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PuPHOS: A Synthetically Useful Chiral Bidentate Ligand for the Intermolecular Pauson−Khand Reaction

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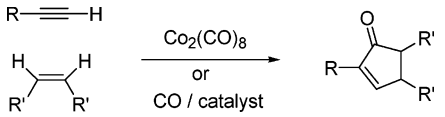
Here we describe the synthesis and use of the Pulegone-derived bidentate P,S ligands PuPHOS and CyPuPHOS in the intermolecular Pauson−Khand reaction. Ligand exchange reaction of hexacarbonyldicobalt−alkyne complexes with PuPHOS provides a diasteromeric mixture of complexes (up to 4.5:1) from which the major isomers can be conveniently separated by simple crystallization. An isomerization−crystallization sequence of the original mixture results in a dynamic resolution that allows the preparation of the pure major $Co_2(\mu\text{-}TMSC_2H)(CO)_4$−PuPHOS (**15a**) in a multigram scale. Pauson−Khand reaction of **15a** with norbornadiene provided, for the first time, the corresponding enone **18** with up to 93% yield and 97% ee. The use of (+)-**18** as a surrogate of chiral cyclopentadienone is also demonstrated. Copper-catalyzed Michael addition of a Grignard reagent followed by removal of the TMS group with TBAF were the most reliable methods to transform (+)-**18** into valuable starting materials **20a**−**e** for the enantioselective synthesis of cyclopentenoid systems.

Introduction

The Pauson−Khand reaction[1] (PKR) is one of the most useful reactions for the construction of cyclopentanic compounds. The number of references on this reaction has grown exponentially in the past decade, which shows the increasing interest of synthetic chemists on this transformation.



Perhaps the greatest unaccomplished target on this field is the development of general catalytic asymmetric versions. Although several useful versions based on the chiral auxiliary approach[2] have been developed, and great progress has been achieved in catalytic intramolecular reactions,[3] many of which are mediated by metals other than cobalt,[4] we are still far from achieving a practical asymmetric process. Probably a logical approach toward this goal would be the development of chiral ligands that (i) bind alkyne−dicobalt hexacarbonyl complexes in high diastereoselectivity, (ii) give stereospecific cyclization reactions (in other words, that diastereomerically pure ligand complexes give enantiomerically pure adducts), and (iii) increase the reaction rate (ligand-accelerated reaction) in relation to the nonligand complexes. In 1988 Brunner pioneered the field by describing the first PKR

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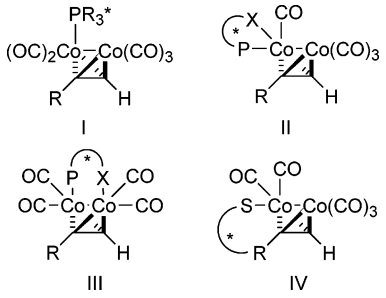
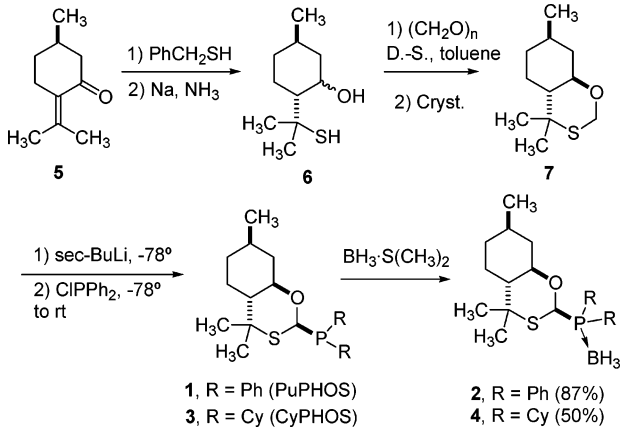


FIGURE 1. Distinct types of chiral cobalt complexes with chiral ligands or chelating auxiliaries.

of a cobalt complex such as **I** coordinated with a chiral ligand (see Figure 1). The use of monophosphine Glyphos allowed a complete stereospecific PKR between phenylacetylene and norbornene.[5] However, the coordination of the phosphine to the complex was unselective affording a 1:1 mixture of diastereomers which, in addition, epimerized at 60 °C in toluene.

The lack of diastereoselectivity in the preparation of complexes **I** directed our efforts toward the use of bidentate ligands able to form conformationally restricted complexes. A bidentate ligand can bind to an alkyne−dicobaltcarbonyl complex in two possible modes, as shown in Figure 1: the chelated complex **II** and the bridged complex **III**. Complexes of type **II** were studied with use of phosphinooxazoline or 2-(2-phosphinoaryl)dihydrooxazole ligands but again the diastereoselectivity in the complexation was very low.[6] Encouraged by the success of chelated chiral auxiliaries **IV**,[7] we studied the use chiral bidentate (P,S) ligands.[8] To this end, we designed and prepared two chiral phosphines[9,10] bearing a R-S-CH-PPh_2 fragment in order to favor the bridged coordination versus the chelated one. Although the best complexation diastereoselectivities were found with camphor-derived ligands,[10] the best results were obtained with the pulegone-derived phosphines[9] which allowed the development of an asymmetric ligand-based methodology of intermolecular PKR. Here we provide a full description of the preparation of the bidentate ligands PuPHOS (**1**) and CyPuPHOS (**3**), their use in PKR, and the synthetic potential of the resulting optically pure intermolecular cycloaddition adducts.[11]

SCHEME 1. Synthesis of Borane-Protected Bidentate Ligands



Results and Discussion

Synthesis of the Ligands. Multigram amounts of the borane-protected PuPHOS **2** can be easily obtained from a four-step procedure starting from natural (+)-pulegone **5** (Scheme 1). Eliel[12] conjugate addition of benzylthiol to **5** followed by Na/NH_3 reduction efficiently afforded mercapto alcohol **6** as a mixture of diastereomers. Dean−Stark reflux of **6**, paraformaldehyde and a catalytic amount of *p*-toluenesulfonic acid in toluene gave a mixture of diastereomeric oxathianes that was crystallized in hexanes at −78 °C.[13] In this way, crystalline oxathiane **7** was obtained in 40% yield from pentane. This compound was treated with *sec*-butyllithium at −78 °C to generate the anion, which was allowed to react with chlorodiphenylphosphine to yield the chiral phosphine **1** as a single diastereomer. PuPHOS was conveniently protected with borane to give **2** as a highly crystalline solid in 87% yield from **7**. Following the same synthetic scheme, borane-protected CyPuPHOS (**4**) was also prepared from **7** by phosphinylation with chlorodicyclohexylphosphine in good overall yield (50%).

The X-ray diffraction of **2** allowed the confirmation of the *S* configuration of the newly formed chiral center, since the phosphorus was placed in the equatorial position in the oxathiane ring (Figure 2).

Ligand Exchange with Dicobalthexacarbonyl Complexes. Free phosphines can be released by treating the borane complexes with 1,4-diazabicyclo[2.2.2]octane (DABCO).[14] Thus, the corresponding P,S-cobalt complexes were prepared in situ by treatment of the parent alkynehexacarbonyl complexes **8**−**11** with the borane-protected P,S ligands in the presence of 2 equiv of DABCO. By heating the mixture in toluene at 80 °C, deprotection and complexation with the free P,S ligand occurred smoothly yielding a mixture of diastereomeric complexes **12a/12b**−**16a/16b** (Table 1). TLC analysis showed that initial complexation when using PuPHOS took place without appreciable diastereoselectivity as previuosly reported for simple phosphines.[5] However,

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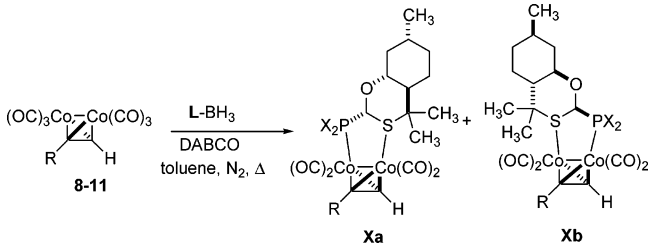
TABLE 1. Thermal Reaction of P,S Ligands with Alkyne−Dicobalthexacarbonyl Complexes



entry	R	starting complex	L	*T* (°C)	time (h)	yield (%)	dr[a]	**Xa/Xb**
1	Ph	**8**[b]	PuPHOS	65	18	91	1:1	**12a/12b**
2	CMe_2OH	**9**	PuPHOS	70	17	84	4.5:1	**13a/13b**
3	Bu^t	**10**	PuPHOS	60	17	99	3:1	**14a/14b**
4	TMS	**11**	PuPHOS	80	17	91	3:1	**15a/15b**
5	TMS	**11**	CyPuPHOS	65	5	87	1:1	**16a/16b**
6	TMS	**11**	CyPuPHOS	85	28	68	1.6:1	**16a/16b**

[a] Established by ^{1}H NMR spectroscopy of the resulting mixture of complexes. [b] Starting complex **8** was prepared in situ ($Co_2(CO)_8$/phenylacetylene/toluene) prior to ligand addition.

