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Chiral ruthenium Lewis acid-catalyzed nitrile oxide cycloadditions

Yasmin Brinkmann,[a] Reniguntala J. Madhushaw,[a] Rodolphe Jazzar,[a] Gerald Bernardinelli[b] and E. Peter Kündig[a,*]

[a]*Department of Organic Chemistry, University of Geneva, 30 Quai Ernest-Ansermet, CH-1211 Geneva 4, Switzerland*
[b]*Laboratory of Crystallography, University of Geneva, 24 Quai Ernest-Ansermet, CH-1211 Geneva 4, Switzerland*

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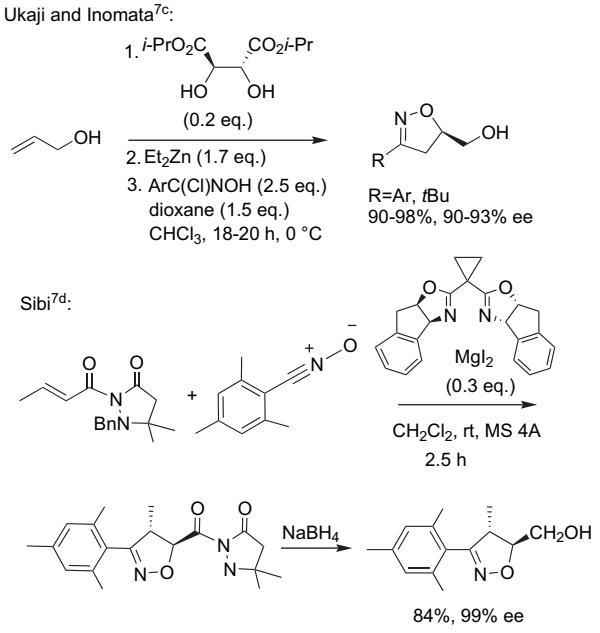
Abstract—The synthesis of the chiral ligand (*R*,*R*)-BIPHOP-F is detailed. Its coordination to a cationic cyclopentadienyl ruthenium fragment generates [Ru (acetone)(*R*,*R*)-BIPHOP-F)Cp][SbF_6], a transition metal Lewis acid that catalyzes the [3+2] dipolar cycloaddition reaction between aryl nitrile oxides and α,β-unsaturated aldehydes to give chiral 2-isoxazolines with yields of 43–98% and asymmetric purity of 60–93% ee. The stereochemistry of the major enantiomer is *S*, consistent with an approach of the nitrile oxide to the C_α-*Si* face of the enal in the *anti-s-trans* conformation in the catalyst site.

1. Introduction

Chiral, enantiopure 2-isoxazolines are important heterocycles and several members of this family of compounds exhibit significant biological activity.[1] They are also precursors to useful chiral acyclic building blocks such as β-hydroxy ketones[2] and γ-aminoalcohols.[3] A convenient one-step route of access to 2-isoxazolines[4] is by 1,3-dipolar cycloaddition reaction of nitrile oxides[5] with alkenes, albeit that the tendency of nitrile oxides to dimerize severely complicates matters.

For chiral non-racemic 2-isoxazolines diastereoselective [3+2] cycloadditions have been developed successfully[6] but enantioselective variants remain scarce (Scheme 1).[7,8] Ukaji and co-workers reported the reaction of nitrile oxides with an allylic alcohol in the presence of an in situ generated chiral Lewis acid derived from $ZnCl_2$ and diisopropyltartrate.[7] More recently, Sibi and co-workers used a chiral Lewis acid prepared from magnesium iodide and a chiral bisoxazoline derived from a 1,2-amino indanol.[8] This catalyst requires a chelating substrate and the best dienophiles were those incorporating a pyrazolidinone. While these results are impressive, we note that catalyst loading is high and that an extension of the methods for this reaction type would be useful. Both reported reactions likely involve two-point binding of the dienophile to the Lewis acid and in Sibi's example, this requires the introduction and removal of an auxiliary group.



Scheme 1. Two examples of chiral Lewis acid-catalyzed cycloaddition reactions of nitrile oxides with alkenes.

Over the past years we have developed one-point binding chiral cationic cyclopentadienyl-FeL* and -RuL* catalysts with well defined coordination spheres and have applied these successfully to Diels–Alder reactions of dienes with α,β-unsaturated aldehydes,[9] and with α,β-unsaturated ketones.[10] Particular relevant to the work described in this article is that the same catalysts were also successful in

* Corresponding author. Tel.: +41 22 379 6093; fax: +41 22 379 3215; e-mail: peter.kundig@chiorg.unige.ch

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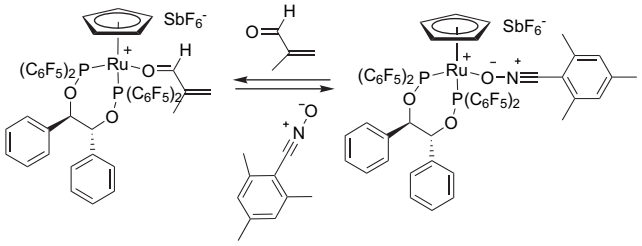
asymmetric [3+2] cycloaddition reactions between enals and nitrones.[11] Ease of generation of the Ru catalysts, stability in solution at ambient temperature, high enantioselectivity in Diels–Alder reactions, efficient catalyst recovery, and large rate differences on variation of the anion are characteristics of these Lewis acids.

The Fe complexes have higher turnover rates but are thermally less stable and cannot be recovered after the reaction. Other arene and cyclopentadienyl half-sandwich complexes have also been used as catalysts in the reactions of enals with dienes and/or of enals with nitrones by the groups of Davies,[12] Carmona and Oro,[13] and Faller.[14] Different chiral one-point binding Lewis acid catalysts for nitrone/enal cycloadditions have recently emerged.[15] Also, MacMillan has reported a successful organocatalytic approach.[16] However, at the time of writing, none of these catalysts have been tested on nitrile oxide cycloaddition reactions. We here report our results in this reaction using as catalyst precursor the complex [Ru(acetone)(*R*,*R*)-BIPHOP-F)(Cp)][SbF_6]. A major concern for this reaction was the high donor ability of the oxygen atom of the dipole.[17] Irreversible nitrile oxide binding would preclude asymmetric catalysis. A parallel situation exists in the reactions of nitrones. Since we have demonstrated reversibility of nitrone coordination to the Lewis acid [Ru(BIPHOP-F)Cp]$^+$,[11] the hypothesis of a similar situation with nitrile oxides (Scheme 2) was worth testing. The results reported here bear this out.

