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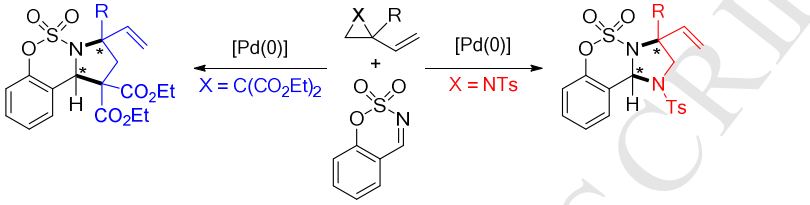

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Vinyl-aziridines and cyclopropanes in Pd-catalyzed (3+2)-cycloaddition reactions with cyclic *N*-sulfonyl imines

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ABSTRACT

Efficient palladium-catalyzed (3+2)-cycloaddition reactions of cyclic *N*-sulfonyl imines and vinyl-aziridines (or cyclopropanes) have been achieved. The reactions, with either vinylic substrate, proceed with excellent yields affording highly functionalized imidazolidine and pyrrolidine derivatives. The cycloadditions take place via the reaction of zwitterionic π-allyl palladium intermediates with cyclic *N*-sulfonyl imines through *i)* the formation of two N–C bonds in the presence of vinylaziridines (synthesis of imidazolidines) and *ii)* one C–C bond and one N–C bond in the presence of vinylcyclopropanes (synthesis of pyrrolidines). Following on preliminary works on the diastereoselective synthesis of imidazolidines, herein we wish to give a broader view on the subject by describing derivatization reactions and attempts towards an enantioselective version. Moreover, we describe and discuss the behavior of each vinylic substrate (aziridine or cyclopropane) on the (3+2)-cycloaddition reactions. Mechanistic and (intriguing) selectivity outcomes are also going to be discussed.

1. Introduction

Following the seminal work of Alper in (3+2)-cycloaddition reactions with heterocumulenes,[1] the palladium-catalyzed ring-opening of vinylaziridines has emerged as a powerful tool for the construction of a plentiful family of N-heterocycle scaffolds (Scheme 1).[2-11] In the presence of a Pd(0) source, the vinyl aziridine is able to form a zwitterionic complex that can be considered as a dipolar intermediate bearing an electrophilic π-allyl palladium complex tethered to a nucleophilic nitrogen atom (Scheme 2; complex A). The nucleophilic moiety is able to react with an external electrophile (*e.g.* CO_2, isocyanates, isothiocycanates, carbodiimides or α,β-unsaturated carbonyl derivatives) leading to a novel nucleophile (Scheme 2; complex B), that can be in turn trapped by the π-allyl palladium leading to the (3+2)-cycloaddition product. Moreover, the cis/trans isomerization of the vinyl aziridine through a π–σ–π isomerization of the π-allyl palladium was early recognized,[12] paving the way for catalytic and asymmetric transformations. Indeed, in 2003, Trost first described the dynamic kinetic asymmetric cycloaddition of isocyanates to racemic vinylaziridines.[2b] It should be emphasized that relatively few catalytic and asymmetric transformations have been described to date (see red arrows in scheme 1). Moreover, the reactivity of 2-substituted vinyl aziridines ($R^4 \neq H$) was also scarcely reported in the literature.[2b]

As we had established a simple and rapid organocatalytic access to 2-substituted vinylaziridines[13] (and vinylcyclopropanes), we were keen to explore their potential in (3+2)-cycloadditions (Scheme 3). In this context, we have recently described an efficient palladium catalyzed (3+2)-cycloadditions of 2-substituted vinylaziridines **3** with cyclic *N*-sulfonyl imines **4**.[14,15]

