A Reusable TNF-Tagged Chiral Bis(oxazoline)–Copper Catalyst for Diels–Alder Transformations

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Abstract: A chiral bis(oxazoline) ligand, substituted on the methylene bridge by a covalent link to an electron-deficient moiety (2,4,7-trinitrofluoren-9-one, TNF), is a useful ligand associated to copper(II) salts to promote enantioselective Diels–Alder reactions between *N*-acyloxazolidinones and cyclopentadiene. Owing to different solubility properties, the corresponding catalyst was precipitated by pentane addition after reaction completion and was easily recovered by filtration. It was successfully reused in up to 20 successive catalytic cycles for the formation of the targeted products with no loss of either the activity or the enantioselectivity along with the recycling.

Key words: asymmetric catalysis, charge transfer complexes, copper, Diels–Alder reaction, catalyst recovery

Bis(oxazoline) ligands have been widely used, associated to various metallic precursors, as efficient and selective promoters for asymmetric catalysis.[1] They are specifically popular for numerous copper-catalyzed reactions leading to targeted compounds in both high yield and selectivity.[2] Many attempts were thus made towards designing efficient procedures for the easy recovery and reuse of these complexes in asymmetric transformations, to minimize environmental and economic losses. These efforts have been recently exhaustively reviewed and concern the covalent linking via the ligand structure on organic or inorganic supports, but also the use of bis(oxazoline)-based catalysts in biphasic conditions allowing for simple separation.[3] Furthermore, the immobilization of chiral catalysts on solid supports via noncovalent interactions has been considered since such a process may involve few synthetic steps to modify the ligand approximately.[4] For instance, Hutchings and coworkers[5] have prepared a copper-exchanged zeolite Y that, in the presence of bis(oxazolines), promoted the enantioselective aziridination of alkenes within the supercages of the microporous materials. Noncovalent interactions on organic supports have also been reported, showing that bis(oxazolines) were efficiently immobilized through electrostatic intercalation with nafion-based supports for cyclopropanation reactions.[6] More recently, García et al. published another strategy based on the formation of a self-supported copper-coordination polymer from a ditopic chiral ligand bearing two aza-bis(oxazoline) moieties.[7] This approach implied the solubilization of the polymeric species under the cyclopropanation reaction conditions for a transformation in homogeneous phase and its heterogeneization by recombination after reaction completion for an easy recovery by filtration and subsequent reuse.

We have previously described another heterogeneization procedure that involves the recovery of bis(oxazoline)-based copper catalysts by the formation of charge-transfer complexes (CTC), as noncovalent interactions between a donor (an electron-rich arene such as anthracene) and a receiver [an electron-deficient 2,4,7-trinitrofluoren-9-one (TNF), for instance]. As CTC present different solubility properties according to the solvent, the efficient precipitation of the catalytic species could occur at the end of the reaction by the addition of an apolar solvent, and the recovery of the active chiral copper complex was performed through simple precipitation.

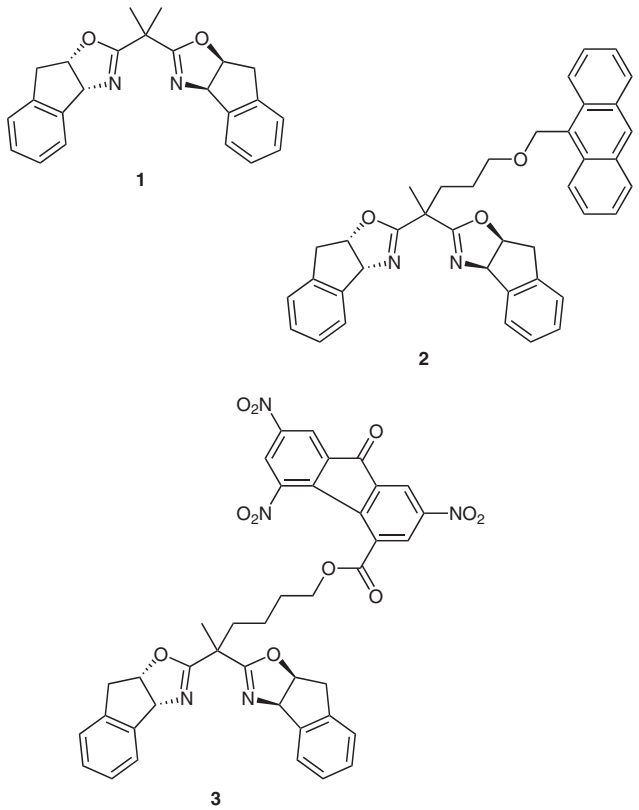

Figure 1 Structure of bis(oxazoline) ligands: indabox (**1**) and its anthracene (**2**) and TNF (**3**) based derivatives

