Asymmetric Pauson−Khand Reactions Using Camphor-Derived Chelating Thiols as Chiral Controllers

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A convenient procedure for the preparation of enantiopure 10-(R-thio)-2-*exo*-bornanethiols from (1*S*)-camphor-10-thiol has been developed. The ethynyl derivatives of these thiols gave excellent diastereoselectivities (up to 98:2) in Pauson−Khand reactions with norbornene and norbornadiene through the intermediacy of a chelated dicobalt pentacarbonyl complex. Thermal reaction conditions starting from the preformed chelated complex gave better results than *N*-oxide-promoted runs with in situ generation of the chelated intermediate. The corresponding adducts have been elaborated through a protocol consisting of conjugate addition, samarium iodide-promoted cleavage of the chiral auxiliary, and retro-Diels−Alder reaction to afford 4-substituted 2-cyclopentenones in high enantiomeric purity.

The search for reliable asymmetric versions of the Pauson−Khand reaction (PKR) is a subject of maximum interest since this reaction has emerged as one of the most powerful tools for the synthesis of cyclopentenones.[1,2] Leaving aside the use of chiral substrates,[3] which in many cases have exhibited high stereoselectivities, several approaches have been explored in order to render the classical cobalt-mediated cyclization enantioselective: (a) chiral phosphines,[4] (b) chiral tertiary amine *N*-oxides[5] to promote the reaction, and (c) chiral auxiliaries bonded either to the alkene or to the alkyne.[6−10]

Although important progress has been recently achieved through the use of chiral phosphines as a source of chirality in PKR,[4] the use of removable chiral auxiliaries

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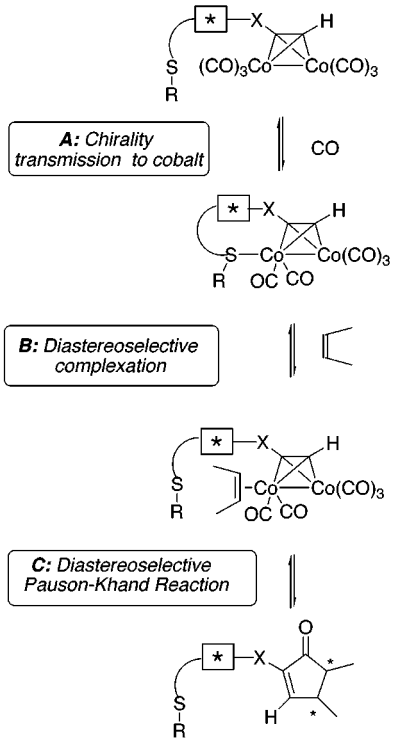


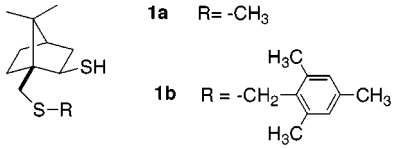
Figure 1. Schematic mode of action of chiral auxiliaries with a thioether functionality able to coordinate to cobalt ("chelating auxiliaries").

is still a reliable approach and, up to now, the only one that has been used in the synthesis of natural products.[6b,7] Whereas in the intramolecular version of the reaction conventional chiral auxiliaries such as *trans*-phenylcyclohexanol or neopentyloxyisoborneol gave good levels of diastereoselection and, in many cases, separable diastereomers, the intermolecular version proved to be more difficult. Nevertheless, excellent results were achieved using alkynyl derivatives of Oppolzer's camphorsultam,[8] chiral oxazolidinone,s[9] or chiral auxiliaries such as 10-methylthioisoborneol[10] with an adequately positioned thioether function.

In earlier studies on the reaction by our group it has been shown that the ability of sulfur to coordinate onto the cobalt atom in the cobalt carbonyl complex was crucial in order to achieve high diastereoselectivity.[11] The substitution of a carbonyl ligand in the hexacarbonyl dicobalt complex by a sulfur atom leads to a new, more reactive pentacarbonyl complex, wherein the diastereotopic cobalt atoms of the cluster are highly differentiated. In this way, the chirality of the auxiliary is transmitted to the metal cluster which, in turn, efficiently controls the absolute configuration of the cyclopentenone product (Figure 1). We have proposed the term *chelating auxiliaries* for species exhibiting such behavior.

One of the problems associated with the use of alcohols as chiral auxiliaries in alkoxyacetylenes participating in PKR is the high tendency of these substrates to undergo polymerization during the preparation of the requisite dicobalt hexacarbonyl complexes. To avoid this problem, the cobalt carbonyl complexes of all terminal alkoxyacetylenes must be prepared by a three-step protocol involving the protection of the terminal acetylenic position by a trimethylsilyl group, complexation, and desilylation.[12] Since acetylenic thioethers exhibit higher stability against hydrolysis than their oxygenated analogues, can be converted without problem into their dicobalt hexacarbonyl complexes, and are appropriate substrates for Pauson−Khand reactions,[13] it seemed reasonable that the use of chiral thiols with a adequately positioned thioether funtion ("chelating thiols") as auxiliaries could improve the scope and selectivity exhibited by their alcohol analogues.

We reasoned that an increase in the steric bulk near the sulfur atom designed as an hemilabile ligand would have a positive effect in the diastereoselectivity of the corresponding PKR. We report here full details[14] on the Pauson−Khand reactions of the alkynyl sulfides derived from the known[15] chiral thiol **1a** bearing a methyl thioether arm able to coordinate to cobalt ("chiral chelating thiol") as well as the synthesis and Pauson−Khand reactions of a new, specifically designed, thiol **1b**.



Results and Discussion

Enantiomerically pure thiol **1a** was prepared from the readily available (1*S*)-camphor-10-thiol[16] **2** through a significant improvement of a described procedure[15] that involves alkylation with methyl iodide, treatment with Lawesson's reagent,[17] and stereoselective reduction of the resulting thione (Scheme 1). In the original procedure, stereochemical control of the reduction step was only possible by performing the reaction at −80 °C, with the undesired cost of a very extended reaction time (12 days). We have now found a more practical alternative for this transformation involving reaction with DIBALH at −20 °C (2 h, 10:1 dr), formation of the *p*-nitrobenzoate of the thiol, purification by simple crystallization, and final saponification. Enantio- and diastereomerically pure **1a** is obtained in 35% overall yield by this protocol.

For the preparation of the new thiol **1b**, the original synthetic sequence was employed since the reduction step takes place in a more convenient way. Thus, (1*S*)-

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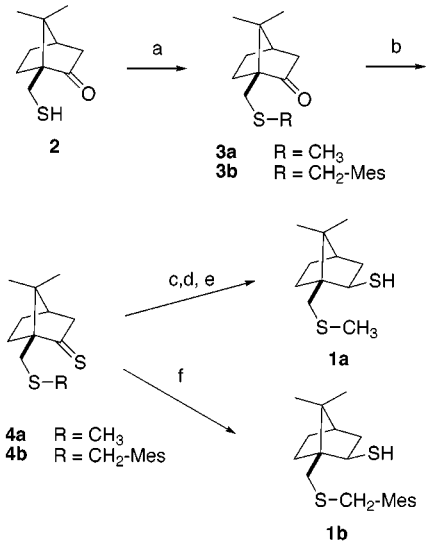
Scheme 1[a]



[a] Key: (a) R−Br, MeOH, NaMeO (**3a**, 79%; **3b**, 81%); (b) Lawesson's reagent (**4a**, 78%; **4b**, 74%); (c) DIBALH, diethyl ether, −20 °C, 88%, 10:1 dr; (d) (i) PNB-Cl, CH_2Cl_2, Pyr, (ii) cryst. 69% overall; (e) NaOH, MeOH, 95%; (f) DIBALH, diethyl ether, −40 °C, 90%.

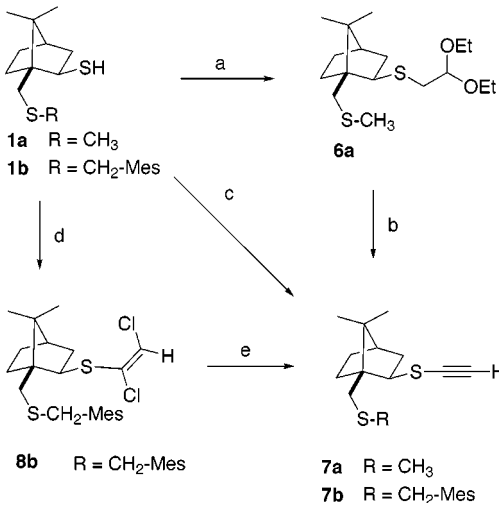
camphor-10-thiol **2** was alkylated by treatment with 2,4,6-trimethylbenzyl bromide[18] and sodium methoxide in methanol to afford the mesytylmethyl derivative **3b** in 81% yield. Conversion of this ketone into the corresponding thione **4b** was accomplished uneventfully in 74% yield using Lawesson's reagent.[17] To our satisfaction, in this case, the DIBALH reduction of the thione **4b** was completely stereoselective at −40 °C yielding diastereomerically pure (exo) thiol **1b** in 90% yield after only 6 h of reaction (Scheme 1). This simple and straightforward preparation of **1b** (54% overall yield from **2**), together with the applications that we have just developed (see below), converts this chiral thiol into a potentially useful chiral auxiliary.

