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Chiral tetrathiafulvalene based phosphine- and thiomethyl-oxazoline ligands. Evaluation in palladium catalysed asymmetric allylic alkylation

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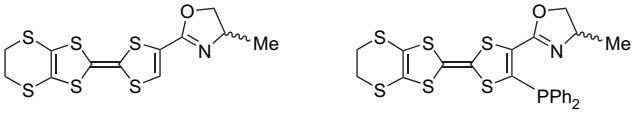
Abstract—New chiral redox active ligands based on ethylenedithio-tetrathiafulvalene (EDT-TTF) bearing racemic or optically pure oxazolines have been synthesised. These auxiliaries possess an additional functionality on the TTF unit, namely a thiomethyl residue or a diphenylphosphino moiety. All ligands have been tested in asymmetric allylic substitutions. The enantioselectivity reached is 85% ee.

1. Introduction

Transition metal catalysed asymmetric allylic alkylations (AAA) provide very useful tools for the formation of stereoselective carbon–carbon bonds.[1] As part of the development of this chemistry, the design and synthesis of new chiral auxiliaries remain a key step. Therefore, a large variety of ligands have been developed for the palladium catalysed AAA[1] and it has been demonstrated that heterobidentate auxiliaries of the P,N type are excellent candidates for that purpose.[1,2] Among those, the phosphine-oxazolines have received increasing attention.[3,4] Within this context, some of us have been involved in the use of chiral aminophosphine-oxazolines in asymmetric catalysis.[5] However, other chiral auxiliaries of the P,S,[6] Se,N[7] and S,N,[8–10] types have been successfully employed as well. On the other hand, some of us have an ongoing interest in the development of electroactive ligands, such as tetrathiafulvalene (TTF) based phosphines[11] or pyridines.[12] Recently, the synthesis of ethylenedithio-tetrathiafulvalene (EDT-TTF) derivatives **1a–c** and **2a–c** based on chiral oxazolines has been reported (Scheme 1).[13] The EDT-TTF-MeOX compounds **1a–c** possess potentially two coordination sites that are the oxazoline unit and the sulfur atoms of the TTF moiety. They have been successfully employed as precursors for chiral molecular metals.[13b] Within the series **2a–c**, the diphenylphosphino moiety tethered to the TTF unit is also able to coordinate a transition metal. Indeed, the X-ray characterisation of the complex (*rac*)-(EDT-TTF-PPh_2-MeOX)$PdCl_2$ showed unambiguously the N,P chelation of racemic **2a** onto the square planar palladium centre.[13a] Because of the potential of N,P type chiral auxiliaries in asymmetric catalysis, we decided to apply them in palladium catalysed AAA. Here, we report on the synthesis of new EDT-TTF based chiral oxazoline ligands and on their use in asymmetric allylic alkylation of the standard substrate (*rac*)-(*E*)-1,3-diphenyl-3-acetoxy-prop-1-ene.



EDT-TTF-MeOX
1a (+/-), **1b** (*R*), **1c** (*S*)

EDT-TTF-PPh_2-MeOX
2a (+/-), **2b** (*R*), **2c** (*S*)

Scheme 1.

2. Results and discussion

In order to increase the steric hindrance on the oxazoline substituent of the chiral auxiliaries of types **1** and **2**, the novel ligands **3a–c** and **4a–c**, bearing an isopropyl residue, have

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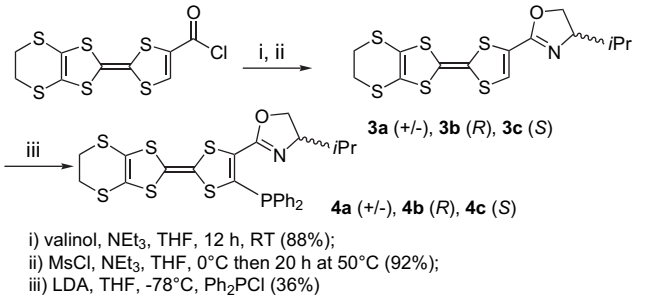
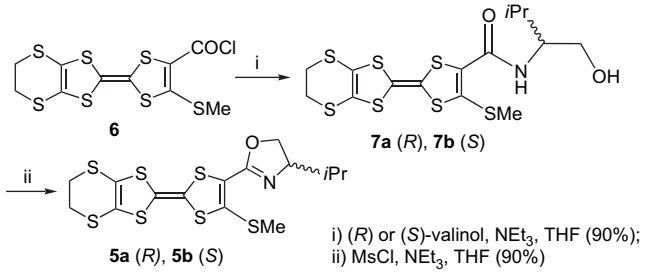
been prepared (Scheme 2). The synthesis of EDT-TTF-*i*PrOX **3a–c** is straightforward following the reported procedure.[14]



Scheme 2.

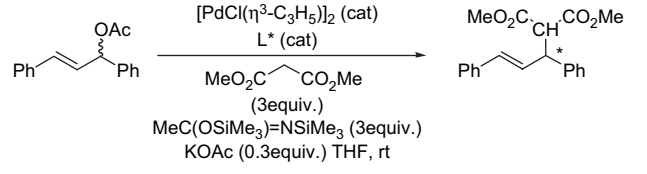
The corresponding phosphinooxazoline ligands EDT-TTF-PPh_2-MeOX **2** and EDT-TTF-PPh_2-*i*PrOX **4** have been prepared following also the procedure described earlier.[13a]

With the aim to examine also the behaviour of auxiliaries containing a thiomethyl residue, rather than a PPh_2 on the TTF unit, we prepared the enantiopure ligands **5a**,**b** according to the route depicted in Scheme 3, the SMe substituent being introduced at an early stage of the synthesis of the acyl chloride **6**.[15] Then, reaction of the latter with the enantiopure (*R*) or (*S*)-valinol afforded the ligands **5a**,**b** via the corresponding β-hydroxy amides **7a**,**b**, thus paralleling the preparation of the non-substituted ligands **3**. The new ligands **4** and **5** have been fully characterised.