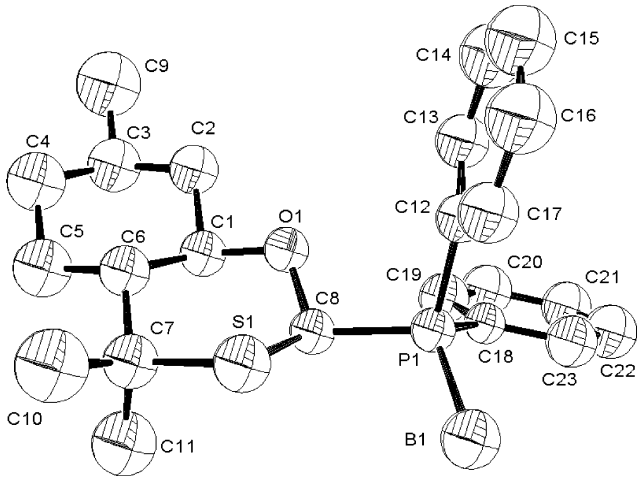


FIGURE 2. Ortep plot of borane-protected phosphine **2** showing 50% probability ellipsoids.

continued heating allowed thermodynamic equilibration to a biased mixture of diastereomers. Although equilibration could not be established for phenylacetylene complex **8**, for complex **9**, prepared from 2-methyl-3-butyn-2-ol, the equilibration ended with a 4.5:1 mixture of diastereomers **13a** and **13b** (Table 1, entry 2). Moreover, complexes derived from *tert*-butylacetylene (**10**) or trimethylsilylacetylene (**11**) gave a 3:1 mixture of isomers. Ligand exchange reaction with the more electron-rich CyPuPHOS occurred in good yield (87%) but with no diastereoselectivity in the first place. Continued heating at 85 °C for 28 h resulted in a biased 1.6:1 mixture of diastereomers (Table 1, entries 5 and 6).

Tetracarbonyl complexes **16a/16b** bearing the CyPuPHOS ligand were viscous red oils which could not be separated by either chromatography or crystallization. Conversely, diastereomeric complexes **12a/12b** with PuPHOS were separated by standard column chromatography. Finally and most conveniently, the major diastereomers **13a**−**15a** were isolated by simple crystallization in a toluene/ethanol solvent mixture. *Thus, by repeating the sequence of equilibration−crystallization, high yields of the major isomer were obtained in a truly dynamic resolution process*. The robustness of complexes **13**−**15**, along with the high yields on the isomerization of the mother liquors (86%) allowed the transformation of virtually all the initial complex mixture into the pure major diastereomer. For example, in the case of complexes **15a/15b**, a 68% yield of **15a** was obtained by means of a single crystallization−isomerization−crystallization sequence. Most remarkably, the present methodology proved to be suitable for the preparation of pure **15a** on a multigram scale.

The stereochemistry of the major isomer **13a** was firmly established by X-ray analysis.[9] The most important features of the crystal structure were the diequatorial binding of the bidentate ligand to the cobalt cluster and the phosphorus coordination to the pro-*R* cobalt atom.[15] To gain further insight into the structure and the relative thermodynamic stability of the two diastereomers, a theoretical study was undertaken. Because of the size of the molecule, a geometry optimization of diastereomers **13a** and **13b** was performed at the semiempirical PM3(tm) level.[16] Although the geometry and structural features of the PM3-modeled major isomer **13a** were quite similar to those of the X-ray structure, the energy of the two isomers was identical, thus indicating that the semiempirical calculations did not accurately reproduce the energy differences between the two diastereomers. However, a DFT single-point calculation at the B3LYP/6-31G(d) level[17] with use of the previously calculated PM3 geometries showed that major **13a** was 0.5 kcal/mol more stable than **13b** in reasonable agreement with experimental data.[18] Finally, a detailed analysis of structures **13a** and **13b** (Figure 3) may provide an explanation for

(15) The nomenclature is referred to the cluster terminal carbon atom. According to the alternative prochirality nomenclature in 2D the pro-*R* (pro-*S*) ligand would correspond to the *Re* (*Si*) ligand, see: Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons: New York, 1994.

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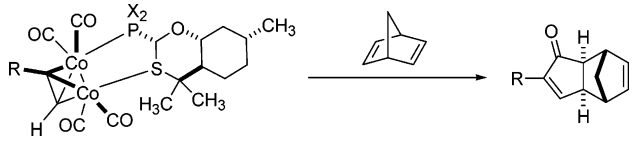
(18) A difference of 1.03 kcal·mol^{-1} would be necessary at 70 °C to attain a 4.5:1 ratio of diastereomers.

TABLE 2. PKR of PuPHOS and CyPuPHOS Complexes with Norbornadiene



entry	complex	R	conditions[a]	time	yield (%)	ee[b]	product
1	**12a**	Ph	Tol./50 °C	30 min	99	99	(+)-**17**
2	**15a**	TMS	Tol./50 °C	3 d	92	57	(+)-**18**
3	**15a**	TMS	CH_2Cl_2/NMO/rt	3 d	93	97	(+)-**18**
4	**15b**	TMS	CH_2Cl_2/NMO/rt	3 d	94	95	(−)-**18**
5	**16a/16b**[c]	TMS	CH_2Cl_2/NMO/45 °C	5 d	52	27	(+)-**18**
6	**13a**	CMe_2OH	CH_2Cl_2/NMO/rt	4 d	98	70	(+)-**19**

[a] All reactions were conducted in Schlenk flasks under nitrogen with 10 equiv of norbornadiene. [b] Enantiomeric excess (%) was determined either by HPLC (Chiracel-OD, **17** and **19**) or GC (β-DEX, **18**). [c] Mixture of diastereomers in a 1.6:1 ratio.

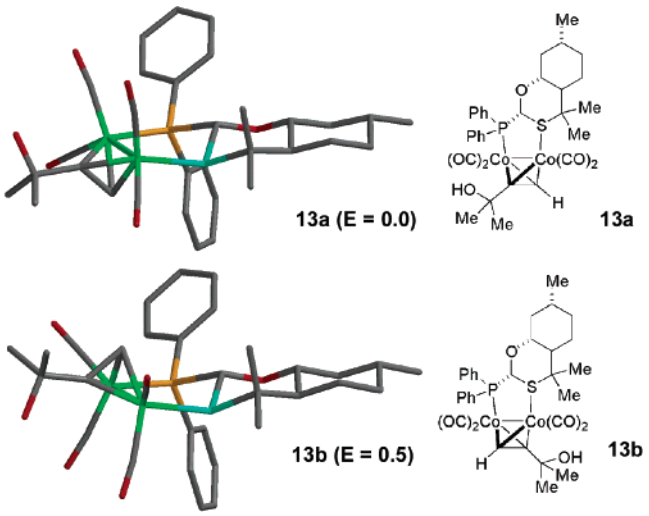


FIGURE 3. PM3 optimized structures of complexes **13a** and **13b** and DFT single-point relative energies.

the energy differences observed between major and minor isomers. A five-membered ring is formed upon coordination of the P,S ligand on two adjacent pseudoequatorial sites of the alkyne−$Co_2(CO)_6$ complex. For isomer **13a**, the diphenylphosphine moiety is linked to the pro-*R* cobalt, in a way that the phenyl groups attached to P and the carbonyl ligands on Co adopt an alternated disposition, thus minimizing steric repulsion. In contrast, minor diastereomer **13b**, where P is attached to a pro-*S* cobalt center, shows an eclipsed disposition of the phenyl and carbonyl groups. Such unfavorable interaction in minor complex **13b** could account for the energy differences observed experimentally.

