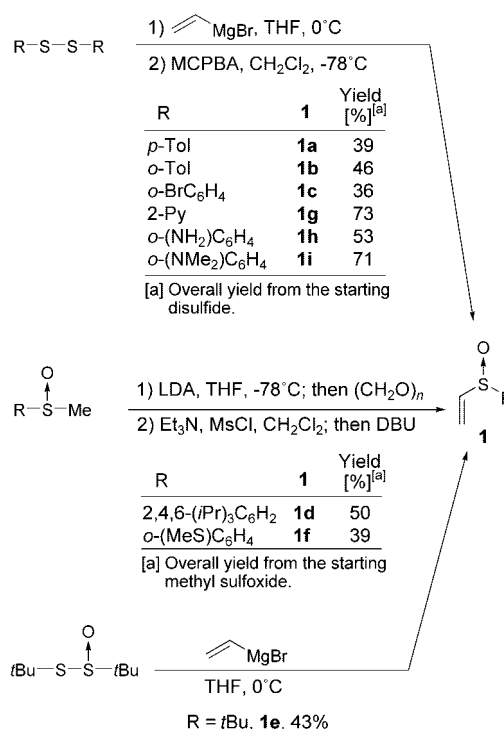


Scheme 7. Structure of the natural product pentenomycin I and the aminocyclopentitol moiety of the hopanoid of *Zymomonas mobilis*.

Results and Discussion

Synthesis of the racemic sulfoxides: First, to check the viability of vinyl sulfoxides as alkenes in intermolecular PK reactions, a variety of substrates with different steric and elec-

tronic environments around the sulfur atom were synthesized. The racemic sulfoxides **1a–i** were readily prepared by one of the following straightforward methods (Scheme 8):



Scheme 8. Synthesis of compounds of type **1**. THF = tetrahydrofuran, MCPBA = meta-chloroperoxybenzoic acid, Tol = tolyl, Py = pyridyl, LDA = lithium diisopropylamide, Ms = mesyl = methane sulfonyl, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

a) reaction of vinyl magnesium bromide with the corresponding disulfide and further MCPBA oxidation; b) condensation of the starting methyl sulfoxide with formaldehyde, followed by mesylation (Et₃N/MsCl) and basic elimination with DBU; or c) direct sulfinylation of vinyl magnesium bromide with *tert*-butylthiosulfinate (for the synthesis of the *tert*-butylsulfoxide **1e**).

PK reaction of vinyl sulfoxides **1a–i with the dicobalthexacarbonyl complex of 1-hexyne:** In the pioneering study of Khand and Pauson on the thermal reaction of alkyne dicobalt complexes with electron-deficient alkenes,^[23] such as ethyl acrylate or acrylonitrile, it was reported that this type of alkenes afforded the 1,3-diene product, instead of the expected cyclopentenone PK adduct, as a result of a competitive fast β-H elimination step after formation of the key cobaltacycle intermediate. These early results are most likely the origin of the extensive belief of the unsuitability of electron-deficient olefins in PK reactions. In contrast to this general assumption, Cazes and co-workers reported in 1999 that certain sterically uncongested electron-poor alkenes, such as methyl acrylate and phenyl vinyl sulfone, gave good yields

of PK adducts when the reactions were carried out in the presence of NMO as the promoter.^[24] Our recent work on 1-sulfinyl-1,6-enynes^[20] and 1-sulfonyl-1,6-enynes^[25] in intramolecular PK reactions proved that, under appropriate experimental conditions, both α,β -unsaturated sulfoxides and α,β -unsaturated sulfones can be excellent substrates in this kind of process.^[26]

Taking into account all these precedents, we first explored the thermal reaction of vinyl sulfoxides **1** with the cobalt complex of 1-hexyne. However, regardless of the substrate (**1a** or **1i**) and solvent used (toluene or acetonitrile at 80°C), we obtained a complex mixture of products in which neither the PK cyclopentenone nor the 1,3-diene could be detected. A similar result was also observed when the reaction was carried out in the presence of cyclohexylamine as the promoter^[5] in toluene at 90°C. As these disappointing results could be due, at least partially, to the low thermal stability of the sulfinyl group, we turned to PK reactions promoted by amine N-oxides, which usually involve the use of very mild reaction conditions (usually 0°C or room temperature). However, under the conditions reported by Cazes and co-workers (excess of NMO, CH₂Cl₂/THF, RT),^[24,27] a sluggish reaction was observed, with the slow metal decomplexation of the alkyne dicobalt complex and recovery of the starting vinyl sulfoxide being the main result. To our delight a much faster reaction occurred when acetonitrile was used as the solvent. The reaction of **1a** with the dicobalt complex of 1-hexyne under these conditions (6 equivalents of NMO·H₂O,^[28] acetonitrile, RT) was completed within 2 h and occurred with complete chemoselectivity (the possible competitive formation of the 1,3-diene product was not detected) and regioselectivity (only the 2,5-disubstituted cyclopentenone was formed). After filtration of the cobalt byproducts and standard silica gel purification, the cyclopentenone **2a** was isolated in 68% yield as a 74:26 mixture of diastereomers.

The most relevant results obtained by using the set of vinyl sulfoxides **1** in the PK reactions with 1-hexyne, under these optimized experimental conditions, are shown in Table 1.

In contrast to the very high alkyne regioselectivity but low alkene regioselectivity usually described in the PK reactions of monosubstituted unfunctionalized alkenes with terminal alkynes,^[17,29] in the case of vinyl sulfoxides **1** all of the reactions were completely regioselective with regard to both alkyne and alkene components, thereby affording exclusively the 2,5-disubstituted cyclopentenones. The same type of PK regioisomer has been previously reported from ethyl acrylate, acrylonitrile, and phenyl vinyl sulfone,^[24] a fact sug-

Table 1. N-Oxide-promoted intermolecular PK reactions of 1-hexyne dicobalt complex with racemic vinyl sulfoxides **1**.

Entry ^[a]	R	1	<i>t</i> [h]	Conversion	2	A:B ratio ^[b]	Yield [%] ^[c]
1	<i>p</i> -Tol	1a	2	> 99	2a	74:26	68
2 ^[d]	<i>o</i> -Tol	1b	24	70	2b	90:10	28
3 ^[d]	<i>o</i> -BrC ₆ H ₄	1c	24	73	2c	86:14	30
4 ^[d]	2,4,6-(<i>i</i> Pr) ₃ C ₆ H ₂	1d	24	60	2d	94:6	24
5 ^[d]	<i>t</i> Bu	1e	24	65	2e	> 98:< 2	20
6 ^[d]	<i>o</i> -MeSC ₆ H ₄	1f	24	< 1	2f	–	–
7	<i>o</i> -Py	1g	1	> 99	2g	73:27	19
8 ^[d]	<i>o</i> -(H ₂ N)C ₆ H ₄	1h	24	> 99	2h	–	–
9	<i>o</i> -(Me ₂ N)C ₆ H ₄	1i	1	> 99	2i	92:8	63
10 ^[e]	<i>o</i> -(Me ₂ N)C ₆ H ₄	1i	4	> 99	2i	93:7	74

[a] Reaction conditions: cobalt complex (1.5 equiv), alkene **1** (1.0 equiv), NMO·H₂O (6.0 equiv), CH₃CN, RT.

[b] Determined by ¹H NMR spectroscopy on the crude mixtures after filtration of the cobalt byproducts.

[c] Pure adducts after chromatography. [d] 3 equivalents of dicobalt complex were used. [e] Reaction run at 0°C.

gesting that this 2,5-regioselectivity is a general trend for electron-deficient alkenes.^[30]

Interestingly, both the reactivity and the stereoselectivity proved to be highly dependent on the substitution at the sulfur center. In the series of noncoordinating sulfoxides (**1a–e**) a correlation between the steric bulk of the sulfoxide and the reactivity was observed. Thus, in contrast to the relatively high reactivity of the *p*-tolyl sulfoxide **1a** (entry 1), whose PK reaction was completed in less than 2 h, the *ortho*-substituted sulfoxides **1b** and **1c** (entries 2 and 3) and, particularly, the very bulky triisopropylphenylsulfoxide **1d** (entry 4) and *tert*-butylsulfoxide **1e** (entry 5), gave incomplete conversions after 24 h, even in the presence of a large excess of the cobalt complex (3-fold excess). Consequently, from these hindered substrates, the corresponding cyclopentenones were isolated in poor yields (20–30%). With regard to the stereoselectivity of the reaction, a qualitative correlation with the bulkiness of the sulfoxide may also be deduced from the data of Table 1: the greater the steric bulk of the sulfoxide, the higher the stereoselectivity, with complete stereocontrol reached in the case of the *tert*-butylsulfoxide **1e** (A:B ratio: > 98:< 2, entry 5).

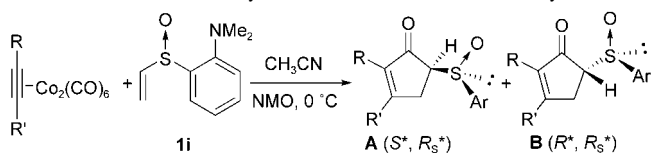
A much more varied outcome was observed in the case of the potentially cobalt-coordinating sulfoxides **1f–i**. Thus, unexpectedly, the methyl thioether **1f** did not react at all^[31] (entry 6), whereas the *ortho*-aminophenyl derivative **1h** (entry 8) evolved completely but with formation of a complex mixture of products.^[32] In the case of the pyridinyl sulfoxide **1g** (entry 7), the PK adduct **2g** could be isolated after purification, albeit in only 19% yield. This poor yield is in contrast with the good results described by Yoshida and co-workers in intermolecular ruthenium-catalyzed PK reactions of α,β -unsaturated pyridinylsilanes.^[11c] In our series of vinyl sulfoxides, the most synthetically interesting result was, by far, the one obtained from the *ortho*-dimethylaminophenyl sulfoxide **1i**, which was the most reactive alkene and afforded the PK adduct **2i** with high diastereoselectivity (entry 9).

This unstrained alkene is reactive enough to perform the reaction at 0 °C, thereby giving rise to the cyclopentenone **2i** in 74 % yield as a 93:7 mixture of diastereomers (entry 10).

At this point it is important to mention that in our previously reported studies on asymmetric Heck reactions with sulfoxides as stereochemical controllers, the *o*-dimethylaminophenylsulfinyl group also provided the best results in terms of reactivity and stereoselectivity,^[33] a result suggesting the broad applicability of this sulfoxide-based chiral auxiliary in transition-metal-mediated reactions.

Scope of the reaction: Having found a highly reactive and stereoselective vinyl sulfoxide for the model PK reaction, we next explored the structural scope of this process with regard to the substitution at the alkyne. The results obtained in the PK reactions of the optimal vinyl sulfoxide **1i** with a variety of alkyne dicobalt complexes under the optimized N-oxide-promoted conditions (NMO·H₂O, CH₃CN, 0 °C) are summarized in Table 2.

Table 2. PK reaction of vinyl sulfoxide **1i** with substituted alkynes.



Entry ^[a]	R	R'	t [h]	Adduct	A:B ratio ^[b]	Yield [%] ^[c]
1	<i>n</i> Bu	H	4	2i	93:7	74
2 ^{[d][e]}	<i>t</i> Bu	H	26	3	>98:<2	55
3 ^[d]	Bn	H	14	4	93:7	58
4	<i>p</i> -Tol	H	12	5	93:7	49
5 ^[e]	TMS	H	16	6	>98:<2	59
6	CH ₂ OTIPS	H	2	7	93:7	62
7	CH ₂ CH ₂ OTIPS	H	7	8	>98:<2	66
8	CH ₂ CH ₂ CH ₂ Br	H	6	9	>98:<2	68
9	Me	Me	24	10	—	—
10 ^[f]	Me	Me	48	10	92:8	33

[a] Reaction conditions: dicobalt complex (1.5 equiv), alkene **1** (1.0 equiv), NMO·H₂O (6.0 equiv), CH₃CN, 0 °C. [b] Determined by ¹H NMR spectroscopy on the crude mixtures after filtration of the cobalt byproducts. [c] Pure adducts after chromatography. [d] 3 equivalents of dicobalt complex were used. [e] Reaction run at RT. [f] Reaction run at 10 Kbar.

Interestingly, reasonable yields of isolated pure adducts (49–74 %), complete regioselectivities, and high to complete diastereoselectivities (*de* = 86–>96 %) were obtained from all terminal alkynes, including primary, benzyl, and tertiary alkyl substituted ones (entries 1–3), aryl acetylenes (entry 4), silylated acetylenes (entry 5), and functionalized alkynes (entries 6–8). Interestingly, the reaction conditions are so mild that even alkynes with a primary bromoalkyl chain can be successfully used (entry 8). As expected, the alkynes substituted with the bulkiest groups, especially *tert*-butyl and TMS (entries 2 and 5), reacted more slowly. In these cases the temperature of the reaction was raised to room temperature and an excess of the alkyne dicobalt complex was used (3-fold excess) in order to assure complete conversion of the starting alkene. In agreement with the

high sensitivity of the process to the steric environment around the C–C triple bond, no reaction at all occurred in the case of an internal alkyne such as 2-butyne (entry 9). This drawback could be partially solved by performing the reaction at high pressure^[34] (10 Kbar) and room temperature for 48 h. Under these conditions the reaction occurred cleanly, albeit with incomplete conversion (30 % of **1i** was recovered), to afford the adducts **10** with high stereoselectivity (entry 10) and in 33 % yield (47 % in converted product).

Configurational assignment of the PK adducts and mechanistic considerations: In the case of the *p*-tolylsulfoxide **2a** the (*S*^{*}, *R*_S^{*}) configuration of the major diastereomer **A** and, consequently, the (*R*^{*}, *R*_S^{*}) configuration of the minor diastereomer **B** were assigned by comparison of the NMR spectroscopy data with those previously reported for structurally very similar *p*-tolylsulfinyl cyclopentenones (for example, 3-ethoxy-5-(*p*-tolylsulfinyl)cyclopent-2-en-1-one).^[35] To support this tentative stereochemical assignment, we obtained suitable crystals of the 2-*tert*-butylcyclopentenone **3A**, which was one of the few solid PK adducts among those depicted in Tables 1 and 2. The unequivocal (*S*^{*}, *R*_S^{*}) configuration of this compound is shown in Figure 1. With

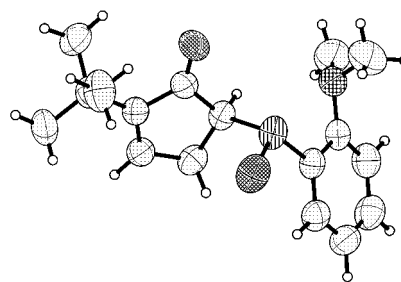
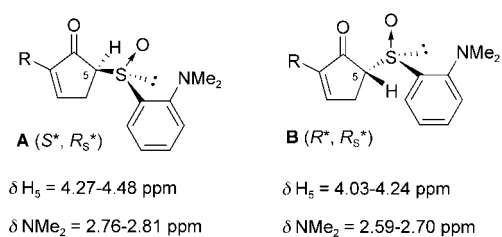


Figure 1. X-ray crystal structure of **3A**.

regard to the conformation around the C–S bond in the crystal, it is interesting to note that the sulfinyl oxygen atom and the aryl group are oriented in such a way as to minimize the steric and electronic interactions with the cyclopentenone ring (dihedral angles: O–S–C⁵–C¹ = 74.77(10)° and C(aryl)–S–C⁵–C¹ = –176.44(9)°). Related to this conformational preference, we noticed a general trend in the chemical shifts of the H⁵ and Me₂N signals in the ¹H NMR spectra of the diastereomers **A** and **B**. Thus, both the H⁵ atom and the Me₂N group always appear significantly more deshielded in the dominant isomer **A** than in the minor isomer **B** (Scheme 9). This very simple spectroscopic criteria can be used for the stereochemical assignment of all the PK adducts obtained from the optimal vinyl sulfoxide **1i**.