For the purposes of this study, thiols **1a**,**b** had to be converted into the corresponding acetylene thioethers. The synthesis of ethynyl sulfide **7a** was initially accomplished using the methodology developed by Cookson.[19] Thus, the sodium thiolate of **1a** was treated with 2-bromoacetaldehyde diethylacetal affording 1,1-diethoxy-2-(R*-thio)ethane **6a** in 80% yield. Subsequent double elimination promoted by LDA yielded the corresponding ethynyl sulfide **7a** in 81% yield.

For small-scale preparations, the methodology developed by Greene starting from thichloroethylene and using potassium hydride as a base[20] was more convenient and afforded (2*R*-*exo*)-10-methylthioisobornyloxyethyne **7a** in 71% yield in a "one-pot" reaction from thiol **1a** (Scheme 2). However, when this method was attempted with thiol **1b** afforded very low yields of the acetylenic thioether **9b**, the intermediate dichloroolefin **8b** being the main product of the reaction.

In any case, this problem could be easily overcome by treating **8b** with butyllithium in diethyl ether to afford almost quantitatively ethynyl sulfide **7b** (Scheme 2).

Scheme 2[a]



[a] Key: (a) $BrCH_2CH(OEt)_2$, NaEtO, EtOH (**6a**, 80%); (b) LDA, diethyl ether (**7a**, 81%); (c) (i) KH, THF, (ii) Cl_2CHCH_2Cl, (iii) *n*-BuLi (**7a**, 71% overall); (d) (i) KH, THF, (ii) Cl_2CHCH_2Cl (**8b**, 70%); (e) *n*-BuLi, diethyl ether (**7b**, 96%).

As anticipated, the preparation of the dicobalt hexacarbonyl complexes of the acetylene thioethers was simple and straightforward. By stirring a solution of the alkynyl thioethers **7a**,**b** in hexanes at room temperature with 1.05 equiv of octacarbonyl dicobalt, the dicobalt hexacarbonyl complexes (**9a**,**b**) were obtained almost quantitatively. The thermal stability of these complexes was clearly superior to that of their oxygenated analogues,[10] allowing complete characterization. However, in their ^1H and ^{13}C spectra, a significative amount (ca. 2−5% in the case of **9a**, 10−30% in the case of **9b**) of new cobalt complexes **10a**,**b**, presumably formed by internal displacement of a carbonyl ligand by the sulfur atom, was observed. As with the oxygenated analogues,[10] an equilibrium appears to exist between hexacarbonyl and chelated complexes. In this case, however, the equilibrium can be almost completely shifted toward the chelated pentacarbonyl species by simply heating the hexane solution of the hexacarbonyl complex at 55 °C under a smooth nitrogen stream or by addition of *N*-methylmorpholine *N*-oxide (NMO) to a dichloromethane solution of **9** at room temperature (Scheme 3). Although both methods for the generation of the pentacarbonyl complexes are almost equivalent in terms of yield (thermal: 89%; NMO: 83% in the case of **10a**), there are several experimental details that should be stressed. First, the ^1H NMR spectra of the thermally generated complex **10a** always showed a small amount (ca. 3−5%) of the starting hexacarbonyl complex **9a**. Conversely, samples of **10a** prepared under oxidative conditions were almost completely free of **9a** by ^1H NMR. As we will see, this fact can be of some concern in reactivity studies. Significantly, and despite the increased steric bulk of the sulfur substituent, the thermal generation of **10b** provided a crude reaction completely free of **9b**.

It is worth noting that two diastereomeric pentacarbonyl complexes **10-(Co-*pro*-*S*)** and **10-(Co-*pro*-*R*)** can be formed by chelation of the alkylthio group to each one of the two diastereotopic cobalt atoms (Figure 2). However, careful inspection of the ^1H and ^{13}C NMR spectra of both pentacarbonyl complexes **10a**,**b**, generated either thermally or by treatment with NMO, revealed only one

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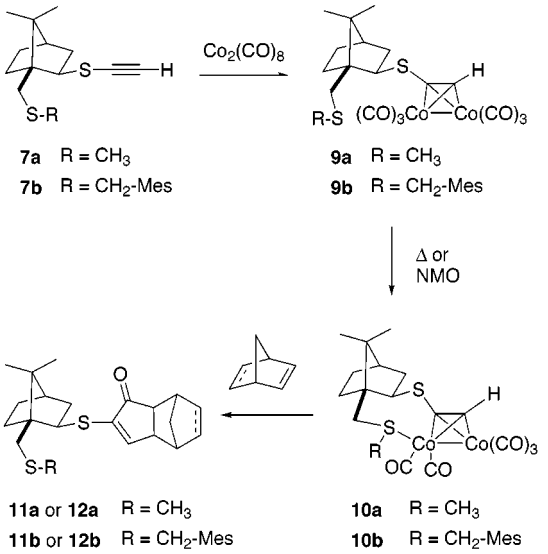
Scheme 3[a]



[a] Conditions and yields for Pauson−Khand reactions are shown in Table 1.

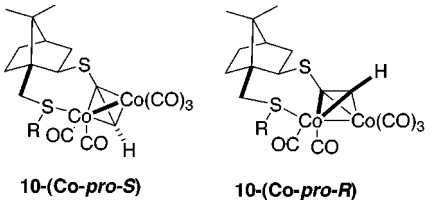
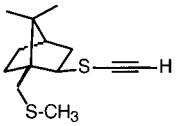
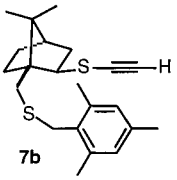


Figure 2. Diastereomeric complexes **10** generated by internal chelation of the sulfide to each diastereotopic cobalt atom.

set of signals. The electronic and geometric changes associated to the conversion of **9a/9b** into **10a/10b** can be readily appreciated by comparison of their NMR spectra (see the Supporting Information). Thus, the main change in the ^{1}H NMR spectra corresponds to the AB system of the $-CH_2S$ group, which shows a large increase in the chemical shift difference of the diastereotopic nuclei, probably reflecting the different geometrical arrangement (axial-like or equatorial-like) of these two protons in the chelated complex. Moreover, the signal of the CH_3S group in the ^{1}H NMR spectrum of **10a** appears significantly shifted downfield (from 2.09 to 2.45 ppm), thus reflecting the reduced electron density of the sulfur atom. On the other hand, the acetylenic proton is correspondingly shifted upfield (6.36/6.34 to 5.89/5.95 ppm) as a consequence of the more electronically rich nature of the C_2Co_2 core. This signal, which appears in a clean region of the spectrum, allows the estimation of the ratio **9/10** after a thermal or oxidative treatment. In the experiments devoted to the generation of **10a**, a very small singlet (ca. 2%) was observed in this zone that could be assigned either to the minor diastereomer of **10a** or to an impurity. By recording the spectrum at low temperature (down to −60 °C), no significant broadening could be observed in either the major or the minor signals. If we make the assumption that the large and the small signals correspond to the major and minor diastereomers of **10a**, it comes out that interconversion between them should be slow at room temperature. Although NOESY studies were performed on **10a** to establish the stereochemistry of the major diastereomer, the high relaxation time of the acetylenic proton (∼9.7 s) prevented the observation of any NOE of this atom with the rest of the molecule. The ^{1}H NMR spectrum of **10b** is clean from 5 to 6.8 ppm, showing only one signal for the acetylenic hydrogen. Although the possibility of a rapid equilibrium between diastereomers cannot be absolutely ruled out, it is much likely that the steric bulk of the mesitylmethyl substitutent is able to completely shift the equilibrium toward one diastereomer, **10-(Co-*pro-S*)** or **10-(Co-*pro-R*)**, as represented in Figure 2.

The Pauson−Khand reactions of the cobalt carbonyl complexes **9**/**10** prepared from alkynyl sulfides **7** were next studied. The results are shown in Table 1. As a control experiment, the thermal reaction between the hexacarbonyl complex **9a** with norbornadiene was performed under a CO atmosphere to minimize the formation of the pentacarbonyl complex. At 0 °C (Table 1, entry 1) the reaction was extremely slow, and after 23 days, only a 31% of a 67:33 diastereomeric mixture of bicyclic cyclopentenones **11a** could be isolated. The *N*-oxide-promoted reaction conditions that had given the best results with the ethynyl ether of 10-methylthioisoborneol[10] were next studied. A solution of the pentacarbonyl complex **10a**, generated by treatment with an excess of NMO (6 equiv) in dichloromethane at room temperature, was cooled to −20 °C and treated with norbornadiene. The reaction was complete in 2.5 days (Table 1, entry 2) but, quite surprisingly, took place without any stereoselectivity leading to equal amounts of the two possible exo adducts. It is worth noting that under the same conditions the analogous oxygenated compound afforded the Pauson−Khand adduct in 77% yield as a 92:8 mixture of diastereomers.[10] The reaction was next studied under thermal conditions starting from the pentacarbonyl complex **10a**, generated in hexanes by heating **7a** at 55 °C. Once the conversion to the pentacarbonyl complex was complete by TLC, the solution was cooled to 0 °C, and norbornadiene was added. After 24 h, the reaction was complete and, in this case, took place with excellent diastereoselectivity (92:8). A further decrease of the reaction temperature (−20 °C, Table 1, entry 4) did not significantly improve the selectivity (93:7), whereas the reaction time increased to 6 days. It was clear from these experiments that an excess of NMO has a deleterious effect on diastereoselectivity (Table 1, entries 2 and 3). On the other hand, it was conceivable that the small amount of the hexacarbonyl complex **9a** present in admixture with **10a** when the latter is generated by thermal activation was responsible for the formation of the minor stereoisomer. In an attempt to develop optimal reaction conditions, **10a** was generated in dichloromethane by treatment with the minimum amount of NMO (3 equiv) and then purified by chromatography. A hexane solution of **10a** completely free of **9a** obtained in this way was subsequently exposed to the employed olefins at different temperatures. At −10 °C, the norbornadiene adduct was obtained in 65% yield and the selectivity increased up to 95:5 (Table 1, entry 5). With norbornene under the same reaction conditions, a 86:14 diastereomeric mixture was obtained in 66% yield after 5 days of reaction (Table 1, entry 8). Thus, while the thermal generation of **10a** seems to be appropriate for achieving high diastereoselectivities, the best results are obtained using the pentacarbonyl complex **10a** generated by oxidative treatment of **9a** followed by complete removal of any excess of NMO or its reduction product.To check whether the presence of the bulky mesitylmethyl group

