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Enantioselective alkylidenecyclopropanation of norbornenes with terminal alkynes catalyzed by palladium–phosphinous acid complexes

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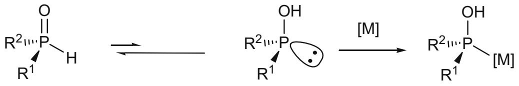
ABSTRACT

Pd(II)-coordinated phosphinous acids catalyzed the formal enantioselective [2+1] cycloaddition of norbornene derivatives with terminal alkynes. The absolute configuration of (+)-**3aa** was assigned using VCD.

1. Introduction

Over the last decade, secondary phosphine oxides (SPOs) have been used as preligands in several transition-metal-catalyzed reactions.[1] The coordination of SPOs to the metal centers occurred through the P(V)–P(III) equilibrium (Scheme 1).[2]



Scheme 1. P(V)–P(III) equilibrium and complex formation with a transition metal.

Interestingly, chiral SPO preligands retain their configuration when being coordinated to the metal,[3] and opportunities for asymmetric catalysis have been reported.[4] Recently, we disclosed a formal [2+1] cycloaddition between terminal alkynes and norbornene derivatives using Pd(II) or Pt(II)–phosphinous acid complexes as catalysts.[5–7] These simple catalytic procedures afforded alkylidenecyclopropane compounds which are chiral when two different substituents were attached to the terminal carbon of the double bond. This unusual chirality is called geometrical enantiomorphic isomerism (*cis–trans* enantiomerism or *Z–E* enantiomerism) (Scheme 2).[8,9]

Herein we report an extensive study on this asymmetric [2+1] cycloaddition catalyzed by palladium(II) associated to chiral SPOs including the effect of carboxylic acids as additives on the enantioselective alkylidenecyclopropanation and VCD studies for the determination of the absolute *E*- and *Z*-configuration of the chiral cycloadducts.

Scheme 2. *Z–E* enantiomerism.

2. Results and discussion

All chiral SPOs were prepared according to our procedures based on the highly diastereoselective ring-opening of an oxazaphospholidine[10a] or on the stereoselective substitution of a (−)-menthyloxy group by an alkyl or aryl lithium of H-menthylphenylphosphinate.[10b] As a model, we first studied the reaction of norbornadiene **1a** with phenylethyne **2a** in the presence of 5 mol % of $Pd(OAc)_2$ and 10 mol % of various chiral SPOs in toluene at 50 °C for 24 h. Table 1 summarizes the results.

These results show that sterically unhindered SPOs, such as (−)-**L1** and (−)-**L2**, afford the expected benzylidenecyclopropane **3aa** in moderate to good yields without asymmetric induction (Table 1, entries 1 and 2). The same results were observed using bisarylphosphine oxides such as (−)-**L4** and (+)-**L5** (Table 1, entries 5 and 6). Among the chiral SPO preligands, *tert*-butylphenylphosphine oxide **L3** appeared to be the most promising in terms of enantioselectivity. Indeed, the enantiomer preligands (*S*)-(−)-**L3** and (*R*)-(+)-**L3** afforded (−)-**3aa** and (+)-**3aa**, respectively, with 58% and 59% enantiomeric excess, respectively (Table 1, entries 3 and 4). However, the palladium catalyst system generated with sterically hindered (*S*)-(−)-**L3** yielded **3aa** with only 40% and was less efficient compared to ligand (−)-**L1** or (−)-**L2**. We wished to improve the yield of the [2+1] cycloaddition catalyzed by $Pd(OAc)_2$/(*S*)-(−)-**L3**. Various solvents such as Et_2O, CH_2Cl_2, THF,

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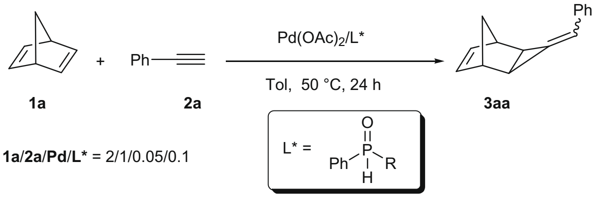
Table 1
Enantioselective benzylidenecyclopropanation of **1a** with **2a** using chiral SPOs

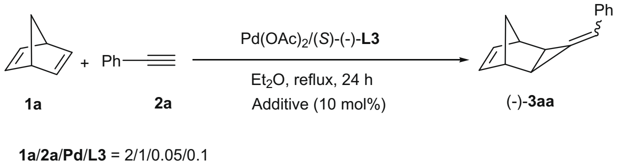


1a/**2a**/**Pd**/**L*** = 2/1/0.05/0.1

Entry	Ligand	Product	Yield[a] (%)	Ee[b] (%)
1	(−)-**L1** R = Me	**3aa**	47	0
2	(−)-**L2** R = *n*-Bu	(−)-**3aa**	62	4
3	(*S*)-(−)-**L3** R = *t*-Bu	(−)-**3aa**	40	58
4	(*R*)-(+)-**L3** R = *t*-Bu	(+)-**3aa**	42	59
5	(−)-**L4** R = 2-biphenyl	(−)-**3aa**	21	0
6	(+)-**L5** R = 2-tolyl	(−)-**3aa**	36	5

[a] Isolated yield.
[b] Ee determined on a Daicel Chiralcel OJ-H column at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99/1, $t_1 = 6.4$ min, and $t_2 = 7.1$ min.

