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Modular chiral gold(I) phosphite complexes†

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Chiral gold(I) phosphite complexes are readily prepared modularly from 3,3'-bis(triphenylsilyl)-1,1'-bi-2-naphthol. These chiral gold(I) phosphite complexes are very reactive precatalysts for the [4+2] cycloaddition of aryl-substituted 1,6-enynes with enantiomeric ratios ranging from 86 : 14 up to 94 : 6.

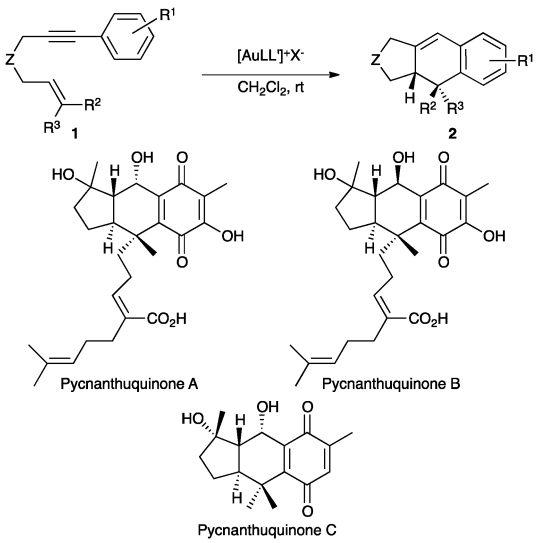
Introduction

Homogeneous gold catalysis provides efficient solutions for the construction of complex carbon skeletons under mild conditions.[1–4] Much of the progress in the enantioselective C–C multiple bond activation catalysed by gold has been achieved in the last few years in intramolecular reactions.[5–15] However, wide-scope enantioselective gold-catalysed transformations are still relatively scarce.

In 2005 we reported the first gold(I)-catalysed enantioselective alkoxycyclization of 1,6-enynes with a cationic catalyst generated *in situ* from [(*R*)-Tol-BINAP(AuCl)$_2$] and $AgSbF_6$.[16] Related enantioselective cyclizations of 1,6-enynes have been carried out more recently with chiral NHC–gold(I)[17] and phosphine–gold[18] complexes, or using platinum catalysts.[19]

We have developed a general gold(I)-catalysed cycloisomerization of substrates **1** by formal [4+2] cycloaddition of arylalkynes with alkenes to form stereospecific cycloadducts **2**,[20] with the core structure of pycnanthuquinones (Scheme 1).[21–23]

As part of a program on the development of general strategies for the synthesis of these terpenoid quinones, we examined an alternative pathway based on the gold-catalysed cyclization of benzyl-substituted 1,5-enynes.[24] In parallel, we also studied the enantioselective cycloaddition of aryl-substituted 1,6-enynes **1** using a variety of gold(I) catalysts with chiral phosphine ligands. Whereas we obtained modest enantioselectivities in most cases,[25] the group of Genêt and Michelet reported good results in the cyclization of two substrates **1a–b** in the presence of a gold(I) catalyst generated *in situ* from DTBM-MeOBIPHEP and AgOTf,[26] although in the case of **1b** the yield was significantly lower than that obtained with achiral catalysts[20] (Scheme 2).



Scheme 1 Gold(I)-catalyzed [4+2] cycloaddition of 1,6-enynes **1** and the structures of pycnanthuquinones A–C.

In an effort at developing general and practical methods for the screening of a large variety of chiral ligands in gold-catalysed reactions, we recently reported a procedure that allows performing enantioselective processes from catalysts prepared *in situ* from a cationic complex [Au(tmbn)$_2$](SbF$_6$) (tmbn = 2,4,6-trimethoxybenzonitrile) and the corresponding chiral ligand.[27] As an alternative, we prepared a series of complexes bearing chiral phosphite ligands based on the BINOL motive using a relatively simple, modular approach from a commercially available 1,1'-bi-2-naphthol. We focused on phosphite ligands over phosphines because of their lower sensitivity to air and other oxidizing agents,[28] and because phosphite gold(I) complexes are the most reactive catalysts for