Table 1. Intermolecular Pauson–Khand Reactions of R*-thioalkynes with Alkenes

Entry	Starting R*thioalkyne	Alkene	Reaction conditions[a] (temperature, time)	Product (yield, d.r.)
1	 **7a**	norbornadiene	A, 0°C, 23 d	**11a** (31%, 67:33)[b]
2		norbornadiene	B, -20°C, 2.5 d	**11a** (67%, 50:50)[b]
3		norbornadiene	C, 0°C, 24 h	**11a** (52%, 92:8)[b]
4		norbornadiene	C, -20°C, 6 d	**11a (53%, 93:7)**[b]
5		norbornadiene	D, -10°C, 3 d	**11a (65%, 95:5)**[b]
6		norbornene	B, 0°C, 48 h	**12a** (66%,37:63)[c]
7		norbornene	C, 0°C, 48 h	**12a** (45%, 82:18)[c]
8		norbornene	D, -10°C, 5 d	**12a** (66%, 86:14)[c]
9	 **7b**	norbornadiene	B, 0°C, 6h	**11b** (28%, 65:35)[c]
10		norbornadiene	C, 0°C, 24 h	**11b (60%, 98:2)**[c]
11		norbornadiene	D, 0°C, 48 h	**11b** (64%, 95:5)[c]
12		norbornene	B, 0°C, 6h	**12b** (26%, 39:61)[c]
13		norbornene	C, 0°C, 4 d	**12b (50%, 96:4)**[c]
14		norbornene	D, 0°C, 48 h	**12b** (30%, 89:11)[c]

[a] Conditions: (A) stirring the dicobalt hexacarbonyl complex **9a**,**b** in hexane at the specified temperature; (B) generation of the pentacarbonyl complex **10a**,**b** by addition of NMO (6 equiv) to a solution of **9a**,**b** in dichloromethane followed by addition of the olefin at the specified temperature; (C) generation of the pentacarbonyl complex **10a**,**b** by heating the solution of **9a**,**b** in hexane at 55 °C followed by addition of the olefin at the specified temperature; (D) generation of the pentacarbonyl complex **10a**,**b** by addition of NMO (3 equiv) to a solution of **9a**,**b** in dichloromethane; purification of **10a**,**b** by chromatography in Al_2O_3 and reaction with the olefin in hexanes at the specified temperature. [b] By HPLC. [c] By ^{13}C NMR.

attached to the chelating sulfur atom in the chiral auxiliary had a positive influence on the diastereoselectivity, the Pauson–Khand reactions of alkynyl sulfide **7b** were tested. As expected from the above-mentioned results, the *N*-oxide-promoted reactions conducted in the presence of excess NMO gave poor yields and selectivities. Gratifyingly enough, however, the thermally generated pentacarbonyl complex **10b** afforded the norbornadiene adduct in 60% yield in excellent diastereoselectivity (98:2) by performing the reaction in hexane at 0 °C (Table 1, entry 10). It is worth mentioning that with this substrate the thermal conversion of the hexacarbonyl complex **9b** into the corresponding chelated species **10b** is complete. In this case, the preparation of **10b** by treatment with NMO followed by chromatography did not improve the selectivity, which decreased to 95:5 (Table 1, entry 11). With norbornene, the thermal reaction from the thermally generated pentacarbonyl complex **10b** also provided excellent diastereoselectivities (Table 1, entry 13). Again, these results were not improved when complex **10b** was prepared by treatment with NMO followed by removal of the excess *N*-oxide (Table 1, entry 14). As a general trend, thiol **1b** behaves as a more efficient chiral controller in intermolecular PKR mediated by internally chelated species such as **10**. Not only is the synthesis of **1b** much simpler and efficient than that of **1a**, but also the experimental procedures associated to its use in intermolecular PKR (i.e., purely thermal generation of the pentacarbonyl complex **10b**) are straightforward and the achieved diastereoselectivities, higher.

Once the formation of the PK adducts was optimized, our efforts were directed to the development of protocols for their conversion into enantiomerically pure, synthetically useful cyclopentenone derivatives with simultaneous recovery of the chiral auxiliary. Most synthetic applications of the Pauson–Khand adducts derived from norbornadiene rely on the possibility of performing on these molecules a retro Diels–Alder reaction leading to a cyclopentenone. In the context of asymmetric Pauson–Khand reactions of chiral enol or ynol ethers, protocols consisting of conjugate addition, samarium iodide-induced cleavage of the carbon–alkoxy linkage, and retro-Diels–Alder reaction has allowed the preparation of enantiomerically pure 4-substituted 2-cyclopentenones and bicyclo[*n*.3.0]alkanones. This strategy has been successfully applied, for instance, to the development of an enantioselective synthesis of brefeldin A.[7a] With the aim of applying the same protocol in the present case, bicyclic adducts **11a** and **11b** were submitted to conjugate addition[21] with *n*-$Bu_2CuCNLi_2$ in diethyl ether. Although the reactions took place cleanly by TLC, cyclopentanones **13a** and **13b** were very unstable and decomposed when chromatographic purification or spectroscopic characterization was attempted. To circumvent this difficulty, the reaction crudes were directly treated with samarium iodide[22] in THF/MeOH to afford the known tricyclic cyclopentanone (−)-**14**. Starting from adduct **11a**, the yield of (−)-**14** was 46% (two steps), 5-butyl-4-hydroxytricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one (**16**) being formed as a significant byproduct (32% yield). On the other hand, starting from **11b**, the reaction was much cleaner and the bicyclic cyclopentenone (−)-**14** was isolated in 64% yield. The starting thiol **1b** could be recovered in 59% yield [91% with respect to (−)-**14**]. The retro Diels–Alder reaction of (−)-**14** was conducted at low temperature (55 °C) under the Lewis acid-catalyzed conditions developed

(21) cf.: Lipschutz, B. H.; Ellsworth, E. L.; Siahaan, I. J.; Shirazi, A. *Tetrahedron Lett.* **1988**, *29*, 6677–6680.

(22) Kende, A. S.; Mendoza, J. S. *Tetrahedron Lett.* **1991**, *32*, 1699–1702.

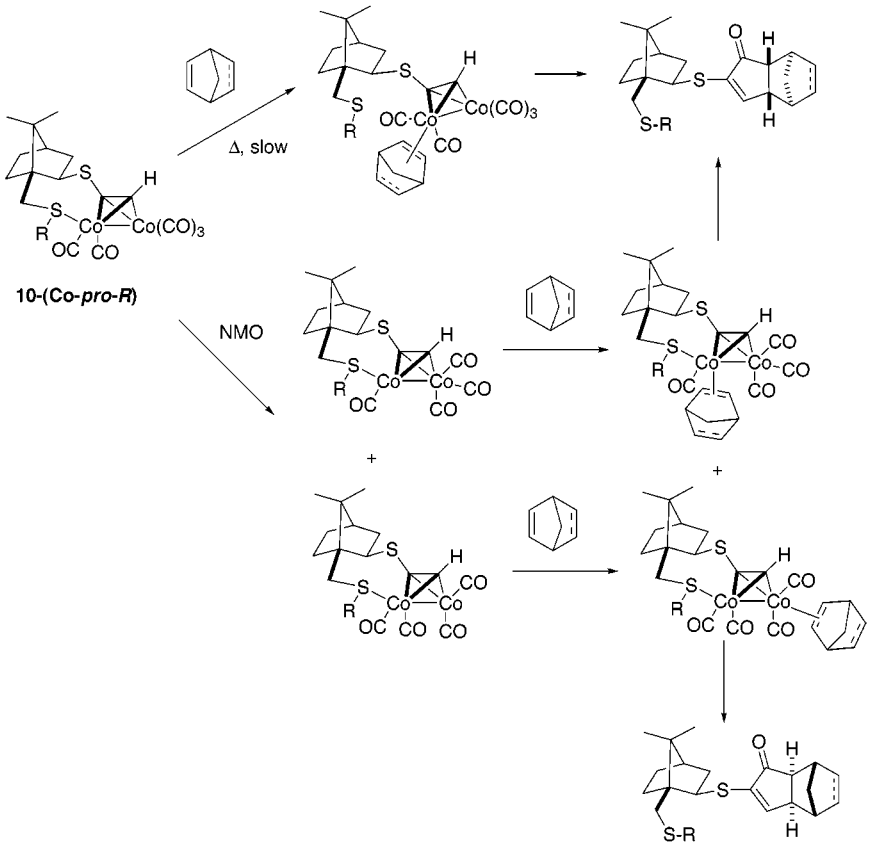
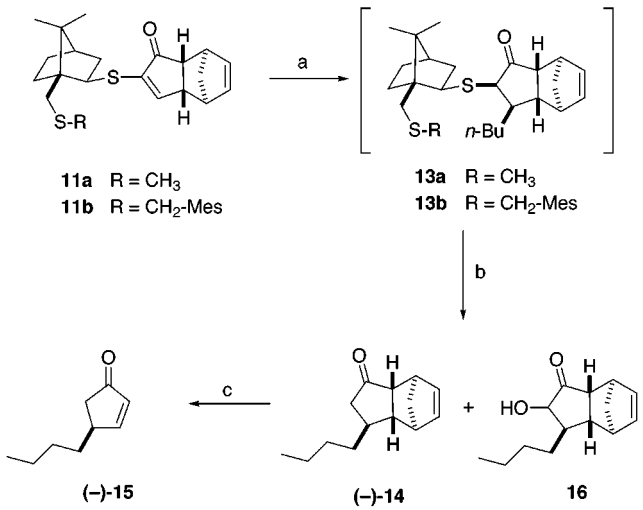