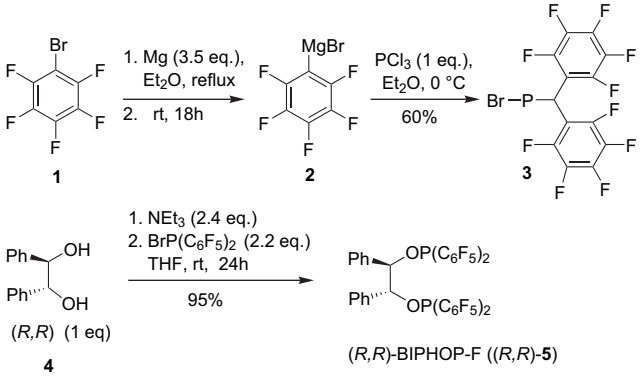


Scheme 2. Reversible coordination of nitrile oxide and enal to the catalyst.

2. Results and discussion

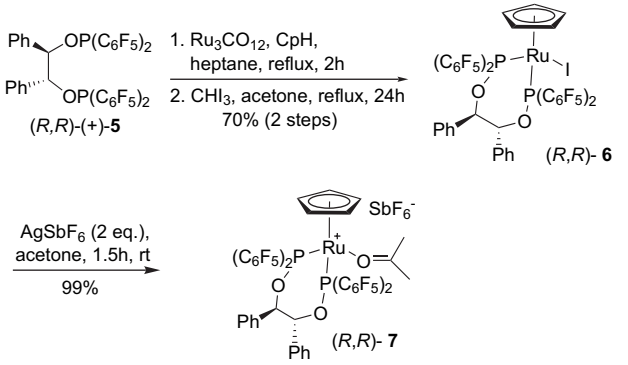
2.1. Ligand and catalyst synthesis

The crystalline, air-stable ligand (*R*,*R*)-BIPHOP-F (**5**) was synthesized as shown in Scheme 3.



Scheme 3. Synthesis of (*R*,*R*)-**5**.

Ligand **5** was then used to assemble the catalyst precursor as detailed in Scheme 4.



Scheme 4. Synthesis of [Ru(acetone)(*R*,*R*)-BIPHOP-F)Cp][SbF_6] ((*R*,*R*)-**7**).

2.2. Synthesis of nitrile oxides

Initial studies were carried out with the stable mesityl nitrile oxide **8a**.[18] As other nitrile oxides dimerize rapidly,[8] they were generated directly prior to use by treatment of the appropriate hydroximoylchlorides with the resin Amberlyst 21. The requisite hydroximoylchlorides were obtained in two steps from commercially available aldehydes.[19]

2.3. Cycloaddition reactions

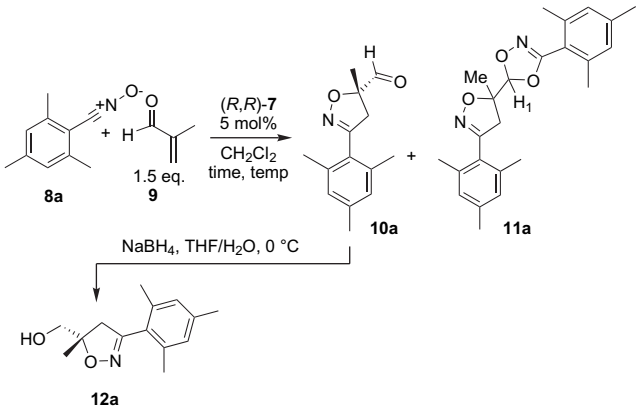
The [3+2] cycloaddition reaction between mesityl nitrile oxide (**8a**) and methacrolein (**9**) in methylene chloride at rt afforded 2-isoxazoline **10a** in 90% yield (Table 1, entry 1). In the presence of catalyst (*R*,*R*)-**7** (5 mol %), an almost quantitative yield of **10a** was obtained at 5 °C after 12 h. Asymmetric induction, measured by chiral HPLC after reduction to **12a** was, however, low (30% ee, entry 2). Lowering the reaction temperature to −10 °C did not improve the ee (entry 3). Thus, either catalyst **7** was not capable of providing better asymmetric induction or the background reaction was important. To test for the latter, the nitrile oxide was added via a syringe pump over a time period of 10 h to a solution of **9** and catalyst **7** in CH_2Cl_2 at −15 °C. This gave a 75% yield of **10a** with 60% ee (entry 4). In the next reaction both **8a** and **9** were added slowly (10 h) to the reaction mixture. While the level of induction was nearly as high as for entry 4, the acetal **11a** formed as side product. Compound **11a** results from the reaction of the isoxazoline aldehyde

Table 1. Cycloaddition reactions of mesityl nitrile oxide (**8a**) and methacrolein (**9**) in the presence of catalyst (*R*,*R*)-**7**

Entry	Time [h]	*T* [°C]	**10a**, yield[a] [%], ee[b] [%]	**11a**, yield[a] [%]
1	18	23	90, 0[c]	—
2	12	5	98, 30	—
3	24	−10	89, 30	—
4[d]	72	−15	75, 60	Traces
5[e]	17	5	60, 58	30

[a] Isolated yield.
[b] Determined by chiral HPLC.
[c] Without catalyst **7**.
[d] Slow addition of mesityl nitrile oxide (10 h).
[e] Slow addition of mesityl nitrile oxide and methacrolein (10 h).

10a with a second molecule of **8a** (entry 5). Further experiments confirmed that more than 1 equiv of nitrile oxide leads to increasing amounts of **11a** to be formed and that an excess of aldehyde results in an erosion of product enantioselectivity due to the uncatalyzed background reaction. High dilution diminished ee values as well.



In the following, the study was extended to other aromatic nitrile oxides bearing electron-donating and electron-withdrawing substituents on the aromatic ring. All nitrile oxides were generated in situ immediately prior to use. Racemic cycloadducts **10b–g** were prepared by reaction of nitrile oxides **8b–g** with methacrolein in CH_2Cl_2 at rt, followed by reduction to give the alcohol derivatives (**12b–g**). In all cases reactions afforded the 3,5-substituted isoxazolines as single regioisomers.

Tentative assignment of the structure was made based on NMR data. As shown in Figure 1 this was confirmed for isoxazoline **12g** by an X-ray structure determination.[20]

Asymmetric reactions were carried out by slow addition (10 h) of the nitrile oxides to the CH_2Cl_2 solutions of methacrolein and catalyst ((*R*,*R*)-**7** (5%) at −5 °C, Table 2). Nitrile oxides with electron-withdrawing substituents in the 4-position on the aromatic ring gave higher ees (entries 5–8) than those having electron-donating substituents (entries 1–4). Yields are lower than for mesityl nitrile oxide because dimerization of the substrates could not be avoided. As a result, small quantities of furoxans, the products of nitrile oxide dimerization, were also formed. Under the conditions used, formation of the double addition products **11b–g** could be avoided. Reaction times are not optimized for entries 7 and 8. The reactivity of the tested substrates differs considerably and the reaction cannot easily be followed by TLC, which complicates optimization.