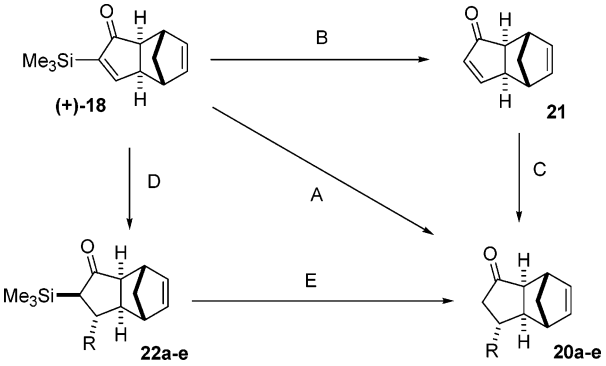
Pauson−Khand Reaction of PuPHOS and CyPuPHOS Complexes. The intermolecular PKR of the resulting P,S−cobalt complexes with norbornadiene was examined under thermal and *N*-oxide activation conditions (Table 2). Heating the diastereomerically pure complex **12a** with 10 equiv of norbornadiene at 50 °C led to rapid cyclization. After 30 min in a stereospecific process the corresponding *exo*-cyclopentenone **17** was obtained in quantitative yield and 99% ee (Table 1, entry 1). Under the same conditions, the PKR of the trimethysilyl complex **15a** provided **18** in high yield but decreased enantiomeric excess (57% ee). The reaction of **15a** in the presence of *N*-methylmorpholine *N*-oxide (NMO) in dichloromethane at room temperature for 3 days again provided the corresponding adduct in high enantiomeric excess, 97% ee (Table 2, entry 3). We assume that thermal activation promotes isomerization of the P,S ligand during the PKR, leading to a nonstereoselective process, while *N*-oxide conditions prevent the undesired isomerization. Submission of the minor diastereomer **15b** to similar reaction conditions provided the final cyclopentenone with opposite absolute configuration. As previously established, coordination of phosphorus to either cobalt center determines the absolute configuration of the final products. Hence, coordination to the pro-*R* cobalt center as in **15a** provides dextrorotatory 4-substituted *exo*-tricyclo[5.2.1.$0^{2,6}$]-4,8-decadien-3-ones with the (1*S*,2*S*,6*R*,7*R*) absolute configuration.

On the basis of the data displayed in Table 2 we conclude that stereoselectivity in the intermolecular PKR of complexes **12**−**16** ultimately depends on the electronic nature of the alkyne moiety. Complex **13a** derived from the electron-rich 2-methyl-3-butyn-2-ol gives a low stereospecific process, even under *N*-oxide promoted conditions (Table 2, entry 6). In contrast, complex **12a** bearing a mild electron-withdrawing phenyl group yields a stereospecific reaction even under thermal activation. Trimethysilylacetylene complex **15a** is a middle ground case. While cyclization under thermal conditions provided low enantiomeric excess, good enantioselectivities were achieved in the presence of NMO. Finally, the PKR of a mixture of complexes **16a/16b** (1.6:1) under *N*-oxide conditions afforded the corresponding cyclopentenone in 27% ee, the expected enantiomeric excess for a completely stereospecific reaction. This observation indicates that the more electron-rich cyclohexylphosphine ligand does not increase the undesired ligand isomerization.

Synthetic Potential of Optically Pure *exo*-4-(Trimethylsilyl)tricyclo[5.2.1.$0^{2,6}$]-4,8-decadien-3-one (18). The intermolecular PKR adducts of norbornadiene are interesting starting materials for the preparation of cyclopentanic compounds. The bicyclo[2.2.1]heptene fragment can be regarded both as a stereoselective controlling group for the conjugate addition to the cyclopentenone and as a masked alkene since it is easily removed through a retro-Diels−Alder reaction (Figure 4). This synthetic strategy has been applied successfully in the synthesis of natural products such as Brefeldin-A with R_1 as a covalently attached chiral auxiliary.[19]

(19) Bernardes, V.; Kann, N.; Riera, A.; Moyano, A.; Pericàs, M. A.; Greene, A. E. *J. Org. Chem.* **1995**, *60*, 6670−6671.

TABLE 3. Reaction Conditions and Yields for Michael Additions and Desilylation Reactions on 18



entry	substrate	route	reagents	R	yield	product
1	(+)-**18**	A	(i) 1.0 equiv of CuI, 2.0 equiv of CH_3Li (ii) 1.3 equiv of HF-Pyr	Me	81	**20a**
2	(+)-**18**	A	(i) 1.0 equiv of CuCN, 2.0 equiv of BuLi (ii) 1.3 equiv of HF-Pyr	*n*-Bu	99	**20b**
3	(+)-**18**	B	1.2 equiv of TBAF anhydrous, THF 3 Å mol sieves	–	99	**21**
4	**21**	C	1.0 equiv of CuI, 2.0 equiv of CH_3Li	Me	73	**20a**
5	**21**	C	1.0 equiv of CuI, 2.0 equiv of *i*-PrMgCl	*i*-Pr	69	**20c**
6	**21**	C	1.0 equiv of CuI, 2.0 equiv of PhLi	Ph	57	**20d**
7	(+)-**18**	D	1.3 equiv of *n*-BuMgCl 0.1 equiv of CuI, Et_2O	*n*-Bu	92	**22b**
8	(+)-**18**	D	1.3 equiv of *i*-PrMgCl 0.1 equiv of CuI, Et_2O	*i*-Pr	92	**22c**
9	(+)-**18**	D	1.3 equiv of PhMgBr 0.1 equiv of CuI, Et_2O	Ph	78	**22d**
10	(+)-**18**	D	1.3 equiv of $CH_2CHMgBr$ 0.1 equiv of CuI, Et_2O	vinyl	80	**22e**
11	**22b**	E	0.1 equiv of TBAF·H_2O, THF	*n*-Bu	82	**20b**
12	**22c**	E	0.1 equiv of TBAF·H_2O, THF	*i*-Pr	92	**20c**
13	**22d**	E	0.1 equiv of TBAF·H_2O, THF	Ph	92	**20d**
14	**22e**	E	0.1 equiv of TBAF·H_2O, THF	vinyl	85	**20e**

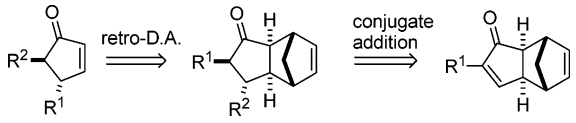


FIGURE 4. Retrosynthetic analysis of cyclopentenones based on PKR adducts.

Among the intermolecular PKR adducts prepared by the present approach, that derived from trimethylsilylacetylene is the most promising from a synthetic point of view. We hypothesized that the characteristics of the norbornadiene adducts in combination with the presumably easy removal of the TMS group make the optically pure adduct **18** a useful "chiral cyclopentadienone synthon".[20] The synthetic potential of this adduct has been recently expanded by Evans et al., who report a promising tandem conjugate addition/Peterson olefination.[21] To further explore the synthetic potential of adduct **18**, we studied the removal of the TMS groups and a wide array of organometallic compounds for Michael addition reactions.

Treatment of (+)-**18** with lithium dimethyl cuprate or lithium dibutylcyanocuprate afforded the corresponding 1,4-addition products, which, under these conditions, were somewhat unstable and difficult to handle. To avoid decomposition the intermediate 1,2-silyl ketones were readily treated with HF-Pyr, producing cyclopentanones **20a** and **20b** in good yield (Table 3, entries 1 and 2). The conjugate addition occurred in a completely stereoselective fashion by attack to the less hindered face of the enone. These compounds were spectroscopically identical with those previously obtained in our chiral auxiliary approach.[2d,e] This methodology, however, was not convenient for less reactive cuprates such as lithium diphenylcuprate, therefore, we examined the removal of the TMS group prior to conjugate addition. Few studies have addressed the desilylation of vinylic silanes. Among these, Krafft described the deprotection of an analogous trimethylsilylenone by treatment with KBu^{t}O/DMSO.[22] Unfortunately, the formation of **21** did not take place under these conditions. The first attempts with HF-Pyr were also unsuccessful. Using TBAF in THF, we isolated the desired product, albeit in low yield. We then established that oxidation of the product during the reaction workup was one of the main side reactions and that anhydrous conditions provided higher yields. After much experimentation, working with strictly anhydrous TBAF under argon we obtained **21** in 99% yield (Table 3, entry 3). The presence of either water or oxygen in the reaction mixture results in the enone-oxide **23** as the major side

(20) Substrate-controlled conjugated addition on **18**, removal of TMS fragment, and retro-Diels–Alder reaction will provide chiral cyclopentenones that could formally arise from the aforementioned achiral cyclopentadienone.

(21) (a) Iqbal, M.; Li, Y.; Evans, P. *Tetrahedron* **2004**, *60*, 2531–2538. (b) Iqbal, M.; Evans, P. *Tetrahedron Lett.* **2003**, *44*, 5741–5745.

(22) Krafft, M. E.; Wright, C. *Tetrahedron Lett.* **1992**, *33*, 151–152.