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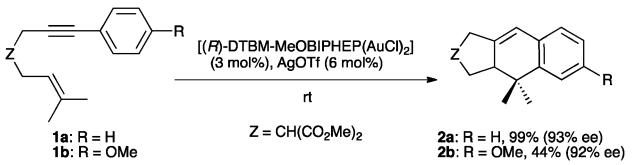
† Electronic supplementary information (ESI) available: Experimental results and NMR data. CCDC 933751 (**L11(AuCl)**), 933752 (**L12(AuCl)a**), 933753 (**L9(AuCl)**), 933754 (**L10(AuCl)**), 933756 (**L8(AuCl)**), 933757 (**L12(AuCl)e**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3cy00250k



Scheme 2 Enantioselective gold(I)-catalysed [4+2] cycloaddition of 1,6-enynes **1a–b**.

the activation of alkynes.[29,30] Herein we report our efforts towards the development of chiral BINOL-derived phosphite gold(I) complexes. Chiral BINOL-derived phosphites have been used as building blocks for synthesis of chiral palladacycles, bis(phosphite) and mixed phosphite–phosphinite PCP-palladium pincer complexes.[31,32] Monodentate phosphite gold(I) complexes with C_3-symmetry[33] and chiral gold phosphoramidite-based catalysts have also been used in a number of gold-catalysed reactions.[10–12,34]

Results and discussion

We initially examined the gold(I)-catalysed cyclization of enyne **1a** to form adduct **2a** using a wide range of complexes as precatalysts (Fig. 1). The structures of complexes **L8(AuCl)** (Fig. 2), **L9(AuCl)**, **L10(AuCl)** (Fig. 3), **L11(AuCl)** (Fig. 4), and **L12(AuCl)a** (Fig. 5) and **L12(AuCl)e** were determined using X-ray diffraction.

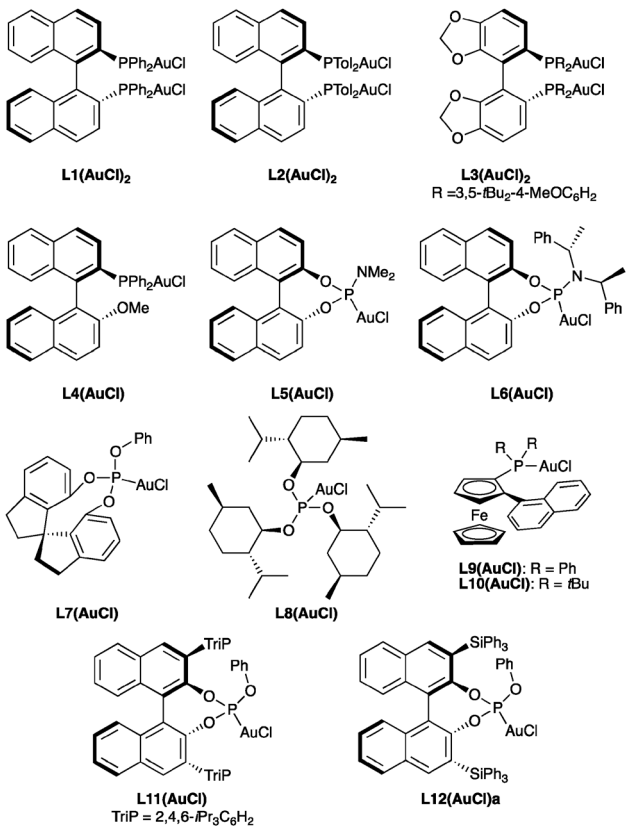


Fig. 1 Chiral gold(I) complexes of the cyclization of 1,6-enyne **1a**.

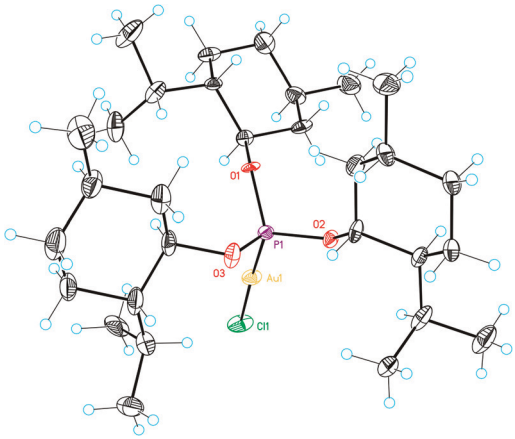


Fig. 2 X-Ray crystal structure of gold complex **L8(AuCl)**. ORTEP plot (50% thermal ellipsoids).