Scheme 3.

Next, the mono or bidentate ligands **2–5** were applied in the palladium catalysed asymmetric allylic alkylation of the standard substrate (*rac*)-(*E*)-1,3-diphenyl-3-acetoxy-prop-1-ene with dimethylmalonate (Scheme 4). The results are summarised in Table 1.



Scheme 4.

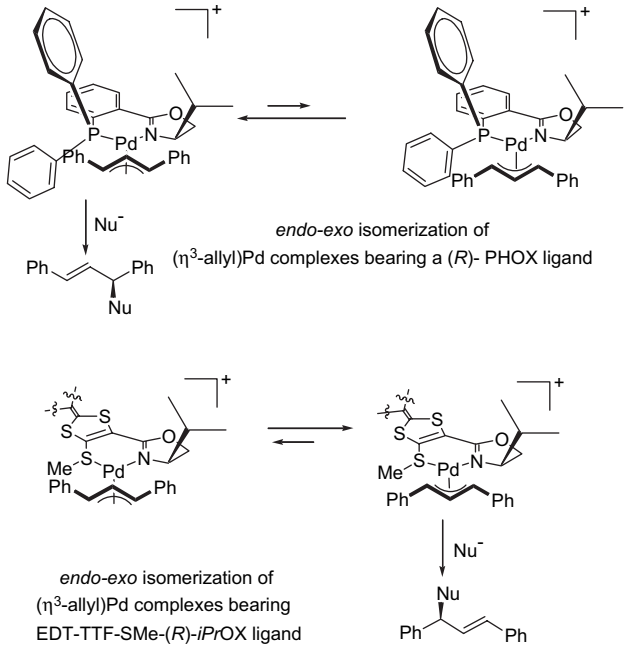
From an experimental standpoint, the precatalysts were generated by reacting $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ with the selected optically pure (*R*) and (*S*)-TTF-ligands in THF during 1 h at room temperature. Then, dimethylmalonate, *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and potassium acetate (KOAc) were added in a solution of THF followed by the substrate (*rac*)-(*E*)-1,3-diphenyl-3-acetoxy-prop-1-ene.[16] The auxiliary **3b** bearing only an oxazoline unit induces a very low selectivity of 6% ee (entry 1), that is much lower than the values reported by Bryce and Chesney for an (*S*)-TTF-*i*PrOx ligand, yet measured by a different method.[8f] On the contrary, the chelating auxiliaries **2b** and **4b**, bearing a diphenylphosphino group besides the oxazoline heterocycle, allowed to reach higher enantioselectivities, up to 85% ee (entries 2–4). Note that, as expected, the use of the racemic ligands provided the racemic mixture of the allyl-malonate, with the same activity as the optically pure counterparts. Interestingly, an enhancement of Δee=55% resulted from the use of the isopropyl- (**4b**) rather than the methyl-oxazoline bearing ligand (**2b**) (entry 3 vs 2).[17] A rationale for the difference in behaviour between catalysts bearing ligands **3** and **4**, with an added PPh_2 group, can be easily deduced from the mechanism of the reaction. Indeed, generally, the selectivity exhibited by catalysts bearing bitopic auxiliaries is related both to the conformation of the most stable palladium-allyl intermediates and to the site of addition of the nucleophile to these palladium species (Scheme 5). Thus, for P,N type ligands, the addition is occurring on the palladium-allyl terminus trans to the better π-acceptor atom, that is the phosphorus one.[18] As a result, both the chiral environment of the ligand and the steric congestion provided by the phenyl residue close to the reacting end of the allyl moiety are profitable for a better enantiodiscrimination. This rationale can be taken into account for the palladium catalyst bearing the auxiliary **4**.

Table 1. Asymmetric allylic substitution reactions with chiral EDT-TTF-oxazoline ligands[a]

Entry	Ligand	[Pd] (mol %)	Time (h)	Conv. (%)[b]	ee % (conf.)[c]
1	EDT-TTF-(*R*)-*i*PrOX **3b**	1.5	20	10	6 (*R*)
2	EDT-TTF-PPh_2-(*R*)-MeOX **2b**	3.0	18	25	30 (*R*)
3	EDT-TTF-PPh_2-(*R*)-*i*PrOX **4b**	1.5	18	10	85 (*R*)
4	EDT-TTF-PPh_2-(*R*)-*i*PrOX **4b**	3.0	70	21	80 (*R*)
5	EDT-TTF-SMe-(*R*)-*i*PrOX **5a**	3.0	18	12	26 (*R*)
6	PHOX+EDT-TTF[e]	3.0	18	8	94 (*R*)
7	EDT-TTF-PPh_2-(*R*)-*i*PrOX[d]	3.0	18	11	79 (*R*)

[a] Reactions were carried out by using $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (0.03 or 0.015 mmol), ligand (1.2 equiv/Pd), the substrate (2 mmol), dimethylmalonate (3 equiv, 6 mmol), BSA (3 equiv, 6 mmol), KOAc (0.3 equiv, 0.6 mmol) in THF (20 ml) at room temperature.
[b] Conversions were determined by ^{1}H NMR analysis.
[c] Enantiomeric excesses were determined by HPLC on a Daicel® Chiralpak® AD column. The absolute configuration was assigned by comparing the sign of absolute optical rotation with reported data.
[d] The reaction was carried out with $[Pd(\eta^3\text{-}C_3H_5)$(EDT-TTF-$PPh_2$-*i*PrOX)$]^{2+}$,$PF_6^-$,$SbF_6^-$ in the same conditions as above.
[e] The reaction was performed in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$/(*R*)-PHOX/EDT-DMC-TTF in 1/1.5/1.5 ratio.