Table 2
Influence of additives on the enantioselective benzylidenecyclopropanation



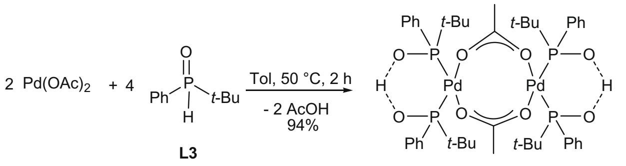
1a/**2a**/**Pd**/**L3** = 2/1/0.05/0.1

Entry	Additive	Yield[a] (%)	Ee[b] (%)
1	(*R*)-(−)-α-Phenylglycine	39	51
2	(*S*)-(−)-Proline	12	55
3	Pivalic acid	52	66
4	Adamantyl acid	32	63
5	(*S*)-(+)-Lactic acid	52	69
6	(*S*)-(+)-Mandelic acid	46	74
7	(*R*)-(−)-Mandelic acid	43	68

[a] Isolated yield.
[b] Ee determined on a Daicel Chiralcel OJ-H column at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99/1, $t_1 = 6.4$ min, and $t_2 = 7.1$ min. All experiments produced the levorotary enantiomer (−)-**3aa**.

and MTBE were examined. The highest yield (55%) was obtained in refluxing Et_2O for 24 h.

Once we had established that the (*S*)-(−)-**L3** or (*R*)-(+)-**L3** enantiomer was the best preligand, we decided to test various additives in order to improve the enantioselectivity. In our previous studies, we showed that the active catalyst **4** for the cycloaddition was obtained by treatment of $Pd(OAc)_2$ with two equivalents of **L3** (Scheme 3). We also observed that the acetic acid released in the medium plays an important role in succeeding the [2+1] cycloaddition.[5,7]



L3

4

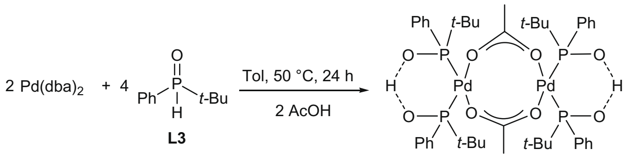
Scheme 3. Palladium(II)–phosphinous acid complex **4**.

This observation led us to examine the effect of chiral or achiral carboxylic acids as additives. We selected some commercially available α-hydroxyacids or α-amino acids as chiral compounds. All reactions were carried out in Et_2O with $Pd(OAc)_2$/(*S*)-(−)-**L3**/additives (1/2/2) as catalyst systems at reflux for 24 h. The results are listed in Table 2.

Under these conditions all enantioselectivities were improved upon (Table 2, entries 3–7), except for (*R*)-(−)-α-phenylglycine and (*S*)-(−)-proline (Table 2, entries 1 and 2). Little improvement in the enantiomeric excess was observed with pivalic acid and adamantyl acid as additives (Table 2, entries 3 and 4). However, the addition of α-hydroxyacids such as (*S*)-(+)-lactic acid proved to be more beneficial (Table 2, entry 5). The best effect was observed with (*S*)-(+)-mandelic acid, affording (−)-**3aa** in 46% yield and 74% ee (Table 2, entry 6). We also showed that by using (*R*)-(−)-mandelic acid instead of the (*S*)-(+)-mandelic acid the enantiomeric excess decreased to 68% (Table 2, entry 7). Whatever be the carboxylic acid used, the enantioselectivity was improved and the chirality of **3aa** depended on the absolute configuration of the preligand. These results suggest that the chiral acid was involved in the catalytic cycle.

Based on the optimization studies (Tables 1 and 2), we decided to test other sources of palladium. In order to avoid the concomitant presence of acetic acid with various chiral α-hydroxyacids, a new route for the synthesis of active catalyst **4** was investigated.

First, we observed by ^{31}P NMR that the active catalyst **4** could be formed upon treatment of $Pd(dba)_2$ with 2 equivalents of (*S*)-(−)-**L3** in presence of AcOH (Scheme 4).