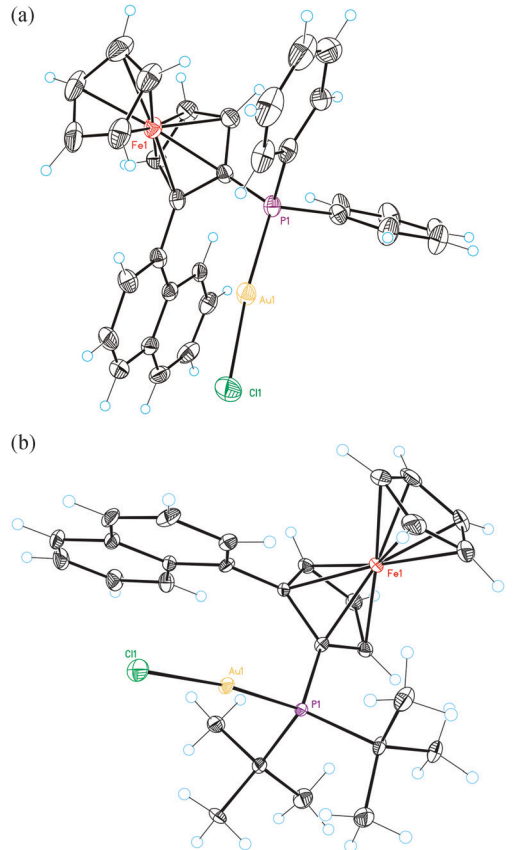


Fig. 3 X-Ray crystal structures of ferrocenylphosphine gold complexes (a) **L9(AuCl)** and (b) **L10(AuCl)**. ORTEP plot (50% thermal ellipsoids).

The cycloadditions were performed either at room temperature (condition A) or under microwave heating (condition B) (Table 1). Diphosphine–digold complexes **L1(AuCl)$_2$**, **L2(AuCl)$_2$**, and **L3(AuCl)$_2$** were investigated first (Table 1, entries 1–9). Cycloadduct **2a** was obtained in all cases in good to excellent yield but only with low to moderate enantioselectivities. The best results with these diphosphine–digold complexes (56% ee) were obtained with **L2(AuCl)$_2$** in

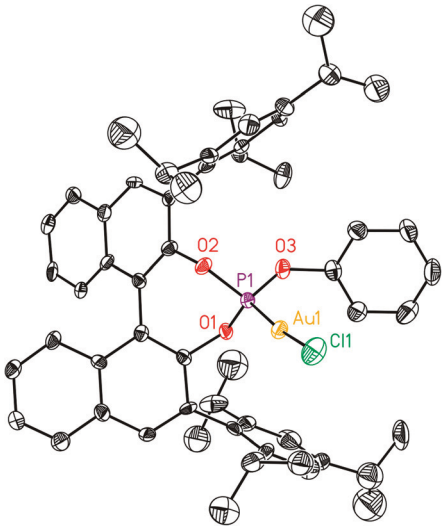


Fig. 4 X-Ray crystal structure of gold complexes **L11(AuCl)** and **L10(AuCl)**. ORTEP plot (50% thermal ellipsoids). Hydrogens are omitted for clarity.

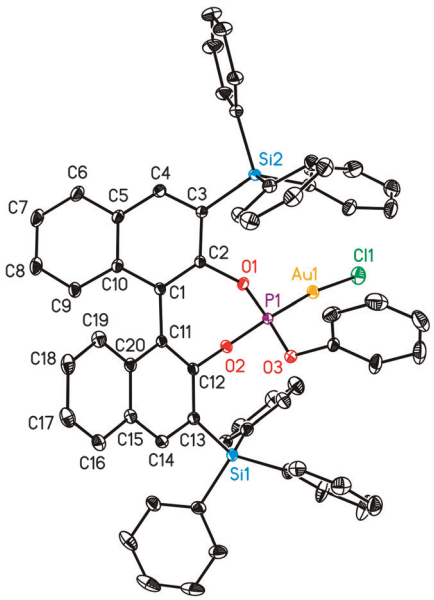


Fig. 5 X-Ray crystal structure of gold complex **L12(AuCl)a**. ORTEP plot (50% thermal ellipsoids). Hydrogens are omitted for clarity.