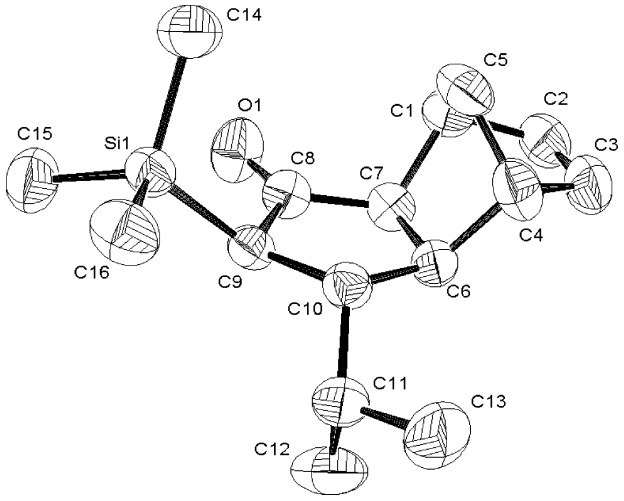
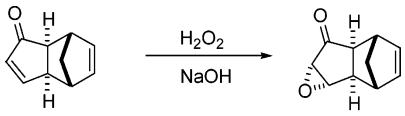


FIGURE 5. Ortep drawing of **22c** showing 50% probability ellipsoids.

SCHEME 2



21 **23**

product in the desilylation procedure. This compound (**23**) was readily prepared in good yield from **21** by oxidation with H_2O_2/NaOH (Scheme 2). Zwanenburg et al.[23] previously reported **23** in racemic form. As expected, **21** was a good substrate for conjugated additions. Stoichiometric amounts of dialkyl and diaryl cuprates afforded the 1,4-addition products in a completely stereoselective manner (Table 3, entries 4−6).

In our search for practical reaction conditions a complementary route to 1,4-addition compounds was studied. The use of magnesiocuprate reagents (RMgX/CuI cat.) was found to be the most convenient from an experimental point of view. The addition of butyl, isopropyl, phenyl, or vinyl radicals provided the stable 1,2-trimethysilyl ketones **22b**−**e** in excellent yield (Table 3, entries 7−10). Single-crystal X-ray diffraction of **22c** allowed us to ascertain that the incoming alkyl group and the TMS group adopted a trans stereochemistry (Figure 5). At this stage, TMS removal with 0.1 equiv of commercial TBAF allowed the preparation of **20b**−**e** in good to excellent yields (Table 3, entries 11−14).

Conclusions

In summary, here we have described the preparation of chiral phosphines PuPHOS and CyPuPHOS and studied their use as bidentated ligands in intermolecular PKR. In the case of PuPHOS, the ligand exchange reaction with alkyne−dicobalt complexes, crystallization of the major isomer, and thermodynamic equilibration of the mother liquors resulted in a practical dynamic resolution that allowed the preparation of diastereomerically pure Co_2−alkyne−PuPHOS complexes. Analysis of the modeled diastereomeric structures indicates that an eclipsed disposition of the $Co(CO)_2$−PPh_2 moiety is likely to account for energy differences between the two diastereomers. Most remarkably, intermolecular PKR of the trimethylsilylacetylene complex **15a** occurred in a completely stereospecific fashion to yield optically enriched cyclopentenone (+)-**18** (97% ee). By means of stereoselective conjugate addition and TMS removal (+)-**18** can be used as a *chiral cyclopentadienone synthon.* The developed procedures pave the way for the use of (+)-**18** as a promising starting material in the enantioselective synthesis of natural cyclopentanic products. This approach is currently being studied in our laboratories.

Experimental Section

[(2*S*,4a*R*,7*R*,8a*R*)-Hexahydro-4,4,7-trimethyl-4*H*-benzoxathiin-2-yl]diphenylphosphine Borane Complex, PuPHOS−BH_3 (2). To a cooled (−78 °C) solution of oxathiane **7** (905 mg, 4.52 mmol) in THF (10 mL) was added dropwise *s*-BuLi 1.3 M in cyclohexane (3.65 mL, 4.74 mmol). The temperature was allowed to rise to −20 °C. After 20 min of stirring at this temperature, chlorodiphenylphosphine (0.94 mL, 4.98 mmol) was then added with a syringe at −20 °C. After that, the temperature was slowly allowed to reach room temperature. After 4.5 h the reaction was quenched at 0 °C by the addition of BH_3·$S(CH_3)_2$ (0.58 mL, 5.88 mmol). The reaction mixture was diluted with Et_2O and water was added (CAUTION! bubbling occurs). The aqueous layer was washed with Et_2O and the combined organic layers were washed with brine and dried ($MgSO_4$). Solvent removal under vacuum afforded a crude product that was purified by flash chromatography (SiO_2, hexane/AcOEt, of increasing polarity) yielding 1.56 g (87%) of **2** as a colorless crystalline solid. Mp 177−179 °C. $[\alpha]_D$ +27.6 (*c* 0.95, $CHCl_3$). IR (KBr) ν_{max} 2923, 2394, 1437, 1148, 1057 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 0.30−1.70 (br m, BH_3), 0.90 (d, J = 6 Hz, 3H), 0.78−1.00 (m, 2H), 1.02−1.17 (m, 1H), 1.25 (s, 3H), 1.45 (s, 3H), 1.51−1.60 (m, 1H), 1.64−1.73 (m, 1H), 1.77−1.89 (m, 2H), 3.37−3.45 (td, J = 4 and 11 Hz, 1H), 5.75 (d, J = 2 Hz, 1H), 7. 40−7.55 (m, 6H), 7.77−7.83 (m, 2H), 7.90−7.97 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.8 (CH_3), 22.1 (CH_3), 24.4 (CH_2), 29.4 (CH_3), 31.4 (CH), 34.7 (CH_2), 41.7 (CH_2), 41.8 (C), 51.5 (CH), 67.2 (CH_2), 76.6 (CH), 128.3 (d, J = 10 Hz, CH), 131.39 (d, J = 15.4, 2.4 Hz, CH), 133.7 (dd, J = 9, 76.1 Hz, CH) ppm. ^{31}P NMR (121 MHz, $CDCl_3$) δ 23.59 ppm. Anal. Calcd for $C_{23}H_{32}BOPS$: C, 69.35; H, 8.10; S, 8.05. Found: C 69.42; H, 8.27; S, 7.81.

[(2*S*,4a*R*,7*R*,8a*R*)-Hexahydro-4,4,7-trimethyl-4*H*-benzoxathiin-2-yl]dicyclohexylphosphine Borane Complex, CyPuPHOS−BH_3 (4). **4** was prepared as described for PuPHOS·BH_3 with chlorodicyclohexylphosphine and BH_3−THF (1.0 M solution in THF) and isolated as a pale yellow crystalline solid after flash chromatography purification (SiO_2, hexane/ethyl acetate 95:5) in 50% yield. Mp 126−128 °C. $[\alpha]_D$ −2.4 (c 0.93, $CHCl_3$). IR (film) ν_{max} 2928, 2852, 2378, 1448, 1386, 1148, 1056, 1003, 914, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.8−2.2 (m, 33H), 0.93 (d, J = 6 Hz, 3H), 1.28 (s, 3H), 3.33 (td, J = 10 and 4 Hz, 1H), 5.43 (d, J_P = 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8 (CH_3), 22.3 (CH_3), 24.5 (CH_2), 26.2 (CH_2, d, J_P = 1 Hz), 26.3 (CH_2, d, J_P = 1 Hz), 26.8−27.6 (4 × CH_2, m), 27.9 (CH_3), 30.4 (CH, d, J_P = 30 Hz), 30.9 (CH, d, J_P = 30 Hz), 31.6 (CH), 34.8 (CH_2), 41.7 (CH_2), 44.2 (Cq, d, J_P = 5 Hz), 51.2 (CH), 74.4 (CH, d, J_P = 37 Hz), 78.9 (CH, d, J_P = 6 Hz) ppm. ^{31}P NMR (121 MHz, $CDCl_3$) δ 36.2 ppm (br doublet). MS (EI) *m/e* 410 (M^+, 1.2%), 409 (M^+ − H, 3.1%), 199 (M^+ − Cy_2PBH_3, 100%). HRMS (EI) Calcd for $C_{23}H_{44}BOPS$ (M^+) 410.2944, found 410.2953.