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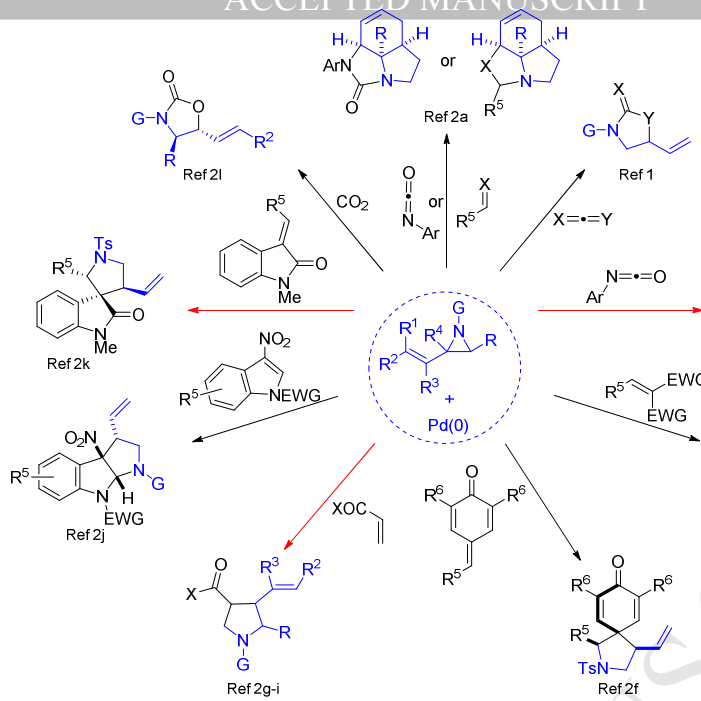
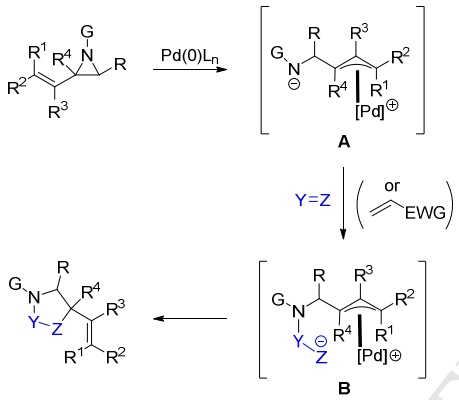
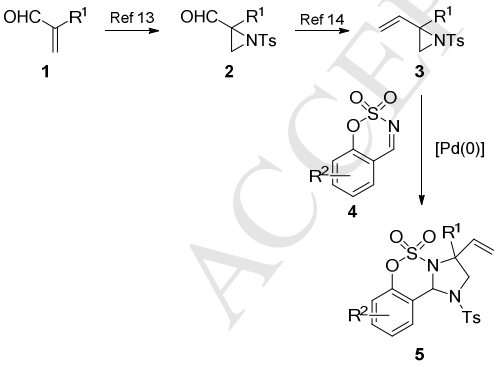


Scheme 1. Pd-catalyzed (3+2)-cycloadditions of vinylaziridines. Red arrows highlight catalytic asymmetric transformations.