For the auxiliary **3b**, the two potential coordination sites are the nitrogen and sulfur atoms, although it is well known that TTF sulfur atoms do not possess good coordination properties, and examples of metal$\cdots S_{TTF}$ coordination are scarce.[19] One can consider that the N=C π* orbital is a better π-acceptor than the sulfur atom, all the more since the latter is included in an electron rich heterocycle.[20] Consequently, for the palladium complexes bearing a ligand **3**, the addition



Scheme 5.

of the nucleophile will occur on the allyl-carbon trans to the oxazoline nitrogen of the chiral auxiliary, as suggested by Bryce and Chesney.[8f] The chiral centre of the ligand will be thus away from the reacting site and, moreover, there is not much steric hindrance on the sulfur site where the nucleophile will add. As a result, several conformers of allyl-palladium complexes of similar stability and reactivity are certainly present in the reaction mixture and are likely to provide a lower selectivity.

In the case of the thiomethyl ligand **5b**, the thioether group is a rather poor π-acceptor,[8l] yet better than the S_{TTF}. Again, the nucleophile certainly adds preferentially onto the carbon located trans to the nitrogen of the oxazoline that is also trans to the chiral environment of the catalyst. Furthermore, the low steric congestion around the SMe sulfur atom of the ligand is not prone to highly selective reactions.

The difference of selectivity observed for catalyses performed in the presence of auxiliaries **2b** and **4b** (Δee= 55%) can be attributed to the overall steric crowding discrimination between the corresponding palladium complexes.

The rates of the reactions require some comments. In all our catalytic experiments, the conversions are low even for prolonged reaction times or with higher catalyst loading. This is indicative of the evolution of the catalytic species during catalysis. We suspect an alteration of the catalyst brought into by the TTF unit furnishing an inactive palladium species. In order to check the likely harmful effect of the TTF residue, we carried out an AAA in the presence of the original (*R*)-PHOX auxiliary and of added EDT-dimethylcarboxylate-TTF (EDT-DMC-TTF). Indeed, in the presence of PHOX, the allyl product is obtained with up to 98% ee.[3] In the presence of added amount of EDT-dimethylcarboxylate-TTF (Pd/PHOX/EDT-DMC-TTF=1/1.5/1.5) while using otherwise identical reaction conditions to the ones given in the table, the conversion dropped to 8% while the stereoselectivity remains at a close level of 94% ee (entry 6). Interestingly, enantioselective hydrogenations performed with iridium catalysts bearing EDT-TTF-PPh_2-*i*PrOX **4** are going to completion.[21] The 'poisoning' of the catalyst by TTF species is thus dependent on the metal used.

Finally, the Tsuji–Trost reaction was also carried out in the presence of oxidised TTF-palladium complexes. Indeed, the TTF unit is redox active, showing stable and reversible changes in oxidation states, the corresponding radical cation species being obtained easily upon chemical or electrochemical oxidation.[20] We therefore envisaged that the use of these TTF containing ligands might allow an electromodulation of the catalytic centre upon changing the electronic density around the metal.[22] This concept was nicely demonstrated by Wrighton et al. in the case of the catalytic hydrogenation of cyclohexene using a cobaltocene-diphosphine based rhodium complex as catalyst, which showed a much higher activity in the reduced cobaltocene form than in the oxidised cobaltocenium one.[23] Very recently, Gibson and Long clearly demonstrated that a ferrocenyl based salen titanium (IV) complex is much more active in the ring-opening polymerisation of lactide in the neutral state, as ferrocene, than in the oxidised state, as ferrocenium salt.[24] Therefore, we prepared first the series of (*rac*), (*R*) and (*S*) cationic palladium complexes [Pd(η^3-C_3H_5){EDT-TTF-PPh_2-*i*PrOX}][PF_6]. Next, we performed the chemical oxidation of these compounds with $NOSbF_6$ as oxidising agent.[25]

Note that the oxidation potentials of the TTF-Pd-allyl complexes (0.81 V vs SCE) corresponding to the equilibrium $TTF \leftrightarrows TTF^{+\bullet}$ are about 180 mV higher than those of the free ligands (0.63 V vs SCE), yet showing a full reversibility of this oxidation process. The corresponding oxidised complexes, thus containing TTF radical cations, were obtained as black, paramagnetic powders, for which satisfactory elemental analyses indicate the expected formulation as [Pd(η^3-C_3H_5){EDT-TTF-PPh_2-*i*PrOX}]$^{2+}$$PF_6^-$,$SbF_6^-$. Moreover, the optical activity of the enantiomeric salts has been demonstrated through circular dichroism measurements (Fig. 1). The new species [Pd(η^3-C_3H_5){EDT-TTF-PPh_2-*i*PrOX}]$^{2+}$$PF_6^-$,$SbF_6^-$ were then applied in the test AAA reaction (Table 1, entry 7). The conversion was slightly lower

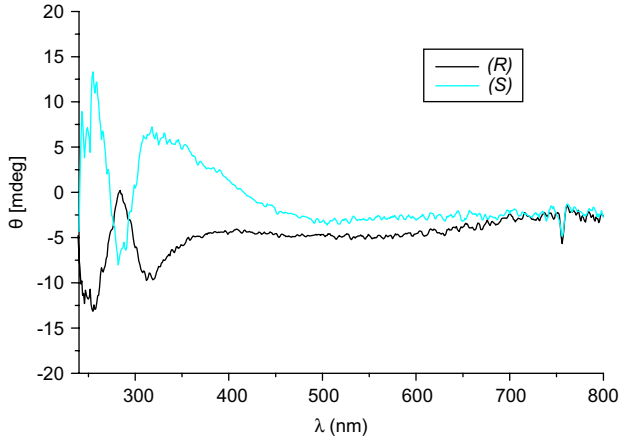


Figure 1. Circular dichroism spectra of the enantiomeric complexes [Pd(η^3-C_3H_5){EDT-TTF-PPh_2-*i*PrOX}]$^{2+}$$PF_6^-$,$SbF_6^-$.