General Procedure for the Synthesis of Tetracarbonyl Complexes: $Co_2(\mu$-$PhC_2H)(CO)_4(\mu$-$C_{23}H_{32}OPS)$, 12a and 12b. A dicobalthexacarbonyl complex of phenylethyne **8** (100 mg, 0.25 mmol), phosphine−borane complex **2** (100 mg, 0.25

(23) Dols, P. P. M. A.; Arnouts, E. G.; Rohaan, J.; Klunder, A. J. H.; Zwanenburg, B. *Tetrahedron* **1994**, *50*, 3473−3490.

mmol), DABCO (41 mg, 0.37 mmol), and toluene (2 mL) were charged in a Schlenk flask under nitrogen. The reaction mixture was heated to 65 °C for 18 h, removing periodically the CO by means of vacuum and nitrogen refilling. Complexation was monitored by TLC. Upon reaction completion the solvent was removed in vacuo. The residue was then purified by flash chromatography on SiO_2 to yield 164 mg (91%) of a **12a/12b** mixture as a red-purple viscous oil. ^{1}H NMR analysis revealed the existence of a 1/1 mixture of diastereomeric complexes. IR (KBr) ν_{max} 1962, 1991, 2022 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): first fraction, δ 0.25−0.45 (m, 2H), 0.71 (d, J = 6 Hz, 3H), 0.75−0.98 (m, 2H), 0.97 (s, 3H), 1.09 (s, 3H), 1.16−1.30 (m, 3H), 1.58−1.68 (m, 1H), 2.75−2.87 (td, J = 4 and 11 Hz, 1H), 4.99 (s, 1H), 5.93 (d, J = 7 Hz, 1H), 7.03−7.25 (m, 9H), 7.88 (d, J = 7 Hz, 2H), 7,93−8.08 (m, 4H) ppm; second fraction, δ 0.20−0.60 (m, 2H), 0.70 (d, J = 6 Hz, 3H), 0.70−1.80 (m, 6H), 0.96 (s, 3H), 1.08 (s, 3H), 2.90−3.10 (m, 1H), 5.44 (b s, 1H), 5.87 (d, J = 6 Hz, 1H), 6.92−7.28 (m, 9H), 7.62−7−78 (m, 2H), 7.81−7.98 (m, 4H) ppm. ^{13}C NMR (75 MHz, C_6D_6): first fraction, δ 18.7, 21.9, 24.8, 27.4, 31.0, 34.1, 41.0, 48.5 (J_P = 6 Hz), 50.0, 73.9, 78.9, 92.5, (J_P = 23 Hz), 98.7 (J_P = 16 Hz), 126.9, 128.2, 128.6, 128.8, 130.0, 130.4, 133.4 (J_P = 12 Hz), 131.7−134.2 (J_P = 34 Hz), 134.7 (J_P = 12 Hz), 135.5−135.9 (J_P = 34 Hz), 142.3, 202.0−207.0 (b, 4CO) ppm; second fraction, δ 18.7 (br), 21.8, 24.6, 27.6, 31.2, 34.3, 41.0, 48.0 (br), 50.4, 73.2, 78.9, 88.2 (br), 126.7, 128.7, 129.9, 130.2, 130.3, 131.7, 132.6 (J_P = 12 Hz), 134.6 (br, J_P = 12 Hz), 142.4, ppm. ^{31}P NMR (121 MHz, C_6D_6) δ -27.99_{first}, -28.78_{scnd} ppm. HRMS (FAB+) calcd for $C_{35}H_{35}Co_2O_5PS$ [M$^+$] 716.0606, found 716.0597.

$Co_2(\mu$-HOMe$_2$CC$_2$H)(CO)$_4(\mu$-C$_{23}$H$_{32}$OPS), 13a and 13b. Dicobalt hexacarbonylcomplex **9** (96 mg, 0.26 mmol), phosphine-borane **2** (100 mg, 0.25 mmol), DABCO (56 mg, 0.5 mmol), and toluene (1.5 mL) were used according to the General Procedure. The reaction mixture was heated at 70 °C for 17 h. Purification by flash chromatography yielded 148 mg (84%) of the **13a/13b** mixture as a red viscous oil that solidified upon standing. ^{1}H NMR analysis showed a 4.5/1 ratio of diastereomeric complexes. Crystallization in toluene/ethanol mixtures afforded the major pure diastereomer. Mp 184 °C. IR (KBr) ν_{max} 1944, 1970, 1979, 2022 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): major fraction, δ 0.25−0.38 (m, 2H), 0.69 (d, J = 6 Hz, 3H), 0.72−0.83 (m, 1H), 0.87−1.02 (m, 1H), 0.97 (s, 3H), 1.11 (s, 3H), 1.10−1.30 (m, 3H), 1.55−1.68 (m, 1H), 1.72 (s, 3H). 1.73 (s, 3H), 1.76 (d, J = 8 Hz, 1H), 2.80 (td, J = 5 and 10 Hz, 1H), 4.95 (s, 1H), 5.52 (d, J = 7 Hz, 1H), 7.01−7.25 (m, 6H), 7.91−8.00 (m, 4H) ppm; distinct signals from the minor fraction,δ 2.94 (br s, 1H), 5.39 (br d, J = 7 Hz, 1H) ppm. ^{13}C NMR (75 MHz, C_6D_6): major, δ 18.8, 21.9, 24.8, 27.3, 31.0, 33.0, 34.2, 41.0, 48.8 (J_P = 7 Hz), 50.0, 72.4, 73.1, 78.8, 92.5 (J_P = 23 Hz), 128.7 (J_P = 9 Hz), 130.1, 130.4, 133.1−133.3 (J_P = 12 Hz), 134.9−135.0 (J_P = 12 Hz) ppm. ^{31}P NMR (121 MHz, C_6D_6): major, δ −28.33 (br s) ppm.

$Co_2(\mu$-Bu^{t}C$_2$H)(CO)$_4(\mu$-C$_{23}$H$_{32}$OPS), 14a and 14b. Dicobalt hexacarbonyl complex **10** (100 mg, 0.27 mmol), phosphine-borane **2** (108 mg, 0.27 mmol), DABCO (45 mg, 0.4 mmol), and toluene (2 mL) were used according to the General Procedure. The reaction mixture was heated at 60 °C for 17 h. Purification by flash chromatography yielded 191 mg (99%) of **14a/14b** as a red solid. ^{1}H NMR analysis revealed a 3/1 ratio of diastereomeric complexes. Crystallization in hexane afforded the major pure diastereomer. IR (KBr) ν_{max} = 1941, 1964, 1977, 2018 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): major fraction, δ 0.26−0.38 (m, 2H), 0.69 (d, J = 6 Hz, 3H), 0.72−0.83 (m, 1H), 0.88−1.02 (m, 1H), 1.00 (s, 3H), 1.10−1.28 (m, 3H), 1.15 (s, 3H), 1.47 (s, 9H), 1.59−1.63 (m, 1H), 2.78−2.87 (td, J = 5 and 10 Hz, 1H), 4.97 (s, 1H), 5.61−5.64 (d, J = 7 Hz, 1H), 7.01−7.25 (m, 6H), 7.91−8.00 (m, 4H) ppm; distinct signals from the minor fraction, δ 1.50 (s, 9H), 2.92−3.05 (br s, 1H), 5.42 (br d, 1H), 5.53 (br s, 1H) ppm. ^{13}C NMR (75 MHz, C_6D_6): major fraction, δ 18.7, 21.9, 24.7, 27.3, 31.0, 33.3, 34.1, 36.9, 41.0, 48.8 (J_P = 7 Hz), 50.0, 73.3, 78.7, 92.5, (J_P = 22 Hz), 128.7 (J_P = 9 Hz), 130.0, 130.2, 133.2 (J_P = 22 Hz), 133.6−134.1 (J_P = 34 Hz), 135.9−136.3 (J_P = 34 Hz) ppm. ^{31}P NMR (121 MHz, C_6D_6): major fraction, δ −27.95 (br s) ppm. HRMS (FAB+) calcd for $C_{32}H_{39}Co_2O_4PS$ [M$^+$ − CO] 668.0970, found 668.0957.

$Co_2(\mu$-Me$_3$SiC$_2$H)(CO)$_4(\mu$-C$_{23}$H$_{32}$OPS), 15a and 15b. Dicobalt hexacarbonylcomplex **11** (100 mg, 0.26 mmol), phosphine-borane **2** (100 mg, 0.25 mmol), DABCO (45 mg, 0.4 mmol), and toluene (2 mL) were used according to the General Procedure. The reaction mixture was heated at 80 °C for 17 h. Purification by flash chromatography yielded 163 mg (91%) of **15a/15b** as a red viscous oil that solidified upon standing. ^{1}H NMR analysis showed a 3/1 ratio of diastereomeric complexes. Crystallization in toluene/ethanol mixtures afforded 92 mg of the major pure diastereomer. Further equilibration of the minor isomer enriched mother liquor at 80 °C for 18 h afforded the starting 3/1 ratio of diastereomers in 86% yield. Mp 163 °C. $[\alpha]_D$ +134.8 (*c* 0.008, $CHCl_3$). IR (KBr) ν_{max} 1956, 1985, 2018 cm^{-1}. ^{1}H NMR (300 MHz, C_6D_6): major fraction, δ 0.25−1.30 (m, 7H), 0.53 (s, 9H), 0.69 (d, J = 6 Hz, 3H), 0.98 (s, 3H), 1.11 (s, 3H), 1.55−1.67 (m, 1H), 2.73−2.85 (m, 1H), 4.85 (s, 1H), 5.99−6.02 (d, J = 8 Hz, 1H), 7.00−7.25 (m, 6H), 7.92−8.03 (m, 4H) ppm; distinct signals from the minor fraction, δ 0.54 (s, 9H), 0.86 (s, 3H), 1.04 (s, 3H), 2.87−3.01 (br s, 1H), 5.51 (br s, 1H), 5.92−5.95 (br d, J = 8 Hz, 1H) ppm. ^{13}C NMR (75 MHz, C_6D_6): major fraction, δ 1.0, 18.16, 21.9, 24.8, 27.3, 31.0, 34.1, 41.0, 48.5, 50.1, 78.8, 86.8, 93.2 (J_P = 22 Hz), 128.6−128.7 (J_P = 9 Hz), 130.0, 133.3−133.5 (J_P = 12 Hz), 134.7−134.8 (J_P = 12 Hz) ppm. ^{31}P NMR (121 MHz, C_6D_6): major fraction, δ −26.42 (br s) ppm. HRMS (FAB+) calcd for $C_{28}H_{39}Co_2OPSSi$ [M$^+$ − 4CO] 600.0892, found 600.0914.