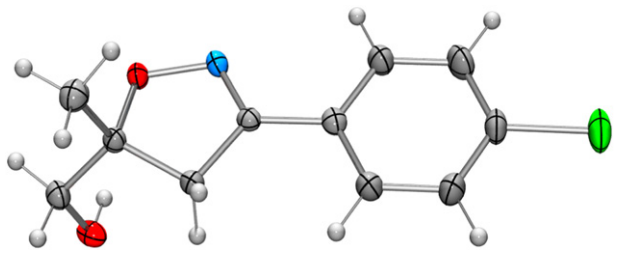
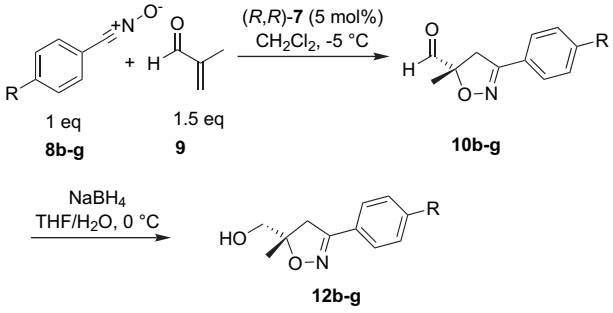


Figure 1. X-ray structure of *rac*-**12g**.

Table 2. Cycloaddition reactions of nitrile oxides (**8b–g**, slow addition) and methacrolein (**9**) in the presence of catalyst (*R*,*R*)-**7**

Entry	Nitrile oxide	Time [h], temp [°C]	**12b–g**, yield[a] [%],	ee[b] [%]
1	**8b**, R=Me	25, −5	51	66
2	**8c**, R=*i*-Pr	38, −5	65	63
3	**8d**, R=OMe	39, −5	57	65
4[c]	**8d**, R=OMe	17, −5	71	63
5	**8e**, R=CF_3	22, −5	58	76
6[d]	**8e**, R=CF_3	16, −20	60	93
7	**8f**, R=F	47, −5	61	76
8	**8g**, R=Cl	24,[e] −5	43	74

[a] Isolated yield.
[b] Determined by chiral HPLC. The *S* configuration is assigned to the major enantiomer.
[c] 1 mmol scale, slightly higher dilution.
[d] Slow addition of both nitrile oxide and methacrolein (10 h).
[e] Reaction incomplete, crystallization of nitrile oxide at syringe pump needle tip.

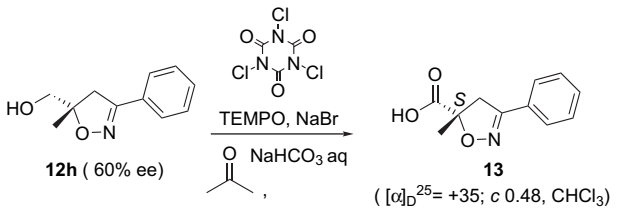


Lowering the temperature to −20 °C led to very inefficient reactions for substrates with electron-rich arenes. With electron-withdrawing substituents, product ee's (**12e–g**) increased slightly (by 2–3%). However, simultaneous slow addition of the reaction partners was beneficial in the case of R=CF_3 (entry 6).

2.4. Absolute configuration

Attempts to obtain an X-ray crystal structure of enantiomerically enriched **12g** have not met with success. Therefore the assignment of the absolute configuration is based on comparison of the optical rotation of 5-methyl-3-phenyl-4,5-dihydro-isoxazole-carboxylic acid **13** with the literature data. Compound **13** was obtained by oxidation of (5-methyl-3-phenyl-4,5-dihydro-isoxazol-5-yl)methanol **12h** (60% ee) with trichloroisocyanuric acid in the presence of catalytic amounts of TEMPO[21] (Scheme 5). Compound **12h** was synthesized by asymmetric [3+2] cycloaddition catalyzed by (*R*,*R*)-**7** like compounds **12b–g**. Compound **13** has an $[\alpha]_D^{25}$ +35 (*c* 0.48, $CHCl_3$). For enantiopure (*R*)-**13** an $[\alpha]_D^{25}$ −131 is reported.[22] Consequently the stereogenic center of the mayor enantiomer is assigned to be *S*. This also ties in with a separate literature report, including CD data, on enantiomerically enriched (*S*)-**13**.[23]

The assigned stereochemistry is in agreement with our proposed model based on the X-ray structure of [Ru ((*S*,*S*)-BIPHOP-F)Cp(methacrolein)][SbF_6].[9] As (*R*,*R*)-BIPHOP (**5**) was used in the present study, we show in Figure 2 the enantiomeric structure of the data published earlier.[9] Methacrolein is bound to (*R*,*R*)-**7** in the *anti-s-trans* conformation



Scheme 5. Synthesis of carboxylic acid **13**.

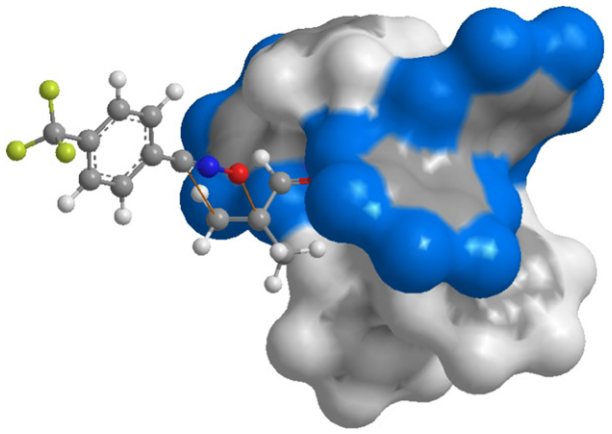


Figure 2. Projection onto the methacrolein C_α-*Si* face in the solid state structure of the complex [Ru((*R*,*R*)-BIPHOP-F)Cp(methacrolein)][SbF_6] and the trajectory of the nitrile oxide **8e**. This model for the [3+2] cycloaddition reaction predicts the isoxazoline product to have the 5*S* configuration.

and nitrile oxide adds to the C_α-*Si* face of the activated enal predicting the product to have the configuration *S* as depicted in the schemes shown above.

3. Conclusions

The first chiral one-point binding catalyst for the [3+2] cycloaddition of aryl nitrile oxides to methacrolein is reported. Modest to very good product enantioselectivities are found and a model rationalizing the regioselectivity and the asymmetric induction is presented. While the mode of stereochemical control is efficient and well understood, the reaction suffers from the rather weak activation provided by the transition metal Lewis acid. The Lewis acid strength of the catalyst resembles that of $ZnCl_2$. Research in this area now focuses on the development of catalysts with higher Lewis acidity but similar geometric features.

