[22] a) W. E. Crowe, J. P. Mitchell, V. C. Gibson, R. R. Schrock, *Macromolecules* **1990**, *23*, 3534 – 3536; b) V. C. Gibson, T. Okada, *Macromolecules* **2000**, *33*, 655 – 656.
[23] The 1,5-dimethyl-1,5-cyclooctadiene (**6**) employed in this study contained 1,6-dimethyl-1,5-cyclooctadiene (20%) as an inseparable mixture.
[24] The ethylene – propylene copolymer obtained was not "perfectly" alternating because of the impurity in 1,5-dimethyl-1,5-cyclooctadiene (**6**).[25] We believe that if pure **6** was polymerized, the poly(isoprene) obtained would have perfectly alternating head-to-tail microstructure, since trisubstituted alkylidenes have not been observed to form. Thus, a perfectly alternating ethylene – propylene would be obtained after hydrogenation.
[25] Z. Wu, R. H. Grubbs, *Macromolecules* **1995**, *28*, 3502 – 3508.

The Phenylsulfonyl Group as an *endo* Stereochemical Controller in Intramolecular Pauson – Khand Reactions of 3-Oxygenated 1,6-Enynes**

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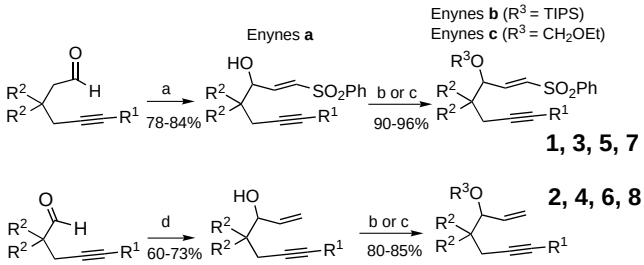
Dedicated to Prof. José Barluenga on the occasion of his 60th birthday

The intramolecular Pauson – Khand (PK) reaction of enynes has become one of the most powerful tools for the construction of cyclopentenone-fused bicyclic compounds. In particular, due to the reliability and efficiency of the cyclization of 1,6-enynes, this reaction has been widely applied to the synthesis of complex products with bicyclo[3.3.0]octane skeletons.[1] In the case of 3-substituted 1,6-enynes, it is well known since the pioneering work of Magnus et al.[2] that the reaction occurs with moderate to high *exo* stereoselectivity[3] (the substituent at the allylic position on the starting enyne ends up on the less sterically crowded *exo* face of the bicyclic product).

Although it is generally assumed that electron-poor alkenes are unsuitable substrates for PK reactions,[1, 4] we recently reported that certain 1-sulfinyl-1,6-enynes undergo intramolecular PK cyclizations in acceptable yields and in a highly stereoselective manner.[5] Encouraged by these results, we envisioned the use of other electron-poor sulfur-substituted olefins, such as vinyl sulfones.[6] Here we report that the readily available racemic or enantiopure 1,6-enynes with γ-oxygenated α,β-unsaturated phenylsulfone structures are not only excellent substrates in intramolecular PK reactions, but also that cyclization takes place with a reversal selectivity, that is, *endo* instead of *exo* selectivity.[7]

Following our usual method of synthesis of (*E*)-γ-hydroxy-α,β-unsaturated phenyl sulfones,[8] several differently substituted 1-phenylsulfonyl-3-hydroxy-1,6-enynes (substrates **1a**, **3a**, **5a**, and **7a**[9]) were prepared in one step by the piperidine-promoted condensation of the corresponding aldehydes with phenylsulfonyl *p*-tolylsulfinylmethane in acetonitrile at 0 °C (78 – 84% yield, Scheme 1). Next, to study the effect of



Scheme 1. Synthesis of the starting 1,6-enynes **1** – **8**. a) $PhSO_2CH_2SOTol$, piperidine, CH_3CN, 0 °C; b) TIPSOTf, 2,6-lutidine, CH_2Cl_2, RT; c) $ClCH_2OEt$, DIPEA, CH_2Cl_2, RT; d) vinylmagnesium bromide, THF, – 78 °C. TIPSOTf = triisopropylsilyl trifluoromethanesulfonate; DIPEA = *N*,*N*-diisopropylethylamine.