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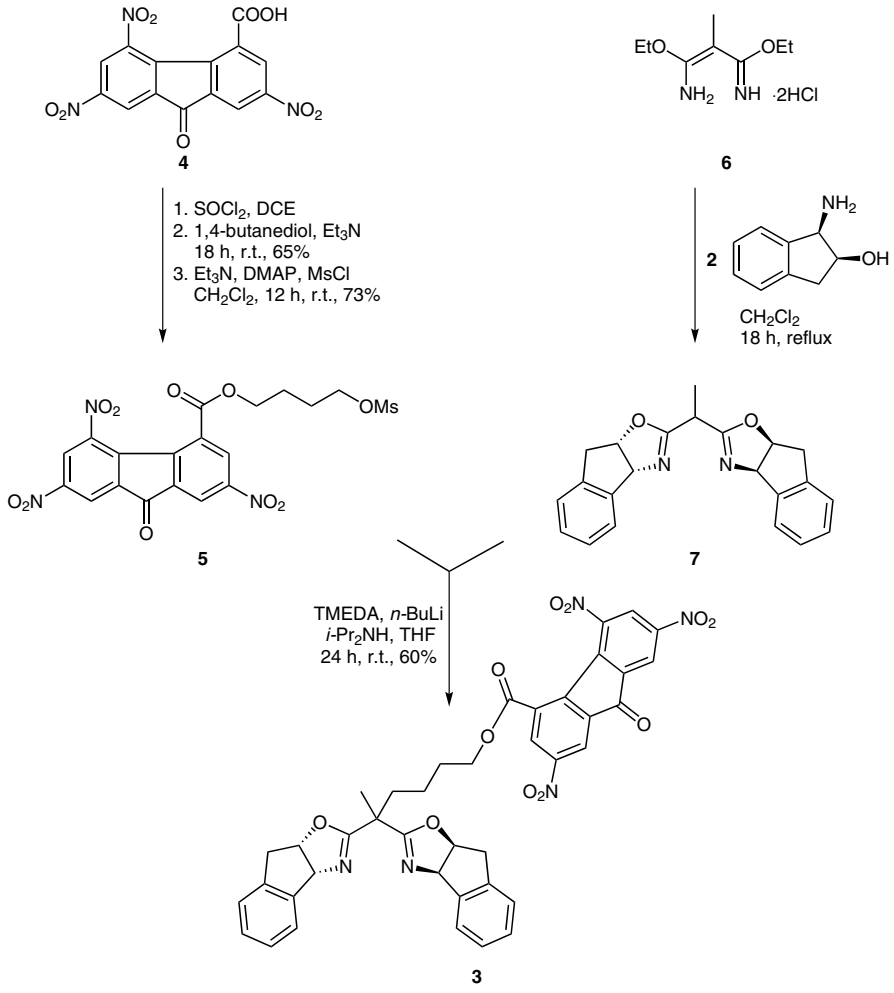
Bis(oxazoline) ligand **2** (Figure 1) was thus prepared and in association to copper triflate [$Cu(OTf)_2$], it promoted Diels–Alder reactions,[8] displaying activities and enantioselectivities comparable to reported results that involved analogous ligands derived from the parent compound **1** (Figure 1).[9]

The recycling procedure was performed by adding TNF at the end of the first run to form the CTC that was precipitated by subsequent addition of pentane, recovered by filtration of the products containing solution and reused up to 12 times without loss of either activity or selectivity.[10] Such a recovery procedure was more recently also proven to be efficient to catalyze Henry reactions[11] but also carbonyl-ene reactions and cyclopropanations.[12] By covalently immobilizing the acceptor moiety on a solid support (polystyrene or silica), charge-transfer interactions allowed the recovery of bis(oxazoline) copper catalysts under heterogeneous conditions.[13]

Having successfully described the switchable binding of a ligand covalently attached to an electron-rich anthracene moiety, we report here the synthesis of bis(oxazoline) ligand **3** (Figure 1) linked to an electron-poor arene moiety such as TNF and the study of its use in copper-catalyzed transformations. We aimed at investigating the possibility of recovering this asymmetric catalyst by formation and precipitation of CTC with anthracene. Furthermore, this type of chiral ligand attached to an electron-deficient moiety could conceivably be immobilized through reversible CTC interactions on a commercially available electron-rich solid support, such as polystyrene, for a direct recovery by filtration, for instance.

Ligand **3** was synthesized in a few synthetic steps with an overall 28% yield (Scheme 1) from 2,5,7-trinitro-9-oxo-9*H*-fluorene-4-carboxylic acid (**4**) that was obtained according to a previously described procedure, starting from diphenic acid in two steps.[14] Intermediate formation of the acyl chloride with thionyl chloride and subsequent addition of the preformed alcoholate of 1,4-butanediol led to the hydroxy ester with 65% yield.[15] It was then transformed into the mesylate derivative **5** in 73% yield. Separately, diethyl 2-methylmalonimidate (**6**)[16] was refluxed in the presence of (1*R*,2*S*)-aminoindanol to yield bis(oxazoline) **7** that was immediately engaged in the next step without further purification. Deprotonation of **7** with LDA, followed by the addition of mesylate **5**, provided ligand **3** in 60% yield as a red solid.