Since the keto–enol tautomerism in the sulfinyl cyclopentenones **2** is expected to be a very favorable process because of the acidity of the hydrogen atom at the C⁵ position, we wondered if the stereoselectivity of the PK reaction would not simply reflect the thermodynamic equilibria between the **A** and **B** epimers. As described below, both theoretical



Scheme 9. Significant 1H NMR spectroscopy data of diastereomers **A** and **B** (in $CDCl_3$).

and experimental studies unequivocally proved that this thermodynamic factor is indeed the origin of the stereoselectivity.

First, we found an excellent agreement between the observed stereoselectivity of the PK reactions and the difference in energy content of both **A** and **B** epimers calculated by theoretical methods. In the interest of time economy, calculations were made with a methyl group located on the double bond of the cyclopentenone ring instead of an *n*-butyl one. Conformation analyses of these 2,5-disubstituted cyclopentenones were performed by using the semiempirical PM3(tm)^[36] procedure, as implemented in HyperChem 6.02.^[37] Then, the low-energy structures were reoptimized by using hybrid DFT (B3LYP)^[38] and the 6-31G*^[39] basis set, as implemented in the Gaussian 03^[40] program package. Frequencies were also computed at the same level of theory/basis and zero-point energy (ZPE) correction was included. The results are summarized in Table 3. The final optimized structures for the modeled **A** and **B** cyclopentenone epimers with the *o*-(*N,N*-dimethylamino)phenyl substituent (**2i'**) are shown in Figure 2.

Table 3. Theoretical calculations on the relative stability of the **A** and **B** epimers.

R	ΔE_{AB} ^[a]	Calculated A/B ratio ^[b] ($R' = Me$)	Experimental A/B ratio ($R' = nBu$)
<i>p</i> -Tol	0.7	77:23	74:26
<i>t</i> Bu	2.5	99:1	> 98: < 2
<i>o</i> -(Me_2N) C_6H_4	1.9	96:4	92:8

[a] ΔE B3LYP/6-31G* + ZPE [kcal mol⁻¹]. [b] At 25 °C.

Structure **A** in Figure 2 shows a conformation (dihedral angles: $O-S-C^5-C^1 = 84.635^\circ$ and $C(Ar)-S-C^5-C^1 = -166.741^\circ$) quite similar to the one adopted by **3A** in the solid state (see Figure 1). In the minor diastereomer **B** the sulfinylic oxygen atom and the aryl group are again oriented in a way that minimizes the steric and electronic interactions with the cyclopentenone ring. The relative orientation between the H^5 atom and the sulfinyl group is almost *anti* in both diastereomers (dihedral angles: **A**: $O-S-C^5-H^5 = -158.384^\circ$; **B**: $O-S-C^5-H^5 = 166.114^\circ$). Thus, the observed trend in the chemical shifts of the H^5 signals in the 1H NMR

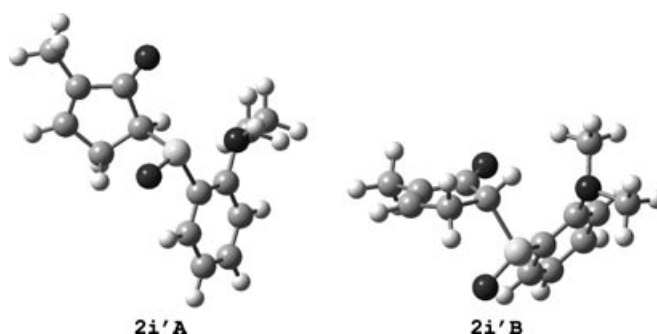
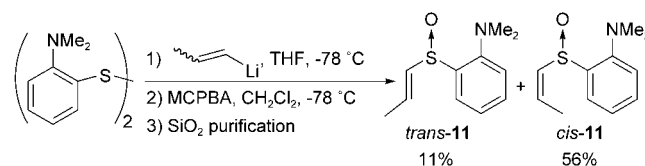


Figure 2. B3LYP/6-31G* optimized structures for cyclopentenones **2i'A** and **2i'B**.

spectra for these epimers (Scheme 9) could be associated to the anisotropic effect exerted by the carbonyl group, which causes a shielding in that proton in diastereomer **B** with respect to **A** (dihedral angles: **A**: $O-C^1-C^5-H^5 = -57.533^\circ$; **B**: $O-C^1-C^5-H^5 = 39.765^\circ$). This effect can be extended to the Me_2N group, which is nearer to the carbonyl group in diastereomer **B** (distance: $CO \cdots H_3CN = 2.586 \text{ \AA}$) than in diastereomer **A** (distance: $CO \cdots H_3CN = 4.067 \text{ \AA}$).

Among the experimental evidence on the easy epimerization process at the C^5 position, we observed that an NMR spectroscopy sample of pure **7A** (obtained from the initial 93:7 diastereomeric mixture by trituration with cold hexane) isomerized again to the 93:7 isomeric ratio in 16 h in $[D_6]$ acetone, in 3 h in CD_3CN (the solvent of the PK reaction), and instantaneously in $[D_6]$ DMSO or CD_3OD . This fast thermodynamic equilibration in polar solvents, even in the absence of any added base, could explain why we failed in all our attempts to separate the **A/B** mixtures by silica gel chromatography.

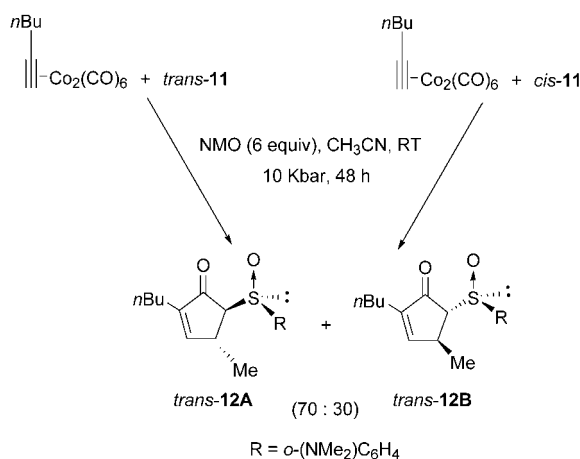
As a third piece of evidence, the behavior of the disubstituted α,β -unsaturated sulfoxides *cis*-**11** and *trans*-**11** was also conclusive. These compounds were readily prepared by reaction of a *cis/trans* mixture of propenyl lithium (generated in situ by treatment of 1-bromo-1-propene with *t*BuLi) with *o*-dimethylaminophenyl disulfide, sulfide-to-sulfoxide oxidation with MCPBA, and final silica gel separation of both isomers. In this way, *trans*-**11** and *cis*-**11** were isolated in 11 % and 56 % overall yields, respectively (Scheme 10). Unlike



Scheme 10. Synthesis of disubstituted α,β -unsaturated sulfoxides *trans*-**11** and *cis*-**11**.

the behavior of the parent vinyl sulfoxide **1i**, the sterically more demanding disubstituted alkenes *cis*-**11** and *trans*-**11** failed to react with the dicobalt complex of 1-hexyne under the standard N-oxide-promoted conditions. Gratifyingly, as

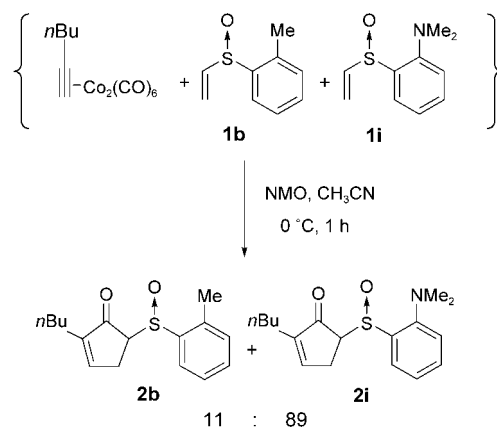
in the case of the PK reaction of disubstituted alkynes, the reaction occurred cleanly under high-pressure conditions (10 Kbar), albeit with incomplete conversions (40–55 % of starting alkene **11** was recovered), to provide the expected regioisomer **12** in 22–31 % yield after chromatography (49–52 % yield in converted product). This reaction is stereochemically quite relevant because the same 70:30 mixture of *trans*-**12A** and *trans*-**12B** isomers was isolated regardless of the starting *cis* or *trans* configuration of the alkene **11** (Scheme 11). This stereochemical convergence can only be



Scheme 11. PK reactions of isomers *trans*-**11** and *cis*-**11** under high pressure.

explained by assuming an easy epimerization at the C⁵ center. The *trans* relative configuration at C⁴/C⁵ in both **12** products was assigned from the low value of the $J_{4,5}$ coupling constant (2.4 and 2.8 Hz for *trans*-**12A** and *trans*-**12B**, respectively), which is in full agreement with typical values in known related *trans*-cyclopentenones.^[41] On the other hand, the relative configuration at the sulfur and C⁵ centers was established following the spectroscopic rule shown in Scheme 9.

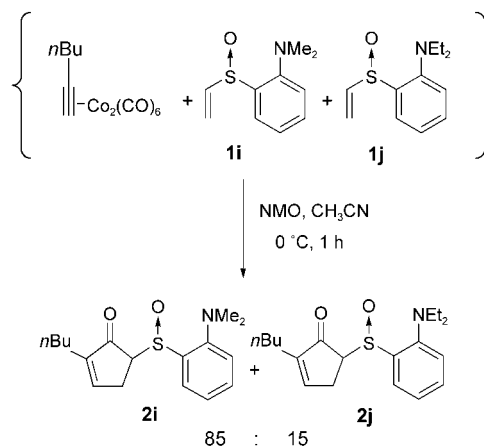
Another very relevant issue of the PK reactions of the vinyl sulfoxides **1** is the mechanistic origin of the high reactivity exhibited by the *o*-dimethylaminophenyl derivative **1i**. To estimate more accurately the magnitude of this effect, we carried out the competitive kinetic experiment shown in Scheme 12, involving two very different *ortho*-substituted phenyl sulfoxides. The reaction of equimolecular amounts of *o*-tolylsulfoxide **1b**, *o*-(dimethylamino)phenyl sulfoxide **1i**, and the dicobaltcarbyl complex of 1-hexyne under the optimal PK reaction conditions (NMO, CH₃CN, 0 °C, 60 min) led to an 11:89 mixture of the corresponding PK adducts **2b** and **2i**. This result clearly shows that substrate **1i**, despite the higher steric bulk of the *o*-dimethylamino group relative to the methyl group in **1b**, is nearly one order of magnitude more reactive than **1b**. The higher reactivity of **1i** suggests that the *o*-dimethylamino group could be acting as a heteroatomic coordinating group at the cobalt center, thus favoring the further coordination of the alkene to the cobalt



Scheme 12. Competitive kinetic experiment involving two very different *ortho*-substituted phenyl sulfoxides.

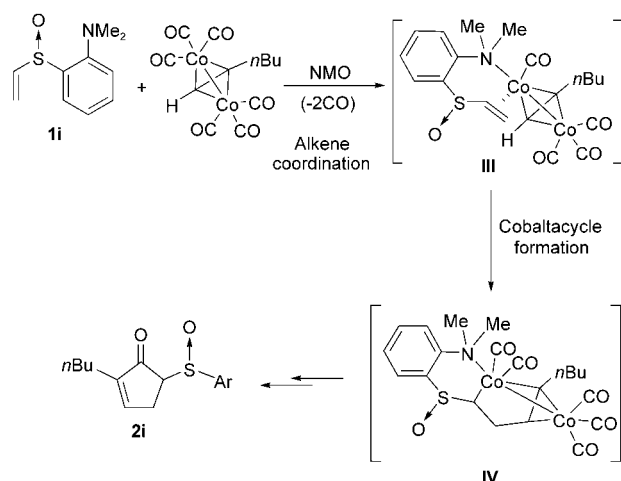
complex; this coordination is supposed to be the rate-determining step in the PK reaction.^[15]

To gain more insight into the subtle contribution of both steric and coordinating effects to the reactivity of vinyl sulfoxide **1i** in the PK reactions, we performed a second competitive experiment with two similar amino-substituted tethered sulfoxides: the optimal *o*-dimethylamino substrate **1i** and the somewhat bulkier *o*-diethylamino derivative **1j** (prepared by following the same method described for **1i**). Equimolecular amounts of **1i**, **1j**, and the dicobaltcarbyl complex were treated as usual (NMO, CH₃CN, 0 °C, 60 min) and gave rise to an 85:15 mixture of the corresponding PK adducts **2i** and **2j** (Scheme 13). This sizeable selectivity indi-



Scheme 13. Competitive kinetic experiment involving two similar *ortho*-substituted phenyl sulfoxides.

cates that a moderate increase in the steric environment around the nitrogen atom has a deeply detrimental effect on the reactivity; this result is in full agreement with the presumed role of the nitrogen atom as a cobalt-coordinating heteroatom in the formation of the key sterically congested alkene–dicobalt complex intermediate **III** (Scheme 14). When the four-bond separation between the C–C double bond and the amine moiety is taken into account, it is ex-

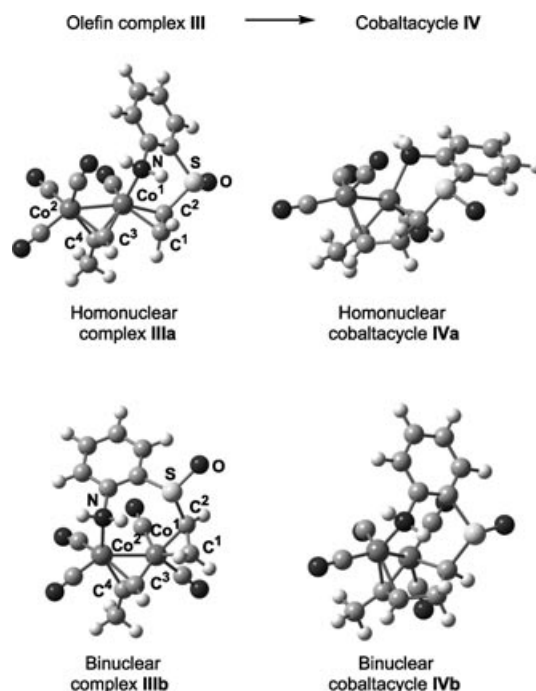
Scheme 14. Presumed intermediates **III** and **IV** in the formation of **2i**.

pected that both groups will coordinate the same cobalt atom on the dicobalt complex. A similar kind of coordination has been proposed in the case of PK reactions of achiral tethered aminoalkenes.^[21]

To shed some light to this point, we performed some theoretical calculations by using, as simplified substrates, the *o*-aminophenyl vinyl sulfoxide as an olefin model and propyne as an alkyne model. In the elucidation of the possible competence of homonuclear coordination (nitrogen and olefin coordinating the same cobalt atom) versus binuclear coordination (nitrogen and olefin coordinating different cobalt atoms), we decided to analyze the relative stability of the starting olefin complexes **III** and their resulting products **IV**. Complexes **III** and cobaltacycles **IV** were fully optimized by semiempirical (PM3^[36]) and DFT (B3LYP^[38]) methods. In this case, the effective core potential LANL2DZ^[42] was used for Co and S, and the STO-3G*^[43] basis set was used for C, H, N, and O. Frequencies were calculated at the same level of theory/basis and ZPE correction was included. The optimized structures found for homonuclear (**IIIa**) and binuclear (**IIIb**) complexes and their corresponding cobaltacycles are shown in Figure 3. Distances and energy differences are collected in Table 4.

As can be seen in Table 4, there are significant differences in the optimized interatomic distances. For instance, the C¹–C³ distance is shorter in **IIIa** than in **IIIb** but the opposite is observed for the Co–N distances.^[44] However, the most interesting outcome of this theoretical study concerns the relative optimized energies: not only is the homonuclear complex **IIIa** more stable than **IIIb** (ΔE_{relat}) but its reaction is much more exothermic (ΔE_{react}), a fact strongly supporting the theory that the homonuclear coordination is the preferred path for this step.