$CHCl_3$ using $AgPF_6$ under both conditions A and B (Table 1, entries 7 and 8). Using a 1:1 ratio of the digold complex to silver salt, under conditions in which the monocationic species are presumably formed, low enantioselectivities were observed. Biaryl gold–phosphine complex **L4(AuCl)** with the (*R*)-MOP ligand gave low enantiomeric excesses (Table 1, entries 11–13). BINOL-derived phosphoramidite complexes **L5(AuCl)** and **L6(AuCl)** also led to **2a** in excellent yield but very poor enantioselectivities (Table 1, entries 14–19). Whereas reactions of complexes **L7(AuCl)**–**L11(AuCl)** led to poor to moderate enantioselectivities (Table 1, entries 20–27), results with phosphite gold complex **L12(AuCl)** were more promising (Table 1, entries 28 and 29). Although the

Table 1 Enantioselective gold(I)-catalysed [4+2] cyclization of 1,6-enyne **1a** to form **2a** with complexes of Fig. 1[a]

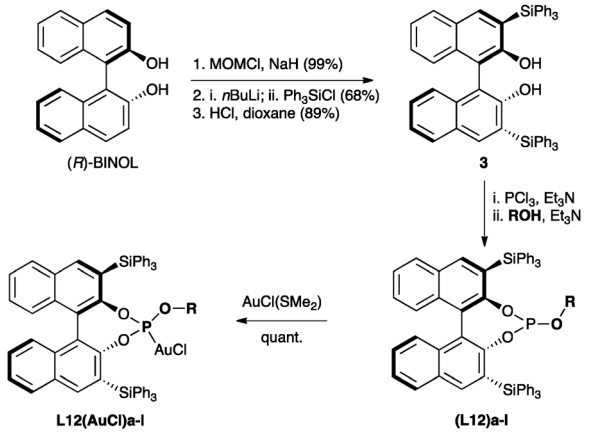
Entry	Au complex	AgX	Conditions	Time	Yield (%)	ee (%)
1	**L1(AuCl)$_2$**	$AgSbF_6$	A	24 h	71	24
2	**L1(AuCl)$_2$**	$AgSbF_6$	B	18 min	92	7
3	**L1(AuCl)$_2$**	$AgPF_6$	A	24 h	81	31
4	**L1(AuCl)$_2$**	$AgPF_6$	B	18 min	90	39
5	**L2(AuCl)$_2$**	$AgSbF_6$	A	30 h	90	25
6	**L2(AuCl)$_2$**	$AgSbF_6$	A[b]	18 min	80	38
7	**L2(AuCl)$_2$**	$AgPF_6$	A[b]	24 h	89	56
8	**L2(AuCl)$_2$**	$AgPF_6$	B[b]	15 min	89	56
9	**L3(AuCl)$_2$**	$AgBF_4$	A	16 h	91	25
10	**L4(AuCl)**	$AgSbF_6$	A	78 h	56	18
11	**L4(AuCl)**	$AgSbF_6$	B	18 min	78	20
12	**L4(AuCl)**	$AgPF_6$	A	78 h	67	23
13	**L4(AuCl)**	$AgPF_6$	B	18 min	84	25
14	**L5(AuCl)**	$AgSbF_6$	A	24 h	91	8
15	**L5(AuCl)**	$AgSbF_6$	B	18 min	95	12
16	**L5(AuCl)**	$AgPF_6$	A	24 h	88	9
17	**L5(AuCl)**	$AgPF_6$	B	18 min	94	14
18	**L6(AuCl)**	$AgSbF_6$	B	18 min	95	5
19	**L6(AuCl)**	$AgPF_6$	B	18 min	94	4
20	**L7(AuCl)**	$AgSbF_6$	A	12 h	92	26
21	**L8(AuCl)**	$AgSbF_6$	A	2 h	98	<1
22	**L9(AuCl)**	$AgSbF_6$	A	24 h	>99[c]	35
23	**L9(AuCl)**	OTf	A[d]	24 h	>99[c]	46
24	**L9(AuCl)**	NTf_2	A[d]	24 h	60[c]	50
25	**L10(AuCl)**	$AgSbF_6$	A[e]	24 h	>99[c]	50
26	**L10(AuCl)**	$AgSbF_6$	A[d]	24 h	>99[c]	39
27	**L11(AuCl)**	$AgSbF_6$	A	12 h	92	26
28	**L12(AuCl)**	$AgSbF_6$	A	12 h	99	57
29	**L12(AuCl)**	$AgBF_4$	A	16 h	90	57

[a] Au complex (2.5 mol%) and AgX (2.5 or 5 mol% for mono and digold complexes, respectively). Conditions A: 23 °C, CH_2Cl_2. Conditions B: microwave heating at 80 °C, CH_2Cl_2. [b] Reaction in $CHCl_3$. [c] Conversion determined using ^1H NMR. [d] Reaction in benzene. [e] Reaction at −20 °C.

enantiomeric excess was only marginally better than that obtained with **L2(AuCl)$_2$**, phosphite gold complex **L12(AuCl)** was a significantly more reactive catalyst, leading to **2a** in nearly quantitative yield in 12 h reaction time (*vs.* 24 h required with **L2(AuCl)$_2$**).