Diels–Alder reactions between *N*-acyloxazolidinones **8** or **10** and cyclopentadiene (Scheme 2) were used as test



Scheme 1 Synthesis of TNF-modified bis(oxazoline) **3**

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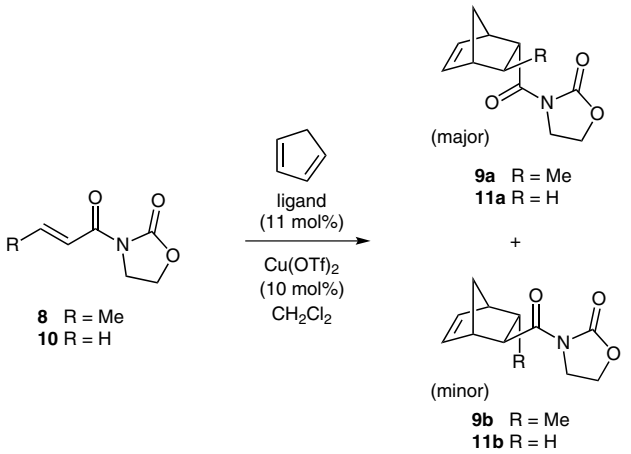
transformations to study the performance of the new catalytic system $Cu(OTf)_2$–**3**. Substrate **8** was thus engaged in a first catalytic run in dichloromethane at room temperature in the presence of 10 mol% $Cu(OTf)_2$ and 11 mol% ligand **3** (Table 1, run 1). Expected products **9a** and **9b** were isolated in high yield (92%) with 78% ee for **9a** as major isomer and 76% de, values comparable to those obtained with ligand **1** under the same conditions.[12] Delightfully, the presence of the TNF group on the bis(oxazoline) ligand did not led to a drop of both the activity and the selectivity of the corresponding catalyst. At the end of this first catalytic run, an equimolar amount of anthracene (10 mol%) was added to the reaction mixture. Pentane was then poured into the solution, leading to the precipitation of a red species that was filtered off, washed, and reengaged in another transformation.



Scheme 2 Diels–Alder reaction between cyclopentadiene and 3-but-2-enoyloxazolidin-2-one (**8**) or 3-acryloyloxazolidin-2-one (**10**)

The ^{1}H NMR analysis of the concentrated crude filtrate revealed, however, that the larger part of the previously added anthracene was recovered along with the products. Nevertheless, the red precipitated species was successfully used in a second catalytic run (Table 1, run 2), affording the same targeted compounds with a high yield (90%) and with similar ee for **9a** as the one obtained in the previous cycle. It thus appeared that, in this case, no CTC formation with anthracene was necessary to allow the efficient recovery of the catalytically active complex $Cu(OTf)_2$–**3**. This species was furthermore easily recovered for four additional catalytic runs by precipitation on addition of pentane and led to the formation of the major adduct **9a** without loss of ee (up to 81%) or yield (Table 1, runs 3–6). During the entire procedure, the de remained unaffected, with a value about 76%. By optimizing the reaction procedure, a complete conversion could be achieved in two hours.[17]

From this first experiment, it seems obvious that $Cu(OTf)_2$–**3** could be easily recovered by precipitation, owing to its different solubility properties, in CH_2Cl_2 or in pentane. The procedure was thus renewed by using solely $Cu(OTf)_2$–**3** without addition of anthracene after the first

Table 1 Diels–Alder Reaction between Cyclopentadiene and **8** in the Presence of $Cu(OTf)_2$–**3** and Anthracene[a]

Run	Time (h)	Conv. (%)[b]	Yield of **9a** + **9b** (%)[c]	ee of **9a** (%)[d]
1	6	>95	92	78 (2*R*)
2	3	>95	90	78 (2*R*)
3	1.5	>95	90	81 (2*R*)
4	2	>95	91	80 (2*R*)
5	2	>95	89	79 (2*R*)
6	2	>95	90	79 (2*R*)

[a] Reaction conditions: **8** (0.5 mmol), cyclopentadiene (3.5 mmol), $Cu(OTf)_2$ (0.05 mmol), **3** (0.055 mmol), r.t., CH_2Cl_2, after the first run addition of anthracene (0.055 mmol).
[b] Determined by ^{1}H NMR spectroscopy.
[c] Isolated yield.
[d] Determined by HPLC analysis (Whelk column), the product configuration was determined by comparison with literature data.[9b]