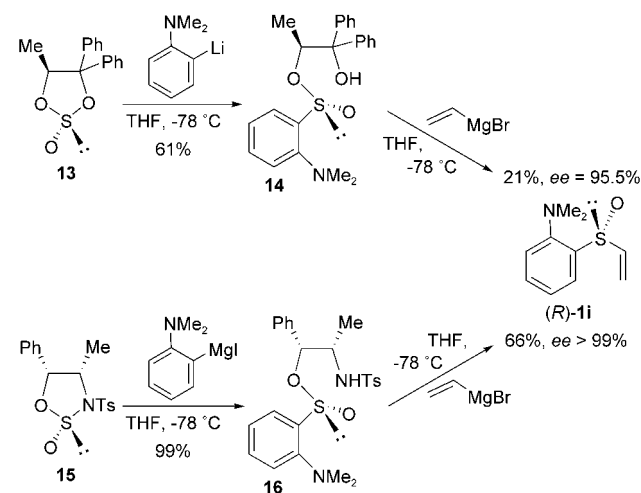
Applications in enantioselective synthesis: Any application of the synthetic potential of this regio- and diastereoselective intermolecular PK methodology to the enantioselective synthesis of polysubstituted cyclopentanoids required, first, the preparation of enantiomerically pure vinyl sulfoxide **1i**. Initially, we applied the sulfite-based method of synthesis of

Figure 3. Optimized calculated structures for olefin complexes **III** and their cobaltacycles **IV**.Table 4. Significant distances [Å] in complexes **III**, relative energies (ΔE_{relat}) between **IIIa** and **IIIb** [Kcal mol⁻¹], and energy differences (ΔE_{react}) between complexes **III** and cobaltacycles **IV** [Kcal mol⁻¹].

	IIIa	IIIb
Co(1)–C(1)	2.121	2.179
Co(1)–C(2)	2.050	2.100
Co–N	2.129	2.077
C(1)–C(2)	1.418	1.414
C(1)–C(3)	2.625	2.762
$\Delta E_{\text{relat}}^{[a]}$	0.0	3.6
$\Delta E_{\text{react}}^{[a]}$	–31.5	–22.6

[a] ZPE correction included.

chiral sulfoxides developed by Kagan and co-workers (Scheme 15).^[45] The ring opening of the commercially available enantiopure sulfite **13** with *o*-(*N,N*-dimethylamino)phen-

Scheme 15. Synthesis of chiral sulfoxide (*R*)-**1i**. Ts = tosyl = toluene-4-sulfonyl.

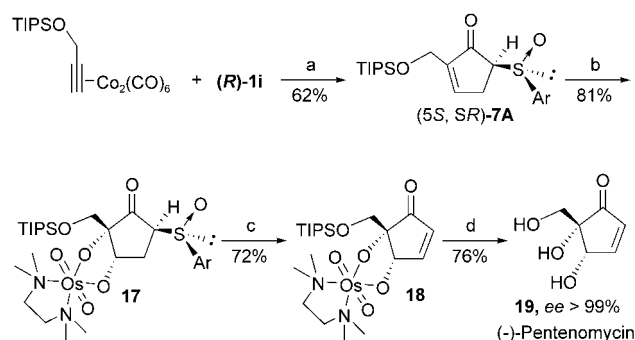
yllithium (generated in situ by treatment of the corresponding iodide with *n*BuLi) in THF at -78°C gave the diastereomerically pure sulfinate **14** as the major regioisomer (61 % yield). Disappointingly, the further reaction of **14** with magnesium vinyl bromide (2 equivalents) under the same reaction conditions (THF, -78°C) provided the expected vinyl sulfoxide (*R*)-**1i** in low yield (21 %) and with incomplete enantioselectivity (95.5 % *ee*, as determined by HPLC with a Chiralcel OD column). The use of a higher amount of the Grignard reagent (4 equivalents) resulted in a more severely detrimental effect on the enantioselectivity (77 % *ee*), thereby showing that this sulfinylation reaction occurs with partial racemization at the sulfur center.

Next, we turned out to the asymmetric synthesis of sulfoxides recently reported by Senanayake and co-workers.^[46] The initial enantiopure sulfinylating reagent, the *N*-tosyl-1,2,3-oxathiazolidine **15**, was prepared in one step from the readily available and inexpensive (1*R*,2*S*)-*N*-tosylnorephedrine. The reaction of **15** with a stoichiometric amount of *o*-(*N,N*-dimethylamino)phenyl magnesium iodide occurred under mild conditions in THF at -78°C with selective cleavage of the S–N bond to give rise to sulfinate **16**, which results from the inversion of configuration at the sulfur atom, in nearly quantitative yield (99 %). To our delight, the reaction of **16** with vinyl magnesium bromide (3 equivalents) in THF at -78°C provided the desired sulfoxide (*R*)-**1i** in 66 % yield and with complete enantioselectivity (Scheme 15), thereby demonstrating that this second substitution at the sulfur atom also took place with complete inversion of configuration.

To highlight the synthetic interest of our novel asymmetric intermolecular version of the PK reaction, we selected two natural cyclopentanoids as synthetic objectives: the antibiotic (–)-pentenomycin I, with a 4,5,5-trisubstituted cyclopentenone structure, and the (–)-aminocyclopentitol moiety of the hopanoid of *Zymomonas mobilis*, which displays a stereochemically complex 1,1,2,3,4,5-hexasubstituted cyclopentane framework (Scheme 7).

(–)-Pentenomycin I was isolated in 1973 from the culture broths of *Streptomyces eurythermus*^[47] and has proved to be moderately active against Gram-positive and Gram-negative bacteria.^[48] To the best of our knowledge, five asymmetric syntheses of this compound have been reported to date,^[49] with four of them requiring carbohydrates as starting materials; this implies the use of long and lineal synthetic sequences (10–20 chemical steps). A very efficient enantioselective four-step synthesis of (–)-pentenomycin I from the vinyl sulfoxide (*R*)-**1i**, taking advantage of the convergent formation of the cyclopentenone ring by a PK reaction, is shown in Scheme 16. After the PK reaction, the rest of the synthetic steps are straightforward: dihydroxylation of the C–C double bond, generation of the enone moiety by sulfoxide pyrolysis, and deprotection of the hydroxy groups.

Treatment of the cobalt complex of the TIPS derivative of propargylic alcohol with enantiopure (*R*)-**1i** (NMO, CH_3CN , 0°C) afforded the adduct **7** in a 93:7 isomer ratio (62 % yield). Trituration of this mixture with cold hexane provided the pure major diastereomer (*S,R_S*)-**7A**. The optical purity of this compound proved to be as high as that of the starting

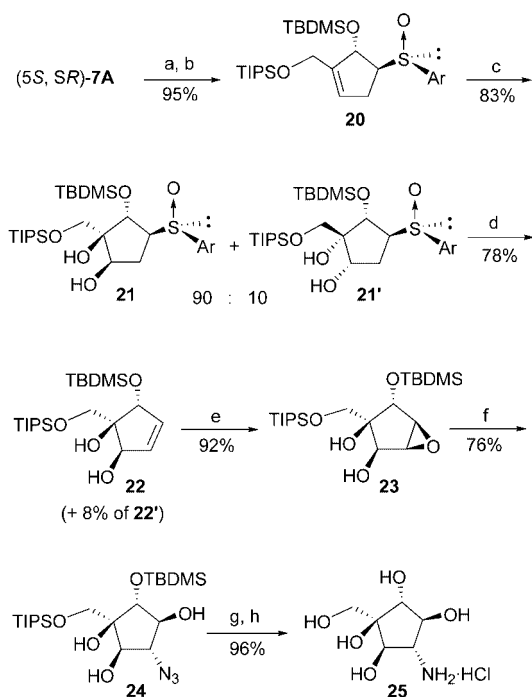


Scheme 16. Synthesis of (–)-pentenomycin. a) NMO, CH_3CN , 0°C ; b) OsO_4 , TMEDA, CH_2Cl_2 , -78°C ; c) toluene, reflux; d) 2M HCl, RT. TIPS = triisopropylsilyl, TMEDA = *N,N,N',N'*-tetramethylethylenediamine.

vinyl sulfoxide (>99 % *ee*, as determined by HPLC with a Chiralcel OD column), thereby proving that the PK reaction took place without any racemization at the sulfur center.^[50] This is an interesting point since it has been reported that the intermolecular PK reaction of norbornene with acetylenic sulfoxides occurs with partial racemization at the sulfur atom.^[18d] Since the dihydroxylation of (*S,R_S*)-**7** with OsO_4 under normal catalytic conditions (3 mol % OsO_4 , NMO, CH_2Cl_2 , 0°C) gave a mixture of stereoisomers, we turned to the procedure of Donohoe et al. for dihydroxylation of alkenes with the stoichiometric pair OsO_4 /TMEDA under extremely mild reaction conditions.^[51] In CH_2Cl_2 at -78°C the reaction was highly stereoselective in favor of dihydroxylation on the expectedly less hindered face of the double bond, that opposite to the sulfinyl group at the C^5 atom. This reaction provided the stable osmate diester **17** in 81 % yield; the (2*S*,3*S*,5*S*) configuration of the product could be established by NOESY experiments (see the Supporting Information for details). Compound **17** suffered a clean sulfoxide pyrolysis in refluxing toluene to afford the enone-osmate diester **18** in 72 % yield. Final acid hydrolysis of the hydroxy-protecting groups (2M HCl) provided the natural (–)-(2*S*,3*S*)-pentenomycin I (**19**), whose absolute rotary power was in full agreement with literature data ($[\alpha]_{\text{D}} = -32$ ($c = 0.2$, EtOH); literature value:^[42] $[\alpha]_{\text{D}} = -32$ ($c = 0.3$, EtOH)). Alternatively, its very high optical purity was unequivocally confirmed by HPLC analysis of the triacetate derivative (>99 % *ee*, as determined by HPLC with a Chiralpak AD column).

Bacteriohopanetetrol ether **II** (Scheme 7) is an abundant triterpenoid of the hopane family, found in the membrane of several bacteria, such as *Methylobacterium organophilum*, *Rhodopseudomonas acidophila*, and *Zymomonas mobilis*.^[52] To our knowledge, to date, only a total synthesis of its aminocyclopentitol unit has been reported, which required D-glucosamine as a commercially available starting material.^[53] An eight-step stereodirected synthesis of the (–) enantiomer of this aminocyclopentitol, from the same PK adduct (*S,R_S*)-**7A**, is shown in Scheme 17.

Stereoselective hydride reduction of the ketone **7A** with DIBALH in THF at -78°C provided a single alcohol, which was protected as the TBDMS derivative **20** (TBDMSCl, imidazole, CH_3CN ; 95 % overall yield from **7**). The *trans* ster-



Scheme 17. Synthesis of the (–)-aminocyclopentitol moiety. a) DIBALH, THF, -78°C ; b) TBDMSCl, imidazole, CH_3CN , RT; c) OsO_4 , NMO, $\text{THF}/\text{H}_2\text{O}$ 10:1, RT; d) NaHCO_3 , toluene, reflux, then SiO_2 purification; e) MCPBA, CH_2Cl_2 , RT; f) NaN_3 , NH_4Cl , DMF, 100°C ; g) H_2 , Pd/C (10%), MeOH; h) HCl/MeOH , RT. TBDMS = *tert*-butyldimethylsilyl, DIBALH = diisobutylaluminum hydride, DMF = *N,N*-dimethylformamide.

eochemistry of **20** was inferred from the well-known stereochemical behavior of β -ketosulfoxides with reducing hydride reagents.^[35] The dihydroxylation of **20** under standard OsO_4 catalytic conditions (3 mol % OsO_4 , NMO, $\text{THF}/\text{H}_2\text{O}$, RT) occurred mainly from the alkene face opposite to the bulky allylic substituent, thereby providing an inseparable 90:10 mixture of both *cis*-diols **21** and **21'** (83% yield). Sulfoxide pyrolysis of this mixture by heating in toluene at 110°C and further silica gel chromatographic separation afforded the cyclopentenediol **22** in 78% yield, along with 8% of its diastereomer **22'**.^[54] As expected from both steric and hydrogen-bond considerations, the epoxidation of **22** with MCPBA (CH_2Cl_2 , RT) was completely stereoselective and occurred on the same side of the allylic hydroxy group (opposite face to the bulky silylated ether) to give a single epoxide **23**. Due to the very different steric environment of both epoxidic carbon atoms, the *trans* opening of **23** with NaN_3 in DMF at 100°C was completely regioselective in favor of attack at the least hindered position (C^3) to provide exclusively the azide **24** (76% yield). Once the configuration of the five stereogenic carbon centers had been controlled, the final hydrogenation of the azide moiety (H_2 , Pd/C), followed by hydroxy deprotection in acid media (HCl , MeOH), afforded the (–)-aminocyclopentitol **25** ($[\alpha]_{\text{D}} = -6$ ($c = 0.3$, MeOH); literature value for the enantiomer:^[53] $[\alpha]_{\text{D}} = +6.2$ ($c = 1.2$, MeOH)). The ^1H and ^{13}C NMR spectroscopy data of this compound were identical to those described in the literature for the (+) enantiomer,^[53] thereby

proving unequivocally the (1*R*,2*R*,3*S*,4*S*,5*R*) configuration and, therefore, the stereochemistry of its synthetic precursors.

Conclusion

We have demonstrated that, under appropriate conditions, α,β -unsaturated sulfoxides behave as efficient acyclic olefinic partners in asymmetric intermolecular PK reactions, to provide substituted 5-sulfinyl-2-cyclopentenones with complete regiocontrol and high stereoselectivity. Among the variety of screened sulfoxides, the cobalt-chelating *o*-(*N,N*-dimethylamino)phenyl vinyl sulfoxide (**1i**) gave the best results in terms of reactivity and stereoselectivity with a wide variety of substituted terminal alkynes. With the readily available sulfoxide (*R*)-**1i**, this methodology opens a new access to the enantioselective synthesis of cyclopentanoids. This synthetic interest has been illustrated by developing efficient stereoselective syntheses of (–)-pentenomycin I and a stereochemically complex aminocyclopentitol. Efforts to further apply the metal-coordinating ability of the *o*-dimethylaminophenyl sulfinyl group as a chiral auxiliary in other stereoselective transition-metal-mediated reactions are underway.

Experimental Section

General: All reagents were obtained from commercial suppliers and were used without further purification except $\text{NMO}\cdot\text{H}_2\text{O}$, which was purified by precipitation from acetone before use. THF, Et_2O , and CH_2Cl_2 were dried over microwave-activated 4 Å molecular sieves. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm Merck silica gel 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 in CDCl_3 (calibrated at $\delta = 7.26$ and 77.0 ppm for ^1H and ^{13}C experiments, respectively), CD_3OD ($\delta = 3.31$ and 49.0 ppm) or D_2O ($\delta = 4.70$ ppm). Mass spectra and high-resolution mass spectra were determined on a Hewlett–Packard HP-5985 mass spectrometer at 70 eV ionising voltage (EI) or under fast atom bombardment (FAB) conditions. Melting points were determined in open-end capillary tubes on a Gallenkamp apparatus. Optical rotations were measured on a Perkin–Elmer 241C polarimeter. HPLC was conducted on an Agilent 1100 instrument, with Daicel Chiralpak AD and Chiralcel OD columns. High-pressure reactions were conducted under 10 Kbar pressure by using a Hofer HP 14 apparatus.