Figure 3. Mechanistic interpretation for the observed loss of stereoselectivity when performing the PKR in the presence of NMO.

by Grieco.[23] In this way, (−)-4-butylcyclopentenone (−)-**15** was obtained in 90% yield.

The enantiomeric purity of (−)-**15** was measured by chiral GC (α-Dex). Samples of (−)-**15** arising either from diastereomerically enriched **11a** or **11b** showed high enantiomeric excesses (94−96% ee) in good agreement with the diasteriomeric ratio of the starting adducts, thus confirming that no significant racemization takes place in the retro-Diels−Alder step.The absolute configuration of adducts **11a** and **11b** (as depicted in Scheme 4) could be established from the sign of the specific rotation of **14**, of known absolute configuration,[10,24] by assuming the universally observed exo configuration of the Pauson−Khand adducts involving norbornene and norbornadiene. The absolute configuration of the major diastereomer of adducts **12a**,**b** was established by chemical correlation since hydrogenation of the major stereoisomer of **11a**,**b** led to the major stereoisomer of **12a**,**b**. It is worth noting that the sense of the induction in the major Pauson−Khand adducts **11a**,**b** and **12a**,**b** is the same as observed using (2*R*)-10-methylthioisoborneol as a chiral auxiliary.[10] This fact strongly suggests that an analogous mechanism, which has been studied in detail,[10b] is operating. According to this mechanism, the coordination of the alkene is directed by the sulfur ligand to a precise cobalt atom (the *pro-R*) which is the one involved in the cobaltacycle formation. This selectivity, linked to the clear energetic preference for the anti-type cobaltacycles would be responsible for the high diastereoselectivity of the process. If the present reactions are compared with those of the analogous acetylenic ethers, the first remarkable difference is in reaction rates. Thus, albeit in a more stereoselective manner, the chelated complexes **10a**,**b** react with strained olefins at considerably lower rates than their oxygenated counterparts. This is clearly indicative of an increased stability of the chelated species, as the possibility of a purely thermal generation or of chromatographic separation also are. This superior stability of the chelated species could provide a clue for the

Scheme 4[a]



[a] Key: (a) *n*-$Bu_2CuCNLi_2$/diethyl ether; (b) SmI_2, THF/MeOH (from **11a**: 46% of (−)-**14**, 32% of **16**; from **11b**: 64% yield of (−)-**14)**; (c) $MeAlCl_2$, maleic anhydride, CH_2Cl_2 (94%).

(23) Grieco, P. A.; Abood, N. *J. Org. Chem.* **1989**, *54*, 6008−6010.
(24) Ackroyd, J.; Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1985**, *68*, 338−344.

understanding of an apparently anomalous result: the complete loss of stereoselectivity when the PKR is conducted in the presence of excess NMO. Once the pentacarbonyl complex is completely formed, if the equilibrium between chelated and nonchelated forms is easily established and a reactive olefin is present in the medium, reaction is predominantly directed toward the cobalt atom involved in chelation. On the other hand, if the chelated form is less reactive and excess NMO is present, further oxidative CO detachment can take place at any of the two diastereotopic cobalt atoms, with the undesired result of a nonselective reaction (Figure 3).

In summary, an extremely efficient asymmetric version of the Pauson−Khand reaction has been developed using camphor-derived chelating thiols. Among them, (2*R*)-10-(mesitylmethylthio)-2-*exo*-bornanethiol **1b** has proved to be an excellent chiral auxiliary: It can be prepared in high yield in only three steps from (1*S*)-camphor-10-thiol, and its ethynyl derivative gives excellent diastereoselectivities (up to 98:2 dr) in Pauson−Khand reactions with norbornene and norbornadiene. These reactions are carried out under purely thermal conditions, by simply generating a stable, chelated pentacarbonyl complex at 55 °C, cooling to 0 °C, and finally adding the reacting olefin at that temperature. The corresponding cycloadducts have been elaborated through a protocol consisting of conjugate addition, samarium iodide-induced cleavage of the chiral auxiliary and retro-Diels−Alder reaction to afford 4-substituted-2-cyclopentenones of high enantiomeric purity.

Experimental Section

General Methods. Melting points were determined in open capillary tubes and are uncorrected. Infrared spectra were recorded in Fourier transform mode, using film (NaCl) or KBr pellet techniques. ^{1}H NMR spectra were recorded at 200, 300, or 500 MHz in $CDCl_3$ unless specified otherwise, with tetramethylsilane as internal standard. *J* values are given in Hertz. ^{13}C NMR spectra were recorded at 50.3, 75.4, or 125.7 MHz in $CDCl_3$ unless specified otherwise. Signal multiplicities were established by DEPT experiments. In all cases, chemical shifts are in ppm downfield of TMS. Elemental analyses were performed by the Servei d'Anàlisis Elementals del CSIC de Barcelona, and exact mass measurements (HRMS) were performed by the Laboratori d'Espectrometria de Masses del CSIC de Barcelona or by the Servicio de Espectrometria de Masas, Universidad de Córdoba. THF and diethyl ether were distilled from sodium benzophenone ketyl. Dichloromethane was distilled from CaH_2. Hexamethyl phosphoramide (HMPA) was purified by distillation from CaH_2 at reduced pressure and stored over 4 Å molecular sieves. All reactions were performed in flame- or oven-dried glassware under a N_2 or Ar atmosphere. Silica gel (70−230 mesh) was used for column chromatography. (1*S*)-Camphor-10-thiol **2**,[16] (1*R*)-10-methylthiocamphorthione **4a**,[15] and 2,4,6-trimethylbenzyl bromide[18] were prepared by literature procedures. All other reagents were purchased commercially and used without further purification.

(2*R*-*exo*)-10-Methylthio-2-bornanethiol [(1*R*,2*R*)-7,7-Dimethyl-1-methylsulfanylmethylbicyclo[2.2.1]heptane-2-thiol] (1a). A. To a cold (−20 °C) solution of (1*R*)-10-methylthiocamphorthione (**4a**) (3.5 g, 16.3 mmol) in diethyl ether (40 mL) was added dropwise under nitrogen a solution of DIBAL-H (80 mL, 1 M in hexane). The reaction was monitored by TLC. After 4−7 h of stirring at −20 °C, cold diethyl ether (50 mL) and saturated NH_4Cl solution (40 mL) were carefully added, and the mixture was slowly allowed to warm to 0 °C. Then, 2 M HCl (ca. 60 mL) was added until two clear phases were formed. The aqueous layer was extracted with diethyl ether and the combined organic phases were washed with 10% $NaHCO_3$, dried over $MgSO_4$, and concentrated in vacuo. The crude oil was purified by column chromatography on Et_3N-pretreated silica gel (2.5% v/v) eluting with hexane to afford 3.1 g (88% yield) of a 10:1 mixture of *exo*- and *endo*-(2*R*)-10-methylthio-2-bornanethiol **1a** as a colorless oil.

B. To a solution of **5a** (0.1 g, 0.27 mmol) in methanol (3 mL) was added 1% NaOH/MeOH (10 mL) under stirring at room temperature. The reaction was monitored by TLC. After 5 min, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with hexane. The organic solution was evaporated and chromatographed on Et_3N-pretreated silica gel (2.5% v/v) eluting with hexane to afford 56 mg (95% yield) of diastereomerically pure **1a**: $[\alpha]_D = -97.3$ (*c* 1.9, $CHCl_3$); IR (film) $\nu_{max} = 2940, 2540, 1450$ cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.8 (m, 1H), 2.97, 2.55 (AB, $J = 11.4$ Hz, 2H), 2.4 (d, $J = 6.2$ Hz, 1H), 2.15 (s, 3H), 2.0−1.1 (m, 7H), 1.04 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.0 (C), 48.7 (C), 46.2 (CH), 43.7 (CH), 39.5 (CH_2), 36.1 (CH_2), 34.7 (CH_2), 27.2 (CH_2), 21.1 (CH_3), 20.1 (CH_3), 17.3 (CH_3); MS (CI-NH_3) *m*/*e* = 215 (M^+ − 1, 100). Anal. Calcd for $C_{11}H_{20}S_2$: C, 61.05; H, 9.32; S, 29.63. Found: C, 61.09; H, 9.52; S, 29.58.