4. Experimental

4.1. General

[Ru((*R*,*R*)-BIPHOP-F)Cp(methacrolein)][SbF_6] (**7**) was synthesized from **5** as described in our previously reported procedures.[9c,d,f] Hydroximoylchlorides, nitrile oxide precursors, were synthesized from commercially available aldehydes following the literature procedures.[19] Reactions were carried out under a positive pressure of nitrogen unless otherwise stated. Glassware was oven-dried, and further dried by placing under vacuum and heating with a heat gun for ca. 5 min. Purification of THF, diethyl ether, *n*-hexane, toluene, and dichloromethane were carried out using a Solvtek© purification system. Commercial chemicals were used as supplied unless otherwise stated. Flash column chromatography was carried out using silica gel (60 Å/32–63 mesh, Brunschwig SA, Basel). Thin layer chromatography was performed on pre-coated aluminum plates (Merck silica 60F_{254}) and visualized using UV light and ethanolic phosphomolybdic acid.

^1H, ^{31}P, ^{19}F, and ^{13}C NMR spectra were recorded on Bruker AMX 200, 300, 400, and 500 spectrometers. Chemical shifts are quoted in parts per million relative to TMS, with coupling constants quoted in hertz. Infrared spectra were recorded on a Perkin–Elmer spectrometer as neat liquids using a Golden Gate© accessory. Polarimetry was performed with a Perkin–Elmer 241 instrument with a Na lamp (589 nm, continuous). Circular dichroism spectra were recorded with a JASCO J-715 spectropolarimeter. LRMS data were acquired using a Varian CH-4 or SM1 spectrometer with the ionizing voltage at 70 eV while HRMS were measured in the ESI or EIMS mode using an Applied Biosystems/Scix (Q-STA) spectrometer. The enantiomeric excess was determined by chiral HPLC Agilent 1100.

4.2. Ligand synthesis

4.2.1. Bis(pentafluorophenyl)bromophosphine ($(C_6F_5)_2PBr$) (3).[24,25] A solution of bromopentafluorobenzene (**1**) (49.5 g, 200 mmol) in Et_2O (40 mL) was added dropwise to dry magnesium turnings (8.5 g, 350 mmol) in 80 mL of Et_2O. The dropwise addition was performed at reflux. The mixture was stirred overnight at rt before being transferred into a dropping funnel over a flask containing PCl_3 (8.73 mL, 100 mmol, 1 equiv) in diethyl ether (60 mL) cooled to 0 °C. The Grignard reagent (C_6F_5)MgBr (**2**) was added dropwise over 3 h under vigorous stirring. The mixture was allowed to warm to rt for 1 h. The reaction mixture was filtered through a Celite pad under N_2. The solvent was removed under vacuum and the crude product was purified by fractional distillation under reduced pressure. Bis(pentafluorophenyl)bromophosphine (**3**) (bp: 120 °C, 1.8 mbar) was obtained as a green-yellow oil (26.4 g, 59%), which solidified to a pale yellow waxy solid when stored in the freezer. ^{31}P NMR (162 MHz, $CDCl_3$): δ=12.2 (m, 1P, J=35.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ=33.9 (m, 4F), 15.7 (ddd, J=20.6, 4.6, 4.6 Hz, 2F), 2.7 (m, 8F).

4.2.2. (*R*,*R*)-Hydrobenzoin-bis(pentafluorophenyl phosphite) (*R*,*R*)-BIPHOP-F (5).[9b] (+)-(*R*,*R*)-Hydrobenzoin (**4**) (2 g, 9.33 mmol), prepared from *trans*-stilbene by Sharpless asymmetric dihydroxylation as described in the literature[26] was dissolved in THF (60 mL). Freshly distilled NEt_3 (3.14 mL, 22.4 mmol) was added and the solution was cooled to −78 °C. Then, a solution of bis(pentafluorophenyl)bromophosphine (**3**) (4.86 mL, 20.53 mmol) in THF (20 mL) was added dropwise. The reaction mixture was allowed to warm up slowly to rt and was stirred for 24 h. After filtration over Celite the solvent was removed in vacuo. The crude product was purified by flash chromatography (pentane/CH_2Cl_2 40:1 to pentane/CH_2Cl_2 4:1). Compound **5** was obtained as a white solid (8.6 g, 92%). IR

(CH_2Cl_2, cm^{-1}): 3054, 2911, 1640, 1586, 1517, 1480, 1380, 1290, 1270, 1202, 1143, 1091, 980, 918, 882, 88, 800, 762, 638, 584; $[\alpha]_D^{25}$ +85 (*c* 2.26, CH_2Cl_2); mp: 118 °C; ^1H NMR (400 MHz, $CDCl_3$): δ=7.05–7.16 (6H, m), 6.98 (4H, dd, *J*=8.3, 1.5 Hz), 5.18 (1H, d, *J*=5.6 Hz), 5.15 (1H, d, *J*=5.6 Hz). ^{13}C NMR (100 MHz, C_6D_6): δ=147, 143, 138, 136, 135, 129, 128, 113, 89. ^{31}P NMR (162 MHz, $CDCl_3$): δ=88.5 (sept, *J*=31.2 Hz, 2P); ^{19}F NMR (376 MHz, C_6D_6): δ=31.6 (m, 4F), 31.0 (m, 4F), 15.5 (m, 2F), 14.4 (m, 2F), 2.7 (m, 8F); MS (70 eV) *m/z*: 561 (100), 381 (65), 365 (55), 180 (78); Elemental analysis, calcd for $C_{38}H_{12}F_{20}O_2P_2$: C, 48.43; H, 1.28. Found: C, 48.54; H, 1.50.

4.3. General procedures for 1,3-dipolar cycloaddition reactions of aromatic nitrile oxides and methacrolein

4.3.1. Generation of nitrile oxides. Nitrile oxides were generated directly prior to use by stirring hydroximoylchloride (60 mg) with the resin Amberlyst 21 (120 mg) in dry CH_2Cl_2 (1.5 mL) at rt. After completion of the reaction (30 min to 2 h) the solution of nitrile oxide was syringed up and the resin was rinsed with additional 0.5 mL of CH_2Cl_2. Stable and storable mesityl nitrile oxide (methyl substituents in *o*,*o*′ positions[18]) did not need an in situ generation.

4.3.2. Synthesis of racemic isoxazolines. For HPLC analysis racemic isoxazolines have been synthesized by reaction of freshly generated nitrile oxide (1 equiv) with methacrolein (10 equiv) in CH_2Cl_2 at rt. After completion of the reaction the solvent was evaporated and the crude aldehyde was diluted in THF/H_2O (4:1). The solution was cooled to 0 °C and $NaBH_4$ (excess) was added slowly, then the reaction was allowed to reach rt. After 2 h the mixture was again cooled to 0 °C before being hydrolyzed with H_2O. Phases were separated and the aqueous layer was extracted two times with AcOEt. The organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude product was purified by flash chromatography affording the pure alcohol.