substitution at the γ-position, the hydroxy group of these enynes was protected as the triisopropylsilyl (TIPS) ether (substrates **b**) and ethoxymethyl ketal derivatives (substrates **c**). To evaluate precisely the effect of the sulfonyl group on the reactivity and stereoselectivity of the PK reaction, the corresponding 1-unsubstituted 3-oxygenated 1,6-enynes were readily prepared by addition of vinylmagnesium bromide to the appropriate aldehyde (synthesis of alcohols **2a**, **4a**, **6a**, and **8a**[9]) followed by protection of the hydroxy group (substrates **2b** – **c**, **4b** – **c**, **6b** – **c**, and **8b** – **c**) (Scheme 1).

Table 1 summarizes the results of the PK cyclizations of enynes **1** – **8** under the usual conditions with an amine *N*-oxide promoter:[10] initial formation of the alkyne dicobalt complex by reaction with $[Co_2(CO)_8]$ in CH_2Cl_2 at room temperature followed by addition of 6 equiv of trimethylamine *N*-oxide (TMANO). Incomplete conversion was observed under these standard conditions with enynes **7**, and so the reaction was performed in the presence of TMANO and molecular sieves[11] (entries 15, 17, and 19).

Remarkably, in spite of the electron-poor character of the C–C double bond of the vinyl sulfones **1**, **3**, **5**, and **7**, these compounds reacted completely after 2 – 3 h to give the corresponding bicyclic PK adducts, in most cases as the only detectable compounds (^{1}H NMR) after removal of the cobalt by-products by filtration through Celite. From a synthetic viewpoint, it is noteworthy that the yields of PK products from 1-sulfonylated 1,6-enynes (70 – 79% yields for cyclopentenones **9**, **11**, **13**, and **15**) are generally higher than those obtained from the corresponding 1-unsubstituted enynes (cyclopentenones **10**, **12**, **14**, and **16**; 38 – 79% yield), and that there is no significant decrease in efficiency on going from the 4,4-dimethyl series **5** and **7** (Thorpe – Ingold effect) to the 4-unsubstituted series **1** and **3**.[12]

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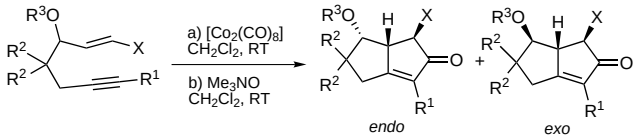
Table 1. Pauson–Khand reactions of enynes **1**–**8**.



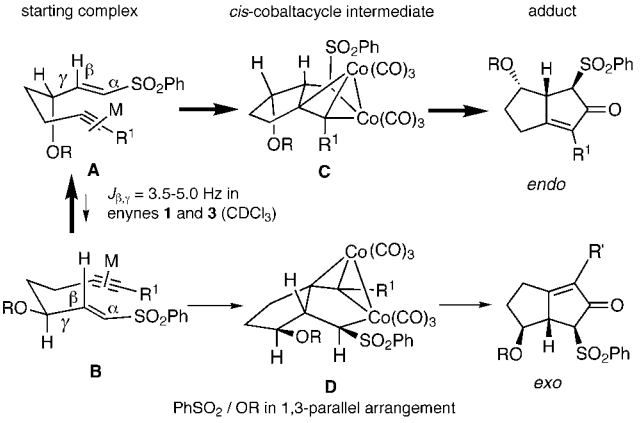
Entry	Enyne	X	R^1	R^2	R^3	Product	*endo*/*exo*[a]	Yield[b] [%] (*endo*[c] [%])
1	**1b**	SO_2Ph	H	H	TIPS	**9b**	**92/8**	74 (66)
2	**2b**	H	H	H	TIPS	**10b**	46/54	54
3	**1c**	SO_2Ph	H	H	CH_2OEt	**9c**	**>98/<2**	76 (76)
4	**2c**	H	H	H	CH_2OEt	**10c**	28/72	72
5	**3b**	SO_2Ph	Me	H	TIPS	**11b**	**91/9**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

[a] Determined by ^{1}H NMR spectroscopy after removal of the cobalt by-products by filtration. [b] Of pure *exo* + *endo* adducts after chromatography on silica gel. [c] In parentheses: yield of pure *endo*-4-sulfonylcyclopentenone after chromatography. [d] The *endo* + *exo* adducts could not be separated by chromatography on silica gel. [e] Reaction conditions: Me_3NO (6 equiv), molecular sieves (4 Å), toluene, RT.