2-*n*-Butyl-5-(*p*-tolylsulfinyl)-2-cyclopentenone (2a): A solution of 1-hexyne (26 μL , 0.23 mmol) and $[\text{Co}_2(\text{CO})_8]$ (77 mg, 0.23 mmol) in CH_3CN (1 mL) was stirred at RT under an argon atmosphere. After 1 h, *N*-methylmorpholine *N*-oxide (106 mg, 0.90 mmol) and a solution of **1a** (25 mg, 0.15 mmol) in CH_3CN (1 mL) were added and the resulting solution was stirred for 2 h. The reaction mixture was diluted with CH_2Cl_2 , treated with trimethylamine *N*-oxide (50 mg) to remove the remaining cobalt complex and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite, which was washed with diethyl ether. The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 3:1) to afford **2aA** and **2aB** as a 74:26 diastereomeric mixture (28 mg, 68%, colorless oil). **A:** ^1H NMR (300 MHz, CDCl_3): $\delta = 7.52$ – 7.21 (m, 5H; Ar, H-3), 3.49 (dd, $J = 2.2$, 6.5 Hz, 1H; H-5), 3.04–2.89 (m, 1H; H-4), 2.41 (s, 3H; ArCH_3), 2.40–2.26 (m, 1H; H-4), 2.18 (m, 2H; H-1'), 1.51–1.09 (m, 4H; H-2', H-3'), 0.88 ppm (t, $J = 7.0$ Hz, 3H; H-4'); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 201.7$, 201.0, 157.7, 156.9, 147.0, 146.8, 142.1, 141.6, 139.1, 135.4, 129.9, 129.5,

125.0, 124.0, 68.1, 66.0, 29.6, 29.5, 29.3, 25.5, 24.7, 24.2, 23.9, 22.3, 22.1, 21.4, 13.8, 13.7 ppm; HRMS (FAB+): calcd for (C₁₆H₂₀O₂S) [M]⁺: 276.1184; found: 276.1177; **B**: ¹H NMR (300 MHz, CDCl₃; significant signals): δ = 7.03 (m, 1H; H-3), 4.20 (dd, *J* = 2.2, 6.5 Hz, 1H; H-5), 2.85–2.70 (m, 1H; H-4), 2.36 (s, 3H; ArCH₃), 1.91 ppm (m, 2H; H-1').

2-*n*-Butyl-5-(*o*-tolylsulfinyl)-2-cyclopentenone (2b): A solution of 1-hexyne (52 μL, 0.45 mmol) and [Co₂(CO)₈] (154 mg, 0.45 mmol) in CH₃CN (2 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (211 mg, 1.80 mmol) and a solution of **1b** (50 mg, 0.30 mmol) in CH₃CN (2 mL) were added. After 10 h at RT, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 14 h at RT. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (200 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 5:1) to afford **2bA** and **2bB** as a 90:10 diastereomeric mixture (23 mg, 28%, colorless oil). **A**: ¹H NMR (300 MHz, CDCl₃): δ = 7.82 (dd, *J* = 2.8, 7.3 Hz, 1H; Ar), 7.44–7.35 (m, 3H; Ar, H-3), 7.21 (dd, *J* = 2.4, 6.1 Hz, 1H; Ar), 3.53 (dd, *J* = 2.4, 6.9 Hz, 1H; H-5), 3.06–2.97 (m, 1H; H-4), 2.42 (s, 3H; ArCH₃), 2.33–2.17 (m, 3H; H-4, H-1'), 1.51–1.23 (m, 4H; H-2', H-3'), 0.89 ppm (t, *J* = 7.3 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 202.0, 158.0, 155.9, 146.9, 140.4, 134.2, 130.9, 126.9, 124.1, 65.0, 29.5, 24.7, 23.2, 22.3, 18.0, 13.7 ppm; HRMS (EI+): calcd for (C₁₆H₂₀O₂S) [M]⁺: 276.1184; found: 276.1182; **B**: ¹H NMR (300 MHz, CDCl₃; significant signals): δ = 3.94 (dd, *J* = 1.6, 6.9 Hz, 1H; H-5), 2.36 ppm (s, 3H; ArCH₃).

2-*n*-Butyl-5-(2-bromophenylsulfinyl)-2-cyclopentenone (2c): A solution of 1-hexyne (22 μL, 0.19 mmol) and [Co₂(CO)₈] (67 mg, 0.19 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (91 mg, 0.78 mmol) and a solution of **1c** (30 mg, 0.13 mmol) in CH₃CN (1 mL) were added. After 12 h at RT, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 12 h at RT. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (90 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 3:1) to afford **2cA** and **2cB** as an 86:14 diastereomeric mixture (15 mg, 30%, colorless oil). **A**: ¹H NMR (300 MHz, CDCl₃): δ = 7.82 (dd, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.57 (t, *J* = 7.5 Hz, 2H; Ar), 7.39 (m, 2H; H-3, Ar), 4.09 (dd, *J* = 2.7, 7.0 Hz, 1H; H-5), 2.89 (m, 1H; H-4), 2.21 (m, 3H; H-1', H-4), 1.56–1.21 (m, 4H; H-2', H-3'), 0.90 ppm (t, *J* = 7.0 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 201.7, 157.7, 147.1, 141.6, 133.2, 132.5, 128.3, 127.1, 118.7, 63.9, 29.5, 24.8, 23.3, 22.4, 13.8 ppm; HRMS (EI+): calcd for (C₁₅H₁₇O₂SB_r) [M]⁺: 340.0133; found: 340.0132; **B**: ¹H NMR (300 MHz, CDCl₃; significant signals): δ = 3.97 (m, 1H; H-5), 3.19 ppm (m, 1H; H-4).

2-*n*-Butyl-5-(2,4,6-triisopropylphenylsulfinyl)-2-cyclopentenone (2d): A solution of 1-hexyne (19 μL, 0.16 mmol) and [Co₂(CO)₈] (55 mg, 0.16 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (76 mg, 0.65 mmol) and a solution of **1d** (30 mg, 0.11 mmol) in CH₃CN (1 mL) were added. After 12 h at RT, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 12 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (70 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 5:1) to afford **2dA** and **2dB** as a 94:6 diastereomeric mixture (10 mg, 24%, colorless oil). **A**: ¹H NMR (300 MHz, CDCl₃): δ = 7.41 (m, 1H; H-3), 7.08 (s, 2H; Ar), 4.18 (dd, *J* = 1.6, 6.5 Hz, 1H; H-5), 3.73 (m, 2H; CH(CH₃)₂), 3.39 (m, 1H; H-4), 2.95 (m, 1H; H-4), 2.90 (m, 1H; CH(CH₃)₂), 2.16 (m, 2H; H-1'), 1.51–1.20 (m, 22H; H-2', H-3', CH(CH₃)₂), 0.89 ppm (t, *J* = 7.3 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 201.6, 156.1, 152.7, 150.1, 146.4, 134.0, 123.0, 66.3, 34.3, 29.6, 28.3, 28.1, 24.6, 23.7, 23.6, 22.3, 13.7 ppm; HRMS (EI+): calcd for (C₂₄H₃₆O₂S) [M]⁺: 388.2436; found: 388.2438; **B**: ¹H NMR (300 MHz, CDCl₃; significant signal): δ = 4.12 ppm (m, 1H; H-5).

2-*n*-Butyl-5-(*tert*-butylsulfinyl)-2-cyclopentenone (2e): A solution of 1-hexyne (39 μL, 0.34 mmol) and [Co₂(CO)₈] (116 mg, 0.34 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (162 mg, 1.38 mmol) and a solution of **1e** (30 mg, 0.23 mmol) in CH₃CN (1 mL) were added. After 12 h at RT, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 12 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (150 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 3:2) to afford **2eA** (10 mg, 20%, colorless oil). ¹H NMR (300 MHz, CDCl₃): δ = 7.38 (m, 1H; H-3), 4.29 (dd, *J* = 2.0, 6.9 Hz, 1H; H-5), 3.25 (m, 1H; H-4), 2.54 (m, 1H; H-4), 2.18 (m, 2H; H-1'), 1.45 (m, 2H; H-2'), 1.31 (m, 2H; H-3'), 1.27 (s, 9H; C(CH₃)₃), 0.89 ppm (t, *J* = 7.3 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 204.7, 158.2, 145.9, 58.1, 55.1, 29.5, 24.6, 23.7, 23.4, 22.3, 13.8 ppm; HRMS (EI+): calcd for (C₉H₁₄O₂S) [M-*t*Bu]⁺: 186.0715; found: 186.0717.

2-*n*-Butyl-5-(2-pyridylsulfinyl)-2-cyclopentenone (2g): A solution of 1-hexyne (29 μL, 0.25 mmol) and [Co₂(CO)₈] (87 mg, 0.25 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (138 mg, 1.17 mmol) and a solution of **1g** (30 mg, 0.20 mmol) in CH₃CN (1 mL) were added and the resulting solution was stirred for 1 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide, and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (aluminum oxide neutral; hexane/ethyl acetate 2:1) to afford **2gA** and **2gB** as a 73:27 diastereomeric mixture (10 mg, 19%, colorless oil). **A**: ¹H NMR (200 MHz, CDCl₃): δ = 8.63 (m, 1H; Ar), 7.95 (m, 2H; Ar), 7.45–7.26 (m, 2H; Ar, H-3), 4.09 (dd, *J* = 2.7, 6.5 Hz, 1H; H-5), 2.90–2.61 (m, 1H; H-4), 2.48–2.26 (m, 1H; H-4), 2.21 (m, 2H; H-1'), 1.54–1.18 (m, 4H; H-2', H-3'), 0.90 ppm (t, *J* = 7.0 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 202.0, 199.8, 163.4, 161.8, 157.4, 155.5, 149.7, 149.3, 148.0, 147.1, 137.9, 137.5, 124.7, 121.3, 120.6, 65.6, 62.8, 29.5, 29.1, 24.7, 24.6, 23.7, 22.3, 13.8, 13.7 ppm; HRMS (FAB+): calcd for (C₁₄H₁₇NO₂S) [M]⁺: 263.0980; found: 263.0975; **B**: ¹H NMR (200 MHz, CDCl₃; significant signals): δ = 4.08 (m, 1H; H-5), 3.09 (m, 1H; H-4), 2.61 (m, 1H; H-4), 2.09 ppm (m, 2H; H-1').

2-*n*-Butyl-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-2-cyclopentenone

(2i): A solution of 1-hexyne (23 μL, 0.20 mmol) and [Co₂(CO)₈] (68 mg, 0.20 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (108 mg, 0.92 mmol) and a solution of **1i** (30 mg, 0.15 mmol) in CH₃CN (1 mL) were added at 0°C and the resulting solution was stirred for 4 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (50 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 3:1) to afford **2iA** and **2iB** as a 93:7 diastereomeric mixture (34 mg, 74%, colorless oil). **A**: ¹H NMR (200 MHz, CDCl₃): δ = 7.79 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.42 (dt, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.30 (m, 1H; H-3), 7.24 (dt, *J* = 1.2, 7.3 Hz, 1H; Ar), 7.09 (dd, *J* = 1.2, 8.1 Hz, 1H; Ar), 4.29 (dd, *J* = 2.4, 6.9 Hz, 1H; H-5), 2.77 (s, 6H; N(CH₃)₂), 2.63 (m, 1H; H-4), 2.18 (m, 2H; H-1'), 2.03 (m, 1H; H-4), 1.50–1.24 (m, 4H; H-2', H-3'), 0.88 ppm (t, *J* = 7.3 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 203.2, 158.0, 150.3, 146.9, 135.4, 131.6, 125.6, 123.7, 119.3, 63.0, 44.6, 29.5, 24.7, 23.6, 22.3, 13.8 ppm; HRMS (FAB+): calcd for (C₁₇H₂₄NO₂S) [M+H]⁺: 306.1528; found: 306.1532; **B**: ¹H NMR (200 MHz, CDCl₃; significant signals): δ = 4.05 (m, 1H; H-5), 2.68 ppm (s, 6H; N(CH₃)₂).

2-*tert*-Butyl-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-2-cyclopentenone

(3): A solution of 3,3-dimethyl-1-butyne (28 μL, 0.23 mmol) and [Co₂(CO)₈] (79 mg, 0.23 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (108 mg, 0.92 mmol) and a solution of **1i** (30 mg, 0.15 mmol) in CH₃CN (1 mL) were added at RT. After 12 h, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 14 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (100 mg), and stirred for 10 min at RT. After removal

of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 4:1) to afford **3A** (26 mg, 55 %, white solid). M.p. 133–136 °C; ¹H NMR (300 MHz, CDCl₃): δ = 7.80 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.43 (dt, *J* = 1.6, 7.3 Hz, 1H; Ar), 7.30 (t, *J* = 2.8 Hz, 1H; H-3), 7.25 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.10 (dd, *J* = 1.2, 8.1 Hz, 1H; Ar), 4.27 (dd, *J* = 2.4, 6.9 Hz, 1H; H-5), 2.78 (s, 6H; N(CH₃)₂), 2.60 (td, *J* = 2.8, 19.0 Hz, 1H; H-4), 1.99 (ddd, *J* = 2.8, 6.9, 19.4 Hz, 1H; H-4), 1.19 ppm (s, 9H; C(CH₃)₃); ¹³C NMR (75 MHz, CDCl₃): δ = 202.5, 156.6, 154.4, 150.4, 135.5, 131.6, 125.7, 123.7, 119.2, 64.1, 44.6, 32.1, 28.1, 22.8 ppm; HRMS (FAB+): calcd for (C₁₇H₂₄NO₂S) [*M*+H]⁺: 306.1528; found: 306.1536.

2-Benzyl-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-2-cyclopentenone (4): A solution of 3-phenyl-1-propyne (19 μL, 0.15 mmol) and [Co₂(CO)₈] (53 mg, 0.15 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (72 mg, 0.61 mmol) and a solution of **1i** (20 mg, 0.10 mmol) in CH₃CN (1 mL) were added at 0 °C. After 5 h, another 1.5 equivalents of the cobalt complex were added and the resulting solution was stirred for 9 h at 0 °C. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (70 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 4:1) to afford **4A** and **4B** as a 93:7 diastereomeric mixture (20 mg, 58 %, colorless oil). **A**: ¹H NMR (200 MHz, CDCl₃): δ = 7.81 (dd, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.44 (dt, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.34–7.07 (m, 8H; H-3, Ar), 4.36 (dd, *J* = 2.7, 7.0 Hz, 1H; H-5), 3.53 (m, 2H; CH₂), 2.78 (s, 6H; N(CH₃)₂), 2.66 (m, 1H; H-4), 2.01 ppm (m, 1H; H-4); ¹³C NMR (75 MHz, CDCl₃): δ = 202.4, 159.4, 150.4, 146.4, 138.1, 135.4, 131.7, 129.0, 128.5, 126.4, 125.7, 123.8, 119.3, 63.2, 44.6, 31.5, 23.6 ppm; HRMS (FAB+): calcd for (C₂₀H₂₂NO₂S) [*M*+H]⁺: 340.1371; found: 340.1376; **B**: ¹H NMR (200 MHz, CDCl₃; significant signals): δ = 4.11 (m, 1H; H-5), 2.70 ppm (s, 6H; N(CH₃)₂).

5-[2-(*N,N*-Dimethylamino)phenylsulfinyl]-2-*p*-tolyl-2-cyclopentenone (5): A solution of 4-ethynyltoluene (29 μL, 0.23 mmol) and [Co₂(CO)₈] (79 mg, 0.23 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (108 mg, 0.92 mmol) and a solution of **1i** (30 mg, 0.15 mmol) in CH₃CN (1 mL) were added at 0 °C and the resulting solution was stirred for 12 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (50 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 3:1) to afford **5A** and **5B** as a 93:7 diastereomeric mixture (26 mg, 49 %, colorless oil). **A**: ¹H NMR (300 MHz, CDCl₃): δ = 7.85 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.80 (t, *J* = 2.8 Hz, 1H; H-3), 7.62 (d, *J* = 8.1 Hz, 2H; *p*-Tol), 7.46 (dt, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.30 (dd, *J* = 1.2, 7.3 Hz, 1H; Ar), 7.18 (d, *J* = 8.5 Hz, 2H; *p*-Tol), 7.13 (dd, *J* = 1.2, 8.1 Hz, 1H; Ar), 4.48 (dd, *J* = 2.8, 6.7 Hz, 1H; H-5), 2.83 (td, *J* = 3.2, 19.8 Hz, 1H; H-4), 2.81 (s, 6H; N(CH₃)₂), 2.35 (s, 3H; ArCH₃), 2.19 ppm (ddd, *J* = 2.8, 6.9, 19.8 Hz, 1H; H-4); ¹³C NMR (75 MHz, CDCl₃): δ = 201.3, 158.3, 150.4, 143.5, 138.6, 135.4, 131.7, 129.1, 128.1, 126.9, 125.7, 123.8, 119.3, 64.4, 44.6, 23.2, 21.3 ppm; HRMS (EI+): calcd for (C₂₀H₂₁NO₂S) [*M*]⁺: 339.1293; found: 339.1302; **B**: ¹H NMR (300 MHz, CDCl₃; significant signals): δ = 4.24 (dd, *J* = 2.4, 6.1 Hz, 1H; H-5), 2.59 (s, 6H; N(CH₃)₂), 2.32 ppm (s, 3H; ArCH₃).