(1*S*,2*R*)-7,7-Dimethyl-1-methylsulfanylmethyl-2-(4-nitrothiobenzoyl)bicyclo[2.2.1]heptane (5a). A solution of a diastereomeric mixture (10:1) of thiol **1a** (1.0 g, 4.67 mmol) in dichloromethane (3 mL) was added, under nitrogen, to a solution of 4-nitrobenzoyl chloride (1.73 g, 9.34 mmol) and pyridine (0.76 mL, 9.34 mmol) in dichloromethane (60 mL). The reaction mixture was stirred at room temperature for 24 h. The reaction was monitored by TLC until no starting material could be observed by TLC. The mixture was then treated with saturated NH_4Cl (3 mL) and water (15 mL) to dissolve all inorganic salts. The aqueous phase was extracted with dichloromethane, dried, and concentrated in vacuo. The crude reaction was chromatographed (3% diethyl ether/hexane) to afford 1.57 g (91% yield) of **5a** as a 10:1 mixture of exo and endo isomers: ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.0 (C), 151.0 (C), 143.0 (C), 128.3 (CH), 123.7 (CH), 53.5 (q), 48.5 (q, minor), 48.7 (q, major), 48.3 (CH), 46.3 (CH, major), 45.8 (CH, minor), 40.2 (CH_2, major), 39.2 (CH_2, minor), 36.6 (CH_2, minor), 36.2 (CH_2, major), 35.1 (CH_2), 29.5 (CH_2, minor), 30.0 (CH_2, minor), 27.1 (CH_2, major), 20.4 (CH_3), 20.2 (CH_3), 19.4 (CH_3, minor), 17.8 (CH_3).

The mixture of diastereomers was crystallized from 35 mL of 40% diethyl ether/hexane at −20 °C yielding 1.17 g of pure **5a** (69% overall yield) as yellow needles: mp 98−99 °C; $[\alpha]_D = -88.2$ (*c* 1.6, $CHCl_3$); IR (film) $\nu_{max} = 2993, 2939, 1667, 1605$ cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.31, 8.27, 8.15, 8.01 (broad s BB′, 4H), 4.1 (dd, 1H), 2.4−2.8 (AB, 2H), 2.07 (s, 3H), 2.1−1.1 (complex signal, 6H), 1.01 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 190.0 (C), 151.0 (C), 143.0 (C), 128.3 (CH), 123.7 (CH), 53.5 (C), 48.7 (C), 48.3 (CH), 46.3 (CH), 40.1 (CH_2), 36.2 (CH_2), 35.1 (CH_2), 27.1 (CH_2), 20.4 (CH_3), 20.2 (CH_3), 17.7 (CH_3). Anal. Calcd for $C_{18}H_{23}NO_3S_2$: C, 59.15; H, 6.34; N, 3.83; S, 17.55. Found: C, 59.06; H, 6.36; N, 3.88; S, 17.31.

(1*S*,4*R*)-7,7-Dimethyl-1-[(2,4,6-trimethylbenzylsulfanyl)-methyl]bicyclo[2.2.1]heptane-2-one (3b). To a suspension of sodium methoxide (1.2 g, 22.2 mmol) in methanol (20 mL) was added a solution of **2** (3.4 g, 18.5 mmol) in methanol (20 mL). After the mixture was stirred 30 min at room temperature, a solution of 2,4,6-trimethylbenzyl bromide (4.9 g, 21.4 mmol) in methanol (20 mL) was added. After the mixture was stirred for 4 h, the solvent was evaporated and the product was chromatographed on silica gel eluting with hexane to afford 4.7 g of **3b** (81% yield): mp 73.3−73.7 °C; $[\alpha]_D = 30.6$ (*c* 1.2, $CHCl_3$); IR (film) $\nu_{max} = 2900, 1710, 1590, 1420$ cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.82 (broad s, 2H), 3.81 (s, 2H), 2.90, 2.59 (AB, $J = 13.4$ Hz, 2H), 2.39 (s, 6H), 2.23 (s, 3H), 2.45−1.20 (complex signal, 7H), 1.02 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.9 (2C), 136.3 (C), 131.2 (C), 128.9 (2CH), 62.0 (C), 47.7 (C), 43.4 (CH), 43.1 (CH_2), 33.6 (CH_2), 29.7 (CH_2), 26.8 (CH_2), 26.6 (CH_2), 20.9 (CH_3), 20.2 (CH_3), 20.1 (CH_3), 19.6 ($2CH_3$) ppm; MS (CI-NH_3) *m*/*e* = 334 (M^+ + 18, 100). Anal. Calcd for $C_{20}H_{28}OS$: C, 75.90; H, 8.92; S, 10.13. Found: C, 75.90; H, 9.01; S, 10.18.

(1*S*,4*R*)-7,7-Dimethyl-1-[(2,4,6-trimethylbenzylsulfanyl)-methyl]bicyclo[2.2.1]heptane-2-thione (4b). To a solution of **3b** (1.85 g, 5.86 mmol) in toluene (5 mL) was added via syringe a solution of Lawesson's reagent (3.5 g, 8.8 mmol) in toluene (25 mL). The reaction mixture was heated under reflux (125 °C) during 12 h, cooled to room temperature, and filtered. The solution was concentrated, and the crude reaction was chromatographed eluting with diethyl ether/hexane (2.5%) to yield 1.43 g of thione **4b** as an orange oil (74% yield): $[\alpha]_D$ = +74.26 (*c* 1.4, $CHCl_3$); IR (film) ν_{max} = 2960, 1620, 1590 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.83 (broad s, 2H), 3,78 (s, 2H), 3.19, 2.73 (AB, *J* = 11.6 Hz, 2H), 2.39 (s, 6H), 2.24 (s, 3H), 2.45−1.20 (complex signal, 7H), 1.09 (s, 3H), 0.85 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ = 136.9 (2C), 136.5 (C), 131.5 (C), 128.9 (2CH), 72.1 (C), 55.3 (CH_2), 49.9 (C), 45.7 (CH), 33.8 (CH_2), 32.8 (CH_2), 30.6 (CH_2), 27.0 (CH_2), 20.9 (CH_3), 20.7 (CH_3), 20.2 (CH_3), 19.7 ($2CH_3$) ppm; HRMS Calcd for $C_{20}H_{28}S_2$ 332.1632, found 332.1639.

(1*S*,2*R*,4*R*)-7,7-Dimethyl-1-[(2,4,6-trimethylbenzylsulfanyl)methyl]bicyclo [2.2.1]heptane-2-thiol (1b). To a cold (−60 °C) solution of thione **4b** (1.06 g, 3.2 mmol) in anhydrous diethyl ether (15 mL) was added via cannula a solution of DIBALH (16 mL, 1 M in hexane). The reaction mixture was allowed to warm to −40 °C and stirred at this temperature until the orange color disappeared. After 6 h, diethyl ether (11 mL) and saturated NH_4Cl (8 mL) were added dropwise with caution. When the gas evolution was finished, the temperature was warmed to 0 °C and the dense mixture was treated with 33 mL of 5% HCl to dissolve all the aluminum salts. The organic layer was separated, and the aqueous phase was extracted with diethyl ether. The combined organic layers were dried and evaporated, yielding a crude that was purified by column chromatography (hexane) to afford 0.96 g of **1b** as a colorless oil (90% yield): $[\alpha]_D$ = −73.1 (*c* 1.5, $CHCl_3$); IR (film) ν_{max} = 2950, 1730, 1620, 1580, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.85 (broad s, 2H), 3.84−3.79 (AB, *J* = 11.2 Hz, 2H), 3.25−2.75 (m, 1H), 3.10,2.67 (AB, *J* = 11.1 Hz, 2H), 2.43 (s, 6 H), 2.38, 2.35 (d, 1H), 2.26 (s, 3H), 1.95−1.00 (complex signal, 7H), 1.07 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8 (2C), 136.4 (C), 131.3 (C), 129.0 (2CH), 51.9 (C), 48.8 (C), 46.2 (CH), 43.8 (CH), 39.5 (CH_2), 34.7 (CH_2), 34.2 (CH_2), 32.5 (CH_2), 27.2 (CH_2), 21.1 (CH_3), 20.9 (CH_3), 20.1 (CH_3), 19.7 ($2CH_3$) ppm; MS (CI-NH_3) *m*/*e* = 352 (M^+ + 18, 100), 335 (M^+ + 1, 29); HRMS calcd for $C_{20}H_{30}S_2$ 334.1789, found 334.1803.