catalytic run. Other recycling procedures involving precipitation by solvent changes have already been described in the literature for the efficient recovery of bis(oxazoline)-based catalysts covalently attached to poly(ethyleneglycol), for example.[18] $Cu(OTf)_2$–**3** was then used and recovered by simple precipitation to promote 14 successive catalytic runs at room temperature involving substrate **8**, affording at each cycle the *endo* products **9a** in up to 79% ee and isolated in continued high yield (up to 92%, Table 2, runs 1–14). Performing the transformation at –10 °C (Table 2, run 12) afforded **9a** with a lower yield (83%) but an enhanced ee of 84%. This could be optimized to 87% ee (Table 2, run 14) when the reaction was conducted at –30 °C, but it was accompanied by an important decrease of the catalyst activity, since the expected product was isolated in only 40% yield even after a prolonged reaction time (44 h). At the 15th run, the recovered catalyst batch was then engaged with substrate **10** at –50 °C. Running the reaction at low temperature is indeed essential to inhibit the competitive noncatalyzed racemic transformation between both substrates that otherwise occurs in a non-negligible extent. The expected products **11a** and **11b** were satisfyingly obtained in high yield (84%) and with a good ee value for the major *endo* product **11a** (87%, Table 2, run 15). Even after 14 successive catalytic cycles, these values perfectly match the one that were obtained for the transformation of **10** under homogeneous conditions with $Cu(OTf)_2$–**1**.[9a] Five more runs were then performed following the same precipitation procedure, and results showed a stable efficiency in terms of yield and enantioselectivity, with an ee up to 89%, and stable de values (91%, Table 2, runs 15–20).

After these transformations, twenty Diels–Alder reactions were thus consecutively carried out with the same catalyst batch involving two different substrates **8** and **10**. No loss of activity or enantioselectivity was observed leading to the targeted compounds with high yields and enantiose-

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lectivities. Due to its efficient recyclability, the formal catalyst-to-substrate ratio used for this enantioselective carbon–carbon bond formation is consequently quite low. It is important to note that typically the use of such low catalyst loadings for these reaction types does not lead to reliable results in terms of both yield and enantioselectivity values.

Table 2 Diels–Alder Reaction between Cyclopentadiene and **8** or **10** in the Presence of $Cu(OTf)_2$–**3**[a]

Run	Substrate	Time (h)	Temp (°C)	Conv. (%)[b]	Yield (%)[c]	ee (%)[d]
1	**8**	1.5	r.t.	77	72	73 (2*R*)
2	**8**	2.5	r.t.	>95	89	76 (2*R*)
3	**8**	2	r.t.	>95	90	79 (2*R*)
4	**8**	2	r.t.	>95	87	79 (2*R*)
5	**8**	2	r.t.	>95	91	77 (2*R*)
6	**8**		r.t.	>95	89	78 (2*R*)
7	**8**	1.5	r.t.	>95	87	77 (2*R*)
8	**8**	1.5	r.t.	>95	90	78 (2*R*)
9	**8**	1.5	r.t.	>95	90	79 (2*R*)
10	**8**	1.5	r.t.	>95	91	79 (2*R*)
11	**8**	1.5	r.t.	>95	89	79 (2*R*)
12	**8**	18	–10	88	83	84 (2*R*)
13	**8**	1.5	r.t.	>95	92	79 (2*R*)
14	**8**	44	–30	48	40	87 (2*R*)
15	**10**	3	–50	93	84	87 (2*R*)
16	**10**	1.5	–50	>95	88	87 (2*R*)
17	**10**	1.5	–50	>95	86	89 (2*R*)
18	**10**	1.5	–50	>95	87	88 (2*R*)
19	**10**	1.5	–50	>95	92	88 (2*R*)
20	**10**	1.5	–50	>95	90	85 (2*R*)

[a] Reaction conditions: **8** or **10** (0.5 mmol), cyclopentadiene (3.5 mmol), $Cu(OTf)_2$ (0.05 mmol), **3** (0.055 mmol), CH_2Cl_2.
[b] Determined by ^1H NMR spectroscopy.
[c] Isolated yield, eq. 1 **9a** + **9b**, eq. 2 **11a** + **11b**.
[d] For substrate **8** and **10** the ee of **9a** and **11a**, respectively, were determined by HPLC analysis (Whelk or OD-H column), the product configurations were determined by comparison with literature data.[9]

We next attempted an analogous procedure aiming at performing direct heterogeneous catalysis on a polymeric support modified by a chiral catalyst through CTC interactions. Complex $Cu(OTf)_2$–**3** was a good candidate to test this concept, possessing an electron-deficient moiety that could led to a reversible immobilization on an electron-rich support such as commercially available cross-linked polystyrene. This process could be of high interest, avoiding the precipitation step and thus the mixture of different solvents and allowing the use of unmodified, cheap supports towards their application in continuous flow reactor. A test was thus performed by mixing $Cu(OTf)_2$–**3** with polystyrene beads (200–400 mesh, 1:8 w/w) in dichloromethane for 12 hours. The supernatant was then filtered out and both the recovered polystyrene and the resulting solution were submitted to a reaction at room temperature between cyclopentadiene and *N*-acyloxazolidinone **8**. Unfortunately, however, no reaction occurred in the presence of the polystyrenyl support, indicating that the catalyst had not been immobilized at its surface under these conditions. On the other hand, a complete conversion in the Diels–Alder cycloadducts **9** (80% ee for major *endo*-**9a**) was obtained with the supernatant solution in six hours at room temperature proving the presence of a high catalyst loading in the solution. CTC interactions between the ligand and the polymeric insoluble support were therefore probably not strong enough to allow its immobilization at the near surface for an efficient anchoring and subsequent recycling. As a perspective, anthracene-modified polystyrene should be prepared and tested as a support with probably higher affinity than the unmodified one to form CTC.