However, the most outstanding result concerns the stereoselectivity of the cyclization. As expected for allylically substituted 1,6-enynes, the PK reactions of enynes **2** and **6** were moderately *exo* selective, and, in agreement with the model proposed by Magnus et al.,[2] which predicts a higher *exo* selectivity with increasing size of the substituent at the alkyne terminus, the PK reactions of the alkyne-substituted series **4** and **8** were somewhat more *exo* selective than those of **2** and **6**, respectively. Interestingly, the PK reactions of the sulfonylated enynes **1**, **3**, **5**, and **7** were *endo* selective in most cases (values in bold in Table 1), even in the alkyne-substituted series **3** and **7**, which proves the strong capacity of the phenylsulfonyl group to reverse the "natural" *exo* selectivity of the process. Thus, in the four sulfonylated series the *endo*-bicyclo[3.3.0]oct-1-en-3-one was obtained with high (entries 7, 9, and 17) or complete stereoselectivity (entry 3), whereby the pronounced reversal of stereoselectivity in the case of the pairs of enynes **1c**/**2c** (entries 3 and 4), **3c**/**4c** (entries 7 and 8) and **7b**/**8b** (entries 17 and 18) is especially remarkable. Furthermore, apart from the adducts **15**, the rest of *endo*/*exo* mixtures of 4-sulfonylcyclopentenones (adducts **9**, **11**, and **13**) were readily separated by simple chromatography on silica gel.

The *exo*/*endo* configuration of the sulfonylated cyclopentenones **9**, **11**, **13**, and **15** was evident from spectroscopic data.[13] In addition, the homogeneity of the stereochemical assignments was confirmed in several cases by hydrolysis of the *O*-protected PK adducts (products **b**,**c**) to the corresponding alcohols (products **a**), and by chemical correlation between sulfonylated and unsulfonylated cyclopentenones. Thus, the reductive desulfonylation of *endo*-**9b**, *endo*-**9c**, and *endo*-**13b** with activated zinc (NH_4Cl, THF/H_2O, RT) furnished in excellent yields *endo*-**10b** (93%), *endo*-**10c** (94%), and *endo*-**14b** (91%), respectively. In addition, the structure of *endo*-**9b** was unequivocally proved by X-ray diffraction.[14]

Although the assumed multistep mechanism of the PK reaction makes rationalization of the stereochemical outcome difficult, two main factors are usually invoked in diastereoselective PK cyclizations: the conformational preferences of the starting complex prior to metallacycle formation[7, 15] and the thermodynamic stability of the putative key *cis*-cobaltacycle intermediates.[2, 16] In the case of the 1-sulfonylated-1,6-enynes, both effects could operate in the same direction, providing a reasonable explanation for the observed major formation of the *endo* isomer (Scheme 2). Thus, as we had

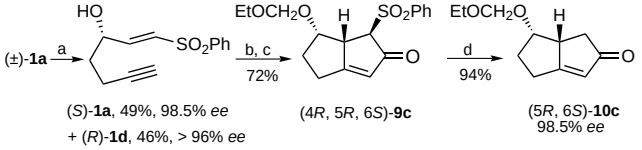


Scheme 2. Proposed mechanism for the observed *endo*-selective reaction.

noticed in other γ-oxygenated α,β-unsaturated phenyl sulfones,[17] the conformation **A** (OR and H_α in 1,3-parallel arrangement) would probably be more stable than conformation **B** (H_α and H_γ in 1,3-parallel arrangement), as is deduced from the low value of $J_{\beta,\gamma}$ (3.5–5.0 Hz, $CDCl_3$) in the starting enynes **1** and **3**. This leads to the *cis*-cobaltacycle **C**, in which the OR and SO_2Ph groups are located on opposite faces of the bicyclic structure, which finally affords the *endo* adduct. In contrast, the less stable conformation **B** (H_β and H_γ in *anti* relationship) would produce the presumably less stable *cis*-cobaltacycle **D** (intermediate in the formation of the *exo*

adduct), which is likely destabilized with respect to **C** due to the 1,3-parallel steric interaction between the OR and SO_2Ph groups (Scheme 2).