4.4. General procedures for catalyzed reactions of nitrile oxides (8a–g) with methacrolein (9)

Compounds **12a**–**g** have been obtained following the general procedure unless otherwise stated. [Ru (acetone) (*R*,*R*)-(BIPHOP-F)(Cp)][SbF_6] (**7**) (26 mg, 5 mol %, 0.02 mmol) was dissolved in CH_2Cl_2 (0.5 mL), then methacrolein (47 μL, 0.56 mmol, 1.5 equiv) was added dropwise under stirring. The solution was cooled to the reaction temperature (−5 °C or −20 °C) and a solution of freshly generated nitrile oxide (50 mg, 0.38 mmol, 1 equiv) in CH_2Cl_2 (2 mL) was added slowly with a syringe pump over 10 h. After stirring for the appropriate reaction time the solvent was evaporated and the residue was taken up in THF/H_2O (4:1, 10 mL). The solution was cooled to 0 °C, $NaBH_4$ (excess) was added slowly, and then the reaction was allowed to reach rt. After 2 h the mixture was again cooled to 0 °C before being hydrolyzed with H_2O, phases were separated and the aqueous layer was extracted twice with AcOEt. The organic layers were dried over anhydrous Na_2SO_4, filtered, and the solvent was evaporated under reduced pressure. The crude was purified by flash chromatography affording the pure alcohol. Enantiomeric excess was determined by chiral HPLC.

4.4.1. 5-Methyl-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-isoxazole-5-carbaldehyde (10a). The catalytic reaction was stopped at the appropriate reaction time. Hexane was added to precipitate **7** and after filtering over Celite, the crude was purified by column chromatography to afford pure **10a**. IR ($CHCl_3$, cm^{-1}): 1735, 1613, 1517, 1434; ^1H NMR (200 MHz, CD_2Cl_2): δ=9.81 (s, 1H), 6.96 (s, 2H), 3.55 (d, *J*=15.0 Hz, 1H), 3.00 (d, *J*=15.0 Hz, 1H), 2.36 (s, 3H), 2.28 (s, 6H), 1.68 (s, 3H); ^{13}C NMR (100 MHz, CD_2Cl_2): δ=199.4, 158.4, 139.3, 136.6, 128.7, 125.6, 88.6, 45.1, 21.3, 19.9, 19.8.

4.4.2. [5-Methyl-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12a). Compound **12a** was obtained following the general procedures or by reduction of **10a** under standard conditions followed by flash chromatography. IR ($CHCl_3$, cm^{-1}): 3384, 2921, 1435, 1334, 1260; HPLC: Chiracel OJ-H, hex/*i*-prop 95:5, 1 mL/min, 60 min, 72% ee; $[\alpha]_D^{25}$ +70 (*c* 0.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ=6.93 (m, 2H), 3.80 (d, *J*=12.0 Hz, 1H), 3.62 (d, *J*=12.0 Hz, 1H), 3.40 (d, *J*=16.0 Hz, 1H), 2.86 (d, *J*=16.0 Hz, 1H), 2.31 (s, 3H), 2.30 (s, 3H), 2.28 (br s, 1H), 1.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=158.1, 138.7, 136.5, 128.4, 126.4, 86.5, 67.2, 46.1, 23.0, 21.7, 19.6; MS (EI): *m/z*: 233 (24), 202 (68), 160 (100); HRMS (ESI^+) calcd for $C_{14}H_{20}NO_2$ $[M+1]^+$: 234.1494; found: 234.1499.

4.4.3. 5-[5-Methyl-3-(2,4,6-trimethyl-phenyl)-4,5-dihydro-isoxazol-5-yl]-3-(2,4,6-trimethyl-phenyl)-[1,4,2]-dioxazole (diastereoisomers 56:44) (11a). The diastereomeric mixture of acetal **11a** has been isolated by column chromatography of the crude reduction product. IR ($CHCl_3$, cm^{-1}): 2921, 1611, 1435, 1332, 1077; ^1H NMR (400 MHz, $CDCl_3$) (major diastereoisomer (56%)): δ=6.91 (s, 2H), 6.89 (s, 2H), 6.13 (1H), 3.43 (d, *J*=17.5 Hz, 1H), 2.97 (d, *J*=17.45 Hz, 1H), 2.40 (s, 6H), 2.37 (s, 6H), 2.22 (s, 6H), 1.65 (s, 3H); ^1H NMR (400 MHz, $CDCl_3$) (minor diastereoisomer (44%)): δ=6.92 (s, 2H), 6.88 (s, 2H), 6.08 (1H), 3.42 (d, *J*=17.7 Hz, 1H), 2.96 (d, *J*=17.7 Hz, 1H), 2.30 (s, 6H), 2.28 (s, 6H), 2.22 (s, 6H), 1.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=158.3, 156.9, 140.9, 138.9, 136.6, 128.6, 125.7, 118.7, 109.0, 85.4, 45.9, 21.7, 21.2, 20.1, 19.5; MS (TS) *m/z*: 233 (24), 202 (68), 160 (100); HRMS (ESI^+) *m/z* calcd for $C_{24}H_{29}N_2O_3$ $[M+H]^+$: 393.2172; found: 393.2173.

4.4.4. [5-Methyl-3-(4-methyl-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12b). IR ($CHCl_3$, cm^{-1}): 3394, 2964, 2933, 1600, 1492, 1261; HPLC: Chiracel OD-H, hex/*i*-prop grad 99:1 to 90:10, 1 mL/min, 60 min, 66% ee; $[\alpha]_D^{25}$ +48 (*c* 1, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): δ=7.53 (d, *J*=8.0 Hz, 2H), 7.16 (d, *J*=8.0 Hz, 2H), 3.72 (d, *J*=12.0 Hz, 1H), 3.56 (d, *J*=12.0 Hz, 1H), 3.45 (d, *J*=16.4 Hz, 1H), 3.00 (d, *J*=16.4 Hz, 1H), 2.35 (s, 3H), 1.86 (br s, 1H), 1.40 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$): δ=157.0, 140.2, 129.3, 126.9, 126.5, 87.2, 67.2, 22.6, 21.4; MS (EI): *m/z*: 205 (16), 174 (45), 132 (100); HRMS (EI^+) calcd for $C_{12}H_{15}NO_2$ $[M]^+$: 205.1103; found: 205.1103.