A new bis(oxazoline) ligand modified by an electron-deficient moiety through a covalent link was thus prepared and proved to promote efficiently the enantioselective Diels–Alder reaction in the presence of copper(II) salts. A charge-transfer complex was formed by addition of anthracene as electron-rich arene aiming at recovering the chiral organometallic complex through its precipitation in pentane. We have demonstrated that under these conditions, the charge-transfer complex is dissociated, and anthracene is removed with the products solution due to its high solubility in apolar solvents. Nevertheless, catalyst $Cu(OTf)_2$–**3** could be entirely recovered by a simple precipitation procedure and reused in subsequent catalytic runs showing its high stability for transforming two different substrates and producing the corresponding compounds in high yields and selectivities. Constant values could indeed be recorded all along 20 runs increasing considerably the TON of the catalyst. Such a methodology combines efficiently the advantages of both homogeneous catalysis, for undemanding mass transfer and short reaction time, together with heterogeneous catalysis for a simple recovery of the active catalyst by filtration. To the best of our knowledge, such a steady catalyst reuse has rarely been described in the literature for enantioselective C–C bond formation.

All reactions were carried out under argon in oven-dried glassware with magnetic stirring. Solvents were distilled before use from CaH_2. Cyclopentadiene was distilled by cracking dicyclopentadiene over CaH_2. ^1H NMR spectra were recorded on a Bruker AM 250 (250 MHz), AM 300 (300 MHz), or AM 360 (360 MHz) as $CDCl_3$ solutions, and data are reported in ppm relative to the solvent (7.27 ppm). ^{13}C NMR spectra were recorded on a Bruker AM 250 (62.5 MHz) or AM 360 (90 MHz) as $CDCl_3$ solutions, and data are reported in ppm relative to the solvent (77.0 ppm). Optical rotations were

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measured as solutions in 10 cm cells using a Perkin-Elmer 241 polarimeter. Melting points were measured with a Reichert instrument. Mass spectra were recorded on a Finnigan MAT 95 S spectrometer. HPLC analyses were carried out on a Perkin-Elmer chromatograph equipped with a diode array UV detector using an OD-H or a Whelk column. IR spectra were recorded as KBr disks using a Perkin-Elmer spectrometer. Elemental analyses were performed by the C.N.R.S. Service of Microanalyses in Gif-sur-Yvette (France). Substrates **8** and **10** were prepared as already described.[10] Poly(styrene-co-divinylbenzene) (2% cross-linked, 200–400 mesh) was purchased from Aldrich.

General Procedure for the Catalytic Diels–Alder Reaction

Ligand **3** (42 mg, 0.055 mmol) dissolved in CH_2Cl_2 (1 mL) was added to $Cu(OTf)_2$ (18 mg, 0.05 mmol), and the blue-green solution was stirred for 1 h at r.t. Then, *N*-acyloxazolidinone (78 mg for **8** or 71 mg for **10**, 0.5 mmol) was added to the previous solution, and the homogeneous mixture was then stirred for 10 additional min at r.t. for **8** or –50 °C for **10**. Cyclopentadiene (260 μL, 3.5 mmol) was then introduced dropwise, and the solution was further stirred at the same temperature. [When the precipitation was done in the presence of anthracene (9 mg, 0.05 mmol), it was added to the green mixture and further stirred for additional 30 min]. The catalyst was precipitated by addition of pentane (10 mL), recovered by filtration, and dried. It was then reused in a renewed catalytic run after solubilization in CH_2Cl_2 (1 mL). The product-containing solution was evaporated under vacuum, the residue was purified by preparative TLC (toluene–EtOAc = 4:1), and analyzed by HPLC for the determination of the ee.

4-(Methylsulfonyloxy)butyl 2,5,7-Trinitro-9-oxo-9*H*-fluorene-4-carboxylate (5)

To a solution of 2,5,7-trinitro-9-oxo-9*H*-fluorene-4-carboxylic acid (**4**, 2.68 g, 7.47 mmol) in DCE (15 mL) was added $SOCl_2$ (8.13 mL, 112.00 mmol) with two drops of DMF, and the mixture was heated to reflux during 16 h. Then solvent was removed under vacuum. In a second Schlenk flask, 1,4-butanediol (3.32 mL, 37.33 mmol) was mixed with Et_3N (2.18 mL, 15.68 mmol) in DCE (33 mL), and the solution was added dropwise to the first Schlenk flask at 0 °C. Then, the dark solution was stirred at r.t. for 18 h. A solution of HCl (10 mL, 1.0 M) was added, and the aqueous layer was extracted with CH_2Cl_2 (2 × 15 mL). Then, the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated to give 3.66 g of the crude hydroxy ester product. It was purified by chromatography on silica gel (CH_2Cl_2–EtOAc = 90:10) to yield the expected compound (2.09 g, 65%) as a yellow solid.[15]