L3

4

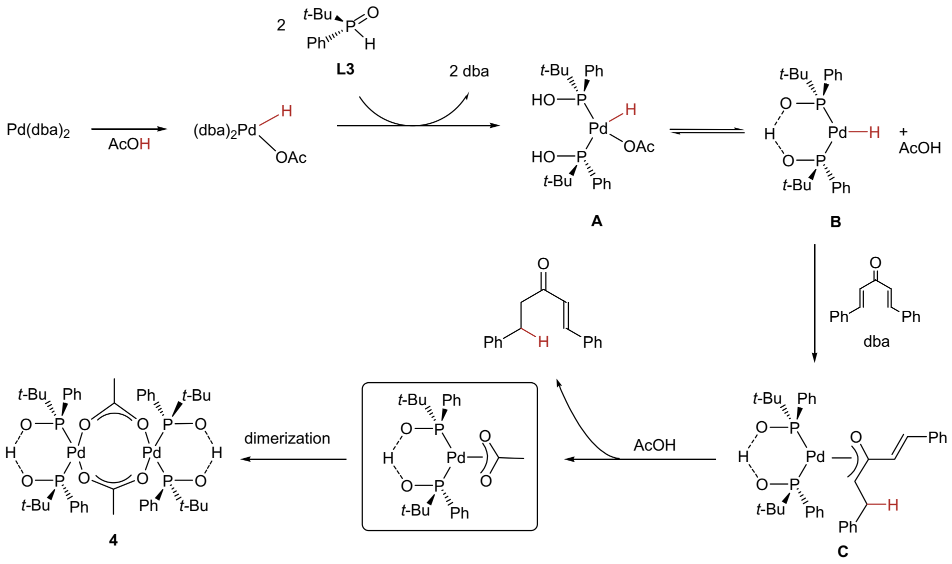
Scheme 4. Synthesis of **4** from $Pd(dba)_2$ and **L3**.

The formation of **4** could be explained as follows. The ligand exchange of dba by SPOs should occur after oxidative addition of AcOH to Pd(0) to give **A**. The loss of AcOH from **A** generated the [HPd] complex **B**, which is able to coordinate the dba partner to give **C** after insertion of the alkene moiety into the Pd–H bond. Acidolysis of the palladium enolate **C** released reduced dba and the desired catalyst **4** (Scheme 5).

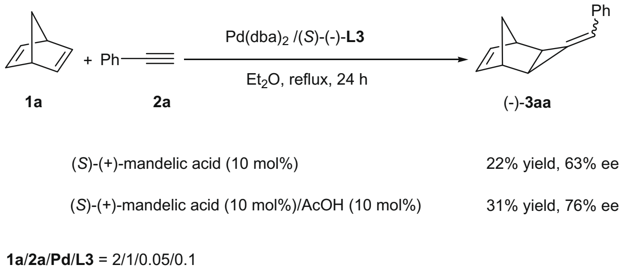
Second, a ^1H NMR analysis of the crude mixture after filtration on a short pad of silica gel confirmed that dba was partially reduced during the formation of **4**.[11]

Using this procedure, the catalyst was generated in situ starting from $Pd(dba)_2$/(*S*)-(−)-**L3**/(*S*)-(+)-mandelic acid and tested in the model reaction. After 24 h in refluxing Et_2O, the desired product (−)-**3aa** was obtained only in 22% yield and 63% ee (Scheme 6). It should be noted that the catalytic system $Pd(OAc)_2$/(*S*)-(−)-**L3**/(*S*)-(+)-mandelic acid afforded (−)-**3aa** in higher enantiomeric excess (74%, Table 2 entry 6) compared to $Pd(dba)_2$/(*S*)-(−)-**L3**/(*S*)-(+)-mandelic acid (scheme 6). Under these conditions, the loss of enantioselectivity was probably due to the lack of AcOH. This assumption was supported by the reaction carried out with $Pd(dba)_2$/(*S*)-(+)-mandelic acid in the presence of 10% of AcOH. In this case, (−)-**3aa** was isolated with the same level of enantiomeric excess (76%, Scheme 6), than the reaction catalyzed with $Pd(OAc)_2$/(*S*)-(−)-**L3**/(*S*)-(+)-mandelic acid.

These results showed that the combination of (*S*)-(+)-mandelic acid/AcOH was crucial in achieving a good level of enantioselectivity. In addition, in situ generation of catalyst **4** from **5** and AgOAc allowed the yield of the reaction to increase to 72% (Scheme 7) without loss of enantiomeric excess (Table 1, entry 3).