4.4.5. [5-Methyl-3-(4-isopropyl-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12c). IR ($CDCl_3$, cm^{-1}): 3369, 2961, 2930, 1611, 1460, 1418, 1361, 1058, 910, 834;

HPLC: Chiracel OJ-H, hex/*i*-prop grad 99:1 to 90:10, 1 mL/min, 60 min, 63% ee; $[\alpha]_D^{25}$ +38 (*c* 1, $CHCl_3$), ^1H NMR (400 MHz, $CDCl_3$): δ=8.14 (d, *J*=8.0 Hz, 2H), 7.81 (d, *J*=8.0 Hz, 2H), 4.29 (dd, *J*=4.3, 3 Hz, 1H), 4.13 (dd, *J*=12.0, 8.5 Hz, 1H), 4.04 (d, *J*=16 Hz, 1H), 3.56 (d, *J*=16 Hz, 1H), 3.49 (m, 1H), 2.32 (br s, 1H), 1.98 (s, 3H), 1.82 (s, 3H), 1.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=157.0, 151.2, 127.2, 126.7, 126.6, 87.2, 67.2, 42.1, 34.0, 23.8, 22.6; MS (EI): *m*/*z*: 233 (23), 202 (60), 160 (100), 43 (49). HRMS (ESI^+) *m*/*z* calcd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1488; found: 234.1482.

4.4.6. [5-Methyl-3-(4-methoxy-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12d). [Ru (acetone) (*R*,*R*)-(BIPHOP-F)(Cp)][SbF_6] (70.12 mg, 5 mol %, 0.05 mmol) was dissolved in CH_2Cl_2 (1.5 mL), then methacrolein (124 μL, 0.56 mmol, 1.5 equiv) was added dropwise under stirring. The solution was cooled to −5 °C and a solution of freshly generated nitrile oxide (149.15 mg, 1 mmol, 1 equiv) in CH_2Cl_2 (6.5 mL) was added slowly with a syringe pump for 10 h. After 17 h hexane was added (20 mL), to precipitate the catalyst, CH_2Cl_2 was removed under vacuum, the solution was filtered through a Celite plug, the catalyst was eluted with acetone, and recycled following our previously published procedures.[9c,d,f] The reduction and purification of the crude reaction was carried out as stated in the general procedures. Pure [3-(4-methoxy-phenyl)-5-methyl-4,5-dihydro-isoxazol-5-yl]-methanol was obtained as a pale yellow solid (157 mg, 71% yield, 63% ee). IR ($CHCl_3$, cm^{-1}): 3503, 2924, 2853, 1607, 1594, 1457, 1437, 1249; HPLC: Chiracel OD-H, hex/*i*-prop grad 95:5 to 85:15, 1 mL/min, 120 min, 65% ee; $[\alpha]_D^{25}$ +45 (*c* 0.59, $CHCl_3$), ^1H NMR (500 MHz, $CDCl_3$): δ=7.63 (d, *J*=8.4 Hz, 2H), 6.95 (d, *J*=8.4 Hz, 2H), 3.88 (s, 3H), 3.75 (d, *J*=12.0 Hz, 1H), 3.60 (d, *J*=12.0 Hz, 1H), 3.48 (d, *J*=16.4 Hz, 1H), 3.04 (d, *J*=16.4 Hz, 1H), 1.89 (br s, 1H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ=160.9, 156.6, 128.06, 122.2, 114.0, 87.0, 67.2, 55.3, 42.2, 22.6; MS (EI): *m*/*z*: 221 (29), 190 (45), 148 (100). HRMS (EI^+) calcd for $C_{12}H_{15}NO_3$ $[M]^+$: 221.1052; found: 221.1051.

4.4.7. [5-Methyl-3-(4-trifluoromethyl-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12e). IR ($CHCl_3$, cm^{-1}): 3384, 2921, 1435, 1327; HPLC: Chiracel OD-H, hex/*i*-prop grad 99:1 to 90:10, 1 mL/min, 60 min, 93% ee; $[\alpha]_D^{25}$ +57 (*c* 0.49, $CHCl_3$), ^1H NMR (200 MHz, $CDCl_3$): δ=7.81 (d, *J*=8.0 Hz, 2H), 7.74 (d, *J*=8.0 Hz, 2H), 3.89 (dd, *J*=12.0, 4.0 Hz, 1H), 3.65 (dd, *J*=12.0, 4.0 Hz, 1H), 3.67 (d, *J*=16.0 Hz, 1H), 3.13 (d, *J*=16.0 Hz, 1H), 1.19 (br s, 1H), 1.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=154.9, 142.1, 138.5, 132.7 (q, *J*=0.8 Hz, CF_3), 126.7, 125.6, 125.5, 88.3, 67.2, 41.6, 22.0; MS (EI): *m*/*z*: 259 (8), 228 (53), 186 (100). HRMS (ESI^+) calcd for $C_{12}H_{12}NO_2F_3Na$ $[M+Na]^+$: 282.0717; found: 282.0719.

4.4.8. [5-Methyl-3-(4-fluoro-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12f). IR ($CHCl_3$, cm^{-1}): 3392, 2932, 1515, 1348; HPLC: Chiracel OJ-H, hex/*i*-prop grad 95:5 to 85:15, 1 mL/min, 120 min, 76% ee; $[\alpha]_D^{25}$ +51 (*c* 0.51, $CHCl_3$), ^1H NMR (300 MHz, $CDCl_3$): δ=7.63 (dd, *J*=8.6, 5.3 Hz, 2H), 7.08 (m, *J*=8.0 Hz, 2H), 3.74 (dd, *J*=12.0, 3.3 Hz, 1H), 3.57 (dd, *J*=11.5, 8.5 Hz, 1H), 3.47 (d, *J*=16.3 Hz, 1H), 2.99 (d, *J*=16.3 Hz, 1H), 2.05 (br s, 1H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=162.0, 156.0, 128.5, 125.9, 115.7, 87.6, 67.2, 42.0, 22.6; MS (TS): *m*/*z* 210 (100), 192 (83), 164 (63); HRMS (ESI^+) calcd for $C_{11}H_{13}NO_2F$ $[M+H]^+$: 210.0924; found: 210.0935.

4.4.9. [5-Methyl-3-(4-chloro-phenyl)-4,5-dihydro-isoxazol-5-yl]-methanol (12g). IR ($CHCl_3$, cm^{-1}): 3391, 2929, 1597, 1495; 1403, 1354; HPLC: Chiracel OJ-H, hex/*i*-prop grad 95:5 to 85:15, 1 mL/min, 120 min, 77% ee; $[\alpha]_D^{25}$ +47 (*c* 0.98, $CHCl_3$), ^1H NMR (300 MHz, $CDCl_3$): δ=7.52 (d, *J*=8.0 Hz, 2H), 7.31 (d, *J*=8.0 Hz, 2H), 3.71 (d, *J*=12.0 Hz, 1H), 3.53 (d, *J*=12.0 Hz, 1H), 3.44 (d, *J*=16.7 Hz, 1H), 2.93 (d, *J*=16.7 Hz, 1H), 2.82 (br s, 1H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=155.9, 135.8, 128.8, 128.1, 127.7, 87.8, 67.0, 41.6, 22.5; MS (TS): *m*/*z* 226 (56), 154 (52), 152 (100); HRMS (ESI^+) calcd for $C_{11}H_{13}NO_2Cl$ $[M+H]^+$: 226.0636; found: 226.0629.