To a solution of this intermediate hydroxy ester (692 mg, 1.60 mmol) in CH_2Cl_2 (20 mL) were added successively Et_3N (447 μL, 3.21 mmol) and DMAP (29 mg, 0.24 mmol) at 0 °C. After 10 min stirring at this temperature, mesyl chloride (310 μL, 4.01 mmol) was added at 0 °C, and the solution was allowed to stir at r.t. for 12 h. A 0.1 M solution of HCl in H_2O (15 mL) was then added, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were successively washed with a sat. solution of $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated to give the crude product. Product **5** was purified on silica gel (CH_2Cl_2–EtOAc = 95:5). The pure product was obtained as a yellow solid (598 mg, 73% yield). R_f = 0.19 (CH_2Cl_2–EtOAc = 95:5); mp 198 °C. ^{1}H NMR (360 MHz, $CDCl_3$): δ = 2.01 (m, 4 H), 3.06 (s, 3 H), 4.35 (t, 2 H, *J* = 5.7 Hz), 4.47 (t, 2 H, *J* = 5.7 Hz), 8.78 (m, 1 H), 8.87 (m, 2 H), 8.97 (m, 1 H). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 24.7, 25.8, 37.4, 66.6, 69.0, 121.8, 122.5, 125.3, 130.5, 132.3, 137.9, 138.9, 139.8, 143.6, 146.6, 149.4, 150.0, 164.5, 185.0. LRMS (ESI$^+$): *m/z* = 532.16 [M + Na$^+$]. HRMS (ESI$^+$): *m/z* cald for $C_{19}H_{15}N_3O_{12}NaS^+$: 532.0274; found: 532.0254. IR (KBr): 1717, 1542, 1341. Anal. Calcd (%) for $C_{19}H_{15}N_3O_{12}S$: C, 44.80; H, 2.97; N, 8.25. Found: C, 44.57; H, 3.11; N, 7.86.

(3a*R*,3a′*R*,8a*S*,8a′*S*)-2,2′-{Ethane-1,1-diyl)bis(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazole} (7)

(1*R*,2*S*)-Aminoindanol (609 mg, 4.08 mmol) was added (as solid) to a suspension of methylimidate **6** (500 mg, 2.04 mmol) in CH_2Cl_2 (40 mL). The mixture was heated to reflux for 18 h. The resulting yellow solution was washed with H_2O, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and then concentrated to give 643 mg of the crude product. For the next synthetic step, the crude mixture could be directly used without further purification. For analysis, the product was recrystallized in *i*-PrOH to give white needles (323 mg, 46% yield); mp 157 °C. ^{1}H NMR (360 MHz, $CDCl_3$): δ = 1.40 (d, 3 H, *J* = 7.1 Hz), 3.06 (dd, 2 H, J_1 = 17.9 Hz, J_2 = 9.1 Hz), 3.31–3.38 (m, 2 H), 3.46 (q, 1 H, *J* = 7.1 Hz), 5.29–5.31 (m, 2 H), 5.54 (d, 2 H, *J* = 7.7 Hz), 7.26–7.28 (m, 6 H), 7.48–7.50 (m, 2 H). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 14.7, 34.1, 39.6, 76.5, 83.3, 125.1, 125.5, 127.4, 128.4, 139.6, 141.7, 165.9. LRMS (ESI$^+$): *m/z* = 344.2 [M$^+$]. $[\alpha]_D$ +245.5 (*c* 1, $CHCl_3$).

5,5-Bis{(3a*R*,8a*S*)-8,8a-dihydro-3a*H*-Indeno[1,2-*d*]oxazol-2-yl}hexyl 2,5,7-Trinitro-9-oxo-9*H*-fluorene-4-carboxylate (3)