(1*S*,2*R*)-2-(2,2-Diethoxyethylsulfanyl)-7,7-dimethyl-1-methylsulfanylmethylbicyclo[2.2.1]heptane (6a). To a stirred suspension of sodium ethoxide in ethanol (47 mg, 2.05 mmol of sodium in 5 mL of ethanol) was added dropwise a solution of **1a** (420 mg, 2.05 mmol) in ethanol (9 mL). After 45 min of stirring at room temperature, 2-bromo-1,1-diethoxyethane (0.31 mL, 2.05 mmol) was added. The reaction mixture was stirred under reflux 1.5 h and then poured into ice/water. The aqueous layer was extracted with dichloromethane, and the combined organic phases were dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography on Et_3N-pretreated silica gel **6a** as an oil: $[\alpha]_D$ = −36.8 (*c* 2.1 $CHCl_3$); IR (film) ν_{max} = 2950, 2870, 1450, 1125 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.61 (t, *J* = 5.7 Hz, 1H), 3.85−3.49 (m, 4H), 2.97, 2.49 (AB, *J* = 11.7 Hz, 2H), 2.95, 2.81 (ABX, *J* = 13.5 Hz, J′= 5.4 Hz, 2H), 2.89 (dd, *J* = 7.8 Hz, 1H), 2.12 (s, 3H), 1.98−1.08 (m, 7H), 1.21 (dt, *J* = 6.9 Hz, J′= 2.4 Hz, 6H), 0.93 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 103.2 (CH), 62.0 (CH_2), 61.5 (CH_2), 53.6 (C), 53.5 (CH), 48.2 (C), 46.2 (CH), 41.6 (CH_2), 38.6 (CH_2), 36.2 (CH_2), 34.9 (CH_2), 27.2 (CH_2), 20.51 (CH_3), 20.45 (CH_3), 17.6 (CH_3), 15.3 (CH_3), 15.3 (CH_3) ppm.; MS (CI-NH_3) *m*/*e* = 350 (M^+ + 18, 6), 333 (M^+ + 1, 1), 215 (100).

(1*S*,2*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-methylsulfanylmethylbicyclo[2.2.1]heptane (7a). Method A. To a cold (60 °C) LDA solution (prepared from diisopropylamine (0.73 mL, 5.2 mmol) and *n*-BuLi (3.6 mL, 1.45 M in hexane, 5.2 mmol) in diethyl ether (30 mL)) was added a solution of **6a** (0.52 g, 1.57 mmol) in diethyl ether (7 mL). The temperature was allowed to warm to 0 °C and the mixture stirred for 3 h. The reaction was quenched by addition of saturated NH_4-Cl solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic phases were dried (Na_2SO_4) and evaporated. The crude product was purified by column chromatography on Et_3N-pretreated silica gel (2.5% v/v) eluting with diethyl ether/hexane mixtures of increasing polarity to yield 0.31 g of **7a** (81%) as an oil.

Method B. To a suspension of oil-free KH (1.74 mmol) in anhydrous THF (2 mL) was added, under nitrogen, a solution of **1a** (0.25 g, 1.16 mmol) in THF (3 mL). After hydrogen evolution subsided (15 min), the mixture was cooled to −50 °C and a solution of trichloroethylene (0.116 mL, 1.28 mmol) in THF (2 mL) was added dropwise. Then, 20 μL of methanol was added, and the reaction mixture was allowed to warm to room temperature. After 1.5 h of stirring, the mixture was cooled to −70 °C and treated with 1 mL of a 2.5 M solution of *n*-BuLi in hexane (2.5 mmol). After 0.5 h at −70 °C, the reaction was slowly warmed to room temperature and stirred for 1.5 h. Then, it was quenched with methanol (0.5 mL) and poured into 6 mL of saturated NH_4Cl solution. The product was extracted with hexane. The combined organic extracts were washed with water, dried, evaporated, and purified by column chromatography (diethyl ether/hexanes 2.5%) yielding 0.20 g of **7a** (71%) as an oil: $[\alpha]_D$ = −86.6 (*c* 1.9 $CDCl_3$); IR (film) ν_{max} = 3280, 2950, 2030, 1450 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.41 (dd, *J* = 9 Hz, J′= 5.7 Hz, 1H), 2.85 (s, 1H), 2.75, 2.58 (AB, *J* = 12 Hz, 2H), 2.15 (s, 3H), 2.1−0.97 (m, 7H), 0.93 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 82.3 (CH), 75.6 (C), 55.9 (CH), 53.5 (C), 48.4 (C), 46.2 (CH), 39.2 (CH_2), 35.5 (CH_2), 34.7 (CH_2), 26.9 (CH_2), 20.5 (CH_3), 20.2 (CH_3), 17.7 (CH_3); MS (EI) *m*/*e* = 240 (M^+, 47), 135 (100); HRMS calcd for $C_{13}H_{20}S_2$ 240.1006, found 240.1003.

(1*S*,2*R*)-2-(1,2-Dichlorovinylsulfanyl)-7.7-dimethyl-1-(2,4,6-trimethylbenzylsulfanyl)methylbicyclo[2.2.1]-heptane (8b). To a stirred suspension of oil-free KH (0.57 g, 5 mmol) in anhydrous THF (10 mL) was added dropwise a solution of thiol **1b** (1.1 g, 3.32 mmol) in THF (10 mL). After hydrogen evolution (20 min), the mixture was cooled to −50 °C and a solution of trichloroethylene (0.47 mL, 5 mmol) in THF (2 mL) was added dropwise, followed by 10 μL of methanol. The reaction mixture was allowed to warm to room temperature (1.5 h) and stirred for 1 h. The reaction was quenched with 1 mL of methanol and concentrated in vacuo. Then, the mixture was treated with saturated NH_4Cl solution (5 mL) and extracted with hexane. The combined organic layers were dried and evaporated. The crude was chromatographed eluting with hexane to afford 0.96 g of **8b** (70% yield): $[\alpha]_D$ = −103.7 (*c* 1.3, $CHCl_3$); IR (film) ν_{max} = 2956, 1613, 1459, 1389 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.82 (broad s, 2H), 6.32 (s, $CDCl_3$ 1H), 3.77 (s, 2H), 3.60 (t, 1H), 2.94, 2.65 (AB, *J* = 12.2 Hz, 2H), 2. 39 (s, 6H), 2.23 (s, 3H), 2.01−1.15 (m, 7H), 1.03 (s, 3H), 0.90 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 136.9 (2C), 136.3 (C), 131.8 (C), 131.3 (C), 128.9 (2CH), 117.4 (CH), 53.5 (C), 52.5 (CH), 48.7 (C), 46.3 (CH), 40.4 (CH_2), 35.0 (CH_2), 33.8 (CH_2), 32.9 (CH_2), 27.1 (CH_2), 20.9 (CH_3), 20.6 ($2CH_3$), 19.6 ($2CH_3$); HRMS calcd for $C_{22}H_{30}S_2Cl_2$ 428.1166, found 428.1149.

(1*S*,2*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-(2,4,6-trimethylbenzylsulfanyl)methylbicyclo[2.2.1]heptane (7b). To a cold (−80 °C) solution of dichloroolefine **8b** (315 mg, 0.74 mmol) in of anhydrous diethyl ether (12 mL) was added a solution of *n*-BuLi (0.65 mL, 2.5 M in hexanes, 1.62 mmol). The mixture was stirred for 30 min at −40 °C, 5 min at 0 °C, and 20 min at room temperature. Then, the reaction mixture was treated with saturated NH_4Cl solution (2 mL), the organic phase was separated, and the aqueous layer was extracted with diethyl ether. The combined organic phases were dried and evaporated to afford 255 mg of **7b** (96% yield): $[\alpha]_D$ = −40.9 (*c* 1.5, $CHCl_3$); IR (film) ν_{max} = 3300, 2960, 2050, 1620 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.83 (broad s, 2H), 3.82 (s, 2H), 3.5−3.38 (m, 1H), 2.85 (s, 1H), 2.85, 2.65 (AB, *J* = 11 Hz, 2H), 2.42 (s, 6H), 2.24 (s, 3H), 2.2−1.05 (complex signal, 7H), 0.97 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 137.0 (2C), 136.4 (C), 131.2 (C), 128.9 (2CH), 82.5 (CH), 55.9 (CH), 53.4 (C), 48.5 (C), 46.3 (CH), 39.4 (CH_2), 34.9 (CH_2), 33.6 (CH_2), 33.0 (CH_2),

27.0 (CH_2), 20.9 (CH_3), 20.6 (CH_3), 20.3 CH_3), 19.7 ($2CH_3$) ppm; HRMS calcd for $C_{22}H_{30}S_2$ 358.1789, found 358.1781.

Dicobalt Hexacarbonyl Complex of (1*S*,2*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-(methylsulfanylmethyl)bicyclo-[2.2.1]heptane (9a). To a solution of **7a** (80 mg, 0.33 mmol) in hexanes (8 mL) was added, under CO atmosphere, $Co_2(CO)_8$ (118 mg, 0.35 mmol) in one portion. The mixture was stirred for 15 min at room temperature (the reaction can be conveniently monitored by TLC). Then, it was filtered through a short Al_2O_3 pad eluting with hexane. The solvent was evaporated in vacuo yielding 160 mg (91%) of **9a**: IR (film) ν_{max} = 2960, 2100, 2060, 2030, 1970 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.36 (s, 1H), 3.13 (dd, J = 9 Hz, J'= 6.3 Hz, 1H), 2.75, 2.57 (AB, J = 11.7 Hz, 2H), 2.21−1.2 (m, 7H), 2.09 (s, 3H), 0.98 (s, 3H), 0.90 (s, 3H);^{13}C NMR (75.4 MHz, $CDCl_3$) δ 199.3 (C), 77.97 (C), 58.7 (CH), 53.9 (C), 48.4 (C), 46.4 (CH), 41.4 (CH_2), 36.4 (CH_2), 35.1 (CH_2), 27.4 (CH_2), 20.8 (CH_3), 20.1 (CH_3), 17.5 (CH_3).