Overall, the structures of Au(I) complexes **L11(AuCl)** and **L12(AuCl)a** in the solid state are similar (Fig. 4 and 5), although the Au–P–OPh angle in **L12(AuCl)a** (102.90°) is significantly more acute than that of **L11(AuCl)** (114.98°). Complex **L12(AuCl)a** shows a cone-shaped binding pocket surrounding with a closest distance of 3.304 Å between the gold centre and a phenyl ring of one of the $SiPh_3$ groups, which is within the range (3.0–3.2 Å) observed in gold(I) complexes in bulky biaryl Buchwald phosphines.[35] This weak Au(I)–arene interaction is not present in complex **L11(AuCl)**.

The preparation of a series of phosphite ligands **(L12)a–n** with different OR groups can be easily carried out using known methods[31,32] from commercially available (*R*)-BINOL[36] by known procedures *via* 3,3'-bis(triphenylsilyl)-1,1'-bi-2-naphthol (**3**) (Scheme 3),[37] which is also commercially available. Ligands **(L12)a–n** were routinely purified by chromatography on silica gel under an inert atmosphere and the corresponding gold(I) complexes **L12(AuCl)a–n** were prepared in quantitative yields by reaction with [$AuCl(SMe_2)$].



Scheme 3 Synthesis of gold(I) phosphite complexes **L12(AuCl)a–l** from **3** and alcohols or phenols.

We assayed the catalytic activity of gold(I) complexes **L12(AuCl)a–l** (5 mol%) by mixing with $AgSbF_6$ (5 mol%) at 0 °C in CH_2Cl_2, followed by addition of substrate **1a** and slowly warming the reaction mixture to 23 °C over 2 h (Table 2).

Under these conditions, **L12(AuCl)a** led to **2a** in 70% ee (Table 2, entry 1). The enantioselectivity was raised further by using phosphite ligands **L12** derived from *p*-alkylsubstituted phenols (Table 2, entries 3–6). The best result (88% ee) was achieved with **L12(AuCl)d** derived from the *tert*-butylphenol group when the reaction was performed at −20 °C (Table 2, entry 6).[38] Satisfactory results were also obtained with **L12(AuCl)g** and **L12(AuCl)k** (Table 2, entries 9 and 13).

The reactions with the best catalyst **L12(AuCl)d** were slower (16–24 h) in 1,2-dichloroethane, ethyl ether, or acetone as solvent (63–82% ee), whereas no reaction was observed in toluene or 1,4-dioxane after 1–2 days. On the other hand, changing the silver salt from $AgSbF_6$ to AgOTf or $AgNTf_2$ did not significantly affect the reactivity and enantioselectivity, while slightly lower enantiomeric excesses were obtained with $AgPF_6$.[39]

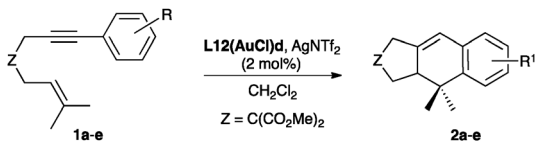
Finally, the optimized phosphite gold(I) catalyst **L12(AuCl)d** was applied for the cyclization of 1,6-enynes **1a–e** using 2 mol% catalyst loadings (Table 3). Substrate **1b** with a *p*-OMe group gave the corresponding cycloadduct **2b** in good yield and enantioselectivity, although a longer reaction time was required (Table 3, entry 2). Good enantioselectivity was also obtained with enyne **2c** bearing a *p*-Me group (Table 3, entry 3). Sterically more demanding substrate **1d** could also be cyclized in 70% yield and 79% ee (Table 3, entry 4). Finally, cyclization of **2e** with a strong electron-withdrawing *p*-NO_2 group at the phenyl ring gave cycloadduct **1d** in 80% yield and 73% ee at 0 °C (Table 3, entry 5).