For the application of the results shown in Table 1 to the synthesis of enantiopure 6-oxygenated *endo*-bicyclo[3.3.0]oct-1-en-3-ones, optically pure 1-sulfonyl-1,6-enynes were required. Some years ago we described a practical lipase-mediated kinetic resolution of a wide structural variety of (±)-γ-hydroxy-α,β-unsaturated sulfones based on their highly enantioselective acetylation with lipase PS (*Pseudomonas cepacia* lipase) as catalyst in an organic solvent.[18] Pleasingly, under these conditions the reaction of (±)-**1a** stopped at 50% conversion (48 h in toluene as solvent) and afforded 49% of the alcohol (*S*)-**1a**[19] and 46% of the acetate (*R*)-**1d**[19] after flash chromatography, both in very high optical purity (98.5% *ee* for (*S*)-**1a** (HPLC, Chiralpak AS) and > 96% *ee* for (*R*)-**1d** (^{1}H NMR, [Pr(hfc)$_3$]). Protection of (*S*)-**1a** as ketal (*S*)-**1c**[19] and subsequent PK cyclization afforded (4*R*,5*R*,6*S*)-**9c**[19] as the only isolated product (72% yield). Finally, zinc-mediated reductive desulfonylation furnished the enantiomerically pure *endo*-substituted cyclopentenone (5*R*,6*S*)-**10c**[19] (94% yield, 98.5% *ee* (HPLC, Chiralcel OD); Scheme 3).



Scheme 3. Enantioselective synthesis of 6-oxygenated *endo*-bicyclo-[3.3.0]oct-1-en-3-ones. a) Lipase PS, vinyl acetate, molecular sieves, toluene, RT; b) $ClCH_2OEt$, DIPEA, CH_2Cl_2, RT; c) [$Co_2(CO)_8$], CH_2Cl_2, RT; TMANO, RT; d) Zn, NH_4Cl, THF/H_2O, RT.

In summary, we have demonstrated that α,β-unsaturated sulfones can be useful substrates in intramolecular PK reactions. Interestingly, unlike the usual stereochemical behavior of allylic substituted 1,6-enynes, the intramolecular PK cyclizations of differently substituted (*E*)-1-phenylsulfonyl-3-oxygenated-1,6-enynes occur with moderate to high *endo* selectivity. As these sulfonylated enynes are readily available in both racemic and enantiopure forms, and the sulfonyl group can be easily removed from the cyclopentenone products, this overall procedure represents an efficient stereocomplementary Pauson–Khand approach to the asymmetric synthesis of 6-substituted bicyclo[3.3.0]oct-1-en-3-ones. The application of this procedure to the stereoselective synthesis of triquinanes is underway.

Experimental Section

(4*R*,5*R*,6*S*)-**9c**: A solution of enyne (*S*)-**1c** (187 mg, 0.61 mmol) in CH_2Cl_2 (5 mL) was added dropwise to a stirred solution of [$Co_2(CO)_8$] (250 mg, 0.73 mmol) in CH_2Cl_2 (5 mL) under argon atmosphere at room temperature (RT). The solution was stirred for 10 min, and TMANO (407 mg, 3.66 mmol) was added in one portion. The resulting solution was stirred for 3 h at RT and filtered through a pad of Celite, which was washed with diethyl ether (30 mL). The combined solvents were evaporated and the residue was purified by flash chromatography (hexane/ethyl acetate 5/1) to afford 155 mg of (4*R*,5*R*,6*S*)-**9c** (76%) as a white solid. M.p. 73–74 °C; $[\alpha]_D^{20} = +241$ ($c = 0.4$, $CHCl_3$); ^{1}H NMR ($CDCl_3$): $\delta = 7.99$–7.96 (m, 2H), 7.70–7.55 (m, 3H), 5.92 (m, 1H), 4.65 (m, AB, 2H), 4.28 (t, $J = 4.1$ Hz, 1H), 4.23 (d, $J = 4.4$ Hz, 1H), 3.59 (m, 1H), 3.51 (m, 2H), 2.71 (m, 2H), 2.24 (m, 2H), 1.21 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR ($CDCl_3$) $\delta = 198.1$, 185.0, 138.6, 134.0, 129.2, 129.1, 125.0, 93.8, 76.3, 68.3, 63.7, 53.2, 32.5, 24.3, 15.1; analysis calcd for $C_{17}H_{20}O_5S$: C 60.70, H 5.99, S 9.53; found: C 60.46, H 6.42, S 9.92.