In a dried Schlenk tube, TMEDA (174 μL, 1.17 mmol) and DIPA (90 μL, 0.64 mmol) were mixed in THF (2 mL), and the solution was cooled to –20 °C. The LDA solution was then obtained by a slow addition of *n*-BuLi (804 μL, 1.6 M in hexane, 1.29 mmol) during 30 min at –20 °C. The uncolored solution was then allowed to stir at r.t. After 1 h, the solution of LDA was transferred in a second Schlenk tube containing **7** (200 mg, 0.59 mmol) in THF (10 mL), and the mixture was stirred at r.t. during 2 h. Compound **5** (420 mg, 0.83 mmol) in THF (4 mL) was then added to the previous solution, and the mixture was stirred during 24 h. Then, H_2O was added to the solution, and the aqueous layer was extracted with EtOAc (10 × 15 mL). The combined organic layers were washed with a sat. solution of NH_4Cl, dried over $MgSO_4$, and then concentrated. The crude product was purified on silica gel (cyclohexane–EtOAc = 1:1) to afford the pure product as a red-brown solid (267 mg, 60% yield). R_f = 0.11 (cyclohexane–EtOAc = 1:1); mp 103–106 °C. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29 (br, s, 3 H), 1.94–2.06 (m, 4 H), 3.28–3.33 (m, 2 H), 3.38–3.51 (m, 4 H), 4.39 (t, 2 H, *J* = 5.6 Hz), 5.45 (td, 2 H, J_1 = 7.8 Hz, J_2 = 2.0 Hz), 5.57 (d, 2 H, *J* = 7.3 Hz), 7.30–7.41 (m, 6 H), 7.55–7.58 (m, 2 H), 8.02 (dd, 2 H, J_1 = 7.5 Hz, J_2 = 1.5 Hz), 8.60 (d, 1 H, *J* = 2.3 Hz), 8.73 (d, 1 H, *J* = 2.5 Hz). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 24.2, 24.7, 25.7, 39.4, 47.2, 66.0, 69.2, 76.6, 84.2, 121.1, 125.2, 125.4, 125.6, 127.6, 128.1, 128.7, 129.6, 130.0, 130.9, 137.1, 137.3, 139.2, 139.4, 141.0, 145.1, 146.2, 148.7, 164.9, 166.0, 187.0. HRMS (ESI$^+$): *m/z* calcd (%) for $C_{40}H_{38}ClN_6O_{12}^+$: 829.2236 [M + NH_4Cl + H_2O + H$^+$]; found: 829.1782 (100); *m/z* calcd for $C_{40}H_{32}N_5O_{11}^+$: 758.2098 [M + H$^+$]; found: 758.2195 (11). $[\alpha]_D^{33}$ +102 (*c* 0.5, $CHCl_3$).

3-{(1*R*,2*R*,3*S*,4*S*)-3-methylbicyclo[2.2.1]hept-5-ene-2-carbonyl}oxazolidin-2-one (9a)

Thanks to a double elution (toluene–EtOAc = 4:1), *exo* (**9a**, R_f = 0.56) and *endo* (**9b**, R_f = 0.56) products were separated for ^{1}H NMR analysis. ^{1}H NMR (360 MHz, $CDCl_3$): δ (*exo*) = 0.88 (d, 3 H, *J* = 6.5 Hz), 1.23 (d, 1 H, *J* = 5.0 Hz), 1.40 (d, 1 H, *J* = 8.4 Hz), 1.68 (d, 1 H, *J* = 8.4 Hz), 2.68–2.75 (m, 1 H), 2.76 (br s, 1 H), 2.89–2.92 (m, 1 H), 4.02–4.08 (m, 2 H), 4.42 (t, 2 H, *J* = 8.1 Hz), 6.18 (dd, 1 H, *J* = 5.8, 2.5 Hz), 6.34 (dd, 1 H, *J* = 5.8, 2.9 Hz); δ (*endo*) = 1.15 (d, 3 H, *J* = 6.8 Hz), 1.47–1.50 (m, 1 H), 1.72 (d, 1 H, *J* = 8.6 Hz), 2.10–2.14 (m, 1 H), 2.55 (br s, 1 H), 3.30 (br s, 1 H), 3.55–3.57 (m, 1 H), 3.91–4.08 (m, 2 H), 4.42 (t, 2 H, *J* = 8.1 Hz), 5.81 (dd, 1 H, *J* = 5.8, 2.9 Hz), 6.39 (dd, 1 H, *J* = 5.8, 3.2 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ (*exo*) = 19.1, 37.7, 43.3, 46.9, 47.8, 50.9, 53.6, 62.0, 135.7, 137.1, 148.8, 175.8; δ (*endo*) = 20.6, 36.7, 43.3, 47.4, 47.7, 49.8, 51.6, 62.1, 131.2, 139.9, 153.6, 174.6. HRMS (ESI$^+$): *m/z* calcd for $C_{12}H_{15}NO_3Na^+$: 244.0944; found: 244.0941. HPLC: Whelk (hexane–EtOH = 99:1, 0.8 mL min^{-1}, 205 nm) t_R (2*S*) = 35.88 min; t_R (2*R*, major) = 38.50 min.

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3-{(1*R*,2*R*,4*R*)-bicyclo[2.2.1]hept-5-ene-2-carbonyl}oxazolidin-2-one (11a)

Inseparable mixture of **11a** and **11b**, with a >95:5 proportion of **11a**. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.38–1.50 (m, 3 H), 1.89–1.99 (m, 1 H), 2.93 (br s, 1 H), 3.30 (br s, 1 H), 3.92–4.06 (m, 3 H), 4.39 (t, 2 H, *J* = 8.7 Hz), 5.86 (dd, 1 H, *J* = 5.5, 3.3 Hz), 6.24 (dd, 1 H, *J* = 5.5, 2.6 Hz). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 29.5, 42.8, 42.9, 43.2, 46.4, 50.2, 61.9, 131.6, 138.0, 153.4, 174.7. HRMS (ESI^+): *m/z* calcd for $C_{11}H_{13}NO_3Na^+$: 230.0788; found: 230.0790. HPLC: OD-H (hexane–*i*-PrOH = 98:2, 0.8 mL min^{-1}, 205 nm): t_R (2*S*) = 65.70 min; t_R (2*R*, major) = 72.87 min.