4.4.10. (5-Methyl-3-phenyl-4,5-dihydro-isoxazol-5-yl)-methanol (12h). The reaction was carried out following the standard procedure starting from 100 mg of phenyl nitrile oxide (0.84 mmol), −5 °C, 22 h, 60% yield. IR ($CHCl_3$, cm^{-1}): 3378, 2929, 1597, 1446, 1359; HPLC: Chiracel OJ-H, hex/*i*-prop grad 95:5 to 85:15, 1 mL/min, 120 min, 60% ee; $[\alpha]_D^{25}$ +27 (*c* 0.98, MeOH), ^1H NMR (300 MHz, $CDCl_3$): δ=7.64 (m, 2H), 7.38 (m, 3H), 3.72 (d, *J*=12.0 Hz, 1H), 3.57 (d, *J*=12.0 Hz, 1H), 3.49 (d, *J*=16.7 Hz, 1H), 2.99 (d, *J*=16.7 Hz, 1H), 2.45 (br s, 1H), 1.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=157.0, 130.0, 129.7, 128.6, 126.5, 87.45, 67.1, 41.9, 22.6; MS (TS): *m*/*z*: 192 (100), 174 (18). HRMS (ESI^+): calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$: 192.1019; found: 192.1019.

4.4.11. 5-Methyl-3-phenyl-4,5-dihydro-isoxazole-5-carboxylic acid (13). The compound was synthesized following the literature procedures.[21] The crude acid was then purified by flash chromatography (30:1 EtOAc/AcOH) to afford **13** as a white solid. IR ($CHCl_3$, cm^{-1}): 2934, 1722, 1447, 1446; 1360; $[\alpha]_D^{25}$ +35 (*c* 0.48, $CHCl_3$), ^1H NMR (300 MHz, $CDCl_3$): δ=7.64 (m, 2H), 7.41 (m, 3H), 3.88 (d, *J*=16.3 Hz, 1H), 3.28 (d, *J*=16.3 Hz, 1H), 1.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=176.1, 156.9, 130.6, 128.8, 128.5, 126.8, 85.8, 44.9, 23.2; MS (TS): *m*/*z*: 206 (100), 188 (76), 160 (20). HRMS (ESI^+) calcd for $C_{11}H_{12}NO_3$ $[M+H]^+$: 206.0811; found: 206.0819.

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References and notes

1. (a) Pirrung, M. C.; Tumey, N. *J. Med. Chem.* **2002**, *45*, 4359; (b) Wade, P. A.; Pillay, M. K.; Singh, S. M. *Tetrahedron Lett.* **1982**, *23*, 4563.
2. (a) Kozikowski, A. P. *Acc. Chem. Res.* **1984**, *17*, 410; (b) *Tetrahedron Symposia-in-Print*; Oppolzer, W., Ed.; 1985; Vol. 41, p 3447.
3. Jäger, V.; Müller, R.; Leibold, T.; Hein, M.; Schwarz, M.; Fengler, M.; Jaroskova, L.; Parzel, M.; Le Roy, P.-Y. *Bull. Soc. Chim. Belg.* **1994**, *103*, 491.