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[2] The *exo* selectivity of the intramolecular PK reaction of allylic substituted 1,6-enynes has been explained by invoking steric repulsion between the *endo* allylic group and the substituent at the alkyne terminus in the *cis*-cobaltacycle intermediate: a) P. Magnus, D. P. Becker, *J. Am. Chem. Soc.* **1987**, *109*, 7495; b) P. Magnus, L. M. Principe, M. J. Slater, *J. Org. Chem.* **1987**, *52*, 1483; c) P. Magnus, L. M. Principe, *Tetrahedron Lett.* **1985**, *26*, 4851; d) P. Magnus, C. Exon, P. Albaugh-Robertson, *Tetrahedron* **1985**, *41*, 5861.

[3] For other examples of *exo* selectivity in PK cyclizations of enynes substituted at allylic or propargylic positions, see a) C. Mukai, J. S. Kim, M. Uchiyama, S. Sakamoto, M. Hanoka, *J. Chem. Soc. Perkin Trans 1* **1998**, 2903; b) C. Mukai, M. Uchiyama, S. Sakamoto, M. Hanaoka, *Tetrahedron Lett.* **1995**, *36*, 5761; c) N. Jeong, S. Hwang, Y. Lee, Y. K. Chung, *J. Am. Chem. Soc.* **1994**, *116*, 3159; d) Y. K. Chung, B. Y. Lee, N. Jeong, M. Hudecek, P. L. Pauson, *Organometallics* **1993**, *12*, 220; e) N. Jeong, B. Y. Lee, S. M. Lee, Y. K. Chung, S.-G. Lee, *Tetrahedron Lett*. **1993**, *34*, 4023; f) S. Yoo, S. H. Lee, N. Jeong, I. Cho, *Tetrahedron Lett.* **1993**, *34*, 3425. g) W. R. Roush, J. C. Park, *Tetrahedron Lett.* **1991**, *32*, 6285; h) N. Jeong, S. Yoo, S. J. Lee, S. H. Lee, Y. K. Chung, *Tetrahedron Lett.* **1991**, *32*, 2137; i) J. Mulzer, K.-D. Graske, B. Kirste, *Liebigs Ann. Chem.* **1988**, 891.

[4] One of the most important limitations of the cyclopentenone synthesis by the PK reaction is that in the reaction of alkyne dicobalt hexacarbonyl complexes with alkenes bearing electron-withdrawing groups (for example, ketone, ester, or cyano), after the olefin insertion step leading to the cobaltacycle intermediate, the reaction proceeds preferentially by β-H elimination rather than by carbonyl insertion, furnishing finally 1,3-dienes instead of cyclopentenones; see a) W. A. Smit, A. S. Gybin, A. S. Shashkov, Y. T. Strychkov, L. G. Kizmina, G. S. Mikaelian, R. Caple, E. D. Swanson, *Tetrahedron Lett.* **1986**, *27*, 1241; b) P. L. Pauson, *Tetrahedron* **1985**, *41*, 5855; c) I. U. Khand, P. L. Pauson, *J. Chem. Soc. Chem. Commun.* **1974**, 379. Only some specific alkynyl enones led to cyclopentenones in cobalt-catalyzed PK reactions: A. L. Veretenov, W. A. Smit, L. G. Vorontsova, M. G. Kurella, R. Caple, A. S. Gibin, *Tetrahedron Lett.* **1991**, *32*, 2109. See also M. Costa, A. Mor, *Tetrahedron Lett.* **1995**, *36*, 2867.

[5] J. Adrio, J. C. Carretero, *J. Am. Chem. Soc.* **1999**, *121*, 7411.