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References and Notes

(1) (a) McManus, H.; Guiry, P. J. *Chem. Rev.* **2004**, *104*, 4151. (b) Hargaden, G. C.; Guiry, P. J. *Chem. Rev.* **2009**, *109*, 2505.

(2) For some very recent examples, see: (a) Livieri, A.; Boiocchi, M.; Desimoni, G.; Faita, G. *Chem. Eur. J.* **2011**, *17*, 516. (b) Wen, L.; Shen, Q.; Wan, X.; Lu, L. *J. Org. Chem.* **2011**, *76*, 2282. (c) Gök, Y.; Noël, T.; van der Eycken, J. *Tetrahedron: Asymmetry* **2011**, *21*, 2275. (d) Bigot, A.; Williamson, A. E.; Gaunt, M. J. *J. Am. Chem. Soc.* **2011**, *133*, 13778. (e) Harvey, J. S.; Simonovich, S. P.; Jamison, C. R.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 13782.

(3) (a) Rechavi, D.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 3467. (b) Fraile, J. M.; García, J. I.; Mayoral, J. A. *Coord. Chem. Rev.* **2008**, *252*, 624. (c) Fraile, J. M.; García, J. I.; Herrerías, C. I.; Mayoral, J. A.; Pires, E.; Salvatella, L. *Catal. Today* **2009**, *140*, 44.

(4) Fraile, J. M.; García, J. I.; Mayoral, J. A. *Chem. Rev.* **2009**, *109*, 360.

(5) Langham, C.; Piaggio, P.; Bethell, D.; Lee, D. F.; McMorn, P.; Bulman Page, P. C.; Willock, D. J.; Sly, C.; Hancock, F. E.; King, F.; Hutchings, G. J. *Chem. Commun.* **1998**, 1601.

(6) Fraile, J. M.; García, J. I.; Mayoral, J. A.; Tarnai, T.; Harmer, M. A. *J. Catal.* **1999**, *186*, 214.

(7) García, J. I.; Lopez-Sanchez, B.; Mayoral, J. A. *Org. Lett.* **2008**, *10*, 4995.

(8) (a) Evans, D. A.; Miller, S. J.; Lectka, T. *J. Am. Chem. Soc.* **1993**, *115*, 6460. (b) Evans, D. A.; Miller, S. J.; Lectka, T.; von Matt, P. *J. Am. Chem. Soc.* **1999**, *121*, 7559.

(9) (a) Davies, I. W.; Senanayake, C. H.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1996**, *37*, 1725. (b) Ghosh, A. K.; Mathivanan, P.; Cappiello, J. *Tetrahedron Lett.* **1996**, *37*, 3815.

(10) (a) Chollet, G.; Rodriguez, F.; Schulz, E. *Org. Lett.* **2006**, *8*, 539. (b) Chollet, G.; Guillerez, M.-G.; Schulz, E. *Chem. Eur. J.* **2007**, *13*, 992.

(11) Didier, D.; Magnier-Bouvier, C.; Schulz, E. *Adv. Synth. Catal.* **2011**, *353*, 1087.

(12) Didier, D.; Schulz, E. *ChemCatChem.* **2011**, *3*, 1880.

(13) (a) Chollet, G.; Didier, D.; Schulz, E. *Catal. Commun.* **2010**, *11*, 351. (b) See also ref. 11.

(14) Sulzberg, T.; Cotter, R. J. *J. Org. Chem.* **1970**, *35*, 2762.

(15) Chuzel, O.; Magnier-Bouvier, C.; Schulz, E. *Tetrahedron: Asymmetry* **2008**, *19*, 1010.

(16) (a) Hosmane, R. S.; Bakthavachalam, V.; Leonard, N. J. *J. Am. Chem. Soc.* **1982**, *104*, 235. (b) Oaks, F. T.; Leonard, N. J. *J. Org. Chem.* **1985**, *50*, 4986.

(17) This simple precipitation procedure was already attempted for a potential recycling of Cu(OTf)–**2** (see ref. 10a). Under analogous conditions, this catalyst could indeed be recovered by pentane precipitation (in this case without the need for TNF addition) but it maintained its activity and selectivity for only three reuses, the 4th recycling leading to a major loss of both the conversion and the enantioselectivity.

(18) (a) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Pitillo, M. *J. Org. Chem.* **2001**, *66*, 3160. (b) Benaglia, M.; Cinquini, M.; Cozzi, F.; Celentano, G. *Org. Biomol. Chem.* **2004**, *2*, 3401. (c) Gissibl, A.; Finn, M. G.; Reiser, O. *Org. Lett.* **2005**, *7*, 2325.

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