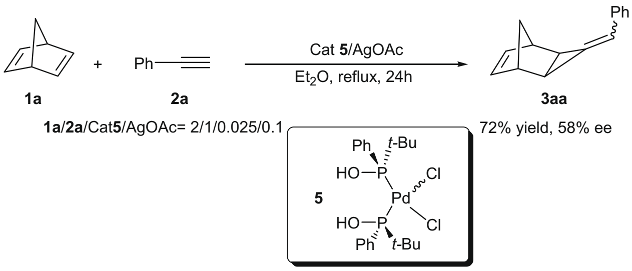
Scheme 5. Proposed reaction pathway for the formation of **4** from Pd(0), **L3,** and AcOH.



Scheme 6. Pd(dba)$_2$/(S)-(−)-**L3**/(S)-(+) mandelic acid as a catalytic system.

Finally, using the best catalytic system complex **5**/AgOAc, the reaction was also examined under different conditions with alkynes **2a**–**c** and norbornadiene **1a**, norbornene **1b,** and benzonorbornadiene **1c** (Table 3).

Without additives, cycloadducts **3aa**, **3ab**, **3ac**, **3ca,** and **3cc** were obtained in moderate yields and enantioselectivities (Table 3, entries 1, 4, 7, 12, and 15). In contrast, the reaction performed with **5**/AgOAc/(S)-(+)-mandelic acid afforded alkylidenecyclopropanes **3aa**, **3ab**, **3ac**, **3ca**, and **3cc** in lower yields but with good levels of enantioselectivities. The most promising result was obtained with norbornadiene **1a** and 1-ethynylcyclohex-1-ene **2c** (1/2 molar ratio). In this case, the enantiomeric excess reached 95% (Table 3, entry 9). For the reaction of norbornene **1b**, the yields of the expected cycloadduct **3ba** dropped dramatically (Table 3, entries 10 and 11). The poor reactivity of norbornene **1b** versus norbornadiene **1a** has been observed in different metal-catalyzed reactions.[12]



Scheme 7. Benzylidenecyclopropanation catalyzed by [complex **5**/AgOAc].

3. VCD study

The absolute configuration of enantiopure (+)-**3aa** was determined by means of vibrational circular dichroism (VCD) by comparing experimental and calculated VCD spectra.[13,14] Density functional theory was used for the calculations. Compound **3aa** was clearly conformationally rigid.[15] We found only one stable conformer (Fig. 1) and normal mode analysis confirmed that it corresponds to a minimum on the potential energy surface since no imaginary frequency was found.

As shown in Figure 2, the calculated VCD and IR spectra (bottom) were in very good agreement with the experimental ones (top). The shape and the relative intensities of the IR and VCD bands were extremely well reproduced by the calculations. It should be noted that VCD spectra of enantiomers have opposite signs. The comparison in Figure 2 provides a high level of confidence for the assignment of the absolute configuration *E* to (+)-**3aa** (Fig. 2).

4. Conclusion

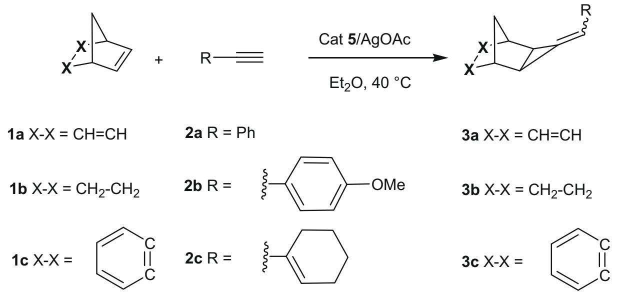
In this article we have described the first asymmetric [2C+1C] cycloaddition catalyzed by Pd(II) complexes with chiral secondary phosphine oxides as preligands involving a terminal carbon atom of the alkyne as the 1C component.[16] This cycloaddition afforded alkylidenecyclopropane compounds exhibiting a geometrical enantiomorphic isomerism. After optimization, we obtained enantioselectivities of up to 95%. Furthermore, by comparison of experimental and theoretical VCD spectra the absolute configuration *E* of (+)-**3aa** has been assigned.

5. Experimental

5.1. Materials and methods

All solvents were purified by standard procedures. THF and Et$_2$O were predried over type 4 Å molecular sieves and distilled prior to use from sodium/benzophenone under nitrogen. Toluene was distilled from sodium and stored over type 4 Å molecular sieves under nitrogen. CH_2Cl_2 and CH_3CN were distilled from CaH_2 under nitrogen prior to use. Light petroleum ether refers to the fraction with bp 40–60 °C. Thin layer chromatography was carried out on Merck