Table 2 Enantioselective gold(I)-catalysed [4+2] cyclization of 1,6-enyne **1a** to form **2a** with complexes **L12(AuCl)a–n**[a]

Entry	Au complex	R	ee (%)
1	**L12(AuCl)a**	Ph	70
2	**L12(AuCl)b**	*m*-Tol	72
3	**L12(AuCl)c**	*p*-Tol	80
4[b]	**L12(AuCl)c**	*p*-Tol	83
5	**L12(AuCl)d**	4-*t*BuC_6H_4	82
6[c]	**L12(AuCl)d**	4-*t*BuC_6H_4	88
7	**L12(AuCl)e**	4-MeOC_6H_4	60
8	**L12(AuCl)f**	2,4-$Me_2C_6H_3$	74
9	**L12(AuCl)g**	3,5-$Me_2C_6H_3$	81
10	**L12(AuCl)h**	2,4,6-$Cl_3C_6H_2$	46
11	**L12(AuCl)i**	2-Napht	70
12	**L12(AuCl)j**	Me	5
13[d]	**L12(AuCl)k**	$PhCH_2$	81
14[e]	**L12(AuCl)l**	3,5-*t*$Bu_2C_6H_3CH_2$	74

[a] Au complex (5 mol%) and $AgSbF_6$ (5 mol%), 0 to 23 °C, 2 h, CH_2Cl_2. [b] Reaction at −20 °C for 4 h. [c] Reaction at −20 °C for 16 h. [d] Reaction at −25 °C for 36 h. [e] Reaction at 0 °C for 7 h.

Table 3 Gold(I)-catalysed [4+2] cycloaddition of 1,6-enynes **1a–n** with catalyst **L12(AuCl)d**



Entry	Enyne	R	*T* (°C)	Time (h)	Product (yield, %)	ee (%)
1	**1a**	H	−20	18	95	88
2	**1b**	*p*-MeO	−20	30	85	86
3	**1c**	*p*-Me	−20	15	98	87
4	**1d**	*o*-Me	−20	30	70	79
5	**1e**	*p*-O_2N	0	15	80	73

Conclusions

We have developed a series of chiral phosphite gold(I) complexes **L12(AuCl)a–n** that are easily prepared in a modular manner from BINOL. Cyclization of aryl-substituted 1,6-enynes with these complexes in the presence of a silver salt occurs with enantiomeric ratios ranging from 86 : 14 up to 94 : 6. It is also important to note that these chiral catalysts rival in reactivity with the most active catalysts for the cyclization of this more challenging class of compounds bearing a disubstituted alkyne.

Acknowledgements

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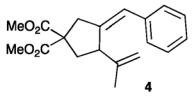
Notes and references

1 E. Jiménez-Núñez and A. M. Echavarren, *Chem. Rev.*, 2008, **108**, 3326–3350.
2 D. J. Gorin, B. D. Sherry and F. D. Toste, *Chem. Rev.*, 2008, **108**, 3351–3378.