5-[2-(*N,N*-Dimethylamino)phenylsulfinyl]-2-trimethylsilyl-2-cyclopentenone (6): A solution of trimethylsilylacetylene (43 μL, 0.31 mmol) and [Co₂(CO)₈] (105 mg, 0.31 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (72 mg, 0.62 mmol) and a solution of **1i** (30 mg, 0.15 mmol) in CH₃CN (1 mL) were added at RT and the resulting solution was stirred for 16 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (70 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 4:1) to afford **6A** (29 mg, 59 %, white

solid). M.p. 133–135 °C; ¹H NMR (300 MHz, CDCl₃): δ = 7.82–7.79 (m, 2H; Ar, H-3), 7.44 (dt, *J* = 1.6, 7.3 Hz, 1H; Ar), 7.26 (t, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.10 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 4.28 (dd, *J* = 2.8, 6.9 Hz, 1H; H-5), 2.81 (dt, *J* = 3.2, 19.4 Hz, 1H; H-4), 2.79 (s, 6H; N(CH₃)₂), 2.16 (ddd, *J* = 2.4, 6.9, 19.8 Hz, 1H; H-4), 0.19 ppm (s, 9H; Si(CH₃)₃); ¹³C NMR (75 MHz, CDCl₃): δ = 206.8, 172.6, 150.3, 147.7, 135.7, 131.6, 125.5, 123.7, 119.2, 63.6, 44.5, 27.2, –2.0 ppm; HRMS (EI+): calcd for (C₁₆H₂₃NO₂SiS) [*M*]⁺: 321.1219; found: 321.1221.

5-[2-(*N,N*-Dimethylamino)phenylsulfinyl]-2-(triisopropylsilyloxy)methyl-2-cyclopentenone (7): A solution of 3-(triisopropylsilyloxy)-1-propyne (244 mg, 1.15 mmol) and [Co₂(CO)₈] (394 mg, 1.15 mmol) in CH₃CN (3 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (540 mg, 4.61 mmol) and a solution of **1i** (150 mg, 0.77 mmol) in CH₃CN (2 mL) were added at 0 °C and the resulting solution was stirred for 2 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (250 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 6:1) to afford **7A** and **7B** (207 mg, 62 %, white solid) as a 93:7 diastereomeric mixture. The mixture was triturated with cold hexane to afford diastereomerically pure **7A** (176 mg, 53 % overall yield). **A**: M.p. 87–88 °C; ¹H NMR (300 MHz, CDCl₃): δ = 7.83 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.60 (m, 1H; H-3), 7.45 (dt, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.27 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.11 (dd, *J* = 1.2, 8.1 Hz, 1H; Ar), 4.47 (m, 2H; H-1'), 4.36 (dd, *J* = 2.4, 6.9 Hz, 1H; H-5), 2.78 (s, 6H; N(CH₃)₂), 2.78–2.67 (m, 1H; H-4), 2.17–2.04 (m, 1H; H-4), 1.05 ppm (m, 21H; TIPS); ¹³C NMR (75 MHz, CDCl₃): δ = 201.6, 158.5, 150.4, 147.0, 135.4, 131.7, 125.7, 123.8, 119.3, 64.0, 58.5, 44.6, 23.9, 17.9, 11.8 ppm; HRMS (FAB+): calcd for (C₂₃H₃₈NO₃SiS) [*M*+H]⁺: 436.2342; found: 436.2338; **B**: ¹H NMR (300 MHz, CDCl₃; significant signals): δ = 4.11 (dd, *J* = 4.0, 4.9 Hz, 1H; H-5), 2.68 ppm (s, 6H; N(CH₃)₂).

Compound (5*S*, *SR*)-**7A** was obtained from (*R*)-**1i**: [*α*]_D = +470 (*c* = 0.2, CHCl₃); HPLC: *ee* > 99 % (Daicel Chiralcel OD column, hexane/isopropanol 98:2 at 0.5 mL min^{–1}, λ = 220 nm; *t*_R = 24.2 min (5*S*, *SR*) and 30.1 min (5*R*, *SS*)).

5-[2-(*N,N*-Dimethylamino)phenylsulfinyl]-2-[2-(triisopropylsilyloxy)ethyl]-2-cyclopentenone (8): A solution of 4-(triisopropylsilyloxy)-1-butyne (35 mg, 0.15 mmol) and [Co₂(CO)₈] (53 mg, 0.15 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (72 mg, 0.61 mmol) and a solution of **1i** (20 mg, 0.10 mmol) in CH₃CN (1 mL) were added at 0 °C and the resulting solution was stirred for 7 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (40 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 5:1) to afford **8A** (30 mg, 66 %, white solid). M.p. 82–83 °C; ¹H NMR (200 MHz, CDCl₃): δ = 7.81 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.49 (m, 1H; H-3), 7.44 (dt, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.26 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.11 (dd, *J* = 1.2, 7.7 Hz, 1H; Ar), 4.30 (dd, *J* = 2.8, 6.9 Hz, 1H; H-5), 3.80 (m, 2H; H-2'), 2.78 (s, 6H; N(CH₃)₂), 2.70 (m, 1H; H-4), 2.47 (m, 2H; H-1'), 2.05 (m, 1H; H-4), 1.03 ppm (m, 21H; TIPS); ¹³C NMR (75 MHz, CDCl₃): δ = 203.0, 160.1, 150.4, 143.8, 135.6, 131.6, 125.7, 123.8, 119.3, 63.0, 61.2, 44.6, 28.7, 23.8, 18.0, 11.9 ppm; HRMS (FAB+): calcd for (C₂₄H₄₀NO₃SiS) [*M*+H]⁺: 450.2498; found: 450.2497.

Compound (5*S*, *SR*)-**8A** was obtained from (*R*)-**1i**: [*α*]_D = +290 (*c* = 0.3, CHCl₃); HPLC: *ee* > 99 % (Daicel Chiralcel OD column, hexane/isopropanol 98:2 at 0.5 mL min^{–1}, λ = 230 nm; *t*_R = 39.8 min (5*S*, *SR*) and 53.4 min (5*R*, *SS*)).

2-(3-Bromopropyl)-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-2-cyclopentenone (9): A solution of 5-bromo-1-pentyne (79 mg, 0.54 mmol) and [Co₂(CO)₈] (184 mg, 0.54 mmol) in CH₃CN (3 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (252 mg, 2.15 mmol) and a solution of **1i** (70 mg, 0.36 mmol) in CH₃CN (2 mL) were added at 0 °C and the resulting solution was stirred for 6 h at this temperature. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (120 mg), and stirred for 10 min at RT.

After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 3:1) to afford **9A** (90 mg, 68%, white solid). M.p. 97–99°C; ¹H NMR (300 MHz, CDCl₃): δ = 7.81 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.45 (dt, *J* = 1.6, 7.6 Hz, 1H; Ar), 7.41 (m, 1H; H-3), 7.27 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.11 (dd, *J* = 1.2, 7.7 Hz, 1H; Ar), 4.33 (dd, *J* = 2.4, 6.9 Hz, 1H; H-5), 3.39 (t, *J* = 6.9 Hz, 2H; H-3'), 2.79 (s, 6H; N(CH₃)₂), 2.67 (m, 1H; H-4), 2.40 (m, 2H; H-1'), 2.13–2.00 ppm (m, 3H; H-4, H-2'); ¹³C NMR (50 MHz, CDCl₃): δ = 202.8, 159.2, 150.3, 144.7, 135.2, 131.6, 125.5, 123.7, 119.3, 62.9, 44.5, 32.8, 30.0, 23.7, 23.6 ppm; HRMS (FAB+): calcd for (C₁₆H₂₁NO₂SBr) [M+H]⁺: 370.0476; found: 370.0470.

2,3-Dimethyl-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-2-cyclopentenone (10): A solution of 2-butyne (18 μL, 0.23 mmol) and [Co₂(CO)₈] (79 mg, 0.23 mmol) in CH₃CN (1 mL) was stirred under an argon atmosphere at 0°C. After 1 h, *N*-methylmorpholine *N*-oxide (54 mg, 0.46 mmol) and a solution of **1i** (15 mg, 0.08 mmol) in CH₃CN (0.5 mL) were added at 0°C. The solution was placed in a teflon reaction vessel and allowed to react at 10 Kbar and RT for 48 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (50 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 2:1) to afford **10A** and **10B** as a 92:8 diastereomeric mixture (7 mg, 33%, conversion = 70%, colorless oil). **A**: ¹H NMR (200 MHz, CDCl₃): δ = 7.81 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.43 (dt, *J* = 1.6, 7.3 Hz, 1H; Ar), 7.26 (t, *J* = 7.7 Hz, 1H; Ar), 7.10 (d, *J* = 8.1 Hz, 1H; Ar), 4.28 (dd, *J* = 2.8, 7.3 Hz, 1H; H-5), 2.78 (s, 6H; N(CH₃)₂), 2.65–2.56 (m, 1H; H-4), 2.01 (s, 3H; CH₃), 1.97–1.81 (m, 1H; H-4), 1.72 ppm (s, 3H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 202.6, 171.1, 150.4, 137.0, 135.7, 131.5, 125.7, 123.7, 119.2, 62.8, 44.6, 28.2, 17.3, 8.1 ppm; HRMS (EI+): calcd for (C₁₅H₁₉NO₂S) [M]⁺: 277.1137; found: 277.1150; **B**: ¹H NMR (200 MHz, CDCl₃; significant signals): δ = 4.06 (dd, *J* = 3.2, 4.9 Hz, 1H; H-5), 2.68 ppm (s, 6H; N(CH₃)₂).

2-*n*-Butyl-5-[2-(*N,N*-dimethylamino)phenylsulfinyl]-4-methyl-2-cyclopentenone (12): A solution of 1-hexyne (33 μL, 0.29 mmol) and [Co₂(CO)₈] (98 mg, 0.29 mmol) in CH₃CN (1.5 mL) was stirred under an argon atmosphere at RT. After 1 h, *N*-methylmorpholine *N*-oxide (67 mg, 0.57 mmol) and a solution of (*Z*)-**1i** (20 mg, 0.10 mmol) in CH₃CN (1 mL) were added. The solution was placed in a teflon reaction vessel and allowed to react at 10 Kbar and RT for 48 h. The reaction mixture was diluted with CH₂Cl₂, treated with trimethylamine *N*-oxide (50 mg), and stirred for 10 min at RT. After removal of the solvent, the crude product was dissolved in diethyl ether and filtered through a pad of celite. The combined organic solvents were evaporated and the residue was purified by chromatography (Et₃N-pretreated SiO₂; hexane/ethyl acetate 5:1) to afford *trans*-**12A** (7 mg, 22%, conversion = 60%, colorless oil) and *trans*-**12B** (3 mg, 9%, colorless oil).

By following the same procedure, (*E*)-**1i** (20 mg, 0.10 mmol) afforded *trans*-**12A** (5 mg, 16%, conversion = 45%) and *trans*-**12B** (2 mg, 6%).

trans-**12A**: ¹H NMR (300 MHz, CDCl₃): δ = 7.85 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.45 (dt, *J* = 1.6, 7.3 Hz, 1H; Ar), 7.28 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.13 (m, 1H; H-3), 7.09 (dd, *J* = 1.2, 7.7 Hz, 1H; Ar), 3.92 (d, *J* = 2.8 Hz, 1H; H-5), 2.92 (m, 1H; H-4), 2.78 (s, 6H; N(CH₃)₂), 2.18 (m, 2H; H-1'), 1.50–1.24 (m, 4H; H-2', H-3'), 0.89 (t, *J* = 7.3 Hz, 3H; H-4'), 0.44 ppm (d, *J* = 7.3 Hz, 3H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 203.0, 163.2, 150.6, 145.7, 135.0, 131.6, 125.6, 124.0, 118.9, 69.7, 44.6, 30.7, 29.5, 24.5, 22.4, 18.6, 13.8 ppm; HRMS (EI+): calcd for C₁₈H₂₅NO₂S [M]⁺: 319.1606; found: 319.1620.

trans-**12B**: ¹H NMR (300 MHz, CDCl₃): δ = 7.81 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.49 (dt, *J* = 1.6, 7.3 Hz, 1H; Ar), 7.33 (dt, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.18 (dd, *J* = 1.2, 7.7 Hz, 1H; Ar), 7.16 (m, 1H; H-3), 3.65 (d, *J* = 2.4 Hz, 1H; H-5), 3.37 (m, 1H; H-4), 2.71 (s, 6H; N(CH₃)₂), 2.09 (m, 2H; H-1'), 1.50–1.24 (m, 4H; H-2', H-3'), 1.30 (d, *J* = 7.3 Hz, 3H; CH₃), 0.87 ppm (t, *J* = 7.3 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 199.6, 160.1, 150.8, 146.8, 135.0, 131.8, 126.5, 124.4, 119.6, 69.5, 44.8, 37.1, 29.6, 24.4, 22.4, 19.9, 13.8 ppm; HRMS (EI+): calcd for C₁₈H₂₅NO₂S [M]⁺: 319.1606; found: 319.1617.

2-*n*-Butyl-5-[2-(*N,N*-diethylamino)phenylsulfinyl]-2-cyclopentenone (2j): **A**: ¹H NMR (200 MHz, CDCl₃): δ = 7.82 (dd, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.43 (dt, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.30 (m, 2H; H-3, Ar), 7.12 (dd, *J* = 1.6, 7.5 Hz, 1H; Ar), 4.47 (dd, *J* = 2.7, 7.0 Hz, 1H; H-5), 3.10 (q, *J* = 7.0 Hz, 4H; N(CH₂CH₃)₂), 2.75–2.60 (m, 1H; H-4), 2.17 (m, 2H; H-1'), 2.12–1.94 (m, 1H; H-4), 1.60–1.22 (m, 4H; H-2', H-3'), 1.06 (t, *J* = 7.0 Hz, 6H; N(CH₂CH₃)₂), 0.90 ppm (t, *J* = 7.0 Hz, 3H; H-4'); ¹³C NMR (75 MHz, CDCl₃): δ = 203.1, 157.9, 147.8, 147.1, 137.6, 131.1, 125.9, 124.2, 122.0, 62.9, 47.7, 29.6, 24.7, 23.7, 22.4, 13.8, 12.1 ppm; HRMS (MALDI-TOF): calcd for C₁₉H₂₈NO₂S [M+H]⁺: 334.1835; found: 334.1827; **B**: ¹H NMR (200 MHz, CDCl₃; significant signal): δ = 4.15 ppm (dd, *J* = 2.7, 7.0 Hz, 1H; H-5).