and the enantioselectivity quite similar to those obtained with the non-oxidised counterparts (entry 4), therefore no clear influence, albeit somewhat negative, of the TTF oxidation state can be drawn. The similarity of the results between neutral TTF and radical cation TTF containing precatalysts can be possibly explained by the in situ reduction of $TTF^{+\bullet}$ in TTF, either by Pd(0) species or because of the basicity of the reaction medium. On the other hand, one possible effect of the TTF oxidation would have been the increase of the π-acceptor ability of the phosphino group, leading to a more favourable trans attack. Nevertheless, one could argue that the effect would be similar on the oxazoline nitrogen atom, all the more because of the conjugation between the TTF and oxazoline moieties. Additional experiments, especially aiming at evaluating the stability of ($TTF^{+\bullet}$)Pd(0) complexes, are necessary to clear up these hypotheses.

3. Conclusion

New chiral EDT-TTF-oxazoline type ligands have been synthesised and evaluated in palladium assisted asymmetric allylic substitution. Up to 85% ee could be obtained for the alkylation of (*rac*)-(*E*)-1,3-diphenyl-3-acetoxy-prop-1-ene with dimethylmalonate, using enantiopure bidentate EDT-TTF-PPh_2-*i*PrOxazoline ligands. The low reaction rates and conversions observed are very likely due to a poisoning of the catalyst by the tetrathiafulvalene. Preliminary investigations with (allyl)Pd(II) complexes containing oxidised TTF-PHOX ligands show no sizeable effect on the selectivity of the same catalytic reaction. The use of these new redox active ligands in other enantioselective reactions will be reported in due time.[21]

4. Experimental

4.1. General

All the reactions were carried out under inert gas atmosphere. Solvents were purified by standard techniques: THF was distilled over sodium and benzophenone; acetonitrile was dried over P_2O_5. Triethylamine was distilled over KOH. Nuclear magnetic resonance spectra were recorded on a Bruker Avance DRX 500 spectrometer operating at 500.04 MHz for ^1H, 125.75 MHz for ^{13}C and 202.39 MHz for ^{31}P. Chemical shifts are expressed in parts per million (ppm) downfield from external TMS. The following abbreviations are used: s, singlet; d, doublet; t, triplet; q, quadruplet; h, heptuplet; o, octuplet; m, multiplet; br, broad. ^{31}P chemical shifts are reported with positive values downfield from external 85% H_3PO_4 in D_2O. MALDI-TOF MS spectra were recorded on Bruker Biflex-IIITM apparatus, equipped with a 337 nm N_2 laser. Elemental analyses were performed by the 'Service d'Analyse du CNRS' at Gif/Yvette, France. No optical rotations could be measured, as the compounds are highly coloured in deep red. Circular dichroism measurements were recorded on a JASCO J-810 spectropolarimeter.

4.2. General procedure for the synthesis of EDT-TTF-PPh_2-*i*PrOX (4a–c)

To a degassed solution of (*R*)-oxazoline **3b**[14] (600 mg, 1.48 mmol) in 100 mL of dry THF, were added 1.2 equiv of LDA (0.25 mL of $(i\text{-Pr})_2NH$ and 0.89 mL of *n*-BuLi solution 2 M, in 10 mL of THF), at −78 °C. After stirring for 4 h at −78 °C, Ph_2PCl (360 mg, 1.61 mmol) was added dropwise. The reaction mixture was then allowed to warm slowly at room temperature, under stirring overnight. The solvent was removed in vacuo to afford a dark oil, which was diluted in dichloromethane and filtered through a pad of Celite®. After concentration under reduced pressure, the product was purified by chromatography column on silica gel, with CH_2Cl_2/cyclohexane 4/1, to afford 310 mg (36% yield) of **4b** as a red solid, after evaporation of solvent.

^1H NMR ($CDCl_3$, δ) 0.71 (d, *J*=6.7 Hz, 3H, CH_3), 0.78 (d, *J*=6.7 Hz, 3H, CH_3), 1.62 (m, 1H, CH(CH_3)$_2$), 3.25 (s, 4H, SCH_2CH_2S), 3.86 (t, *J*=7.9 Hz, C$H_{syn/i\text{-Pr}}$H′O), 3.92 (m, 1H, NCHCH_2O), 4.16 (dd, *J*=9.2 and 7.9 Hz, 1H, CH$H'_{anti/i\text{-Pr}}$O), 7.34–7.43 (m, 10H, CH_{aro}); ^{13}C NMR ($CDCl_3$, δ) 18.0 (*C*H_3), 18.5 (*C*H_3), 30.1 (S*C*H_2CH_2S), 30.2 (SCH_2*C*H_2S), 32.5 (*C*H(CH_3)$_2$), 71.0 (*C*HN), 72.6 (*C*H_2O), 105.9–113.7–114.1–116.5 (2*C*=*C*), 125.6 (d, J_{C-P}= 20.4 Hz, C=*C*–C=N), 128.5 (2d, J_{C-P}=7.5 Hz, *C*H$_{aro,meta}$), 129.6 (d, J_{C-P}=15.1 Hz, *C*H$_{aro,para}$), 133.5 (2d, J_{C-P}= 21.2 Hz, *C*H$_{aro,ortho}$), 135.4 and 135.8 (d, J_{C-P}=11.3 Hz, *C*$_{ipso}$), 141.2 (d, J_{C-P}=54.5 Hz, C=*C*–PPh_2), 156.8 (d, J_{C-P}= 2.8 Hz, *C*=N); ^{31}P NMR ($CDCl_3$, δ) −10.6; IR (KBr, cm^{-1}): 1628 ($\nu_{C=N}$); *m*/*z* (MALDI-TOF): 588.96 (M^+). Anal. Calcd for $C_{26}H_{24}NOPS_6$: C, 52.94; H, 4.10; N, 2.37. Found: C, 53.01; H, 4.11; N, 2.32.