Dicobalt Hexacarbonyl Complex of (1*S*,2*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-[(2,4,6-trimethylbenzylsulfanyl)methyl]bicyclo[2.2.1]heptane (9b). To a solution of **7b** (0.2 g, 0.57 mmol) in hexanes (9 mL) was added, under N_2, $Co_2(CO)_8$ (0.21 g, 0.61 mmol) in one portion. The mixture was stirred for 20 min at room temperature (the reaction can be conveniently monitored by TLC). The resulting solution was used without further purification in the subsequent reactions. Evaporation of a sample allowed its characterization although some pentacarbonyl complex **10b** was observed in the spectra: IR (film) ν_{max} = 2958, 2092, 2063, 2012, 1962 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.81 (broad s, 2H), 6.34 (s, 1H), 3.80−3.67 (AB, J = 11.55 Hz, 2H), 3.15 (dd, J = 8.1 Hz, J'=4.8 Hz, 1H), 2.95, 2.49 (AB, J = 12.5 Hz, 2H), 2.36 (s, 6H), 2.23 (s, 3H), 2.2−0.8 (m, 7H), 0.99 (s, 3H), 0.88 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.8 (C), 136.2 (2C), 131.6 (C), 128.8 (2CH), 78.0 (CH), 58.8 (CH), 54.3 (C), 48.3 (C), 46.6 (CH), 41.3 (CH_2), 35.2 (CH_2), 34.4 (CH_2), 33.1 (CH_2), 27.3 (CH_2), 20.9 (CH_3), 20.2 (CH_3), 20.1 ($2CH_3$), 19.7 (CH_3) ppm.

Dicobalt Pentacarbonyl Complex of (1*S*,2*R*,4*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-(methylsulfanylmethyl)-bicyclo[2.2.1]heptane (10a). Thermal Generation. A hexane solution of dicobalt hexacarbonyl complex **9a** prepared from **7a** (80 mg, 0.33 mmol) was heated at 55 °C under a stream of anhydrous nitrogen during 1 h (the reaction can be conveniently monitored by TLC; the red spot of the hexacarbonyl complex disappears while a brown, more polar complex is formed). The mixture was filtered through Al_2O_3 eluting with hexanes, and the solvent was removed in vacuo to afford 146 mg (89% yield, two steps) of the dicobalt pentacarbonyl complex **10a**.

NMO Promoted. To a solution of dicobalt hexacarbonyl complex **9a** prepared from **7a** (60 mg, 0.25 mmol) in CH_2Cl_2 (5 mL) was added, under nitrogen atmosphere, NMO (88 mg, 3 equiv, 0.75 mmol). After 10 min of stirring at room temperature, only the pentacarbonyl complex could be observed by TLC. Pentane (15 mL) was added to the mixture, and the solution was concentrated to a final volume of ca. 5−10 mL. The crude was chromatographed on Al_2O_3 eluting with pentane, yielding 80 mg (65% yield, two steps) of **10a**: IR (film) ν_{max} = 2950, 2070, 2005, 1965 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.89 (s, 1H), 3.51, 2.44 (AB, J = 11.4 Hz, 2H), 2.94 (dd, J = 9 Hz, J' = 6.3 Hz, 1H), 2.45 (s, 3H), 2−1.26 (m, 6H), 1.07 (s, 3H), 0.98−0.95 (m, 1H), 0.89 (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 200 (C), 77.8 (C), 57.7 (CH), 53.9 (C), 48.9 (C), 46.5 (CH), 44.4 (CH_2), 36.1 (CH_2), 34.8 (CH_2), 28.7 (CH_3), 27.1 (CH_2), 20.5 (CH_3), 19.8 (CH_3).

Dicobalt Pentacarbonyl Complex of (1*S*,2*R*,4*R*)-2-Ethynylsulfanyl-7,7-dimethyl-1-[(2,4,6-trimethylbenzylsulfanyl)methyl]bicyclo[2.2.1]heptane (10b). Thermal Generation. The procedure described in the generation of **10a** starting from **7b** (0.2 g, 0.57 mmol) and $Co_2(CO)_8$ (0.21 g, 0.61 mmol) afforded a solution of **10b** that was used without purification.

NMO Promoted. To a solution of hexacarbonyl complex **9b** prepared as described above from **7b** (0.119 g, 0.33 mmol) was added NMO (0.24 g, 2.06 mmols, 6 equiv). After 20 min of stirring at room temperature, only the pentacarbonyl complex could be observed by TLC. The solution was used without further purification. Evaporation of a sample allowed its characterization: $[\alpha]_D$ = −853.3 (*c* 0.4, $CHCl_3$); IR (film) ν_{max} = 2956, 2063, 2012, 1962, 1654 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.88 (broad s, 2H), 5.95 (s, 1H), 4.02,3.80 (AB, J = 13.0 Hz, 2H), 3.31 (d, J = 11.1 Hz, 1H), 2.9, 2.8 (m, 1H), 2.35 (s, 6H), 2.27 (s, 3H), 2.1−0.8 (m, 8H), 1.01 (s, 3H), 0.54 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7 (C), 137.3 (2C), 129,4 (2CH), 128.7 (C), 78.5 (CH), 57.5 (CH), 54.1 (C), 48.6 (C), 46.6 (CH), 41.2 (CH_2), 38.6 (CH_2), 36.1 (CH_2), 34.4 (CH_2), 26.9 (CH_2), 20.1 ($2CH_3$), 20.1 (CH_3), 19.8 (CH_3) ppm; MS (FAB, NBA) 588 (M^+ − CO, 2), 560 (M^+ − 2CO, 30), 476 (M^+ − 5CO, 100).

General Procedures for Pauson−Khand Reactions. Cycloadduct of 7a with Norbornadiene. Reaction Conditions A. To a solution of alkynyl thioether **7a** (40 mg, 0.17 mmol) in hexanes (4 mL) in CO atmosphere was added $Co_2(CO)_8$ (61 mg, 0.18 mmol) in one portion. After 15 min of stirring at room temperature, the dark red solution was cooled to 0 °C, and 2,5-norbornadiene (0.17 mL, 1.7 mmol) was added. The mixture was stored at 0−5 °C during 23 days. Then, the crude reaction was filtered and the solvent was evaporated. Flash column chromatography (2% v/v NEt_3 pretreated SiO_2, hexanes/diethyl ether) afforded 19 mg (31% yield, two steps) of **11a** (67:33 diastereomeric ratio).

Reaction Conditions B. To a solution of thioether **7a** (40 mg, 0.17 mmol) in dichloromethane (4 mL) was added $Co_2(CO)_8$ (61 mg, 0.18 mmol) in one portion. After 15 min of stirring at room temperature, NMO (119 mg, 1.02 mmol) was added. After 10 min of stirring, the solution was cooled to 0 °C, and 2,5-norbornadiene (0.17 mL, 1.7 mmol) was added. The mixture was stirred for 24 h at 0 °C, filtered, and chromatographed yielding 39 mg (64% yield) of a 2.1:1 diastereomeric mixture of adducts **11a**. The same reaction conditions but performing the reaction at −20 °C during 60 h afforded 41 mg (67% yield, two steps) of **11a** (50:50 diastereomeric ratio).

Reaction Conditions C. To a solution of a thermally generated pentacarbonyl complex **10a** (146 mg, 0.29 mmol) in hexanes (6 mL) at 0 °C was added 2,5-norbornadiene (0.29 mL, 2.9 mmol). The reaction was stirred 24 h at 0 °C. The mixture was filtered through Celite washing with CH_2Cl_2. The solution was concentrated and chromatographed to afford 55 mg (52% yield) of a 92:8 diastereomeric mixture of **11a**. The same reaction conditions but performing the reaction at −20 °C during 6 days afforded 57 mg (53% yield) of **11a** (93:7 diastereomeric ratio).

Reaction Conditions D. To a solution of an NMO-generated pentacarbonyl complex **10a** (451 mg, 0.9 mmol) in hexanes (17 mL) was added 2,5-norbornadiene (0.95 mL, 9 mmol) at −10 °C. The reaction was stirred for 76 h at this temperature. The mixture was filtered through Celite, concentrated, and chromatographed to afford 211 mg (65% yield) of **11a** (95:5 diastereomeric ratio).

4-[(1*S*,2*R*,4*R*)-7,7-Dimethyl-1-methylsulfanylmethyl-bicyclo[2.2.1]hept-2-ylsulfanyl]tricyclo[5.2.1.0^{2,6}]deca-4,8-dien-3-one (11a): IR (film) ν_{max} = 3060, 2940, 1700, 1560 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (minor), 7.10 (major) (d, J = 3 Hz, 1H), 6.27−6.17 (m, 2H), 3.39 (minor), 3.33 (major) (dd, J = 8.7 Hz, J'= 5.7 Hz, 1H), 2.92 (s, 1H), 2.84−2.5 (m, 2H), 2.77 (s, 1H), 2.69 (s, 1H), 2.36−2.34 (m, 1H), 2.08 (major), 2.05 (minor) (s, 3H), 2.04−1.18 (m, 9H), 1.02 (major), 0.99 (minor) (s, 3H), 0.88 (major), 0.87 (minor) (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 206.1 (C), 153.7 (CH, minor), 153.5 (CH), 146.2 (C), 146.1 (C, minor), 138.3 (CH), 137.1 (CH), 53.7 (C), 52.6 (CH), 52.5 (CH, minor), 50.5 (CH), 50.2 (CH, minor), 48.7 (C), 48.6 (CH, minor), 48.6 (CH), 46.4 (CH), 46.3 (CH, minor), 44.0 (CH, minor), 43.9 (CH), 43.7 (CH, minor), 43.7 (CH), 41.6 (CH_2), 41.5 (CH_2, minor), 40.8 (CH_2), 40.7 (CH_2, minor), 35.9 (CH_2, minor), 35.8 (CH_2), 35.3 (CH_2), 35.1 (CH_2, minor), 27.4 (CH_2), 27.3 (CH_2, minor), 20.7 (CH_3), 20.7 (CH_3), 20.6 (CH_3, minor), 17.8 (CH_3); MS (EI) *m/e* = 360 (M^+,16), 183 (100); HRMS calcd for $C_{21}H_{28}OS_2$ 360.1582, found 360.1580; HPLC analysis (Nucleosil C_{18}, 25 cm) MeOH/H_2O 80/20 (1 mL/min, λ = 220 nm) t_R (major) = 16.5 min, t_R (minor) = 17.3 min.