(1*R*,2*S*)-2-(*p*-Tolylsulfonylamino)-1-phenylpropyl (S)-2-(*N,N*-dimethylamino)phenyl sulfinate (16): A solution of *N,N*-dimethyl-2-iodoaniline (1.02 g, 4.13 mmol) and I₂ in dry Et₂O (4 mL) was added to a flask containing Mg (150 mg, 6.19 mmol) at RT under an argon atmosphere. The reaction mixture was heated until complete formation of the magnesium iodide. It was then diluted with dry THF (15 mL) and cooled to –78°C. A solution of **15**^[46] (725 mg, 2.06 mmol) in dry THF (10 mL) was added. The solution was stirred at –78°C for 1 h and saturated aqueous NH₄Cl (20 mL) was then added. The mixture was extracted with ethyl acetate (2 × 15 mL) and the combined organic layers were dried (Na₂SO₄) and evaporated. The crude product was purified by flash chromatography (hexane/ethyl acetate 4:1) to afford **16** (975 mg, 99%, colorless oil). [α]_D = –147 (c = 1.2, CHCl₃); ¹H NMR (200 MHz, CDCl₃): δ = 7.99 (dd, *J* = 1.6, 8.1 Hz, 1H; Ar), 7.83 (d, *J* = 8.1 Hz, 2H; Ar), 7.51 (dt, *J* = 1.6, 7.5 Hz, 1H; Ar), 7.35–7.20 (m, 6H; Ar), 7.09 (m, 3H; Ar), 5.70 (d, *J* = 9.7 Hz, 1H; H-1), 5.11 (d, *J* = 2.7 Hz, 1H; NH), 3.64 (m, 1H; H-2), 2.62 (s, 6H; N(CH₃)₂), 2.43 (s, 3H; ArCH₃), 0.93 ppm (d, *J* = 7.0 Hz, 3H; H-3); ¹³C NMR (75 MHz, CDCl₃): δ = 152.4, 143.2, 138.6, 138.3, 137.5, 133.5, 129.6, 128.2, 127.9, 127.1, 125.9, 125.0, 123.2, 119.7, 84.1, 54.3, 45.1, 21.5, 14.7 ppm; HRMS (FAB+): calcd for (C₂₄H₂₉N₂O₄S₂) [M+H]⁺: 473.1569; found: 473.1573.

(*R*)-2-(*N,N*-Dimethylamino)phenyl vinyl sulfoxide ((*R*)-1i**):** Vinyl magnesium bromide (1 M in THF, 5.24 mL, 5.24 mmol) was added to a solution of sulfinate **16** (825 mg, 1.75 mmol) in THF (15 mL) at –78°C. The solution was stirred at –78°C for 2 h and saturated aqueous NH₄Cl (20 mL) was then added. The mixture was extracted with ethyl acetate (2 × 15 mL) and the combined organic layers were dried (Na₂SO₄) and evaporated. The crude product was purified by flash chromatography (hexane/diethyl ether 1:1) to afford the sulfoxide (*R*)-**1i** (225 mg, 66%, colorless oil). The spectral data were identical to those described for (*S*)-**1i**. [α]_D = +551 (c = 1.0, CHCl₃); HPLC: *ee* > 99% (Daicel Chiralpak AD column, hexane/isopropanol 95:5 at 0.5 mL min^{–1}, λ = 254 nm; *t*_R = 19.5 min (*S*) and 21.4 min (*R*)).

(2*S*,3*S*,5*S*,5*R*)-[5-[2-(*N,N*-Dimethylamino)phenylsulfinyl]-2,3-osmadioxy-2-(triisopropylsilyloxy)methylcyclopentan-1-one]-[*N,N,N',N'*-tetramethylethylenediamine] osmate diester (17): A solution of OsO₄ (71 mg, 0.28 mmol) in CH₂Cl₂ (2 mL) was added to a solution of cyclopentanone (5*S*,5*R*)-**7A** (110 mg, 0.25 mmol) and TMEDA (42 μL, 0.28 mmol) in CH₂Cl₂ (3 mL) cooled to –78°C under an argon atmosphere. After being stirred at –78°C for 1 h, the reaction mixture was treated with saturated aqueous Na₂SO₃ (5 mL) and stirred for 2 h at RT. The mixture was extracted with AcOEt (5 × 10 mL) and the combined organic layers were dried (Na₂SO₄) and evaporated. The crude product was triturated with hexane and filtered to afford **17** (165 mg, 81%, brown solid). M.p. > 140°C (decomp); [α]_D = –99 (c = 0.2, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ = 7.83 (dd, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.39 (dt, *J* = 1.6, 7.7 Hz, 1H; Ar), 7.25 (dt, *J* = 1.2, 7.3 Hz, 1H; Ar), 7.06 (dd, *J* = 1.2, 7.7 Hz, 1H; Ar), 5.03 (dd, *J* = 1.6, 4.4 Hz, 1H; H-3), 4.36 (dd, *J* = 8.9, 11.3 Hz, 1H; H-5), 4.23/4.02 (AB system, *J* = 10.9 Hz, 2H; H-1'), 3.02 (m, 4H; NCH₂CH₂N), 2.84 (s, 3H; N(CH₃)₂), 2.83 (s, 3H; N(CH₃)₂), 2.82 (m, 1H; H-4), 2.80 (s, 3H; N(CH₃)₂), 2.73 (s, 3H; N(CH₃)₂), 2.68 (s, 6H; N(CH₃)₂), 1.76 (m, 1H; H-4), 1.13 ppm (m, 21H; TIPS); ¹³C NMR (75 MHz, CDCl₃): δ = 212.5, 150.3, 136.5, 131.0, 125.7, 123.8, 119.3, 99.7, 88.7, 65.7, 64.3, 64.0, 61.8, 51.7, 51.4, 51.3, 46.0, 44.5, 23.8, 17.9, 11.8 ppm; HRMS (FAB+): calcd for (C₂₉H₅₄N₃O₇Si₃) [M+H]⁺: 808.3067; found: 808.3066.

(2*S*,3*S*)-[2,3-Osmadioxy-2-(triisopropylsilyloxy)methyl-4-cyclopentenone]-[*N,N,N',N'*-tetramethylethylenediamine] osmate diester (18): A solution of sulfoxide **17** (110 mg, 0.14 mmol) in toluene (5 mL) was heated

to reflux for 1 h. The mixture was then cooled to RT, the solvent was evaporated under reduced pressure, and the residue was purified by chromatography (CH_3CN) to afford **18** (64 mg, 72 %, brown solid). M.p. $>200^\circ\text{C}$ (decomp); $[\alpha]_{\text{D}}^{25} = +245$ ($c=0.1$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta=7.61$ (dd, $J=2.0$, 5.7 Hz, 1H; H-3), 6.26 (dd, $J=1.2$, 6.1 Hz, 1H; H-2), 5.58 (dd, $J=1.2$, 2.4 Hz, 1H; H-4), 4.23/4.00 (AB system, $J=8.9$ Hz, 2H; H-1'), 3.05 (m, 4H; $\text{NCH}_2\text{CH}_2\text{N}$), 2.86 (s, 3H; $\text{N}(\text{CH}_3)_2$), 2.84 (s, 3H; $\text{N}(\text{CH}_3)_2$), 2.83 (s, 3H; $\text{N}(\text{CH}_3)_2$), 2.75 (s, 3H; $\text{N}(\text{CH}_3)_2$), 1.02 ppm (m, 21H; TIPS); ^{13}C NMR (50 MHz, CDCl_3): $\delta=206.7$, 162.9, 133.2, 94.1, 64.4, 62.3, 52.1, 51.6, 17.9, 11.9 ppm; HRMS (FAB+): calcd for $(\text{C}_{21}\text{H}_{43}\text{N}_2\text{O}_6\text{SiO}_5) [\text{M}+\text{H}]^+$: 639.2505; found: 639.2487.

(–)-Pentenomycin **1** (**19**):^[48] A solution of cyclopentenone **18** (64 mg, 0.10 mmol) in 2 M HCl (4 mL) was stirred at RT for 6 h. The mixture was washed with CH_2Cl_2 (3×5 mL) and the aqueous layer was concentrated. The residue was purified by chromatography (ethyl acetate/methanol 10:1) to afford (–)-(2*S*,3*S*)-pentenomycin (11 mg, 76 %, colorless oil). $[\alpha]_{\text{D}}^{25} = -32$ ($c=0.2$, EtOH) (natural product:^[48] $[\alpha]_{\text{D}}^{25} = -32$ ($c=0.3$, EtOH)); ^1H NMR (300 MHz, D_2O): $\delta=7.78$ (dd, $J=2.4$, 6.1 Hz, 1H; H-3), 6.39 (dd, $J=1.2$, 6.1 Hz, 1H; H-2), 4.78 (dd, $J=1.2$, 2.8 Hz, 1H; H-4), 3.77/3.71 ppm (AB system, $J=11.3$ Hz, 2H; H-6); ^{13}C NMR (75 MHz, D_2O): $\delta=213.3$, 168.0, 136.9, 79.8, 75.1, 66.8 ppm.

(–)-Pentenomycin **1** triacetate:^[55] Acetic anhydride (101 μL , 1.07 mmol) was added to a solution of pentenomycin (11 mg, 0.08 mmol) in ice-cold pyridine (204 μL , 2.52 mmol) under an argon atmosphere. After 24 h at RT, water (5 mL) was added and the mixture was extracted with ethyl acetate (3×5 mL). The combined organic solvents were evaporated and the residue was purified by chromatography (hexane/ethyl acetate 2:1) to afford (–)-pentenomycin triacetate (13 mg, 63 %, white solid). M.p. 111–112 $^\circ\text{C}$ (literature value:^[55] m.p. 112–114 $^\circ\text{C}$); $[\alpha]_{\text{D}}^{25} = -8$ ($c=0.2$, EtOH) (literature value:^[55] $[\alpha]_{\text{D}}^{25} = -8$ ($c=0.5$, EtOH)); ^1H NMR (300 MHz, CDCl_3): $\delta=7.45$ (dd, $J=2.8$, 6.1 Hz, 1H; H-3), 6.51 (dd, $J=1.6$, 6.5 Hz, 1H; H-2), 5.81 (dd, $J=1.6$, 2.8 Hz, 1H; H-4), 4.36 (s, 2H; H-6), 2.10 (s, 3H; Ac), 2.08 (s, 3H; Ac), 2.05 ppm (s, 3H; Ac); ^{13}C NMR (75 MHz, CDCl_3): $\delta=199.7$, 170.0, 169.5, 168.6, 154.3, 135.8, 77.2, 72.1, 64.3, 20.6, 20.4, 20.1 ppm; HPLC: $ee > 99\%$ (Daicel Chiralpak AD column, hexane/isopropanol 95:5 at 0.5 mL min $^{-1}$, $\lambda=220$ nm; $t_{\text{R}}=33.0$ min (2*S*,3*S*) and 36.5 min (2*R*,3*R*)).

(1*S*,5*S*,5*R*)-5-[2-(*N,N*-Dimethylamino)phenylsulfenyl]-2-(triisopropylsilyloxy)methyl-2-cyclopenten-1-ol: DIBALH (1.0 M in THF, 1.89 mL, 1.89 mmol) was added to a solution of cyclopentenone (5*S*,5*R*)-**7A** (275 mg, 0.63 mmol) in dry THF (10 mL) cooled to -78°C under argon atmosphere. After being stirred at this temperature for 1 h, the mixture was poured into an Erlenmeyer flask containing saturated aqueous potassium–sodium tartrate (25 mL) and AcOEt (25 mL). The two layers were stirred at RT for 30 min and separated. The aqueous layer was extracted with AcOEt (4×15 mL) and the combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (Et_3N -pretreated SiO_2 ; hexane/ethyl acetate 3:1) to afford the alcohol (265 mg, 96 %, colorless oil). $[\alpha]_{\text{D}}^{25} = +250$ ($c=1.0$, CHCl_3); ^1H NMR (200 MHz, CDCl_3): $\delta=7.80$ (d, $J=8.1$ Hz, 1H; Ar), 7.41 (t, $J=7.5$ Hz, 1H; Ar), 7.23 (t, $J=7.5$ Hz, 1H; Ar), 7.10 (d, $J=8.1$ Hz, 1H; Ar), 5.63 (s, 1H; H-3), 5.37 (m, 1H; H-1), 4.44 (m, 2H; H-1'), 3.84 (m, 1H; H-5), 3.47 (d, $J=2.7$ Hz, 1H; OH), 2.75 (s, 6H; $\text{N}(\text{CH}_3)_2$), 2.56–2.42 (m, 1H; H-4), 1.90 (dd, $J=8.6$, 17.8 Hz, 1H; H-4), 1.08 ppm (m, 21H; TIPS); ^{13}C NMR (50 MHz, CDCl_3): $\delta=150.6$, 142.9, 136.1, 131.3, 126.8, 125.5, 123.7, 119.3, 78.6, 66.4, 61.9, 44.5, 26.5, 17.9, 11.7 ppm; HRMS (FAB+): calcd for $\text{C}_{23}\text{H}_{40}\text{NO}_3\text{SiS} [\text{M}+\text{H}]^+$: 438.2498; found: 438.2487.

(3*S*,4*S*,5*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-[2-(*N,N*-dimethylamino)phenylsulfenyl]-2-(triisopropylsilyloxy)methylcyclopentene (**20**): TBDMSCl (456 mg, 3.03 mmol) was added to a solution of the alcohol (265 mg, 0.61 mmol) and imidazole (124 mg, 1.82 mmol) in dry CH_3CN (8 mL) under an argon atmosphere. After 14 h at RT, water (5 mL) was added. The organic layer was separated, the aqueous layer was extracted with AcOEt (2×10 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (Et_3N -pretreated SiO_2 ; hexane/ethyl acetate 8:1) to afford **20** (330 mg, 99 %, white solid). M.p. 78–80 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{25} = +166$ ($c=1.0$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta=7.80$ (dd, $J=1.6$, 7.5 Hz, 1H; Ar), 7.44 (dt, $J=1.6$, 7.5 Hz, 1H; Ar), 7.25 (dt, $J=1.6$, 7.5 Hz, 1H; Ar), 7.15 (dd, $J=1.1$, 7.5 Hz, 1H; Ar), 5.66 (m, 1H; H-5), 5.23 (m, 1H; H-2), 4.26 (m, 2H; H-1'), 3.76 (m, 1H; H-3), 2.69 (s, 6H; $\text{N}(\text{CH}_3)_2$), 2.55–2.41 (m, 1H;

H-4), 1.75–1.60 (m, 1H; H-4), 1.05 (m, 21H; TIPS), 0.95 (s, 9H; *t*BuSi), 0.26 (s, 3H; CH_3Si), 0.17 ppm (s, 3H; CH_3Si); ^{13}C NMR (75 MHz, CDCl_3): $\delta=150.8$, 144.9, 137.4, 131.3, 125.6, 124.5, 124.4, 119.9, 77.6, 67.9, 60.7, 45.0, 25.7, 18.0, 11.9, -4.4 , -4.6 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{29}\text{H}_{54}\text{NO}_3\text{Si}_2\text{S} [\text{M}+\text{H}]^+$: 552.3358; found: 552.3373; HPLC: $ee > 99\%$ (Daicel Chiralcel OD column, hexane/isopropanol 99.3:0.7 at 0.5 mL min $^{-1}$, $\lambda=245$ nm; $t_{\text{R}}=18.3$ min (2*S*,3*S*,5*R*) and 22.2 min (2*R*,3*R*,5*S*)).