4.2.1. (+/−)-EDT-TTF-PPh_2-*i*PrOX (4a). From 600 mg of **3a**,[15] red solid (460 mg, 53% yield). Anal. Calcd for $C_{26}H_{24}NOPS_6$: C, 52.94; H, 4.10; N, 2.37. Found: C, 52.95; H, 4.21; N, 2.24.

4.2.2. (*S*)-EDT-TTF-PPh_2-*i*PrOX (4c). From 600 mg of **3c**,[15] red solid (200 mg, 23% yield). Anal. Calcd for $C_{26}H_{24}NOPS_6$: C, 52.94; H, 4.10; N, 2.37. Found: C, 52.78; H, 4.03; N, 2.34.

4.3. General procedure for the synthesis of β-hydroxy amides (7a,b)

(*R*)-2-Amino-3-methyl-1-butanol or (*R*)-valinol (225 mg, 2.14 mmol) and distilled triethylamine (0.48 mL, 3.42 mmol) were placed in 10 mL THF. This colourless solution was stirred for 10 min under N_2 at room temperature, then a freshly prepared solution of EDT-TTF-TM-COCl **6**[15] (690 mg, 1.71 mmol in 70 mL THF, purple colour) was added dropwise. The reaction mixture became orange and a precipitate was formed. After stirring overnight at room temperature, the brown-red mixture was filtrated through Celite and the solvent evaporated. The crude product was purified on silica gel (eluant: THF), then the solvent evaporated. The oil thus obtained was diluted in a small volume of THF (5–8 mL) and dropped onto 400–500 mL petroleum ether to afford **7a** as a brown-pink powder (720 mg, 90% yield).

Mp=136 °C; ^1H NMR ($CDCl_3$, δ): 0.97 (d, ^3J=6.8 Hz, 3H, CH_3), 0.99 (d, ^3J=6.8 Hz, 3H, CH_3), 1.97 (o, ^3J=6.8 Hz, 1H, CH(CH_3)$_2$), 2.55 (s, 3H, SCH_3), 2.75 (br s, 1H, O*H*), 3.29 (s, 4H, SCH_2CH_2S), 3.72 (m, 2H, CH_2O), 3.83 (m, 1H, NH–C*H*–CH_2O), 7.37 (d, ^3J=8.0 Hz, 1H, N*H*); ^{13}C NMR

($CDCl_3$, δ): 18.7 (CH_3), 19.6 (CH_3), 20.0 (SCH_3), 29.0 ($CH(CH_3)_2$), 30.2 (SCH_2CH_2S), 57.8 (CH–NH), 63.8 (CH_2OH), 109.6–111.1–113.5–114.4 (2C=C), 129.9 (=C–SMe), 132.7 (=C–C=O), 160.3 (NH–C=O); *m/z* (MALDI-TOF): 468.89 (M^+) (calcd: 468.95). Anal. Calcd for $C_{15}H_{19}NO_2S_7$: C, 38.35; H, 4.08; N, 2.98. Found: C, 38.39; H, 4.04; N, 2.87.

4.3.1. (*S*)-EDT-TTF-SMe-β-hydroxyamide (7b). From 0.25 mL (2.14 mmol) (*S*)-2-amino-3-methyl-1-butanol or (*S*)-valinol, brown-pink powder (690 mg, 86% yield). Anal. Calcd for $C_{15}H_{19}NO_2S_7$: C, 38.35; H, 4.08; N, 2.98. Found: C, 38.13; H, 4.06; N, 2.85.

4.4. General procedure for the synthesis of EDT-TTF-SMe-*i*PrOX (5a,b)

A solution of hydroxyamide **7a** (670 mg, 1.43 mmol) and distilled NEt_3 (0.34 mL, 2.44 mmol) in 30 mL THF was cooled at 0 °C, and then, mesyl chloride (0.19 mL, 2.43 mmol) was added at once. After 30 min of stirring at 0 °C, more NEt_3 (1.53 mL, 10.98 mmol) was added and the reaction mixture was subsequently heated at 50 °C until the intermediate mesylate disappeared (checked by TLC: AcOEt/cyclohexane 1/1), after ca. 20 h. After filtration through Celite, the solvent was evaporated and the crude product was purified by silica gel chromatography (eluant: AcOEt/cyclohexane 1/1), to afford **5a** as a red powder (580 mg, 90% yield) after evaporation of solvents.

Mp=129 °C; ^1H NMR ($CDCl_3$, δ) 0.88 (d, J=6.7 Hz, 3H, CH_3), 0.97 (d, J=6.7 Hz, 3H, CH_3), 1.78 (o, J=6.7 Hz, 1H, $CH(CH_3)_2$), 2.54 (s, 3H, SCH_3), 3.29 (s, 4H, SCH_2CH_2S), 4.02–4.08 (m, 2H, $NCH(CH_3)$ and $CH_{syn/i\text{-}Pr}$ H′O), 4.32 (dd, J=8.9 and 7.8 Hz, 1H, $CHH'_{anti/i\text{-}Pr}O$); ^{13}C NMR ($CDCl_3$, δ) 18.1 (CH_3), 18.8 (CH_3), 18.6 (SCH_3), 30.2 (SCH_2CH_2S), 32.7 ($CH(CH_3)_2$), 70.9 (CHN), 72.6 (CH_2O), 108.4–112.9–113.5–114.3 (2C=C and C=C–SMe), 137.7 (C=C–C=N), 157.0 (C=N); *m/z* (MALDI-TOF): 450.97 (M^+). Anal. Calcd for $C_{15}H_{17}NOS_7$: C, 39.88; H, 3.79; N, 3.10. Found: C, 39.73; H, 3.79; N, 2.95.