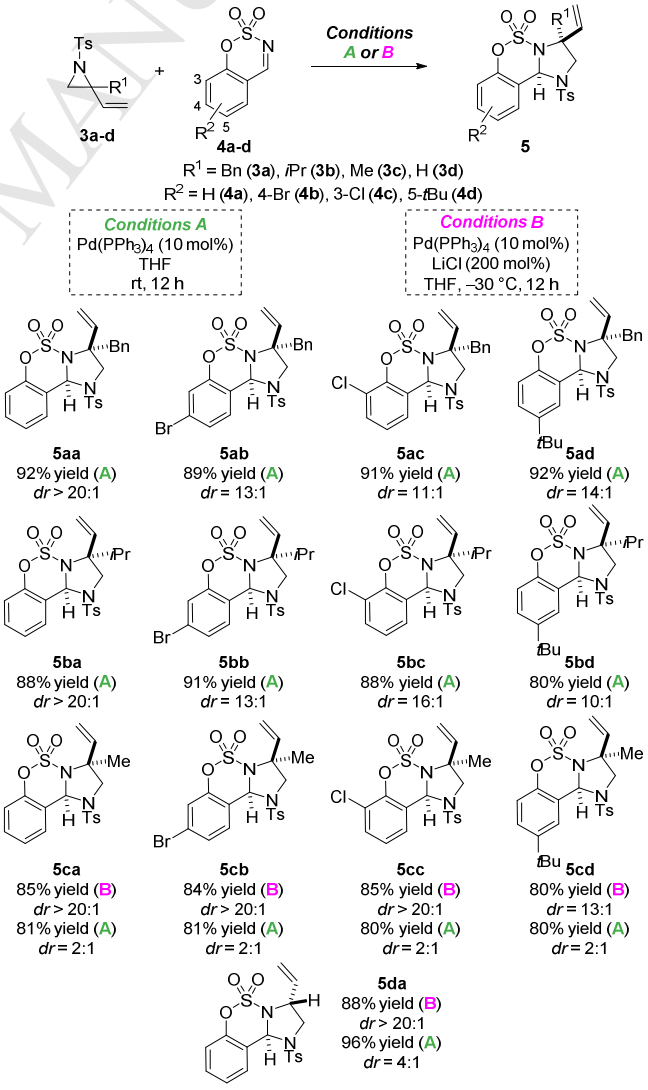


Scheme 2. Simplified mechanism for the (3+2)-cycloadditions.



Scheme 3. Straightforward access to 2-substituted vinylaziridines **3** and reaction with cyclic *N*-sulfonyl imines **4**.

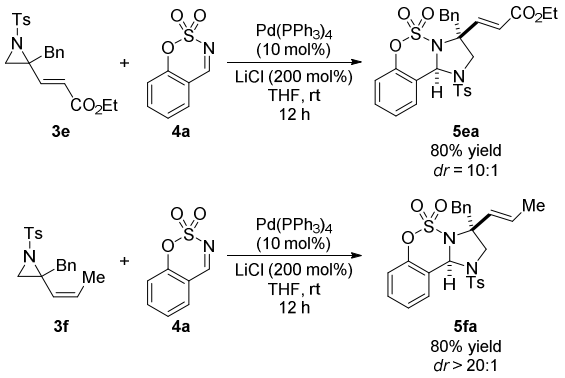
In the presence of $Pd(PPh_3)_4$ in THF at room temperature, the imidazolidines **5** have been obtained in high yields and diastereoselectivities: a general overview of the scope of the reaction is shown in scheme 4 (see examples with conditions A). It was also noticed that in the presence of less bulky substituents (*i.e.* R^1 = Me, H), low diastereoselectivities were generally observed (Scheme 4, conditions A).



Scheme 4. Pd-catalyzed (3+2)-cycloaddition reactions between 2-substituted vinylaziridines **3** and cyclic *N*-sulfonyl imines **4**.

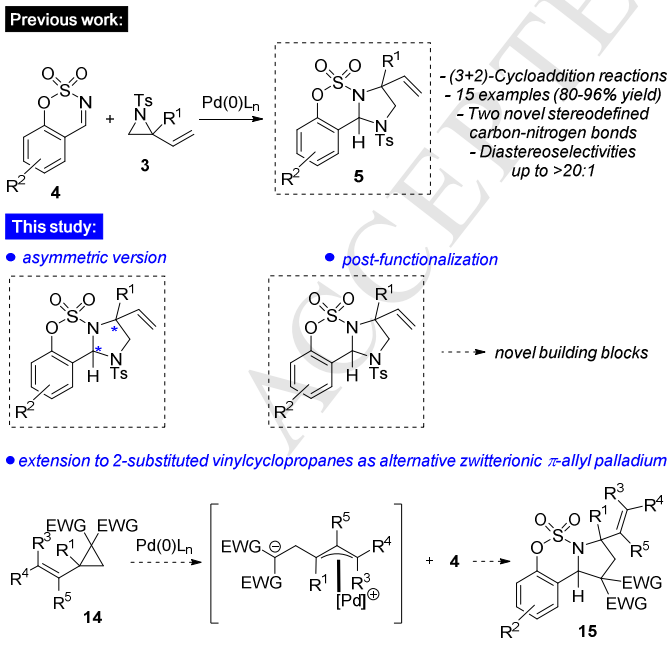
Anticipating that accelerating a π–σ–π isomerization could have a beneficial impact on the diastereoselectivity outcome, the reaction was carried out in the presence of two equivalents of LiCl.[16] Finally, by combining the use of LiCl and decreasing the reaction temperature down to –30 °C, the imidazolidines **5ca-5cd** and **5da** were obtained in excellent yields and diastereoselectivities (Scheme 4, conditions B). The diastereoselectivity of the imidazolidines **5** could be ascertained by the determination of the X-ray structure of compound **5aa**.[14]

The reaction could also be extended to *Z* and *E* substituted double bonds substrates **3e** and **3f** obtained by either Wittig or Horner-Wadsworth-Emmons from aldehyde **2a** (see scheme 3). In the case of imidazolidine **5fa**, the isomerization of the Z double bond was interpreted as a confirmation of the π–σ–π isomerization of the π-allyl palladium intermediate.