[6] Vinyl sulfones had never been successfully used in PK reactions. As a related reported precedent, the treatment of divinyl sulfone with alkyne dicobalt complexes did not give the cyclopentenone PK product (I. U. Khand, P. L. Pauson, *Heterocycles* **1978**, *11*, 59) in accordance with the accepted behavior of alkenes with electron-withdrawing substituents (see ref. [4]).

[7] To the best of our knowledge, the only reported case of *endo* selectivity in a PK reaction of an allylic substituted 1,6-enyne concerns a specific 3,4-disubstituted enyne: J. A. Casalnuovo, R. W. Scott, E. A. Harwood, N. E. Schore, *Tetrahedron Lett.* **1994**, *35*, 1153. Similarly, for a study of the *endo*/*exo* selectivity in 3,4-disubstituted-1,7-enynes, see C. Mukai, J. S. Kim, H. Sonobe, M. Hanaoka, *J. Org. Chem.* **1999**, *64*, 6822.

[8] a) B. M. Trost, T. A. Greese, *J. Org. Chem.* **1991**, *56*, 3189; b) E. Domínguez, J. C. Carretero, *Tetrahedron* **1990**, *46*, 7197.

[9] Alternatively, the phenyl-substituted alkynes **7a** and **8a** were readily prepared by Sonogashira reaction of the corresponding terminal alkynes **5a** and **6a** with phenyl iodide ($Pd(OAc)_2$ 10 mol%, CuI 10 mol%; PPh_3 20 mol%, Et_3N 200 mol% in benzene at RT; 81 and 75% yield, respectively).

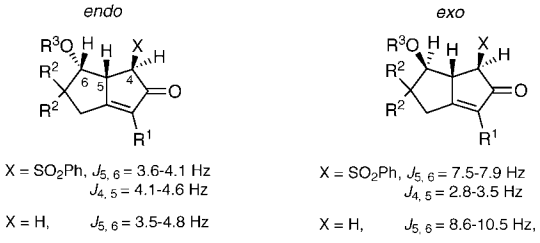
  0044-8249/00/11216-3030 $ 17.50+.50/0

[10] Very similar yields and diastereoselectivities were obtained in the thermal PK reaction (CH_3CN, 80 °C) of the dicobalt complexes of the enynes **1** and **3**.

[11] The combination TMANO/molecular sieves has been recently reported as an efficient promoter in PK reactions: L. Pérez-Serrano, L. Casarrubios, G. Domínguez, J. Pérez-Castells, *Org. Lett.* **1999**, *1*, 1187.

[12] Except for the free alcohols **1a** and **3a**, which proved to be rather unreactive in PK reactions. For instance, the alkyne dicobalt hexacarbonyl complex of **1a** did not react at all under thermal (CH_3CN, 80 °C) or TMANO-promoted conditions (CH_2Cl_2, RT). A very low yield of PK products **9a** (25% yield, *endo*/*exo* = 85/15) was obtained when the reaction was performed in the presence of TMANO and molecular sieves. In this case, instead of the PK cyclopentenone, the main product was the corresponding exocyclic 1,3-diene (see ref. [4]).

[13] As is usual in other 6-substituted bicyclo[3.3.0]octen-3-ones (for example, ref. [2c]), the coupling constant between H_5 and H_6 is a very simple and excellent criterion for stereochemical diagnosis. Thus, $J_{5,6}$ is much smaller in the *endo* isomers ($J_{5,6} = 3.6-4.8$ Hz, H_5/H_6 in *cis* relationship) than in the *exo* isomers ($J_{5,6} = 7.5-10.5$ Hz, H_5/H_6 in *trans* arrangement). Also, a characteristic trend was observed for the chemical shift of H_6 in the C-4 sulfonylated adducts: H_6 is significantly more deshielded in the *endo* isomer than in the *exo* isomer (see below), in accordance with the strong deshielding effect of the phenylsulfonyl group on the hydrogen atom in the 1,3-parallel arrangement. Additionally, these stereochemical assignments have been confirmed by NOESY experiments on the pairs of isomers *endo*/*exo* **9b** and *endo*/*exo* **13c**.



[14] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-141942. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[15] Recent examples: S. Fonquerna, R. Rios, A. Moyano, M. A. Pericàs, A. Riera, *Eur. J. Org. Chem.* **1999**, 3459, and references therein.