3 (*a*) A. Fürstner and P. W. Davies, *Angew. Chem., Int. Ed.*, 2007, **46**, 3410–3449; (*b*) A. Fürstner, *Chem. Soc. Rev.*, 2009, **38**, 3208–3221.
4 V. Michelet, P. Y. Toulleca and J.-P. Genêt, *Angew. Chem., Int. Ed.*, 2008, **47**, 4268–4315.
5 (*a*) N. Huguet and A. M. Echavarren, in *Asymmetric Synthesis II*, ed. M. Christmann and S. Bräse, Wiley-VCH Verlag, 2012, ch. 26, pp. 205–212; (*b*) R. A. Widenhoefer, *Chem.–Eur. J.*, 2008, **14**, 5382–5391; (*c*) N. Bongers and N. Krause, *Angew. Chem., Int. Ed.*, 2008, **47**, 2178–2181; (*d*) S. Sengupta and X. Shi, *ChemCatChem*, 2010, **2**, 609–619; (*e*) P. Pradal, P. Y. Toullec and V. Michelet, *Synthesis*, 2011, 1501–1514; (*f*) A. Marinetti, H. Jullien and A. Voituriez, *Chem. Soc. Rev.*, 2012, **41**, 4884–4908.
6 (*a*) M. J. Johansson, D. J. Gorin, S. T. Staben and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 18002–18003; (*b*) F. Kleinbeck and F. D. Toste, *J. Am. Chem. Soc.*, 2009, **131**, 9178–9179; (*c*) G. L. Hamilton, E. J. Kang, M. Mba and F. D. Toste, *Science*, 2007, **317**, 496–499.
7 (*a*) C. Liu and R. A. Widenhoefer, *Org. Lett.*, 2007, **9**, 1935–1938; (*b*) P. Mukherjee and R. A. Widenhoefer, *Angew. Chem., Int. Ed.*, 2012, **51**, 1405–1407.
8 C.-M. Chao, D. Beltrami, P. Y. Toullec and V. Michelet, *Chem. Commun.*, 2009, 6988–6990.
9 A. Martínez, P. García-García, M. A. Fernández-Rodríguez, F. Rodríguez and R. Sanz, *Angew. Chem., Int. Ed.*, 2010, **49**, 4633–4637.
10 I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós and J. L. Mascareñas, *J. Am. Chem. Soc.*, 2009, **131**, 13020–13030.
11 A. Z. González, D. Benitez, E. Tkatchouk, W. A. Goddard III and F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 5500–5507.
12 S. Suárez-Pantiga, C. Hernández-Díaz, E. Rubio and J. M. González, *Angew. Chem., Int. Ed.*, 2012, **51**, 11552–11555.
13 L.-I. Rodríguez, T. Roth, J. L. Fillol, H. Wadepohl and L. H. Gade, *Chem.–Eur. J.*, 2012, **18**, 3721–3728.
14 S. Handa and L. M. Slaughter, *Angew. Chem., Int. Ed.*, 2012, **51**, 2912–2915.
15 S. G. Sethofer, T. Mayer and F. D. Toste, *J. Am. Chem. Soc.*, 2010, **132**, 8276–8277.
16 M. P. Muñoz, J. Adrio, J. C. Carretero and A. M. Echavarren, *Organometallics*, 2005, **24**, 1293–1300.
17 (*a*) Y. Matsumoto, K. B. Selim, H. Nakanishi, K. Yamada, Y. Yamamoto and K. Tomioka, *Tetrahedron Lett.*, 2010, **51**, 404–406; (*b*) W. Wang, J. Yang, F. Wang and M. Shi, *Organometallics*, 2011, **30**, 3859–3869.
18 C.-M. Chao, E. Genin, P. Y. Toullec, J.-P. Genêt and V. Michelet, *J. Organomet. Chem.*, 2009, **694**, 538–545.
19 (*a*) D. Brissy, M. Skander, P. Retailleau and A. Marinetti, *Organometallics*, 2007, **26**, 5782–5785; (*b*) P. Y. Toullec, C.-M. Chao, Q. Chen, S. Gladiali, J.-P. Genêt and V. Michelet, *Adv. Synth. Catal.*, 2008, **350**, 2401–2408; (*c*) D. Brissy, M. Skander, H. Jullien, P. Retailleau and A. Marinetti, *Org. Lett.*, 2009, **11**, 2137–2139; (*d*) H. Jullien, D. Brissy, P. Retailleau and A. Marinetti, *Eur. J. Inorg. Chem.*, 2011, 5083–5086; (*e*) H. Jullien, D. Brissy, R. Sylvain, P. Retailleau, J.-V. Naubron, S. Gladiali and A. Marinetti, *Adv. Synth. Catal.*, 2011, **353**, 1109–1124.
20 (*a*) C. Nieto-Oberhuber, S. López and A. M. Echavarren, *J. Am. Chem. Soc.*, 2005, **127**, 6178–6179; (*b*) C. Nieto-Oberhuber, P. Pérez-Galán, E. Herrero-Gómez, T. Lauterbach, C. Rodríguez, S. López, C. Bour, A. Rosellón, D. J. Cárdenas and A. M. Echavarren, *J. Am. Chem. Soc.*, 2008, **130**, 269–279.