Scheme 5. Vinyl-substituted aziridines **3e** and **3f** as substrates in Pd-catalyzed (3+2)-cycloaddition reaction.

With the objective to extend the scope of this methodology and to better understand the mechanistic scenario, we decided through this study, to focus our attention on *i)* asymmetric versions, *ii)* the post-transformation of the aminals **5**, and *iii)* the use of alternative zwitterionic π-allyl palladium intermediates starting from vinylcyclopropanes (Scheme 6).

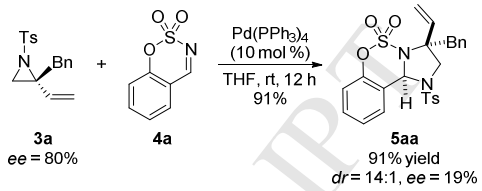


Scheme 6. New targeted objectives within the Pd-catalyzed (3+2)-cycloaddition reactions with 2-substituted vinyl-aziridines and cyclopropanes.

2. Results and discussion

Asymmetric reactions

With these aims in mind, we have thus started our studies first seeking to devise an asymmetric version of the previous developed Pd-catalyzed (3+2)-cycloaddition. In our previous study, we have shown that enantioenriched vinylaziridine **3a** (80% *ee*) in the presence of **4a** enabled the formation of **5aa** in 91% yield with a marked erosion of the enantiomeric purity (19% *ee*) (Scheme 7).



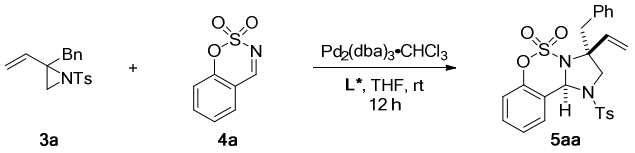
Scheme 7. Prior trial on an asymmetric version from enantioenriched 2-substituted vinylaziridine **3a** (80% *ee*).

This observation suggesting a rapid π–σ–π interconversion of the π-allyl palladium (correlated with the double bond isomerization in **3f** → **5fa**) thus paved the way to the development of a dynamic kinetic asymmetric transformation (DYKAT).[17] The use of chiral ligands in the **3a** + **4a** → **5aa** model reaction was thus investigated. Extensive work (more than 22 different chiral ligands under various conditions) was thus undertaken to embrace a general overview of the nature of the chiral ligand on the selectivity outcome (conversion, yield, diastereo- and enantioselectivities). Results are summarized in table 1.

Concerning a mono-catalytic system strategy, differently substituted phosphoramidites were first tried (entries 1-10). With these ligands, the reaction was, for some yet unclear reason, very sensitive to the ligand structure (compare for example entries 1-2) leading to either no reactivity or complete conversion. **L2** proved to be the more efficient one leading to **5aa** in 80% yield, good *ee* (70%) but with a moderate diastereoselectivity (*dr* = 3:1) (entry 2). Moving to biphosphines (entries 11-16), low enantioselectivities have been generally observed (up to 40% *ee* using BINAP but in a very low conversion, entry 11) and, as observed with phosphoramidites, small modifications in their structure have a dramatic impact on the reactivity: compare Josiphos and Taniaphos (entries 13 and 15). Classical Trost ligand **L16**, widely used in DYKAT Tsuji-Trost reactions, gave the expected compound in very good yield and diastereoselectivity albeit with a low *ee* (16%) (entry 16). A dual catalysis combining a Pd source and the activation of the electrophile (*i.e.* with a chiral Lewis acid or a Brønsted acid) was attempted with albeit deceiving results in terms of conversion and enantioselectivities (entries 17, 20 and 21). According to the general mechanism proposed in scheme 6, the generation of the first stereogenic center is mediated by the attack of the TsN^- anion to the imine partner. Therefore, using a chiral counterion could be interesting to promote this addition in an enantioselective way. Thus, chiral ammoniums **L18** and **L19**, have been tested, albeit unsuccessfully regarding enantioselectivities.