3-(*tert*-Butyldimethylsilyloxy)-4-[2-(*N,N*-dimethylamino)phenylsulfenyl]-2-(triisopropylsilyloxy)methyl-1,2-cyclopentanediol (**21** and **21'**): OsO_4 (2.5 % in *t*BuOH, 126 μL , 0.01 mmol) was added to a solution of **20** (230 mg, 0.42 mmol) and NMO (98 mg, 0.83 mmol) in THF/ H_2O 10:1 (22 mL). After being stirred at RT for 7 h, the reaction mixture was treated with saturated aqueous Na_2SO_3 (10 mL) and stirred for 30 min at RT. The organic layer was separated, the aqueous layer was extracted with AcOEt (4×10 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (Et_3N -pretreated SiO_2 ; hexane/ethyl acetate 6:1) to afford (1*R*,2*S*,3*S*,4*S*,5*R*)-**21** and (1*S*,2*S*,3*S*,4*S*,5*R*)-**21'** as an inseparable mixture (90:10) (203 mg, 83 %, colorless oil). (1*R*,2*S*,3*S*,4*S*,5*R*)-**21**: ^1H NMR (300 MHz, CDCl_3): $\delta=7.74$ (dd, $J=1.6$, 7.7 Hz, 1H; Ar), 7.42 (dt, $J=1.6$, 7.7 Hz, 1H; Ar), 7.28 (dt, $J=1.2$, 7.3 Hz, 1H; Ar), 7.14 (dt, $J=1.2$, 7.7 Hz, 1H; Ar), 4.45 (dd, $J=5.3$ Hz, 1H; H-2), 3.96–3.91 (m, 1H; H-3), 3.81 (s, 2H; H-1'), 3.54 (ddd, $J=4.9$, 9.7, 12.1 Hz, 1H; H-5), 3.50 (s, 1H; OH), 3.06 (d, $J=12.9$ Hz, 1H; OH), 2.68 (s, 6H; $\text{N}(\text{CH}_3)_2$), 1.87 (ddd, $J=5.7$, 10.5, 15.8 Hz, 1H; H-4), 1.64 (ddd, $J=3.2$, 4.9, 15.4 Hz, 1H; H-4), 1.04 (m, 21H; TIPS), 0.94 (s, 9H; *t*BuSi), 0.22 (s, 3H; CH_3Si), 0.19 ppm (s, 3H; CH_3Si); ^{13}C NMR (75 MHz, CDCl_3): $\delta=151.0$, 135.5, 131.9, 126.2, 124.8, 120.1, 82.8, 79.6, 72.6, 65.3, 64.7, 45.0, 27.1, 25.7, 18.0, 11.9, -4.4 , -4.9 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{29}\text{H}_{56}\text{NO}_3\text{Si}_2\text{S} [\text{M}+\text{H}]^+$: 586.3412; found: 586.3402; (1*S*,2*S*,3*S*,4*S*,5*R*)-**21'**: ^1H NMR (300 MHz, CDCl_3 ; significant signals): $\delta=4.49$ (d, $J=7.7$ Hz, 1H; H-2), 2.66 ppm (s, 6H; $\text{N}(\text{CH}_3)_2$).

5-(*tert*-Butyldimethylsilyloxy)-1-(triisopropylsilyloxy)methyl-3-cyclopentene-1,2-diol (**22**): A two-necked round-bottomed flask, equipped with a stirrer and a reflux condenser and containing NaHCO_3 (1.15 g, 13.65 mmol), was flame-dried in an argon stream. A solution of the sulfonides **21** and **21'** (200 mg, 0.34 mmol) in toluene (8 mL) was added through a cannula and the mixture was stirred vigorously and heated at reflux for 16 h. The mixture was cooled to RT and filtered over celite. The residue was purified by flash chromatography (Et_3N -pretreated SiO_2 ; hexane/ethyl acetate 10:1) to afford (1*R*,2*R*,5*R*)-**22** (111 mg, 78 %, colorless oil) and (1*S*,2*S*,5*R*)-**22'** (11 mg, 8 %, colorless oil). (1*R*,2*R*,5*R*)-**22**: $[\alpha]_{\text{D}}^{25} = -84$ ($c=1.0$, CHCl_3); ^1H NMR (200 MHz, CDCl_3): $\delta=5.93$ (m, 1H; H-3), 5.86 (m, 1H; H-4), 4.69 (s, 1H; H-5), 4.63 (m, 1H; H-2), 3.97/3.74 (AB system, $J=9.7$ Hz, 2H; H-1'), 3.22 (s, 1H; OH), 2.56 (d, $J=5.4$ Hz, 1H; OH), 1.09 (m, 21H; TIPS), 0.87 (s, 9H; *t*BuSi), 0.08 (s, 3H; CH_3Si), 0.06 ppm (s, 3H; CH_3Si); ^{13}C NMR (50 MHz, CDCl_3): $\delta=135.8$, 134.5, 80.9, 79.9, 77.3, 65.5, 25.8, 17.9, 11.9, -4.6 , -4.9 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{21}\text{H}_{44}\text{O}_4\text{Si}_2\text{Na} [\text{M}+\text{Na}]^+$: 439.2670; found: 439.2674; (1*S*,2*S*,5*R*)-**22'**: $[\alpha]_{\text{D}}^{25} = +3$ ($c=1.0$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta=5.88$ (dt, $J=1.6$, 6.1 Hz, 1H; H-3), 5.65 (dt, $J=1.6$, 6.1 Hz, 1H; H-4), 4.78 (c, $J=1.6$ Hz, 1H; H-5), 4.55 (dq, $J=1.6$, 10.1 Hz, 1H; H-2), 3.78/3.60 (AB system, $J=9.7$ Hz, 2H; H-1'), 3.56 (s, 1H; OH), 2.89 (d, $J=9.7$ Hz, 1H; OH), 1.06 (m, 21H; TIPS), 0.92 (s, 9H; *t*BuSi), 0.15 (s, 3H; CH_3Si), 0.14 ppm (s, 3H; CH_3Si); ^{13}C NMR (75 MHz, CDCl_3): $\delta=135.9$, 132.0, 79.4, 75.2, 74.8, 63.3, 25.7, 18.0, 12.0, -4.4 , -4.8 ppm.

(1*S*,2*R*,3*R*,4*R*,5*S*)-4-(*tert*-Butyldimethylsilyloxy)-3-(triisopropylsilyloxy)-methyl-6-oxabicyclo[3.1.0]hexane-2,3-diol (**23**): A solution of MCPBA (70 %, 222 mg, 0.90 mmol) in CH_2Cl_2 (10 mL) was added to a solution of **22** (125 mg, 0.30 mmol) in CH_2Cl_2 (5 mL). After 3 days at RT, saturated aqueous Na_2SO_3 (5 mL) was added, followed by saturated aqueous NaHCO_3 (20 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 4:1) to afford **23** (120 mg, 92 %, colorless oil). $[\alpha]_{\text{D}}^{25} = -49$ ($c=1.0$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta=4.25$ (m, 1H; H-2), 4.07 (s, 1H; H-4), 3.85/3.78 (AB system, $J=9.7$ Hz, 2H; H-1'), 3.66 (m, 1H; H-1), 3.37 (d, $J=2.7$ Hz, 1H; H-5), 2.96 (brs, 1H; OH), 2.73 (brs, 1H; OH), 1.05 (m, 21H; TIPS), 0.87 (s, 9H; *t*BuSi), 0.10 (s, 3H; CH_3Si), 0.08 ppm (s, 3H; CH_3Si); ^{13}C NMR

(75 MHz, CDCl_3): δ = 78.0, 76.2, 74.8, 66.7, 58.8, 56.2, 25.6, 17.9, 11.8, –4.8, –5.2 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{21}\text{H}_{44}\text{O}_5\text{NaSi}_2$ [$M+\text{Na}$] $^+$: 445.2619; found: 445.2612.

(1R,2R,3S,4S,5R)-3-Azido-5-(tert-butyldimethylsilyloxy)-1-(triisopropylsilyloxy)methyl-1,2,4-cyclopentanetriol (24): A solution of epoxide **23** (70 mg, 0.16 mmol) in DMF (7 mL) was added to a mixture of NH_4Cl (104 mg, 1.94 mmol) and NaN_3 (126 mg, 1.94 mmol) in DMF (7 mL) under an argon atmosphere. The reaction mixture was stirred at 100 °C for 20 h and water (10 mL) was then added. The organic layer was separated and the aqueous layer was extracted with AcOEt (2×10 mL). The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (hexane/ethyl acetate 10:1) to afford **24** (58 mg, 76%, white solid). M.p. 49–50 °C; $[\alpha]_D^{25}$ = –12 (c = 1.0, CHCl_3); ^1H NMR (300 MHz, CDCl_3): δ = 4.01 (dd, J = 4.5, 7.7 Hz, 1H; H-2), 3.87 (m, 1H; H-5), 3.86/3.82 (AB system, J = 10.1 Hz, 2H; H-1'), 3.71 (m, 1H; H-3), 3.67 (m, 1H; H-4), 3.35 (s, 1H; OH), 2.67 (d, J = 4.5 Hz, 1H; OH), 2.46 (d, J = 7.7 Hz, 1H; OH), 1.08 (m, 21H; TIPS), 0.88 (s, 9H; $t\text{BuSi}$), 0.11 (s, 3H; CH_3Si), 0.09 ppm (s, 3H; CH_3Si); ^{13}C NMR (75 MHz, CDCl_3): δ = 80.9, 80.6, 78.8, 78.0, 71.5, 66.9, 25.6, 17.9, 11.7, –4.6, –5.1 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{27}\text{H}_{48}\text{N}_3\text{O}_5\text{Si}_2\text{Na}$ [$M+\text{Na}$] $^+$: 498.2790; found: 498.2805.

(1R,2R,3S,4S,5R)-3-Amino-5-(tert-butyldimethylsilyloxy)-1-(triisopropylsilyloxy)methyl-1,2,4-cyclopentanetriol: 10% Pd/C (7 mg) was added to a solution of azide **24** (35 mg, 0.07 mmol) in MeOH (3 mL) and the resulting suspension was stirred under an H_2 atmosphere for 1 h. The solution was filtered over celite, the filter cake was rinsed with methanol, and the combined filtrate was evaporated to afford the amine (33 mg, 99%, colorless oil). $[\alpha]_D^{25}$ = +1 (c = 0.8, CH_3OH); ^1H NMR (300 MHz, CD_3OD): δ = 3.82 (d, J = 7.3 Hz, 1H; H-5), 3.77 (s, 2H; H-1'), 3.67 (d, J = 8.5 Hz, 1H; H-2), 3.39 (dd, J = 7.3, 8.3 Hz, 1H; H-4), 2.85 (t, J = 8.9 Hz, 1H; H-3), 1.12 (m, 21H; TIPS), 0.92 (s, 9H; $t\text{BuSi}$), 0.13 ppm (s, 6H; CH_3Si); ^{13}C NMR (75 MHz, CD_3OD): δ = 84.9, 80.6, 78.0, 77.8, 68.9, 61.7, 26.5, 18.6, 13.2, –4.2, –4.6 ppm; HRMS (MALDI-TOF): calcd for $\text{C}_{27}\text{H}_{48}\text{NO}_5\text{Si}_2$ [$M+\text{H}$] $^+$: 450.3066; found: 450.3074.

(1R,2R,3S,4S,5R)-4-Amino-1-hydroxymethyl-1,2,3,5-cyclopentanetetrol hydrochloride (25):^[53] A solution of the amine (35 mg, 0.07 mmol) in MeOH/HCl (1 mL) was stirred at RT for 4 h. The solvent was evaporated and the resulting residue was washed with dry diethyl ether to afford **25** as a highly hygroscopic white solid (14 mg, 97%). $[\alpha]_D^{25}$ = –6 (c = 0.3, CH_3OH) (literature value for the enantiomer:^[53] $[\alpha]_D^{25}$ = +6.2 (c = 1.2, CH_3OH)); ^1H NMR (300 MHz, CD_3OD): δ = 3.94 (d, J = 9.7 Hz, 1H; H-5), 3.81 (d, J = 6.1 Hz, 1H; H-2), 3.71 (dd, J = 6.1, 8.9 Hz, 1H; H-3), 3.67/3.56 (AB system, J = 10.9 Hz, 2H; H-1'), 3.22 ppm (t, J = 9.3 Hz, 1H; H-4); ^{13}C NMR (75 MHz, CD_3OD): δ = 84.1, 78.2, 77.5, 72.7, 64.7, 60.9 ppm.

Acknowledgment

Financial support of this work by the McYT (Ministerio de Ciencia y Tecnología) is gratefully acknowledged (Projects: BQU2000-0226 and BQU2003-0508). M.R.R. thanks the MEC (Ministerio de Educación) for a predoctoral fellowship. We also thank J. C. de la Rosa for some experimental work, the Centro de Computación Científica (Universidad Autónoma de Madrid) for computation time, and Dr. M. Alcamí (Universidad Autónoma de Madrid) for helpful discussions.

- [1] a) *Comprehensive Organometallic Chemistry II* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Elsevier, New York, **1995**; b) *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**; c) *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**.
- [2] For reviews on PK reactions, see: a) P. L. Pauson, *Tetrahedron* **1985**, *41*, 5855–5860; b) N. E. Schore, *Chem. Rev.* **1988**, *88*, 1081–1119; c) N. E. Schore, *Org. React.* **1991**, *40*, 1–90; d) N. E. Schore in *Comprehensive Organic Synthesis*, Vol. 5 (Eds.: B. M. Trost, I. Fleming), Pergamon, Oxford, **1991**, pp. 1037–1064; e) N. E. Schore in *Comprehensive Organometallic Chemistry II*, Vol. 12 (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson), Elsevier, New York, **1995**, pp. 703–739; f) H.-W. Frühauf, *Chem. Rev.* **1997**, *97*, 523–596; g) O. Geis, H.-