Table 3
Enantioselective alkylidenecyclopropanation of norbornenes



Entry	Alkene	Alkyne	Ratio (**1**/**2**)	Additive	Time (h)	Product[a]	Yield[b] (%)	Ee[c] (%)
1	**1a**	**2a**	2/1	—	24	(−)-**3aa**	72	58
2	**1a**	**2a**	2/1	(*S*)-(+) Mandelic acid	24	(−)-**3aa**	65	70
3	**1a**	**2a**	1/2	(*S*)-(+) Mandelic acid	24	(−)-**3aa**	44	70
4	**1a**	**2b**	2/1	—	64	(−)-**3ab**	72	42
5	**1a**	**2b**	2/1	(*S*)-(+) Mandelic acid	64	(−)-**3ab**	46	60
6	**1a**	**2b**	1/2	(*S*)-(+) Mandelic acid	64	**3ab**	—	—
7	**1a**	**2c**	2/1	—	62	(−)-**3ac**	35	49
8	**1a**	**2c**	2/1	(*S*)-(+) Mandelic acid	48	(−)-**3ac**	28	80
9	**1a**	**2c**	1/2	(*S*)-(+) Mandelic acid	64	(−)-**3ac**	21	95
10	**1b**	**2a**	2/1	—	62	(−)-**3ba**	13	30
11	**1b**	**2a**	2/1	(*S*)-(+) Mandelic acid	48	(−)-**3ba**	18	46
12	**1c**	**2a**	2/1	—	62	(+)-**3ca**	45	37
13	**1c**	**2a**	2/1	(*S*)-(+) Mandelic acid	48	(+)-**3ca**	20	67
14	**1c**	**2a**	1/2	(*S*)-(+) Mandelic acid	67	(+)-**3ca**	42	58
15	**1c**	**2c**	2/1	—	52	(+)-**3cc**	35	38
16	**1c**	**2c**	2/1	(*S*)-(+) Mandelic acid	63	(+)-**3cc**	25	72
17	**1c**	**2c**	1/2	(*S*)-(+) Mandelic acid	67	**3cc**	—	—

[a] Non racemic products obtained from (*S*)-(−)-**L3** preligand.
[b] Yield after purification.
[c] Enantiomeric excesses were determined by HPLC analyses.

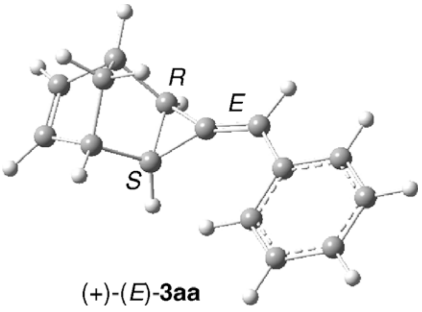


Figure 1. Stable conformation of compound **3aa** optimized at B3PW91/6–311+G(d,p) theoretical level.

Silica Gel 60 F_{254} and visualized under ultraviolet light (254 and 366 nm), or through spraying with 5% phosphomolybdic acid in EtOH, or by placing in iodine vapor. Flash chromatography was performed with Merck Silica Gel 60 (230–400 mesh). All reactions were carried out under an argon atmosphere. Palladium complex **5** was synthesized according our procedure.[5]

5.2. Physical and analytical measurements

Melting points (uncorrected) were determined in a capillary tube with a Metler LP61 apparatus. IR spectra were recorded on an IRTF Perking-Elmer 1700X spectrophotometer. $[\alpha]_D^{20}$ values were determined with a Perking-Elmer Polarimeter 341. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker Avance spectrometers at 200 MHz for ^{1}H, 50 MHz for ^{13}C, and 81 MHz for ^{31}P, with $CDCl_3$ unless otherwise stated. As external reference for ^{31}P NMR spectra, 85% phosphoric acid was used. Chemical shifts (δ) are reported in ppm relative to $CHCl_3$ ($\delta = 7.26$ for ^{1}H and $\delta = 77.0$ for ^{13}C). *J* values are given in hertz. The solvents for chiral chromatography (*n*-hexane, 2-PrOH, EtOH) are of HPLC grade from SDS (Peypin, France). They are degassed and filtered on Millipore membrane 0.45 μm before use. CHIRALPAK IA, CHIRALCEL OD-H, CHIRALCEL OJ-H, and CHIRALPAK AD-H (0.46 × 25 cm) columns are available from Merck-Eurolab. The chiral HPLC analyses were performed on a screening unit composed of Merck D-7000 system manager, Merck-Lachrom L-7100 pump, Merck-Lachrom L-7360 oven, Merck-Lachrom L-7400 UV detector, and Jasco OR-1590 polarimeter. Mass spectra were recorded on API III plus triple quadrupole mass spectrometer (Sciex, Toronto, Canada) equipped with a pneumatically assisted electrospray source. Elemental analyses were performed by the Elemental Microanalysis Service of the 'Faculté de Saint Jérôme'.