Pauson−Khand Reaction of 7a with Norbornene. Procedure B using as reagents **7a** (50 mg, 0.21 mmol), $Co_2(CO)_8$ (75 mg, 0.22 mmol), NMO (147 mg, 1.25 mmol), and norbornene (197 mg, 2.1 mmol) was followed. The reaction was conducted at 0 °C during 48 h affording 50 mg (66% yield, two steps) of **12a** (37:63 diastereomeric ratio as determined by ^{13}C NMR).

Procedure C using as reagents **7a** (50 mg, 0.21 mmol), $Co_2(CO)_8$ (75 mg, 0.22 mmol), and norbornene (197 mg, 2.1 mmol) was followed. The reaction was conducted at 0 °C during 48 h affording 34 mg (45% yield, two steps) of **12a** (82:18 diastereomeric ratio as determined by ^{13}C NMR).

Procedure D using as reagents **10a** (83 mg, 0.17 mmol), and norbornene (167 mg, 1.7 mmol) was followed. The reaction was conducted at −10 °C during 120 h affording 40 mg (66% yield, two steps) of **12a** (86:14 diastereomeric ratio as determined by ^{13}C NMR).

4-[(1*S*,2*R*,4*R*)-7,7-Dimethyl-1-methylsulfanylmethylbicyclo[2.2.1]hept-2-ylsulfanyl]tricyclo[5.2.1.0^{2,6}]dec-4-en-3-one (12a): IR (film) ν_{max} = 2960, 2880, 1705, 1570 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.08 (minor), 7.03 (major) (d, J = 3 Hz, 1H), 3.39 (minor), 3.33 (major) (dd, J = 9 Hz, J' = 5.7 Hz, 1H), 2.83−2.78 (m, 1H), 2.66−2.63 (m, 1H), 2.6−2.5 (m, 1H), 2.41 (d, J = 3.6 Hz, 1H), 2.26 (d, J = 4.5 Hz, 1H), 2.18 (d, J = 4 Hz, 1H), 2.08 (major), 2.06 (minor) (s, 3H), 2.06−0.9 (m, 13H), 1.02 (major), 0.99 (minor) (s, 3H), 0.88 (major), 0.87 (minor) (s, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 207.4 (C), 153.5 (CH, minor), 153.2 (CH), 145.2 (C), 53.85 (CH, minor), 53.82 (CH), 53.6 (C), 50.4 (CH), 50.2 (CH, minor), 49.26 (CH), 49.20 (CH, minor), 48.63 (C), 48.58 (C, minor), 46.28 (CH), 46.23 (CH, minor), 40.7 (CH_2), 40.6 (CH_2, minor), 39.3 (CH, minor), 39.2 (CH), 38.6 (CH, minor), 38.6 (CH), 35.8 (CH_2, minor), 35.7 (CH_2), 35.2 (CH_2), 35.0 (CH_2, minor), 31.3 (CH_2), 31.3 (CH_2, minor), 28.8 (CH_2, minor), 28.8 (CH_2), 28.3 (CH_2, minor), 28.3 (CH_2), 27.2 (CH_2), 27.2 (CH_2, minor), 20.5 (CH_3, minor), 20.6 (CH_3), 20.6 (CH_3), 17.6 (CH_3); MS (CI-CH_4) m/e = 363 (M^+ + 1, 100).

(1*R*,2*R*,6*S*,7*S*)-5-Butyl-4-[(1*S*,2*R*,4*R*)-7,7-dimethyl-1-methylsulfanylmethylbicyclo[2.2.1]hept-2-ylsulfanyl]-tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (13a). A solution of $Bu_2CuCNLi_2$ in diethyl ether was prepared as follows: To a cold (−50 °C) suspension of CuCN (95 mg, 1.06 mmol) in deoxygenated diethyl ether (12 mL) was added, under argon, *n*-BuLi (1.6 M in hexanes, 1.32 mL, 2.12 mmol), and the resulting solution was stirred for 30 min at −30 °C. To this cuprate solution, cooled to −78 °C, was added via cannula under argon a solution of enone **11a** (0.19 g, 0.53 mmol) in diethyl ether (2 mL). After 10 min of stirring, wet but deoxygenated diethyl ether (6 mL) was added. The reaction mixture was allowed to warm to 0 °C, and 10% NH_4OH in saturated NH_4Cl solution (20 mL) was added. The reaction was vigorously stirred at room temperature 30 min and extracted with dichloromethane. The combined organic phases were dried (Na_2SO_4) and evaporated yielding 0.2 g of an oil that was immediately used in the next step without characterization.

(1*R*,2*R*,6*S*,7*S*)-5-Butyl-4-[(1*S*,2*R*,4*R*)-7,7-dimethyl-1-(2,4,6-trimethylbenzylsulfanyl)methylbicyclo[2.2.1]hept-2-ylsulfanyl]tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one (13b). The cuprate addition was performed following the procedure described above for **13a** but starting from adduct **11b** (139 mg, 0.29 mmol) to give 156 mg of an oil that was immediately used in the next step without characterization.

(1*R*,2*R*,5*S*,6*S*,7*S*)-5-Butyltricyclo[5.2.1.0^{2,6}]-8-decen-3-one [(−)-14].[10,23] **From 13a.** A solution of SmI_2 was prepared as follows: Samarium powder (259 mg, 1.72 mmol) and 1,2-diiodoethane (485 mg, 1.72 mmol) were placed under argon in a Schlenk flask.. Then THF (2.6 mL) was added and the mixture vigorously stirred 2 h at room temperature. The crude reaction **13a** was dissolved in a mixture of THF/MeOH (2:1) and added via cannula to a freshly prepared, cold (0 °C) SmI_2 solution in THF. After 10−15 min, no starting material was observed by TLC. Then, wet THF, hexane, and saturated Na_2CO_3 solution were sequentially added. The phases were separated, and the aqueous layer was extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4) and evaporated yielding 0.18 g of a residue that was chromatographed eluting with hexane/diethyl ether mixtures to afford 50 mg (46% yield, two steps) of (−)-**14** [$[\alpha]_D$ = −115.8 (*c* 1.0, $CHCl_3$)] along with 20 mg of thiol **1a** (17% yield), 47 mg of disulfide (41% yield) and 37 mg of 5-butyl-4-hydroxytricyclo-[5.2.1.0^{2,6}]deca-4,8-dien-3-one.

From 13b. The crude reaction **13b** was treated with 4 equiv of SmI_2 solution in THF prepared as described. Once the reaction with SmI_2 was complete, it was quenched by bubbling oxygen into the reaction followed by addition of wet THF (4 mL) and saturated 10/1 K_2CO_3/potassium tartrate solution (4 mL). The mixture was extracted with hexane, and the organic phases were dried ($MgSO_4$), evaporated, and chromatographed on NEt_3 pretreated SiO_2 eluting with 0.5% diethyl ether/hexane to afford 38 mg (64% yield, two steps) of (−)-**14** along with 75 mg (59%) of thiol **1b**. The spectroscopic data of **14** were fully coincident with those described in ref 10.

(−)-(*S*)-4-Butyl-2-cyclopentenone (−)-15.[10,24] In a round-bottomed flask under nitrogen were placed (−)-**14** (130 mg, 0.63 mmol), maleic anhydride (0.3 g, 3.1 mmol), and CH_2Cl_2 (4 mL). To this solution was added $MeAlCl_2$ (1 M in hexane, 0.7 mL, 0.7 mmol) via syringe. The reaction mixture was then heated at 55 °C for 2 h, cooled to room temperature, quenched with saturated K_2CO_3 solution, and filtered through Celite. The residue was purified by flash column chromatography (2% v/v NEt_3 pretreated SiO_2, hexane/diethyl ether) and afforded 85 mg (90%) of (−)-(*S*)-4-butyl-2-cyclopentenone as a colorless oil. Enantiomeric purity: CG (α-Dex 120) 30 m, 0.25 mm i.d. 45 min isocratic at 70 °C, then 0.2 °C/min until 90 °C; t_R (min) = 128.8 (maj), 133.5 (min). The product obtained from a sample of **11a** of 95% de showed an enantiomeric purity of 96% ee. The product obtained from **11b** (96% de) showed an enantiomeric purity of 94% ee. Spectroscopic data of **15** were fully coincident with those described in ref 10.

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Supporting Information Available: ^1H NMR spectra of cobalt carbonyl complexes **9a**,**b** and **10a**,**b**. Experimental procedures and product characterization of the Pauson−Khand reactions of **7b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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