4. (a) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565; (b) Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633; For reviews: (c) Kanemasa, S.; Tsuge, O. *Heterocycles* **1990**, *30*, 719; (d) *Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products*; Padwa, A., Pearson, W. H., Eds.; Wiley: Chichester, UK, 2002.
5. (a) Torssell, K. B. G. *Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis*; VCH: New York, NY, 1988; (b) Caramella, P.; Gruenanger, P. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, NY, 1984; Vol. 1, p 291.
6. Reviews on asymmetric cycloadditions of nitrile oxides: (a) Karlsson, S.; Hogberg, E. H. *Org. Prep. Proced. Int.* **2001**, *33*, 103; (b) Gothelf, K. V.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 863; (c) Pellissier, H. *Tetrahedron* **2007**, *63*, 3235.
7. (a) Ukaji, Y.; Sada, K.; Inomata, K. *Chem. Lett.* **1993**, 1847; (b) Shimizu, M.; Ukaji, Y.; Inomata, K. *Chem. Lett.* **1996**, 455; (c) Tsuji, M.; Ukaji, Y.; Inomata, K. *Chem. Lett.* **2002**, 1112.
8. Sibi, M. P.; Itoh, K.; Jasperse, C. P. *J. Am. Chem. Soc.* **2004**, *126*, 5366.
9. (a) Kündig, E. P.; Bourdin, B.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1856; (b) Bruin, M. E.; Kündig, E. P. *Chem. Commun.* **1998**, 2635; (c) Kündig, E. P.; Saudan, C. M.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1219; (d) Kündig, E. P.; Saudan, C. M.; Alezra, V.; Viton, F.; Bernardinelli, G. *Angew. Chem., Int. Ed.* **2001**, *40*, 4481; (e) Kündig, E. P.; Saudan, C. M.; Viton, F. T. *Adv. Synth. Catal.* **2001**, *343*, 51; (f) Alezra, A.; Bernadinelli, G.; Corminboeuf, C.; Frey, U.; Kündig, E. P.; Merbach, A. E.; Saudan, C. M.; Viton, F.; Weber, J. T. *J. Am. Chem. Soc.* **2004**, *126*, 4843; (g) Kumar, P. G. A.; Pregosin, P. S.; Vallet, M.; Bernardinelli, G.; Jazzar, R. F.; Viton, F.; Kündig, E. P. *Organometallics* **2004**, *23*, 5410.
10. Rickerby, J.; Vallet, M.; Bernadinelli, G.; Viton, F.; Kündig, E. P. *Chem.—Eur. J.* **2007**, *13*, 354.
11. Viton, F.; Bernardinelli, G.; Kündig, E. P. *J. Am. Chem. Soc.* **2002**, *124*, 4968.
12. (a) Davies, D. L.; Fawcett, J.; Garratt, S. A.; Russell, D. R. *Chem. Commun.* **1997**, 1351; (b) Davenport, A. J.; Davies, D. L.; Fawcett, J.; Russell, D. R. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1500; (c) Davies, D. L.; Fawcett, J.; Garratt, S. A.; Russell, D. R. *Organometallics* **2001**, *20*, 3029; (d) Davies, D. L.; Fawcett, J.; Garratt, S. A.; Russell, D. R. *J. Organomet. Chem.* **2002**, *662*, 43.
13. (a) Carmona, D.; Cativiela, C.; Garcia Correas, R.; Lahoz, F. J.; Lamata, M. P.; Lopez, J. A.; De Viu, M.; Oro, L. A.; San Jose, E.; Viguri, F. *Chem. Commun.* **1996**, 1247; (b) Carmona, D.; Lahoz, F. J.; Elipe, S.; Oro, L. A.; Lamata, M. P.; Viguri, F.; Mir, C.; Cativiela, C.; De Viu, M. *Organometallics* **1998**, *17*, 2986; (c) Carmona, D.; Lamata, M. P.; Oro, L. A. *Coord. Chem. Rev.* **2000**, *200*, 717; (d) Carmona, D.; Lamata, M. P.; Viguri, F.; Rodriguez, R.; Oro, L. A.; Balana, A. I.; Lahoz, F. J.; Tejero, T.; Merino, P.; Franco, S.; Montesa, I. *J. Am. Chem. Soc.* **2004**, *126*, 2716; (e) Carmona, D.; Lamata, M. P.; Viguri, F.; Rodriguez, R.; Oro, L. A.; Lahoz, F. J.; Balana, A. I.; Tejero, T.; Merino, P. *J. Am. Chem. Soc.* **2005**, *127*, 13386; (f) Carmona, D.; Vega, C.; Garcia, N.; Lahoz, F. J.; Elipe, S.; Oro, L. A.; Lamata, M. P.; Viguri, F.; Borao, R. *Organometallics* **2006**, *25*, 1592; (g) Carmona, D.; Lamata, M. P.; Viguri, F.; Ferrer, J.; Garcia, N.; Lahoz, F. J.; Martin, M. L.; Oro, L. A. *Eur. J. Inorg. Chem.* **2006**, 3155; (h) Barba, C.; Carmona, D.; Garcia, J. I.; Lamata, M. P.; Mayoral, J. A.; Salvatella, L.; Viguri, F. *J. Org. Chem.* **2006**, *71*, 9831.
14. (a) Faller, J. W.; Lavoie, A. *J. Organomet. Chem.* **2001**, *630*, 17; (b) Faller, J. W.; Grimmond, B. J. *Organometallics* **2001**, *20*, 2454; (c) Faller, J. W.; Grimmond, B. J.; D'Alliessi, D. G. *J. Am. Chem. Soc.* **2001**, *123*, 2525; (d) Faller, J. W.; Fontaine, P. P. *Organometallics* **2005**, *24*, 4132; (e) Faller, J. W.; Parr, J. *Curr. Org. Chem.* **2006**, *10*, 151.
15. (a) Mita, T.; Ohtsuki, N.; Ikeno, T.; Yamada, T. *Org. Lett.* **2002**, *4*, 2457; (b) Kanemasa, S.; Ueno, N.; Shirahase, M. *Tetrahedron Lett.* **2002**, *43*, 657; (c) Kanemasa, S. *Synlett* **2002**, 1371; (d) Kezuka, S.; Ohtsuki, N.; Mita, T.; Kogami, Y.; Ashizawa, T.; Ikeno, T.; Yamada, T. *Bull. Chem. Soc. Jpn.* **2003**, *76*, 2197; (e) Ohtsuki, N.; Kezuka, S.; Kogami, Y.; Mita, T.; Ashizawa, T.; Ikeno, T.; Yamada, T. *Synthesis* **2003**, 1462; (f) Shirahase, M.; Kanemasa, S.; Oderaotoshi, Y. *Org. Lett.* **2004**, *6*, 675; (g) Kano, T.; Hashimoto, T.; Maruoka, K. *J. Am. Chem. Soc.* **2005**, *127*, 11926.
16. Jen, W. S.; Wiener, J. J. M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 9874.
17. Coordination of metal to nitrile oxide: (a) Kanemasa, S.; Nishiuchi, M.; Kamimura, A.; Hori, K. *J. Am. Chem. Soc.* **1994**, *116*, 2324; (b) Yamamoto, Y.; Watanabe, S.; Kadotani, K.; Hasegawa, M.; Noguchi, M.; Kanemasa, S. *Tetrahedron Lett.* **2000**, *41*, 3131; (c) Faita, G.; Paio, A.; Quadrelli, P.; Rancati, F.; Seneci, P. *Tetrahedron* **2001**, *57*, 8313; (d) Rasmussen, B. S.; Elezcano, U.; Skrydstrup, T. *J. Chem. Soc., Perkin Trans. 1* **2002**, 1723.
18. Grundmann, C.; Dean, J. M. *J. Org. Chem.* **1965**, *30*, 2809.
19. Liu, K. L.; Shelton, B. R.; Howe, R. K. *J. Org. Chem.* **1980**, *45*, 3916.
20. Crystallographic data for **12g**: cell dimensions and intensities were measured at 150 K on a Stoe IPDS diffractometer with graphite-monochromated Mo Kα radiation. (λ=0.71073 Å). Data were corrected for Lorentz and polarization effects and for absorption. ($C_{11}H_{12}NO_2Cl$), M_r=225.7, monoclinic, *P*21/*c*, *a*=11.6995(13), *b*=10.5564(8), *c*=9.1556(12) Å, *b*=94.333(14)°, *V*=1127.5(2) Å^3, *Z*=4, μ=0.318 mm^{-1} (Mo Kα), d*x*=1.329 g cm^{-3}, *S*=1.08(2), *R*=0.034, *R*=0.032. CCDC 644678 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223 336 033; or deposit@ccdc.cam.ac.uk).
21. De Luca, L.; Giacomelli, G.; Masala, S.; Porcheddu, A. *J. Org. Chem.* **2003**, *68*, 4999.
22. Ros, A.; Alvarez, E.; Dietrich, H.; Fernandez, R.; Lassaletta, J. M. *Synlett* **2005**, 2899.
23. Yang, S.; Hayden, W.; Griengl, H. *Monatsh. Chem.* **1994**, *125*, 469.
24. (a) Fild, M.; Glemser, O.; Hollenberg, I. *Z. Naturforsch., B.* **1966**, *21*, 920; (b) Ali, R.; Dillon, K. B. *J. Chem. Soc., Dalton Trans.* **1990**, 2593.
25. The details of the procedure are repeated here because in the earlier report two lines in the experimental part were missing. Kündig, E. P.; Dupre, C.; Cunningham, A., Jr.; Pons, D. *Helv. Chim. Acta* **1994**, *77*, 421.
26. (a) Sharpless, K. B.; Amberg, W.; Bennani, Y. L.; Crispino, G. A.; Hartung, K.-S.; Jeong; Kwong, H.-L.; Morikawa, K.; Wang, Z.-W.; Xu, D.; Zhang, X. L. *J. Org. Chem.* **1992**, *57*, 2768; (b) Wang, Z. M.; Sharpless, K. B. *J. Org. Chem.* **1994**, *59*, 8302.