Based on Oii's work on (3+2)-cycloadditions with vinyloxazolidinones,[7b,18] original ligand **L22** bearing a phosphine with a remote ammonium salt could be efficiently obtained from the commercially available cinchona **7** in one step and in 57% yield (Scheme 8). Even though good yield (80%) and diastereoselectivity (>20:1) have been observed in the model

Table 1. Screening of chiral ligands **L1**–**L22** for Pd-catalyzed (3+2)-cycloaddition reactions with 2-substituted vinylaziridines and cyclic *N*-sulfonyl imines.[a]



Entry	Strategy	Ligand Class	Ligands **L**	Conversion[b] (%)	Yield[c] (%)	*dr*[d]	*ee*[e] (%)
1	Mono-catalysis	Phosphoramidites	**L1**	–	ND	ND	ND
2			**L2**	**100**	**80**	**3:1**	**70**
3			**L3**	–	ND	ND	ND
4			**L4**	–	ND	ND	ND
5			**L5**	–	ND	ND	ND
6			**L6**	–	ND	ND	ND
7			**L7**	100	82	6:1	55
8			**L8**	50	37	8:1	33
9			**L9**	33	20	6:1	9
10			**L10**	–	ND	ND	ND
11		Biphosphines	BINAP (**L11**)	<10	<10	>20:1	40
12			2-Furyl-MeOBIPHEP (**L12**)	100	80	>20:1	0
13			JOSIPHOS (**L13**)	<5	ND	ND	ND
14			DTBM-SEGPHOS (**L14**)	5	ND	ND	ND
15			TANIAPHOS (**L15**)	64	52	3:1	21
16			Trost ligand (**L16**)	100	80	>20:1	16
17[f]	Dual-catalysis	Bisoxazoline	*t*Bu-bisoxazoline (**L17**)	–	ND	ND	ND
18[g]		Chiral ammoniums	**L18**	100	86	13:1	0
19[g]			**L19**	100	86	13:1	0
20[g]		Phosphoric acids	**L20**	100	60	12:1	0
21[g]			**L21**	100	60	12:1	0
22		Phosphine/ ammonium salt	**L22**	100	80	>20:1	0

[a] Reaction conditions: Unless otherwise noted, reactions were conducted with aziridine **3a** (0.13 mmol) and imine **4a** (0.16 mmol) under $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) catalyst, ligand **L*** (6 or 12 mol%) in THF (1.5 mL) at rt for 12 h. [b] Conversion determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [c] Isolated yield after purification on column chromatography. [d] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [e] Enantiomeric excesses were determined by HPLC on a chiral stationary phase. [f] The reaction was carried with $Cu(OTf)_2$ (10 mol %), **L17** (11 mol %) and $Pd(PPh_3)_4$ (10 mol%) in THF at rt for 12 h. [g] $Pd(PPh_3)_4$ (10 mol%) was used as catalyst with 10 mol% of chiral phosphoric acid (**L20**/**L21**) or ammonium salts (**L18**/**L19**). ND = Not Determined.