4.4.1. (*S*)-EDT-TTF-SMe-*i*PrOX (5b). From 640 mg (1.36 mmol) hydroxyamide **7c**, red crystalline solid (540 mg, 88% yield). Anal. Calcd for $C_{15}H_{17}NOS_7$: C, 39.88; H, 3.79; N, 3.10. Found: C, 40.02; H, 3.75; N, 2.97.

4.5. Synthesis of the palladium complexes

4.5.1. Synthesis of complexes (+/−), (*R*) and (*S*)-[Pd(η³-C_3H_5)(EDT-TTF-PPh_2-*i*PrOX)]PF_6. The ligand (*R*)-EDT-TTF-PPh_2-*i*PrOX **4b** (59 mg, 0.1 mmol) and the precursor $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (18.6 mg, 0.05 mmol) were dissolved in THF (5 ml). The dark red solution was stirred for 1 h at room temperature followed by the addition of $TlPF_6$ (36 mg, 0.1 mmol). After 15 min of stirring, a filtration through a pad of dry Celite afforded the complex [Pd(η³-C_3H_5)(**4b**)]PF_6 as a dark powder (78.2 mg, 89% yield).

^1H NMR (CD_2Cl_2, δ): 0.55 (d, ^3J=7.1 Hz, 3H, CH_3), 0.89 (d, J=7.1 Hz, 3H, CH_3), 2.03 (dh, J=7.1 and 3.9 Hz, 1H, $CH(CH_3)_2$), 3.02 (br m, 1H, H_{allyl}), 3.29 (m, 4H, SCH_2CH_2S), 3.92 (br m, 1H, H_{allyl}), 4.41 (ddd, J=9.6, 5.1 and 3.9 Hz, 1H, N–CH–(*i*-Pr)–CH_2O), 4.47 (dd, J=9.0 and 5.1 Hz, 1H, $CH_{anti/i\text{-}Pr}H'O$), 4.58 (t, J=9.0 Hz, 1H, $CHH'_{syn/i\text{-}Pr}O$), 4.93 (br m, 1H, H_{allyl}), 5.33 (br m, 1H, H_{allyl}), 5.85 (q, J=10.3 Hz, 1H, $H_{allyl\ central}$), 7.42–7.71 (m, 10H, CH_{aro}); ^{13}C NMR (CD_2Cl_2, δ): 14.5 and 18.3 (s, $2CH_3$), 30.0 (s, $CH(CH_3)_2$), 31.9 (s, SCH_2CH_2S), 68.1 (s, CH–N), 70.5 (s, CH_2O), 76.8 (s, $CH_{2allyl\ trans/N}$), 109.8–113.9–114.3 and 114.6 (s, 2C=C), 123.1 (d, J_{C-P}=6.0 Hz, C=C–C=N), 126.9 and 128.1 (d, J_{C-P}=48.5 Hz, $CH_{2allyl\ trans/P}$), 128.6 (s, $CH_{allyl\ central}$), 130.0 and 130.4 (d, J_{C-P}=11.6 Hz, $CH_{aro,meta}$), 132.2 (d, J_{C-P}=14.0 Hz, C_{ipso}), 132.9 and 133.7 (d, J_{C-P}=14.6 Hz, $CH_{aro,ortho}$), 133.2 and 133.4 (d, J_{C-P}=2.4 Hz, $CH_{aro,para}$), 137.5 (d, J_{C-P}=17.5 Hz, C=C–PPh_2), 159.4 (d, J_{C-P}=6.7 Hz, C=N); ^{31}P NMR (CD_2Cl_2, δ): 16.0; *m/z* (MALDI-TOF): 735.71 (M^+). Anal. Calcd for $C_{29}H_{29}F_6NOP_2PdS_6$: C, 39.48; H, 3.31; N, 1.59. Found: C, 40.82; H, 3.73; N, 1.15 (crude product).

4.5.1.1. [Pd(η³-C_3H_5)(4a)]PF_6. Same amounts of reagents, dark powder (87.2 mg, 99% yield). Anal. Calcd for $C_{29}H_{29}F_6NOP_2PdS_6$: C, 39.48; H, 3.31; N, 1.59. Found: C, 40.92; H, 3.83; N, 1.09 (crude product).

4.5.1.2. [Pd(η³-C_3H_5)(4c)]PF_6. Same amounts of reagents, dark powder (85.2 mg, 97% yield). Anal. Calcd for $C_{29}H_{29}F_6NOP_2PdS_6$: C, 39.48; H, 3.31; N, 1.59. Found: C, 40.87; H, 3.78; N, 1.12 (crude product).

4.5.2. Synthesis of complexes (+/−), (*R*) and (*S*)-[Pd(η³-C_3H_5)(EDT-TTF-PPh_2-*i*PrOX)]$^{2+}$,PF_6^-,SbF_6^-. The complex [Pd(η³-C_3H_5)(**4b**)]PF_6 (80 mg, 0.09 mmol) and the oxidising agent $NOSbF_6$ (24 mg, 0.09 mmol) were dissolved in acetonitrile (8 ml). The solution was stirred for 1 h at room temperature, and then CH_3CN was removed under reduced pressure. The oxidised complex [Pd(η³-C_3H_5)(**4b**)]$^{2+}$, PF_6^-,SbF_6^- was thus isolated as a black powder (88.4 mg, 88% yield). Anal. Calcd for $C_{29}H_{29}F_{12}NOP_2PdS_6Sb$: C, 31.21; H, 2.44; N, 1.26. Found: C, 30.44; H, 3.32; N, 1.45 (crude product).