5.3. IR and VCD measurements

Infrared (IR) and vibrational circular dichroism (VCD) spectra were recorded on a Bruker PMA 50 accessory coupled to a Tensor 27 Fourier transform infrared spectrometer. A photoelastic modulator (Hinds PEM 90) set at l/4 retardation was used to modulate the handedness of the circular polarized light at 50 kHz. Demodulation was performed by a lock-in amplifier (SR830 DSP). An optical low-pass filter (<1800 cm^{-1}) before the photoelastic modulator was used to enhance the signal/noise ratio. A transmission cell equipped with CaF_2 windows and a 25 μm spacer was used and the liquid samples were measured neat. A spectrum of the racemic sample recorded in VCD mode was subtracted from the VCD spectrum of the enantiopure sample. Both for the enantiopure and for the racemic samples the interferogram was averaged over totally three hours in time slices of 1 h at a resolution of 4 cm^{-1},

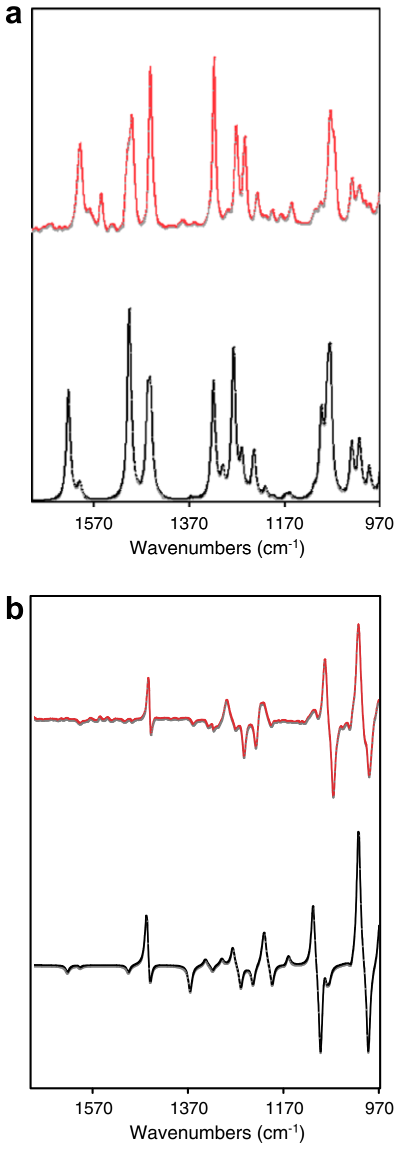


Figure 2. Comparison of the experimental (top) and calculated (bottom) IR (a) and VCD (b) spectra. (+)-**3aa** was used for the experiments. Calculations at the B3PW91/6-311+G(d,p) level were performed for the *E* configuration. For predicted spectra, wavenumbers are scaled by a factor of 0.97.

corresponding to a total of about 12,000 scans. For the infrared spectrum the empty cell served as reference. The spectra are presented without smoothing and further data processing.

5.4. DFT calculations

The geometry optimizations, vibrational frequencies, IR absorption, and VCD intensities were calculated with Density Functional Theory (DFT) using B3PW91 functional and a 6-311+G(d,p) basis set. Frequencies were scaled by a factor of 0.97. IR absorption and VCD spectra were constructed from calculated dipole and rotational strengths assuming Lorentzian band shape with a half-width at half maximum of 4 cm^{-1}. All calculations were performed using GAUSSIAN03[17] package.

5.5. General procedure for palladium-catalyzed alkylidenecyclopropanation

In a 10 mL flame-dried Schlenk flask, complex **5** (0.05 mmol, 27.0 mg) from (*S*)-(−)-**L3** and acetate silver (0.10 mmol, 16.7 mg) were dissolved under argon in dry and degassed Et_2O (2 mL). The resulting solution was stirred at room temperature. After 30 min, the solution was filtered on Celite under argon and introduced in a flame-dried Schlenk flask. Then were added successively a solution of norbornadiene or others (2 mmol), alkyne (1 mmol), and (*S*)-(+)-mandelic acid (0.10 mmol, 15.2 mg), respectively, in 1, 1, and 1 mL of dry and degassed Et_2O. The resulting mixture was stirred at reflux for 20–72 h, filtered on Celite, and the solvent was concentrated then in vacuum to afford a crude product. Purification by flash chromatography afforded alkylidenecyclopropanes.