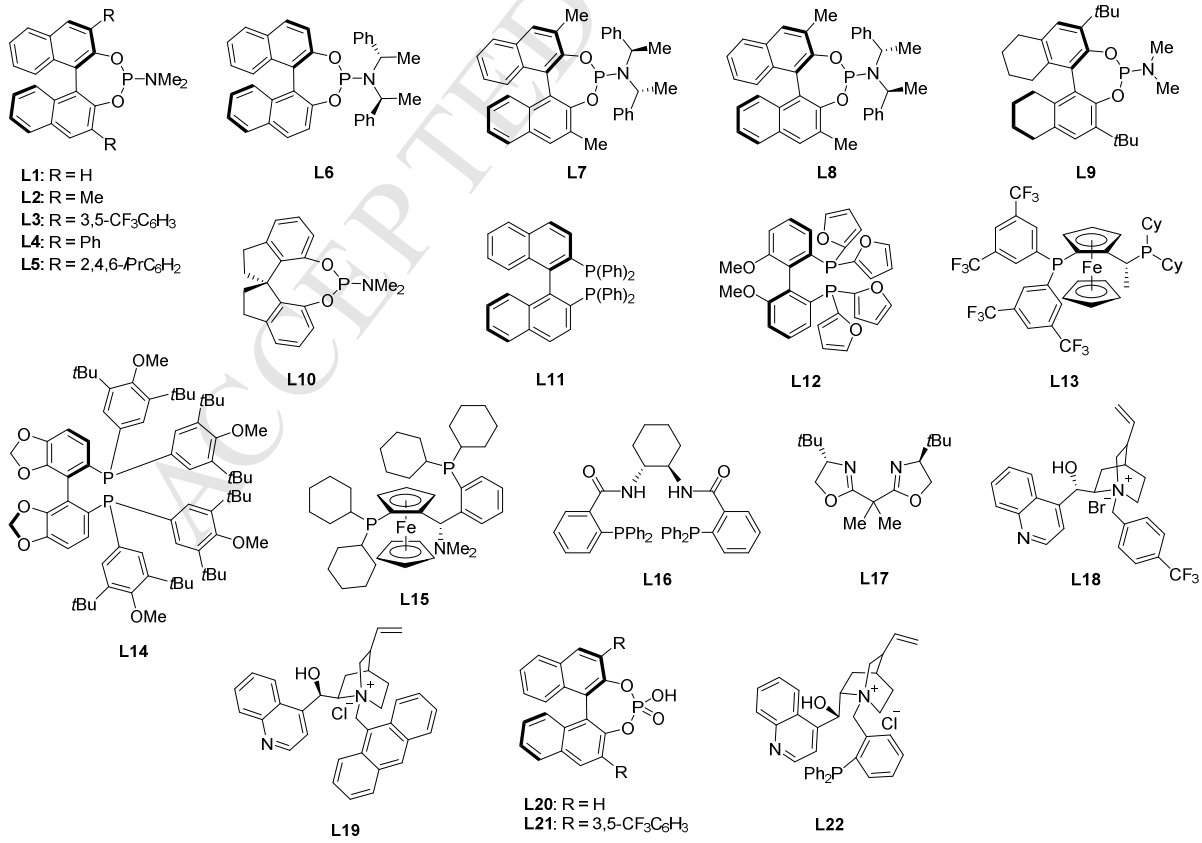
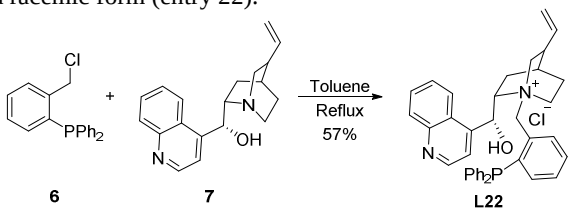


Figure 1. Structures of chiral ligands **L1**-**22** screened on this study.

reaction of **3a** with cyclic *N*-sulfonyl imine **4a**, **5aa** was obtained in a racemic form (entry 22).

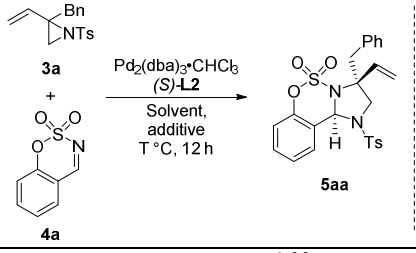


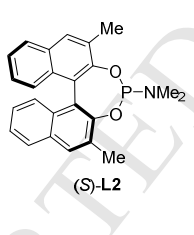
6 7 L22

Scheme 8. Synthesis of phosphine tethering an ammonium salt ligand **L22**.

After this chiral ligands' overview, the reaction was re-optimized in order to improve not only the enantioselectivity (70%) but also, ideally, the 3:1 diastereoselectivity. Changing the solvent to DMF or toluene has no impact on the diastereoselectivity outcome (Table 2, entries 2-3) but a small enantioselectivity improvement was observed with toluene (75% vs 70% *ee*). Decreasing the reaction temperature to −30 °C led to a marked improvement of the enantioselectivity to 82% (entry 4) but no further improvement could be observed at −78 °C (entry 5). We previously observed in our original communication, that the diastereoselectivity could be improved by using additives to promote a rapid π–σ–π interconversion of the π-allyl intermediate. Indeed when the reaction was carried out in toluene at −30 °C, in the presence of two equivalents of TBACl,[2g] the diastereoselectivity raised up to >20:1 but unexpectedly the compound was obtained in a racemic form (entry 6). In a control experiment, the same reaction in the presence of only 20 mol% of TBACl led to the originally observed 3:1 diastereoselectivity and 56% *ee* (entry 7).