$Co_2(\mu$-Me$_3$SiC$_2$H)(CO)$_4(\mu$-C$_{23}$H$_{41}$OPS), 16a and 16b. Dicobalt hexacarbonylcomplex **11**, phosphine-borane **4**, DABCO, and toluene were used according to the General Procedure. The reaction mixture was heated at 65 °C for 5 h. Purification by flash chromatography yielded 87% of **16a/16b** as a red viscous oil that solidified upon standing. ^{1}H NMR analysis showed a 1:1 ratio of diastereomeric complexes. Further heating (85 °C, 28 h) of the initial mixture provided a 1.6:1 biased mixture of diastereomers. IR (film) ν_{max} 2014, 1980, 1952 cm^{-1}. ^{1}H NMR (400 MHz, C_6D_6): mixture of diastereomers, δ 0.26−2.46 (m), 0.57_{maj} (s, 9H), 0.58_{min} (s, 9H), 0.71_{maj} (t, J = 6 Hz, 3H), 0.71_{min} (t, J = 6 Hz, 3H), 1.04 (s, 3H), 1.05 (s, 3H), 1.19 (s, 3H), 2.93_{maj} (td, J = 10 and 4 Hz, 1H), 3.12_{min} (td, J = 10 and 4 Hz, 1H), 4.62_{maj} (s, 1H), 5.11_{min} (s, 1H), 5.78_{min} (d, J_P = 8 Hz, 1H), 5.99_{maj} (d, J_P = 7 Hz, 1H) ppm. ^{13}C NMR (100 MHz, C_6D_6): characteristic signals of the diastereomeric mixture, δ 1.2 (CH_3), 1.3 (CH_3), 79.6 (CH), 78.8 (CH), 85.6 (CH), 83.6 (CH), 91.3 (d, J_p = 17 Hz, CH), 205.3 (br, CO) ppm. ^{31}P NMR (121 MHz, C_6D_6) δ -15.45_{maj}, -18.75_{min} ppm. MS (ESI) *m/e* 725 (M$^+$ + H), 697 (M$^+$ + H − CO), 669 (M$^+$ + H − 2CO), 641 (M$^+$ + H − 3CO), 613 (M$^+$ + H − 4CO). HRMS (FAB, NBA) calcd for $C_{29}H_{51}Co_2O_2PSSi$ (M$^+$ − 3CO) 640.1781, found 640.1780.

(+)-(1*S*,2*S*,6*S*,7*R*)-4-Phenyltricyclo[5.2.1.0 ^{2,6}]deca-4,8-dien-3-one, 17.[6,9] The first fraction of pure major **12a** (29 mg, 0.040 mmol), norbornadiene (40 μL, 0.4 mmol), and toluene (2 mL) were charged in a Schlenk flask under nitrogen and heated to 50 °C with stirring. TLC monitoring showed the reaction was complete after 30 min. Purification by flash chromatography on SiO_2 (hexane/AcOEt, 5%) yielded 9 mg (99%) of (+)-**17** as a white solid (99% ee). HPLC analysis: CHIRALCEL OD (25 cm), 2% IPA−98% hexane, 0.5 mL/min, λ = 254 nm. t_R (+) isomer = 16.8 min, t_R (−) isomer = 20.6 min.

(+)-(1*S*,2*S*,6*S*,7*R*)-4-(1-Hydroxy-1-methylethyl)tricyclo-[5.2.1.0 ^{2,6}]deca-4,8-dien-3-one, 19.[9,5a] The major crystalline diastereomer **13a** (15 mg, 0.021 mmol), norbornadiene (21 μL, 0.21 mmol), *N*-methylmorpholine *N*-oxide (14 mg, 0.12 mmol), and CH_2Cl_2 (1.5 mL) were charged in a Schlenk flask tube under nitrogen and stirred at room temperature for 4 days to yield 4.3 mg (98%) of (−)-**19** in 50% ee as calculated by HPLC

analysis: CHIRALCEL OD (25 cm), 5% IPA-−5% hexane, 1.0 mL/min, λ = 254 nm. t_R (−) isomer = 6.5 min, t_R (+) isomer = 7.3 min.

(+)-(1*S*,2*S*,6*R*,7*R*)-4-(Trimethylsilyl)tricyclo[5.2.1.0 ^{2,6}]-deca-4,8-dien-3-one, 18.[9,16] **Thermal conditions:** The major crystalline diastereomer **15a** (16 mg, 0.022 mmol), norbornadiene (20 μL, 0.2 mmol), and toluene (1.0 mL) were charged in a Schlenk flask under nitrogen and heated at 50 °C for 3 days. This procedure resulted in complete conversion of the starting complex (TLC) and yielded (+)-**18** in 57% ee as calculated by GC analysis. ***N*-Oxide conditions:** The major crystalline diastereomer **15a** (21 mg, 0.029 mmol), norbornadiene (50 μL, 0.5 mmol), *N*-methylmorpholine *N*-oxide (20 mg, 0.17 mmol), and CH_2Cl_2 (1.0 mL) were charged in a Schlenk flask under nitrogen and stirred at room temperature for 3 days to yield 6 mg (93%) of (+)-**18** in 97% ee as calculated by GC analysis: Supelco β-DEX 120, 30 m, 150 °C. t_R (−) isomer = 31.7 min, t_R (+) isomer = 33.4 min. Mp 102−103 °C. $[\alpha]_D$ +78.5 (*c* 0.88, $CHCl_3$). IR (KBr) υ_{max} 3064, 3029, 2977, 1684, 1570, 1302, 1254, 1246 cm^{-1}.^{1}H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 9H), 1.17 (d, J = 9 Hz), 1.36 (dt, J = 2 and 9 Hz, 1H), 2.26 (dt, J = 2 and 6 Hz, 1H), 2.67 (s, 1H), 2.82 (dt, J = 1 and 5 Hz, 1H), 2.88 (s, 1H), 6.16−6.27 (2 × dd, J_A = 3 and 5 Hz, J_B = 3 and 6 Hz, 2H), 7.58 (d, J = 3 Hz, 1H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$) δ −1.9 (CH_3), 41.3 (CH_2), 42.9 (CH), 43.8 (CH), 52.0 (CH), 53.4 (CH), 137.4 (CH), 138.2 (CH), 152.1 (C), 172.8 (CH), 213.0 (C) ppm. E.M. (CI−NH_3) *m/z* 219 (M^+ + 1, 50%), 236 (M^+ + 18, 100%). HRMS (CI−NH_3) calcd for $C_{13}H_{18}OSi$ 218.1127, found 218.1122.

(−)-(1*R*,2*R*,6*S*,7*S*)-4-(Trimethylsilyl)tricyclo[5.2.1.0 ^{2,6}]-deca-4,8-dien-3-one, 18. *N*-Oxide conditions: Pure minor diastereomer **15b** yielded under analogous reaction conditions (−)-**18** in 95% ee as calculated by GC analysis.