5.5.1. (−)-3-Benzylidenetricyclo[3.2.1.0^{2,4}]oct-6-ene (−)-3aa

Enantiomeric excess: 70%. Colorless oil. $[\alpha]_D^{20} = -96.7$ (*c* 0.52, $CHCl_3$). IR ν_{max} (thin film, NaCl plate): 3115, 3062, 2976, 1597, 1554 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.97 (d, *J* = 8.4 Hz, 1H), 1.14 (d, *J* = 8.4 Hz, 1H), 1.63 (d, *J* = 8.0 Hz, 1H), 1.87 (dd, *J* = 7.9, 1.1 Hz, 1H), 3.11 (d, *J* = 1.5 Hz, 1H), 3.23 (d, *J* = 1.5 Hz, 1H), 6.43 (m, 2H), 6.56 (s, 1H), 7.16–7.37 (m, 3H), 7.48–7.53 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 25.0, 28.5, 42.5, 44.5, 45.1, 117.2, 126.5 (*2), 126.6, 128.4 (*2), 137.8, 139.2, 139.7, 141.1. ESIMS (low resolution) *m/z*: Calcd for $C_{15}H_{14}$ $(M+H)^+$: 195. Found: 195 $(M+H)^+$, 212 $(M+NH_4)^+$, 233 $(M+K)^+$. Anal. Calcd for $C_{15}H_{14}$: C, 92.74; H, 7.26. Found: C, 92.81; H, 7.18. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99/1, t_R: (+) = 6.0 min, (−) = 6.8 min.

The semi-preparative chiral HPLC separation of (±)-**3aa** was performed by successive injections, on an unit composed of Merck D-7000 system manager, Merck-Hitachi L-6000 pump, Rheodyne valve with a 500 μL loop, and a Merck-Hitachi L-4000 UV-detector. CHIRALCEL OJ (250 × 10 mm) was used with hexane/2-PrOH (99/1) as mobile phase, 4.5 mL/min as flow rate, and UV at 254 nm. 100 μL of a 30 mg/mL solution were injected every 3 min. After injection of 3 mL of the solution and collection of the enantiomers **3aa**, 40 mg of the first enantiomer (+)-**3aa**, $[\alpha]_D^{20} = +140.8$ (*c* 0.21, $CHCl_3$), was obtained with ee >99% and 35 mg of the second enantiomer (−)-**3aa**, $[\alpha]_D^{20} = -136.7$ (*c* 0.21, $CHCl_3$), was obtained with ee = 97%.

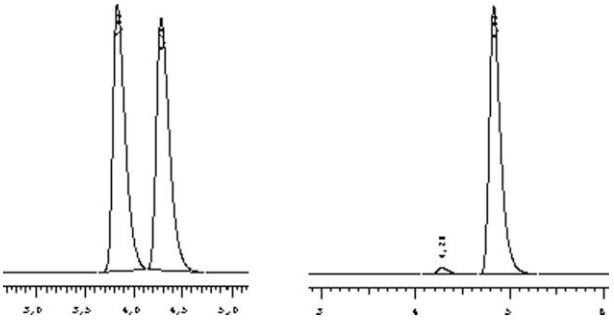
5.5.2. (−)-3-*p*-Methoxybenzylidenetricyclo[3.2.1.0^{2,4}]oct-6-ene (−)-3ab

Enantiomeric excess: 60%. White solid mp 54–55 °C. $[\alpha]_D^{20} = -83.6$ (*c* 0.5, $CHCl_3$). IR ν_{max} (thin film, NaCl plate): 3052, 3002, 2976, 2836, 1607, 1511, 1248, 1038 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.98 d, *J* = 8.5 Hz, 1H), 1.16 (d, *J* = 8.5 Hz, 1H), 1.63 (d, *J* = 7.9 Hz, 1H), 1.85 (dd, *J* = 7.7, 1.1 Hz, 1H), 3.1 (d, *J* = 1.5 Hz, 1H), 3.2 (d, *J* = 1.7 Hz, 1H), 3.8 (s, 3H), 6.44–6.45 (m, 2H), 6.53 (s, 1H), 6.90 (d, *J* = 8.9 Hz, 2H), 7.45 (d, *J* = 8.9 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): 24.9, 28.2, 42.5, 44.3, 45.0, 55.2, 113.9, 116.5, 127.6, 130.8, 138.7, 139.2, 139.7, 158.5. ESIMS (low resolution) *m/z*: Calcd for $C_{16}H_{16}O$ $(M+H)^+$: 225. Found: 225 $(M+H)^+$, 242 $(M+NH_4)^+$. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; hexane/*i*-PrOH 95/5, t_R: (+) = 9.30 min, (−) = 12.9 min.