[16] For instance, see a) P. M. Breczinski, A. Stumpf, H. Hope, M. E. Krafft, J. A. Casalnuovo, N. E. Schore, *Tetrahedron* **1999**, *55*, 6797; b) J. Castro, A. Moyano, M. A. Pericàs, A. Riera, *Tetrahedron* **1995**, *51*, 6541.

[17] a) J. C. Carretero, R. Gómez Arrayás, *J. Org. Chem*. **1998**, *63*, 2993; b) J. Adrio, J. C. Carretero, R. Gómez Arrayás, *Synlett* **1996**, 640. Similar conformational preferences have been reported for γ-oxygenated α,β-unsaturated esters, see: c) B. W. Gung, M. B. Francis, *Tetrahedron Lett.* **1995**, *36*, 2579; d) B. W. Gung, M. B. Francis, *J. Org. Chem.* **1993**, *58*, 6177.

[18] In all the studied cases, only the *R* enantiomer of the (±)-(*E*)-γ-hydroxy-α,β-unsaturated sulfone was acetylated (J. C. Carretero, E. Domínguez, *J. Org. Chem.* **1992**, *57*, 3867).

[19] Specific rotations: (*S*)-**1a**: $[\alpha]_D^{20} = +28.0$ ($c = 1$, $CHCl_3$); (*R*)-**1d**: $[\alpha]_D^{20} = +5.1$ ($c = 1$, $CHCl_3$); (*S*)-**1c**: $[\alpha]_D^{20} = -25.1$ ($c = 1.8$, $CHCl_3$); (4*R*,5*R*,6*S*)-**9c**: $[\alpha]_D^{20} = +241$ ($c = 0.4$, $CHCl_3$); (5*R*,6*S*)-**10c**: $[\alpha]_D^{20} = +90.2$ ($c = 0.2$, $CHCl_3$).

Cyclization of Terminal Diynes Catalyzed by Thiolate-Bridged Diruthenium Complexes: A Simple Synthetic Route to *endo*-Macrocyclic (*Z*)-1-En-3-ynes**

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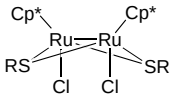
Homogeneous catalysis by polynuclear transition metal complexes has been receiving much attention because the multimetallic sites are expected to provide unique reaction sites for activation and transformation of substrate molecules. These sites are anticipated to differ significantly from those of conventional monometallic centers coordinated by ancillary ligands.[1] Toward this end, our studies have long been focused on the synthesis and reactivity of polynuclear noble-metal complexes with bridging sulfur ligands.[2] Recently, we found that the thiolate-bridged diruthenium complexes $[Cp^*RuCl(\mu_2\text{-}SR)_2RuCp^*Cl]$ (**1**–**3**)($Cp^* = \eta^5\text{-}C_5Me_5$; R = Me, Et, *n*Pr) catalyze the head-to-head *Z* dimerization of terminal alkynes containing straight-chain aliphatic and functional groups.[3] Although mononuclear ruthenium complexes such as $[Cp^*Ru(L)H_3]$ (L = phosphane) also catalyze the dimerization of terminal alkynes, such a highly regio- and stereoselective dimerization of a wide range of terminal alkynes has never been realized.[4] We have now extended our study of the catalytic activity of the diruthenium complexes to include the cyclization of terminal diynes. Preliminary results are described here.



1; R = Me
2; R = Et
3; R = *n*Pr
4; R = *i*Pr

Trost and co-workers have reported the palladium-catalyzed cyclization of α,ω-diynes to give the corresponding *exo*-macrocyclic 1-en-3-ynes in moderate yields and high regio- and stereoselectivities.[5] In sharp contrast, synthetic routes to *endo*-macrocyclic 1-en-3-ynes are extremely limited.[6] Actually, six steps are necessary to prepare (*Z*)-1-cyclododecen-3-yne from cyclododecanone and the total yield is less than 5%.[6] To the best of our knowledge, there is no report of a synthetic method for *endo*-macrocyclic (*Z*)-1-en-3-ynes from α,ω-diynes.[7]

Treatment of 1,15-hexadecadiyne[8] (**6a**) in methanol in the presence of $[Cp^*RuCl(\mu_2\text{-}SMe)_2RuCp^*Cl]$ (**1**) (10 mol%) at

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