(+)-(1*S*,2*S*,5*R*,6*R*,7*R*)-5-Methyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 20a. [2e,24] **Route A:** Copper(I) iodide (0.12 g, 0.63 mmol) and ether (6 mL) were placed under nitrogen in a round-bottomed flask. The resulting slurry was cooled to −50 °C, and 1.6 M MeLi (0.78 mL, 1.25 mmol) was added via syringe. The mixture was stirred at −50 °C for 30 min and then allowed to gradually warm to −10 °C. A solution of (+)-**18** in ether (5 mL) was added via cannula. After 10 min at this temperature, no more starting material was visible by TLC. At this point, hexane and NH_4Cl/NH_3 10% were added to the crude until two phases were clearly obtained. The aqueous phase was extracted with ether, and the combined extracts were washed with NH_4Cl/NH_3 10% until a colorless aqueous phase was obtained. The organic phase was then washed with brine, dried ($MgSO_4$), and concentrated in vacuo to yield 119 mg of **22a** as a yellow oil, which was immediately used without further purification. A solution of **22a** (119 mg, 0.48 mmol) in acetonitrile (100 μL) was treated with HF-pyr 60% (20 μL, 0.59 mmol). The reaction mixture was stirred at room temperature until TLC analysis revealed complete conversion of the starting material. Next, saturated $NaHCO_3$ solution was added, and the aqueous phase was extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Purification by column chromatography (2% v/v NEt_3 pretreated SiO_2, hexane/AcOEt 10%) yielded 63 mg of **20a** as a colorless oil (81%). $[\alpha]_D$ +115° (*c* 1.0, $CHCl_3$). IR (film) υ_{max} 3070, 2970, 1740, 1465, 825, 700 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.19 (d, J = 6 Hz, 3H), 1.15−1.25 (m, 1H), 1.38−1.48 (m, 1H), 2.15−2.70 (ABX, J_{ab} = 18 Hz, J_{ax} = 7 Hz, J_{bx} = 10 Hz, 2H), 2.28−2.35 (m, 1H, m), 2.78 (s, 1H), 3.09 (s, 1H), 6.10−6.22 (m, 2H) ppm.

(+)-(1*S*,2*S*,6*R*,7*R*)-Tricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 21.[25] **Route B:** In a two-necked, 50-mL flask fitted with a septum and an argon inlet were weighed (+)-**18** (200 mg, 0.916 mmol) and 400 mg of 3 Å molecular sieves in pellets. The system was flushed with argon and 10 mL of anhydrous THF was added. Then 1.1 mL of a 1.0 M solution of TBAF in THF (1.10 mmol, 1.2 equiv) dried over 3 Å molecular sieves were added dropwise. When complete disappearance of the starting product was observed by TLC (ca. 1 h) 10 mL of ether and then 15 mL of saturated aqueous NH_4Cl solution were added. The organic layer was quickly separated and the aqueous one was extracted twice with ether. The combined organic layers were dried with $MgSO_4$, filtered, and evaporated under reduced pressure. The crude was immediately purified by flash chromatography (SiO_2/CH_2Cl_2) to afford 134 mg (quant.) of a yellow oil that solidified on the freezer at −20 °C. $[\alpha]_D$ +261 (*c* 0.15, $CHCl_3$). IR (film) ν_{max} 2973, 1703, 1579, 1341, 1178, 710 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, J = 9 Hz, 1H), 1.41 (dt, J = 9 and 1 Hz, 1H), 2.27 (ddd, J = 5, 1 and 1 Hz, 1H), 2.72 (m, 1H), 2.86 (m, 1H), 2.93 (m, 1H), 6.22 (dd, J = 6 and 3 Hz, 1H), 6.26 (dd, J = 6 and 2 Hz, 1H), 6.29 (dd, J = 6 and 3 Hz, 1H), 7.57 (dd, J = 6 and 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 41.3 (CH_2), 42.8 (CH), 43.7 (CH), 50.6 (CH), 52.1 (CH), 137.4 (CH), 138.4 (CH), 138.4 (CH), 166.1 (CH), 210.5 (C=O) ppm.

(+)-(1*S*,2*R*,5*S*,6*R*,7*R*)-5-Methyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 20a.[2e] **Route C:** Dry CuI (366 mg, 1.92 mmol) was placed in a 25-mL flask fitted with a septum and an argon inlet. The system was flushed with argon and 5 mL of anhydrous Et_2O was added. The resulting suspension was cooled to −78 °C, and 1.6 M MeLi in ether (2.4 mL, 3.84 mmol) was then added dropwise. After 20 min, a solution of enone **21** (140 mg, 0.96 mmol) in ether (4 mL) was added to the transparent solution via cannula. When no starting material could be detected by TLC (ca. 25 min) the reaction was treated under vigorous stirring with aqueous NH_4Cl (10 mL) for 1 h. The blue aqueous layer was extracted with ether (2 × 20 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in a vacuum to yield 113 mg (73%) of **20a** as a pale yellow oil. $[\alpha]_D$ +115 (*c* 1.0, $CHCl_3$).

(+)-(1*S*,2*S*,4*R*,5*S*,6*R*,7*R*)-5-Isopropyl-4-trimethylsilyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 22c. Route D: Into a 100-mL flask provided with magnetic stirring, rubber septum, and argon atmosphere was placed a suspension of anhydrous CuI (35 mg, 0.186 mmol, 0.1 equiv) (freshly recrystallized) in 25 mL of anhydrous diethyl ether. The flask was cooled to −78 °C and 1.1 mL (2.23 mmol, 1.2 equiv) of 2.0 M isopropylmagnesium chloride solution in ether was added dropwise. After the mixture was stirred for 10 min a solution of (+)-**18** (406 mg, 1.86 mmol) in 5 mL of anhydrous ether was added dropwise. The solution rapidly turned dark and was allowed to warm to −40 °C over 2 h during which the color became orange. The mixture was then treated with equal volumes of saturated aqueous NH_4Cl and aqueous NH_4OH for 20 min. The aqueous layer was sepaated and extracted twice with ether. The combined organic layers were washed with brine, dried with anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure to yield 451 mg (92%) of the **22c** as a colorless crystalline solid. $[\alpha]_D$ +83.5 (*c* 1.60, $CHCl_3$). Mp (DSC) 57 °C. IR (film) ν_{max} 2956, 1706, 1247, 1202, 860, 838, 702 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.11 (s, 9H), 0.87 (d, J = 6 Hz, 3H), 0.99 (d, J = 6 Hz, 3H), 1.22 (d, J = 9 Hz, 1H), 1.39 (dt, J = 9 and 2 Hz, 1H), 1.71 (m, 1H), 1.81 (dt, J = 9 and 4 Hz, 1H), 2.08 (dd, J = 9 and 5 Hz, 1H), 2.16 (dd, J = 9 and 2 Hz, 1H), 2.25 (d, J = 9 Hz, 1H), 2.67 (s, 1H), 3.05 (s, 1H), 6.15 (dd, J = 5 and 3 Hz, 1H), 6.19 (dd, J = 5 and 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ −0.9 (CH_3), 16.5 (CH_3), 21.4 (CH_3), 32.1 (CH), 44.6 (CH + CH_2), 46.9 (CH), 48.3 (CH), 50.0 (CH), 50.1 (CH), 57.8 (CH), 138.0 (CH), 138.9 (CH), 221.5 (C=O) ppm. Anal. Calcd for $C_{16}H_{26}OSi$: C,73.22, H, 9.98. Found: C, 72.85, H, 10.25.

(+)-(1*S*,2*S*,4*R*,5*S*,6*R*,7*R*)-5-*n*-Butyl-4-trimethylsilyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 22b. Following the procedure described for **22c** (Route D) but using a 2.0 M butylmagnesium chloride the target compound **22b** was obtained in 92% yield

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as a pale yellow oil. $[\alpha]_D$ +74.0 (*c* 2.0, $CHCl_3$). IR (film) ν_{max} 2957, 2925, 1733, 1457 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 9H), 0.94 (t, J = 7 Hz, 3H), 1.18 (d, J = 9 Hz, 1H), 1.25−1.37 (m, 4H), 1.40 (d, J = 9 Hz, 1H), 1.44−1.62 (m, 2H), 1.69 (m, 1H), 1.96 (dd, J = 10 and 2 Hz, 1H), 2.00 (dd, J = 9 and 5 Hz, 1H), 2.33 (d, J = 9 Hz, 1H), 2.72 (s, 1H), 3.05 (s, 1H), 6.15 (dd, J = 6 and 3 Hz, 1H), 6.19 (dd, J = 6 and 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.4 (CH_3), 14.3 (CH_3), 23.0 (CH_2), 29.8 (CH_2), 39.0 (CH_2), 42.5 (CH), 44.7 (CH_2), 46.4 (CH), 49.5 (CH), 50.6 (CH), 52.9 (CH), 57.9 (CH), 138.1 (CH), 138.7 (CH), 221.1 (C=O) ppm. MS (CI−CH_4) *m/e* 277 (M^+ + H, 4.9%), 276 (M^+, 2.5%), 235 ($M^+ - C_3H_5$, 59.8%), 210 ($M^+ - C_5H_6$, 48.2%), 73 ($C_3H_9Si^+$, 100%), 66 ($C_5H_6^+$, 62.4%). HRMS (CI−CH_4) calcd for $C_{17}H_{29}OSi$ (M^+ + H) 277.1988, found 277.1989.