- G. Schmalz, *Angew. Chem.* **1998**, *110*, 955–958; *Angew. Chem. Int. Ed.* **1998**, *37*, 911–914; h) N. Jeong in *Transition Metals for Organic Synthesis* (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, pp. 560–577; i) Y. K. Chung, *Coord. Chem. Rev.* **1999**, *188*, 297–341; j) A. J. Fletcher, S. D. R. Christie, *J. Chem. Soc. Perkin Trans. 1* **2000**, 1657–1668; k) K. M. Brummond, J. L. Kent, *Tetrahedron* **2000**, *56*, 3263–3283; l) T. Sugihara, M. Yamaguchi, M. Nishizawa, *Chem. Eur. J.* **2001**, *7*, 3315–3318; m) B. E. Hanson, *Comments Inorg. Chem.* **2002**, *23*, 289–318; n) J. Blanco-Urgoiti, L. Añorbe, L. Pérez-Serrano, G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev.* **2004**, *33*, 32–42.
- [3] a) I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, *J. Chem. Soc. Chem. Commun.* **1971**, 36; b) I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, *J. Chem. Soc. Perkin Trans. 1* **1973**, 975–977; c) I. U. Khand, G. R. Knox, P. L. Pauson, W. E. Watts, M. I. Foreman, *J. Chem. Soc. Perkin Trans. 1* **1973**, 977–981.
- [4] a) P. S. Shambayati, W. E. Crowe, S. L. Schreiber, *Tetrahedron Lett.* **1990**, *31*, 5289–5292; b) N. Jeong, Y. K. Chung, B. Y. Lee, S. H. Lee, S.-E. Yoo, *Synlett* **1991**, 204–207.
- [5] T. Sugihara, M. Yamada, H. Ban, M. Yamaguchi, C. Kaneko, *Angew. Chem.* **1997**, *109*, 2884–2886; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2801–2804.
- [6] T. Sugihara, M. Yamada, M. Yamaguchi, M. Nishizawa, *Synlett* **1999**, 771–773.
- [7] a) W. A. Smit, A. S. Gybin, A. S. Shashkov, Y. T. Strychkov, L. G. Kyzmina, G. S. Mikaelian, R. Caple, E. D. Swanson, *Tetrahedron Lett.* **1986**, *27*, 1241–1244. b) S. O. Simonian, W. A. Smit, A. S. Gybin, A. S. Shashkov, G. S. Mikaelian, V. A. Tarasov, I. I. Ibragimov, R. Caple, D. E. Froen, *Tetrahedron Lett.* **1986**, *27*, 1245–1248.
- [8] a) L. Pérez-Serrano, L. Casarrubios, G. Domínguez, J. Pérez-Castells, *Org. Lett.* **1999**, *1*, 1187–1188; b) L. Pérez-Serrano, J. Blanco-Urgoiti, L. Casarrubios, G. Domínguez, J. Pérez-Castells, *J. Org. Chem.* **2000**, *65*, 3513–3519.
- [9] For a review on catalytic PK reactions, see: S. E. Gibson, A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844–1854; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800–1810.
- [10] For recent references, see: a) N. Jeong, B. K. Sung, J. S. Kim, S. B. Park, S. D. Seo, J. Y. Shin, K. Y. In, Y. K. Choi, *Pure Appl. Chem.* **2002**, *74*, 85–91; b) T. Shibata, N. Toshida, K. Takagi, *J. Org. Chem.* **2002**, *67*, 7446–7450; c) P. A. Wender, N. M. Deschamps, G. G. Gamber, *Angew. Chem.* **2003**, *115*, 1897–1901; *Angew. Chem. Int. Ed.* **2003**, *42*, 1853–1857; d) K. Fujii, T. Morimoto, K. Tsutsumi, K. Kakiuchi, *Angew. Chem.* **2003**, *115*, 2511–2513; *Angew. Chem. Int. Ed.* **2003**, *42*, 2409–2411; e) W. H. Suh, M. Choi, S. I. Lee, Y. K. Chung, *Synthesis* **2003**, 2169–2172.
- [11] For recent references, see: a) T. Morimoto, N. Chatani, Y. Fukumoto, S. Murai, *J. Org. Chem.* **1997**, *62*, 3762–3765; b) T. Kondo, N. Suzuki, T. Okada, T. Mitsudo, *J. Am. Chem. Soc.* **1997**, *119*, 6187–6188; c) K. Itami, K. Mitsudo, J. Yoshida, *Angew. Chem.* **2002**, *114*, 3631–3634; *Angew. Chem. Int. Ed.* **2002**, *41*, 3481–3484.
- [12] For recent references, see: a) F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1996**, *118*, 11688–11689; b) S. J. Sturla, S. L. Buchwald, *J. Org. Chem.* **1999**, *64*, 5547–5550; c) F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 7026–7033; d) S. J. Sturla, S. L. Buchwald, *Organometallics* **2002**, *21*, 739–748.
- [13] For recent references, see: a) T. Shibata, K. Takagi, *J. Am. Chem. Soc.* **2000**, *122*, 9852–9853; b) T. Shibata, S. Kadowaki, M. Hirase, K. Takagi, *Synlett* **2003**, 573–575; c) H. Cao, S. R. Mundla, J. M. Cook, *Tetrahedron Lett.* **2003**, *44*, 6165–6168.
- [14] For recent references, see: a) J. Cassayre, F. Gagosz, S. Z. Zard, *Angew. Chem.* **2002**, *114*, 1861–1863; *Angew. Chem. Int. Ed.* **2002**, *41*, 1783–1785; b) I. Nomura, C. Mukai, *J. Org. Chem.* **2004**, *69*, 1803–1812; c) B. Jiang, M. Xu, *Angew. Chem.* **2004**, *116*, 2597–2600; *Angew. Chem. Int. Ed.* **2004**, *43*, 2543–2546.
- [15] a) M. Yamanaka, E. Nakamura, *J. Am. Chem. Soc.* **2001**, *123*, 1703–1708; b) F. Robert, A. Milet, Y. Gimbert, D. Konya, A. E. Greene, *J. Am. Chem. Soc.* **2001**, *123*, 5396–5400; c) T. J. M. de Bruin, A. Milet, F. Robert, Y. Gimbert, A. E. Greene, *J. Am. Chem. Soc.* **2001**, *123*, 7184–7185; d) M. A. Pericàs, J. Balsells, J. Castro, I. Marchueta, A. Moyano, A. Riera, J. Vázquez, X. Verdager, *Pure Appl. Chem.* **2002**, *74*, 167–174; e) T. J. M. de Bruin, A. Milet, A. E. Greene, Y. Gimbert, *J. Org. Chem.* **2004**, *69*, 1075–1080.

- [16] For specific reviews on asymmetric PK reactions, see: a) S. T. Ingate, J. Marco-Contelles, *Org. Prep. Proced. Int.* **1998**, *30*, 121–143; b) S. L. Buchwald, F. A. Hicks in *Comprehensive Asymmetric Catalysis*, Vol. 2 (Eds.: E. N. Jacobsen, A. Pfaltz, H. Yamamoto), Springer-Verlag, Berlin, **1999**, pp. 491–510.
- [17] I. U. Khand, P. L. Pauson, *J. Chem. Res. Synop.* **1977**, 9.
- [18] For recent references, see: a) S. Fonquerna, A. Moyano, M. A. Pericàs, A. Riera, *J. Am. Chem. Soc.* **1997**, *119*, 10225–10226; b) E. Montenegro, M. Poch, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron Lett.* **1998**, *39*, 335–338; c) X. Verdager, J. Vázquez, V. Bernardes-Génisson, A. E. Greene, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **1998**, *63*, 7037–7052; d) E. Montenegro, A. Moyano, M. A. Pericàs, A. Riera, A. Alvarez-Larena, J. F. Piniella, *Tetrahedron: Asymmetry* **1999**, *10*, 457–471; e) J. Balsells, A. Moyano, M. A. Pericàs, A. Riera, *Org. Lett.* **1999**, *1*, 1981–1984; f) S. Fonquerna, R. Rios, A. Moyano, M. A. Pericàs, A. Riera, *Eur. J. Org. Chem.* **1999**, 3459–3478; g) J. Balsells, J. Vázquez, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2000**, *65*, 7291–7302; h) J. Vázquez, S. Fonquerna, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron: Asymmetry* **2001**, *12*, 1837–1850; i) I. Marchueña, E. Montenegro, D. Panov, M. Poch, X. Verdager, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2001**, *66*, 6400–6409. See also: j) K. Hiroi, T. Watanabe, *Tetrahedron Lett.* **2000**, *41*, 3935–3939; k) L. Shen, R. P. Hsung, *Tetrahedron Lett.* **2003**, *44*, 9353–9358.
- [19] a) J. Castro, A. Moyano, M. A. Pericàs, A. Riera, A. Alvarez-Larena, J. F. Piniella, *J. Organomet. Chem.* **1999**, *585*, 53–58; b) J. Castro, A. Moyano, M. A. Pericàs, A. Riera, A. Alvarez-Larena, J. F. Piniella, *J. Am. Chem. Soc.* **2000**, *122*, 7944–7952; c) X. Verdager, A. Moyano, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahía, *J. Am. Chem. Soc.* **2000**, *122*, 10242–10243; d) X. Verdager, M. A. Pericàs, A. Riera, M. A. Maestro, J. Mahía, *Organometallics* **2003**, *22*, 1868–1877. See also: e) P. Bladon, P. L. Pauson, H. Brunner, R. Eder, *J. Organomet. Chem.* **1988**, *355*, 449–454; f) H. Brunner, A. Niedernhuber, *Tetrahedron: Asymmetry* **1990**, *1*, 711–714; g) H.-J. Park, B. Y. Lee, Y. K. Kang, Y. K. Chung, *Organometallics* **1995**, *14*, 3104–3107; h) A. M. Hay, W. J. Kerr, G. G. Kirk, D. Middlemiss, *Organometallics* **1995**, *14*, 4986–4988; i) Y. Gimbert, F. Robert, A. Durif, M.-T. Averbuch, N. Kann, A. E. Greene, *J. Org. Chem.* **1999**, *64*, 3492–3497; j) S. E. Gibson, S. E. Lewis, J. A. Loch, J. W. Steed, M. J. Tozer, *Organometallics* **2003**, *22*, 5382–5384.
- [20] a) J. Adrio, J. C. Carretero, *J. Am. Chem. Soc.* **1999**, *121*, 7411–7412; b) J. C. Carretero, J. Adrio, *Synthesis* **2001**, 1888–1896.
- [21] a) M. E. Krafft, *J. Am. Chem. Soc.* **1988**, *110*, 968–970; b) M. E. Krafft, C. A. Juliano, I. L. Scott, C. Wright, M. D. McEachin, *J. Am. Chem. Soc.* **1991**, *113*, 1693–1703.
- [22] Previous communication: M. Rodríguez Rivero, J. C. de la Rosa, J. C. Carretero, *J. Am. Chem. Soc.* **2003**, *125*, 14992–14993.
- [23] a) I. U. Khand, P. L. Pauson, *J. Chem. Soc. Chem. Commun.* **1974**, 379; b) I. U. Khand, P. L. Pauson, *Heterocycles* **1978**, *11*, 59–67.
- [24] M. Ahmar, F. Antras, B. Cazes, *Tetrahedron Lett.* **1999**, *40*, 5503–5506.
- [25] a) J. Adrio, M. Rodríguez Rivero, J. C. Carretero, *Angew. Chem.* **2000**, *112*, 3028–3031; *Angew. Chem. Int. Ed.* **2000**, *39*, 2906–2909; b) J. Adrio, M. Rodríguez Rivero, J. C. Carretero, *Chem. Eur. J.* **2001**, *7*, 2435–2448.
- [26] For a review on PK reactions of electron-poor alkenes, see: M. Rodríguez Rivero, J. Adrio, J. C. Carretero, *Eur. J. Org. Chem.* **2002**, 2881–2889.
- [27] A similar outcome was observed with trimethylamine *N*-oxide (TMANO) or TMANO/molecular sieves as promoters.
- [28] The best results were obtained by using freshly purified samples of commercially available monohydrated NMO (NMO·H₂O). This prior purification is readily performed by precipitation from acetone. The use of dry acetonitrile had a deleterious effect on the reaction.
- [29] a) M. E. Krafft, *Tetrahedron Lett.* **1988**, *29*, 999–1002; b) N. Jeong, Y. K. Chung, B. Y. Lee, S. H. Lee, S.-E. Yoo, *Synlett* **1991**, 204–206.
- [30] For electronic effects on alkene regioselectivity in the PK reaction, see also: a) S. E. MacWhorter, V. Sampath, M. M. Olmstead, N. E. Schore, *J. Org. Chem.* **1988**, *53*, 203–205; b) P. Mayo, W. Tam, *Tetrahedron* **2001**, *57*, 5943–5952.
- [31] For precedents regarding the isolation and PK reactions of sulfur-coordinated dicobaltcarbonyl alkyne complexes, see refs. [18b,c,i]. See also: M. E. Krafft, I. L. Scott, R. H. Romero, S. Feibelmann, C. E. Van Pelt, *J. Am. Chem. Soc.* **1993**, *115*, 7199–7207.
- [32] We obtained essentially the same results regardless of the particular acid/base protocol used in the isolation of the reaction mixture from the basic substrates **1h** and **1i**. This outcome suggests the formation of strong nitrogen–cobalt coordinated side products.
- [33] a) N. Díaz Buezo, I. Alonso, J. C. Carretero, *J. Am. Chem. Soc.* **1998**, *120*, 7129–7130; b) N. Díaz Buezo, J. C. de la Rosa, J. Priego, I. Alonso, J. C. Carretero, *Chem. Eur. J.* **2001**, *7*, 3890–3900.
- [34] For a review on the use of high pressure in transition-metal-mediated reactions, see: O. Reiser in *High Pressure Chemistry* (Eds.: R. Van Eldik, F.-G. Klaerner), Wiley-VCH, Weinheim, **2002**, pp. 223–238.
- [35] A. B. Bueno, M. C. Carreño, J. L. García Ruano, R. Gómez Arrayás, M. M. Zarzuelo, *J. Org. Chem.* **1997**, *62*, 2139–2143.
- [36] a) J. J. P. Stewart, *J. Comput. Chem.* **1989**, *10*, 209–220; b) J. J. P. Stewart, *J. Comput. Chem.* **1989**, *10*, 221–264.
- [37] *HyperChem 6.02*; Hypercube Inc., Gainesville, FL, **1999**.
- [38] a) C. Lee, W. Yang, R. G. Parr, *Phys. Rev. B* **1988**, *37*, 785–789; b) A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 1372–1377.
- [39] a) R. Ditchfield, W. J. Hehre, J. A. Pople, *J. Chem. Phys.* **1971**, *54*, 724–728; b) W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257–2261; c) P. C. Hariharan, J. A. Pople, *Theor. Chim. Acta* **1973**, *28*, 213–223.
- [40] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03* (revision B.03), Gaussian Inc., Pittsburgh, PA, **2003**.
- [41] A. A. Ahmed, T. Gati, T. A. Hussein, A. T. Ali, O. A. Tzakou, M. A. Couladis, T. J. Mabry, G. Toth, *Tetrahedron* **2003**, *59*, 3729–3735.
- [42] P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270–283.
- [43] a) W. J. Hehre, R. F. Stewart, J. A. Pople, *J. Chem. Phys.* **1969**, *51*, 2657–2664; b) J. B. Collins, P. R. Schleyer, J. S. Binkley, J. A. Pople, *J. Chem. Phys.* **1976**, *64*, 5142–5151.
- [44] A shorter Co–N distance was found for the homonuclear complex than for binuclear in a model with a three-bond distance between the C–C double bond and the amino moiety (see ref. [15a]).
- [45] F. Rebiere, O. Samuel, L. Ricard, H. B. Kagan, *J. Org. Chem.* **1991**, *56*, 5991–5999.
- [46] Z. Han, D. Krishnamurthy, P. Grover, H. S. Wilkinson, Q. K. Fang, X. Su, Z.-H. Lu, D. Magiera, C. H. Senanayake, *Angew. Chem.* **2003**, *115*, 2078–2081; *Angew. Chem. Int. Ed.* **2003**, *42*, 2032–2035.
- [47] K. Umino, T. Furama, N. Matzuzawa, Y. Awataguchi, Y. Ito, T. Okuda, *J. Antibiot.* **1973**, *26*, 506–512.
- [48] K. Umino, N. Takeda, Y. Ito, T. Okuda, *Chem. Pharm. Bull.* **1974**, *22*, 1233–1238.
- [49] For asymmetric syntheses of pentenomycin, see: a) J. P. H. Verhagen, A. C. Richardson, R. S. Bhatt, B. D. Grant, W. L. Fitch, J. G. Moffatt, *Pure Appl. Chem.* **1978**, *50*, 1363–1383; b) M. Hetmanski, N. Purcell, R. J. Stoodley, *J. Chem. Soc. Perkin Trans. 1* **1984**, 2089–2096; c) T. Sugahara, K. Ogasawara, *Synlett* **1999**, 419–420; d) M. Seepersaud, Y. Al-Abed, *Tetrahedron Lett.* **2000**, *41*, 4291–4293; e) J. K. Gallos, K. C. Damianou, C. C. Dellios, *Tetrahedron Lett.* **2001**, *42*, 5769–5771.

- [50] As a second example of the lack of racemization at the sulfur center in the asymmetric version of this PK reaction, adduct (5*S*,*SR*)-**8A** was obtained in >99% *ee* from enantiopure vinylsulfoxide (*R*)-**1i**.
- [51] T. J. Donohoe, K. Blades, P. R. Moore, M. J. Waring, J. J. G. Winter, M. Helliwell, N. J. Newcombe, G. Stemp, *J. Org. Chem.* **2002**, 67, 7946–7956.
- [52] a) J.-M. Renoux, M. Rohmer, *Eur. J. Biochem.* **1985**, 151, 405–410; b) S. Neunlist, P. Bissere, M. Rohmer, *Eur. J. Biochem.* **1988**, 171, 245–252; c) D. Herrmann, P. Bissere, J. Connan, M. Rohmer, *Tetrahedron Lett.* **1996**, 37, 1791–1794.
- [53] J. L. Chiara, I. Storch de Gracia, A. Bastida, *Chem. Commun.* **2003**, 1874–1875.
- [54] The stereochemistry of **22** and **22'** was confirmed by NOESY experiments.
- [55] M. Hetmanski, N. Purcell, R. J. Stoodley, *J. Chem. Soc. Perkin Trans. 1* **1984**, 2089–2096.

Received: May 6, 2004
Published online: September 23, 2004