21 D. M. Fort, R. P. Ubillas, C. D. Mendez, S. D. Jolad, W. D. Inman, J. R. Carney, J. L. Chen, T. T. Ianiro, C. Hasbun, R. C. Bruening, J. Luo, M. J. Reed, M. Iwu, T. J. Carlson, S. R. King, D. E. Bierer and R. Cooper, *J. Org. Chem.*, 2000, **65**, 6534–6539.
22 D. W. Laird, R. Poole, M. Wikström and I. A. van Altena, *J. Nat. Prod.*, 2007, **70**, 671–674.
23 Total synthesis of (−)-pycnanthuquinone C: F. Löbermann, P. Mayer and D. Trauner, *Angew. Chem., Int. Ed.*, 2010, **49**, 6199–6202.
24 V. López-Carrillo, N. Huguet, Á. Mosquera and A. M. Echavarren, *Chem.–Eur. J.*, 2011, **17**, 10972–10978.
25 P. Pérez-Galán, PhD thesis, ICIQ-URV, 2005–2010N. Delpont, PhD thesis, ICIQ-URV, 2007–2011.
26 C.-M. Chao, M. R. Vitale, P. Y. Toullec, J.-P. Genêt and V. Michelet, *Chem.–Eur. J.*, 2009, **15**, 1319–1323.
27 M. Raducan, C. Rodríguez-Escrich, X. C. Cambeiro, E. Escudero-Adán, M. A. Pericàs and A. M. Echavarren, *Chem. Commun.*, 2011, **47**, 4893–4895.
28 P. W. N. M. van Leeuwen, P. C. J. Kamer, C. Claver, O. Pàmies and M. Diéguez, *Chem. Rev.*, 2011, **111**, 2077–2118.
29 H. M. Amijs, V. López-Carrillo, M. Raducan, P. Pérez-Galán, C. Ferrer and A. M. Echavarren, *J. Org. Chem.*, 2008, **73**, 7721–7730.
30 D. Benitez, N. D. Shapiro, E. Tkatchouk, Y. Wang, W. A. Goddard III and D. F. Toste, *Nat. Chem.*, 2009, **1**, 482–486.
31 (*a*) R. B. Bedford, Y.-N. Chang, M. F. Haddow and C. L. McMullin, *Dalton Trans.*, 2011, **40**, 9034–9041; (*b*) R. B. Bedford, Y.-N. Chang, M. F. Haddow and C. L. McMullin, *Dalton Trans.*, 2011, **40**, 9042–9050.
32 (*a*) Phopshite **L11**: M. Kawasaki, P. Li and H. Yamamoto, *Angew. Chem., Int. Ed.*, 2008, **47**, 3795–3597; (*b*) Phopshite **L12a**: A. Sakakura, M. Sakuma and K. Ishihara, *Org. Lett.*, 2011, **13**, 3130–3797.
33 A. Z. González and F. D. Toste, *Org. Lett.*, 2009, **12**, 200–203.
34 (*a*) H. Teller, S. Flügge, R. Goddard and A. Fürstner, *Angew. Chem., Int. Ed.*, 2010, **49**, 1949–1953; (*b*) H. Teller, M. Corbet, L. Mantilli, G. Gopakumar, R. Goddard, W. Thiel and A. Fürstner, *J. Am. Chem. Soc.*, 2012, **134**, 15331–15342.
35 (*a*) E. Herrero-Gómez, C. Nieto-Oberhuber, S. López, J. Benet-Buchholz and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2006, **45**, 5455–5459; (*b*) P. Pérez-Galán, N. Delpont, E. Herrero-Gómez, F. Maseras and A. M. Echavarren, *Chem.–Eur. J.*, 2010, **16**, 5324–5332.
36 J. M. Brunel, *Chem. Rev.*, 2005, **105**, 4233.

37 V. E. Albrow, A. J. Blake, R. Fryatt, C. Wilson and S. Woodward, *Eur. J. Org. Chem.*, 2006, 2549–2557.

38 (*a*) Adduct **2a** of 88% ee (determined by HPLC) has $[\alpha]_D^{20}$ – 25.0 ± 2.0 (*c* = 0.11, $CHCl_3$). This value contrasts with that reported for **2a** of 93% ee, $[\alpha]_D^{21}$ + 14.8, (*c* = 0.93, $CHCl_3$) in ref. 26. When the cyclization of **2a** with $L(AuCl)_2$ (L = (*R*)-4-MeO-3,5-(^{t}Bu)$_2$MeOBIPHEP = DTBM-MeO-BIPHEP) (3 mol%) and AgOTf (6 mol%) in Et_2O, in addition to **2a** (74 ee, estimated by chiral HPLC), known **4** (ref. 38*b*) was also obtained (72 : 28 ratio). We could not find conditions that would allow the full resolution of **4** and the enantiomers of **2a** by chiral HPLC; (*b*) S. Porcel and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2007, **46**, 2672–2676.



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39 See ESI† for details.