4.5.2.1. [Pd(η³-C_3H_5)(4a)]$^{2+}$,PF_6^-,SbF_6^-. Same amounts, black powder (80.5 mg, 80% yield). Anal. Calcd for $C_{29}H_{29}F_{12}NOP_2PdS_6Sb$: C, 31.21; H, 2.44; N, 1.26. Found: C, 30.49; H, 3.36; N, 1.41 (crude product).

4.5.2.2. [Pd(η³-C_3H_5)(4c)]$^{2+}$,PF_6^-,SbF_6^-. Same amounts, black powder (81.7 mg, 81% yield). Anal. Calcd for $C_{29}H_{29}F_{12}NOP_2PdS_6Sb$: C, 31.21; H, 2.44; N, 1.26. Found C, 30.51; H, 3.34; N, 1.38 (crude product).

4.6. General procedure for the asymmetric allylic alkylation

In a Schlenk tube, the selected chiral auxiliary (0.036 mmol) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (6 mg, 0.016 mmol) were dissolved in anhydrous THF (10 mL). The red solution was stirred for 1 h at room temperature. In a second Schlenk tube, the base KOAc (60 mg), BSA (1.6 mL) and the nucleophile dimethylmalonate (0.7 mL) were mixed in THF (5 mL). The solution containing the palladium precatalyst was transferred onto the above mixture followed by the substrate (505 mg, 2 mmol) in solution in THF (5 mL). The reaction mixture was stirred during the desired reaction time. Then,

a saturated solution of $NaHCO_3$ (20 mL) was added. The product was extracted with diethylether (3×20 mL). The organic layers were dried over $MgSO_4$. After filtration and evaporation of the solvent, an oil was obtained, which was analysed by ^1H NMR in order to determine the conversion and by HPLC (Daicel® Chiralpak® AD column, hexane/isopropanol: 90/10, flow rate=1mL/min; λ=254 nm) to determine the enantiomeric excess.