(+)-(1*S*,2*S*,4*R*,5*R*,6*R*,7*R*)-5-Phenyl-4-trimethylsilyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 22d. The procedure described for **22c** (Route D) was followed but starting from (+)-**18** (109 mg) and using 1.0 M phenylmagnesium bromide solution in THF (very slow addition of the enone was required to avoid 1,2 addition of phenylmagnesium bromide). After purification by flash chromatography on SiO_2 with a hexane/AcOEt mixture (98:2), 115 mg of **22d** (78%) was obtained as a colorless solid. Mp (DSC) 97 °C. $[\alpha]_D$ +74.4 (*c* 2.15, $CHCl_3$). IR (KBr) ν_{max} 2983, 2959, 1707, 1242, 1183, 869, 841, 722, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ = −0.03 (s, 9H), 1.31 (d, J = 9 Hz, 1H), 1.51 (d, J = 9 Hz, 1H), 2.33 (dd, J = 9 and 6 Hz, 1H), 2.54 (d, J = 9 Hz, 1H), 2.57 (dd, J = 11 and 2 Hz, 1H), 2.85 (dd, J = 11 and 6 Hz, 1H), 2.89 (s, 1H), 3.15 (s, 1H), 6.08 (dd, J = 6 and 3 Hz, 1H), 6.16 (dd, J = 6 and 3 Hz, 1H), 7.28 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.6 (CH_3), 44.6 (CH_2), 46.3 (CH), 48.1 (CH), 49.8 (CH), 54.3 (CH), 54.4 (CH), 57.8 (CH), 126.6 (CH), 127.5 (CH), 128.8 (CH), 138.3 (CH), 138.6 (CH), 147.3 (Cq), 219.8 (C=O) ppm. Anal. Calcd. for $C_{19}H_{24}OSi$: C, 76.97, H, 8.16. Found: C, 76.60, H, 8.42.

(+)-(1*S*,2*S*,4*R*,5*S*,6*R*,7*R*)-5-Vinyl-4-trimethylsilyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 22e. Following the procedure described for **22c** (Route D) but with 1.0 M vinylmagnesium bromide solution in THF, **22e** was obtained in 80% yield as a pale yellow oil. $[\alpha]_D$ +78.9 (*c* 0.90, $CHCl_3$). IR (film) ν_{max} 2959, 2942, 1732, 1641, 1389, 849 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.09 (s, 9H), 1.20 (d, J = 9 Hz, 1H), 1.46 (dt, J = 9 and 2 Hz, 1H), 2.11 (m, 1H), 2.15 (dd, J = 11 and 2 Hz, 1H), 2.34 (m, 1H+1H), 2.82 (s, 1H), 3.08 (s, 1H), 4.96 (ddd, J = 10, 2, and 1 Hz, 1H), 5.03 (ddd, J = 17, 2, and 1 Hz, 1H), 5.82 (ddd, J = 17, 10, and 8 Hz), 6.16 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ −1.4 (CH_3), 44.8 (CH_2), 46.3 (CH), 47.7 (CH), 47.8 (CH), 50.8 (CH), 51.5 (CH), 57.3 (CH), 113.6 (CH_2), 138.3 (CH), 138.6 (CH), 143.8 (CH), 219.9 (C=O) ppm. MS (CI−CH_4) *m/e* 180 ($M^+ - C_5H_6$, 13.1%), 167 (36.4%), 149 (100%), 73 ($C_3H_9Si^+$, 34.5%). HRMS (CI−CH_4) Calcd. for $C_{15}H_{16}OSi$ ($M^+ - C_5H_6$) 180.0970, found 180.0970.

(+)-(1*S*,2*S*,5*R*,6*S*,7*R*)-5-Phenyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 20d.[19,26] **Route E:** In a 25-mL flask equipped with a magnetic stirring was placed a solution of **22d** (100 mg, 0.337 mmol) in THF (4 mL). TBAF·H_2O (8.8 mg, 0.03 mmol, 0.1 equiv) was added and the mixture stirred for 45 min until disappearance of the starting product by TLC. Water (2 mL) and diethyl ether (2 mL) were added to the reaction mixture and the aqueous layer was separated and extracted twice with ether. The combined organic layers were dried with anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography on SiO_2 with a hexane/ethyl acetate mixture (98:2) to yield **20d** (70 mg, 92% yield) as a colorless oil. $[\alpha]_D$ +107 (*c* 1.50, $CHCl_3$). IR (film) ν_{max} 2965, 1733, 1186, 763, 751, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.40 (d, J = 9 Hz, 1H), 1.53 (dt, J = 9 and 1 Hz, 1H), 2.44 (m, 1H), 2.52 (d, J = 1 Hz, 1H), 2.82 (ddd, J = 17, 12, and 1 Hz, 1H), 2.86 (m, 1H), 2.92 (s, 1H), 2.93 (m, 1H), 3.21 (s, 1H), 6.15 (dd, J = 6 and 3 Hz, 1H), 6.18 (dd, J = 6 and 3 Hz, 1H), 7.27 (m, 3H), 7.35 (m, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 44.5 (CH_2), 45.3 (CH), 45.4 (CH), 47.6 (CH), 51.3 (CH_2), 52.1 (CH), 55.1 (CH), 126.7 (CH), 127.0 (CH), 128.9 (CH), 137.7 (CH), 138.4 (CH), 145.4 (Cq), 217.3 (C=O) ppm.

(+)-(1*S*,2*S*,5*S*,6*R*,7*R*)-5-Isopropyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 20c. Following the procedure described for **20d** (Route E) **20c** was obtained in 92% yield as a colorless oil. $[\alpha]_D$ +83.2 (*c* 1.05, $CHCl_3$). IR (film) ν_{max} 2960, 2872, 1731, 694 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (d, J = 6 Hz, 3H), 1.01 (d, 7 Hz, 3H), 1.23 (d, J = 9 Hz, 1H), 1.41 (dt, J = 9 and 2 Hz, 1H), 1.48 (m, 1H), 1.62 (m, 1H), 2.06 (dd, J = 7 and 7 Hz, 1H), 2.32 (ddd, J = 18, 11, and 2 Hz, 1H), 2.29 (m, 1H), 2.74 (s, 1H), 3.11 (s, 1H), 6.14 (dd, J = 6 and 3 Hz, 1H), 6.20 (dd, J = 6 and 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7 (CH_3), 34.9 (CH), 44.6 (CH_2), 45.4 (CH), 46.5 (CH), 47.8 (CH), 48.1 (CH_2), 48.8 (CH), 55.3 (CH), 137.6 (CH), 138.5 (CH), 218.9 (C=O) ppm. MS (CI−NH_3) *m/e* 190 (M^+, 4.2%), 191 (M^+ + H, 19.9%), 125 ($M^+ - C_5H_5$, 100%). HRMS (CI−NH_3) calcd for $C_{13}H_{19}O$ (M^+ + H) 191.1436, found 191.1442.

(+)-(1*S*,2*S*,5*S*,6*R*,7*R*)-5-Vinyltricyclo[5.2.1.0^{2,6}]dec-8-en-3-one, 20e. Following the procedure described for **20d** (Route E) **20e** was obtained in 85% yield as a colorless oil. $[\alpha]_D$ +79.5 (*c* 0.80, $CHCl_3$). IR (film) ν_{max} 2963, 1729, 1640 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (d, J = 9 Hz, 1H), 1.47 (dt, J = 9 and 2 Hz, 1H), 2.15 (dd, J = 7 and 8 Hz, 1H), 2.32 (d, J = 9 Hz, 1H), 2.39 (m, 1H), 2.51 (ddd, J = 17, 11, and 2 Hz, 1H), 2.61 (dd, J = 17 and 9 Hz, 1H), 2.83 (s, 1H), 3.13 (d, J = 1 Hz, 1H), 5.01 (dd, J = 10 and 1 Hz, 1H), 5.06 (ddd, J = 17, 1, and 1 Hz, 1H), 5.90 (ddd, J = 17, 10, and 7 Hz, 1H), 6.16 (dd, J = 5 and 3 Hz, 1H), 6.19 (dd, J = 5 and 3 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.9 (CH), 44.9 (CH_2), 45.4 (CH), 47.3 (CH), 49.4 (CH_2), 49.6 (CH), 54.8 (CH), 114.1 (CH_2), 138.0 (CH), 138.7 (CH), 142.0 (CH), 217.5 (C=O) ppm. MS (CI−CH_4) *m/e* 175 (M^+ + H, 6.8%), 174 (M^+, 5.1%), 163 (8.2%), 149 (17%), 137 (6.7%), 109 ($M^+ - C_5H_5$, 100%), 91 (20.4%), 79 (16.7%). HRMS (CI−CH_4) calcd for $C_{12}H_{15}O$ (M^+ + H) 175.1045, found 175.1043

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Supporting Information Available: Tables of complete X-ray crystal data, including ORTEP drawings, refinement parameters, atomic coordinates, and bond distances and angles for **2** and **22c**; general experimental methods; and ^1H and ^{13}C NMR spectra of compounds **4**, **12**−**16**, **20c**, **20e**, **22b**−**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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