5.5.3. (−)-3-Cyclohex-1-enylmethylene-tricyclo[3.2.1.0^{2,4}]oct-6-ene (−)-3ac

Enantiomeric excess: 95%. White solid mp: 64–65 °C. $[\alpha]_D^{20} = -34.3$ (*c* 0.3, $CHCl_3$). IR ν_{max} (thin film, NaCl plate): 2981, 2961, 2938, 2921, 1630, 1446, 1317, 1253, 904 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.90 (d, *J* = 8.5 Hz, 1H), 1.1 (d, *J* = 8.3 Hz, 1H), 1.45–1.70 (m, 6H), 2.12–2.14 (m, 2H), 2.26–2.33 (m, 2H), 2.98 (br s, 2H), 5.68–5.70 (m, 1H), 6.19 (s, 1H), 6.36 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.5, 22.7, 24.7, 25.5, 25.8, 28.6, 42.2, 44.5, 44.7, 120.9, 126.9, 136.6, 137.0, 139.0, 139.5. ESIMS (low resolution) *m/z*: Calcd for $C_{15}H_{18}$ $(M+H)^+$: 199. Found: 199 $(M+H)^+$, 216 $(M+NH_4)^+$. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL

OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99.5/0.5, t_R: (+) = 4.3 min, (−) = 4.8 min.



5.5.4. (−)-3-Benzylidenetricyclo[3.2.1.0^{2,4}]octane (−)-3ba

Enantiomeric excess: 46%. Colorless oil. $[\alpha]_D^{20} = -63.3$ (*c* 0.175, $CDCl_3$) IR ν_{max} (thin film, NaCl plate): 3077, 2955, 1596 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 0.81 (d, *J* = 9.9 Hz, 1H), 1.02 (d, *J* = 9.9 Hz, 1H), 1.34 (d, *J* = 7.3 Hz, 1H), 1.39–1.64 (m, 5H), 2.50 (m, 1H), 2.62 (m, 1H), 6.62 (s, 1H), 7.13–7.37 (m, 3H), 7.43–7.53 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 19.5, 23.1, 28.6, 28.9, 30.9, 38.0, 38.4, 119.5, 126.4 (*2), 126.5, 128.4 (*2), 130.7, 138.1. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.54; H, 8.14. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99/1, t_R: (+) = 5.6 min, (−) = 7.2 min.

5.5.5. (+)-10-Benzylidenetetracyclo[6.3.1.0^{2,7}.0^{9,11}]dodeca-2,4,6-triene (+)-3ca

Enantiomeric excess: 67%. White solid mp: 84–85 °C. $[\alpha]_D^{20} = +66.4$ (*c* 0.51, $CHCl_3$). IR ν_{max} (thin film, NaCl plate): 3068, 2976, 1590 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.37 (d, *J* = 9.2 Hz, 1H), 1.52 (d, *J* = 9.2 Hz, 1H), 1.68 (d, *J* = 7.6 Hz, 1H), 1.92 (dd, *J* = 7.6, 1.0 Hz, 1H), 3.54 (br s, 1H), 3.67 (br s, 1H), 6.72 (s, 1H), 7.08 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.13 (dd, *J* = 7.7, 4.6 Hz, 1H), 7.20–7.41 (m, 5H), 7.50–7.60 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 24.2, 27.6, 42.1, 45.3, 45.9, 119.8, 121.2, 121.3, 125.3 (*2), 126.5 (*2), 126.9, 128.5 (*2), 137.2, 137.5, 149.5, 149.8. Anal. Calcd for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.12; H, 6.59. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99/1, t_R: (−) = 12.8 min, (+) =16.9 min.

5.5.6. (+)-10-Cyclohex-1-enylmethylenetetracyclo[6.3.1.0^{2,7}.0^{9,11}]dodeca-2,4,6-triene (+)-3cc

Enantiomeric excess: 72%. White solid mp: 89–90 °C. $[\alpha]_D^{20} = +46.0$ (*c* = 0.52, $CHCl_3$). IR ν_{max} (thin film, NaCl plate): 3014, 2977, 2933, 2833, 1630, 1457, 1264, 753, 731 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 1.36 (d, *J* = 9.2 Hz, 1H), 1.52–1.60 (m, 2H), 1.67–1.80 (m, 5H), 2.20 (br s, 2H), 2.40–2.43 (m, 2H), 3.48 (dd, *J* = 4.3, 0.7 Hz, 2H), 5.80–5.83 (m, 1H), 6.40 (s, 1H), 7.10–7.16 (m, 2H), 7.27–7.30 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 22.5, 22.7, 23.9, 25.6, 25.8, 27.7, 41.7, 45.5, 45.7, 121.1, 123.5, 125.1, 127.7, 132.9, 136.5, 149.7, 150.0. ESIMS (low resolution) *m/z*: Calcd for $C_{19}H_{20}$ $(M+H)^+$: 249. Found: 249 $(M+H)^+$, 266 $(M+NH_4)^+$. Enantiomeric excesses were determined by HPLC analysis on CHIRALCEL OJ-H (0.46 × 25 cm) at $\lambda = 254$ nm; flow rate 1 mL/min; eluent: hexane/*i*-PrOH 99.875/0.125, t_R: (+) = 7.6 min, (−) = 8.7 min.

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