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References and notes

1. (a) Trost, B. M.; VanVranken, D. L. *Chem. Rev.* **1996**, *96*, 395–422; (b) Trost, B. M.; Lee, C. *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, NY, 2000; Chapter 8E, pp 503–650; (c) Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921–2943; (d) Pfaltz, A.; Lautens, M. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. II; Chapter 24, pp 833–884.
2. For reviews on P,N auxiliaries in enantioselective catalysis, see: (a) Fache, F.; Schulz, E.; Tommasino, L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159–2231; (b) Chelucci, G.; Orru, G.; Pinna, G. A. *Tetrahedron* **2003**, *59*, 9471–9515; (c) Guiry, P. J.; Saunders, C. P. *Adv. Synth. Catal.* **2004**, *346*, 497–537.
3. For first reports on chiral phosphine-oxazoline auxiliaries, see: (a) Sprinz, J.; Helmchen, G. *Tetrahedron Lett.* **1993**, *34*, 1769–1772; (b) Von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566–568; (c) Dawson, G. J.; Frost, C. G.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 3149–3150.
4. (a) Helmchen, G.; Kudis, S.; Sennhenn, P.; Steinhagen, H. *Pure Appl. Chem.* **1997**, *69*, 513–518; (b) Helmchen, G.; Pfaltz, A. *Acc. Chem. Res.* **2000**, *33*, 336–345; (c) Braunstein, P.; Naud, F. *Angew. Chem., Int. Ed.* **2001**, *40*, 680–699.
5. (a) Blanc, C.; Hannedouche, J.; Agbossou-Niedercorn, F. *Tetrahedron Lett.* **2003**, *44*, 6469–6473; (b) Blanc, C.; Agbossou-Niedercorn, F.; Nowogrocki, G. *Tetrahedron: Asymmetry* **2004**, *15*, 2159–2163.
6. (a) Hiroi, K.; Suzuki, Y. *Tetrahedron Lett.* **1998**, *39*, 6499–6502; (b) Enders, D.; Peters, R.; Runsink, J.; Bats, J. W. *Org. Lett.* **1999**, *1*, 1863–1866.
7. (a) Sprinz, J.; Kiefer, M.; Helmchen, G.; Huttner, G.; Walter, O.; Zsolnai, L.; Reggelin, M. *Tetrahedron Lett.* **1994**, *35*, 1523–1526; (b) Hou, X.-L.; Wu, X.-W.; Dai, L.-X.; Cao, B.-X.; Sun, J. *Chem. Commun.* **2000**, 1195–1196; (c) Braga, A. L.; Vargas, F.; Sehnem, J. A.; Braga, R. C. *J. Org. Chem.* **2005**, *70*, 9021–9024; (d) Braga, A. L.; Lüdtke, D. S.; Sehnem, J. A.; Alberto, E. E. *Tetrahedron* **2005**, *61*, 11664–11671; (e) Braga, A. L.; Paixao, M. W.; Marin, G. *Synlett* **2005**, 1975–1978.
8. (a) Dawson, G. J.; Frost, C. G.; Martin, C. J.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 7793–7796; (b) Allen, J. V.; Bower, J. F.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1994**, *5*, 1895–1898; (c) Frost, C. G.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1993**, *4*, 1785–1788; (d) Allen, J. V.; Coote, S. J.; Dawson, G. J.; Frost, C. G.; Martin, C. J.; Williams, J. M. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2065–2072; (e) Morimoto, T.; Tachibana, K.; Achiwa, K. *Synlett* **1997**, 783–786; (f) Chesney, A.; Bryce, M. R. *Tetrahedron: Asymmetry* **1996**, *7*, 3247–3254; (g) Chesney, A.; Bryce, M. R.; Chubb, R. W.; Batsanov, A. S.; Howard, J. A. *Tetrahedron: Asymmetry* **1997**, *8*, 2337–2346; (h) Park, J.; Quan, Z.; Lee, S.; Ahn, K. H.; Cho, C.-W. *J. Organomet. Chem.* **1999**, *584*, 140–146; (i) Koning, B.; Meetsma, A.; Kellogg, R. M. *J. Org. Chem.* **1998**, *63*, 5533–5540; (j) Anderson, J. C.; James, D. S.; Mathias, J. P. *Tetrahedron: Asymmetry* **1998**, *9*, 753–756; (k) Boog-Wick, K.; Pregosin, P. S.; Trabesinger, G. *Organometallics* **1998**, *17*, 3254–3264; (l) Adams, H.; Anderson, J. C.; Cubbon, R.; James, D. S.; Mathias, J. P. *J. Org. Chem.* **1999**, *64*, 8256–8262; (m) Cheluci, G.; Cabras, M. A. *Tetrahedron: Asymmetry* **1996**, *7*, 965–966; (n) Tietze, L. F.; Lohmann, J. K. *Synlett* **2002**, 2083–2085; (o) Braga, A. L.; Paixao, M. W.; Milani, P.; Silveira, C. C.; Rodrigues, O. E. D. *Synlett* **2004**, 1297–1299.
9. (a) Voiturier, A.; Fiaud, J.-C.; Schulz, E. *Tetrahedron Lett.* **2002**, *43*, 4907–4909; (b) Voituriez, A.; Schulz, E. *Tetrahedron: Asymmetry* **2003**, *14*, 339–346; (c) Schulz, E.; Voituriez, A. *Russ. Chem. Bull. (Int. Ed.)* **2003**, *52*, 2588–2594.
10. You, S.-L.; Zhou, Y.-G.; Hou, X.-L.; Dai, L.-X. *Chem. Commun.* **1998**, 2765–2766.
11. (a) Avarvari, N.; Martin, D.; Fourmigué, M. *J. Organomet. Chem.* **2002**, *643–644*, 292–300; (b) Avarvari, N.; Fourmigué, M. *Chem. Commun.* **2004**, 2794–2795; (c) Avarvari, N.; Fourmigué, M. *Chem. Commun.* **2004**, 1300–1301; (d) Gouverd, C.; Biaso, F.; Cataldo, L.; Berclaz, T.; Geoffroy, M.; Levillain, E.; Avarvari, N.; Fourmigué, M.; Sauvage, F. X.; Wartelle, C. *Phys. Chem. Chem. Phys.* **2005**, *7*, 85–93.
12. (a) Devic, T.; Avarvari, N.; Batail, P. *Chem.—Eur. J.* **2004**, *10*, 3696–3707; (b) Devic, T.; Rondeau, D.; Şahin, Y.; Levillain, E.; Clérac, R.; Batail, P.; Avarvari, N. *Dalton Trans.* **2006**, 1331–1337.
13. (a) Réthoré, C.; Fourmigué, M.; Avarvari, N. *Chem. Commun.* **2004**, 1384–1385; (b) Réthoré, C.; Avarvari, N.; Canadell, E.; Auban-Senzier, P.; Fourmigué, M. *J. Am. Chem. Soc.* **2005**, *127*, 5748–5749.
14. Réthoré, C.; Fourmigué, M.; Avarvari, N. *Tetrahedron* **2005**, *61*, 10935–10942.
15. The detailed synthesis of the acyl chloride **6** will be reported elsewhere: Réthoré, C.; Madalan, A. M.; Fourmigué, M.; Canadell, E.; Lopes, E.; Almeida, M.; Clérac, R.; Avarvari, N., in preparation.
16. Hayashi, T.; Yamamoto, A.; Ito, Y.; Nishiok, E.; Miura, H.; Yanagi, K. *J. Am. Chem. Soc.* **1989**, *111*, 6301–6311.
17. The reactions carried out with the ligands of (*S*) configuration are leading to the enantiomeric product with the same results.
18. Kollmar, M.; Goldfuss, B.; Reggelin, M.; Rominger, F.; Helmchen, G. *Chem.—Eur. J.* **2001**, *7*, 4913–4927.
19. (a) Matsubayashi, G.; Yokoyama, K.; Tanaka, T. *J. Chem. Soc., Dalton Trans.* **1988**, 3059–3062; (b) Kuroda-Sowa, T.; Hirata, M.; Munakata, M.; Maekawa, M. *Chem. Lett.* **1998**, 499–500.
20. Segura, J. L.; Martin, N. *Angew. Chem., Int. Ed.* **2001**, *40*, 1372–1409.
21. Réthoré, C.; Suisse, I.; Agbossou-Niedercorn, F.; Fourmigué, M.; Avarvari, N., in preparation.
22. Allgeier, A. M.; Mirkin, C. A. *Angew. Chem., Int. Ed.* **1998**, *37*, 894–908.
23. Lorkovic, I. M.; Duff, R. R., Jr.; Wrighton, M. S. *J. Am. Chem. Soc.* **1995**, *117*, 3617–3618.
24. Gregson, C. K. A.; Gibson, V. C.; Long, N. J.; Marshall, E. L.; Oxford, P. J.; White, A. J. P. *J. Am. Chem. Soc.* **2006**, *128*, 7410–7411.
25. Connely, N. G.; Geiger, W. E. *Chem. Rev.* **1996**, *96*, 877–910.