Table 2. Re-optimization of the reaction conditions in the presence of chiral ligand (*S*)-**L2**.[a]





Entry	Solvent	T °C	Additive (mol%)	Yield[b] (%)	*dr*[c]	*ee*[d] (%)
1	THF	rt	–	85	3:1	70
2	DMF	rt	–	84	3:1	40
3	toluene	rt	–	86	3:1	75
4	toluene	–30	–	86	3:1	82
5	toluene	–78	–	88	3:1	79
6	toluene	–30	TBACl (200)	83	>20:1	0
7	toluene	–30	TBACl (20)	88	3:1	56
8	**toluene**	**–30**	**AcOH (10)**	**85**	**3:1**	**90**
9	toluene	–30	$PhCO_2H$ (10)	80	2:1	67
10	toluene	–30	Pivalic acid (10)	87	2:1	83
11	THF	–30	AcOH (10)	86	2:1	80
12	toluene	–30	TBACl (200) AcOH (10)	84	20:1	0

[a] Reaction conditions: Unless otherwise noted, reactions were conducted with aziridine **3a** (0.13 mmol) and imine **4a** (0.16 mmol) under $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) catalyst, ligand (*S*)-**L2** (12 mol%) and additive (X mol%) in solvent (1.5 mL) at T °C for 12 h. [b] Isolated yield after purification on column chromatography. [c] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [d] Enantiomeric excesses were determined by HPLC on a chiral stationary phase.

These very disappointing results (for mechanistic discussion *vide infra*) prompted us to investigate the use of other additives. The use of acetic acid as additive has been first described by Trost raising up the enantioselectivity from 42 to 82% *ee* in the cycloaddition of vinylaziridine with isocyanates.[2b] When the reaction was performed in toluene at −30 °C in the presence of 10 mol% of acetic acid, the *ee* raised up to 90% with no modification of the diastereoselectivity (entry 8). Playing on the pka of the carboxylic acid (acetic acid; pKa = 4.8) by using either benzoic acid (pKa = 4.2) or pivalic acid (pKa = 5.0) proved detrimental: 67 and 83% *ee* were respectively obtained (entries 9 and 10). Similar behavior was observed when the reaction was carried out in THF at −30 °C in presence of 10 mol% of acetic acid: 80% *ee* (entry 11). In order to obtain a synergistic effect, we have tried the combination of TBACl (that increased our *dr* ratios) and AcOH (that provided higher *ees*). Unfortunately, even though excellent diastereoselectivity and yield could be maintained (*dr* = 20:1 and 84% yield) the compound was isolated in a racemic form (entry 12).

Interestingly, compound **5aa** obtained in 90% *ee* and 3:1 *dr* (entry 8) could be recrystallized in a CH_2Cl_2/pentane system to give the diastereomeric pure compound in >99% *ee*. An X-ray analysis could be thus realized establishing the absolute configuration of the two stereocenters as *R* and *S* for the C5 and C7 stereocenters respectively (Figure 2).[19]

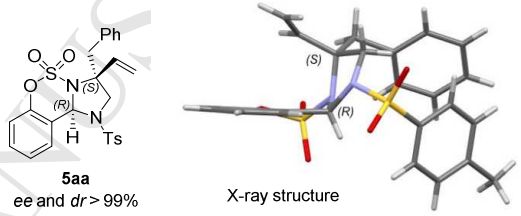
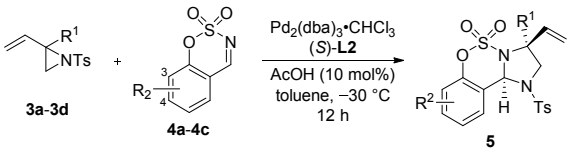


Figure 2. X-ray analysis of **5aa** in >99% *ee* and *dr*.

These optimized conditions have been next tested on differently substituted vinylaziridines **3a-3d** and *N*-sulfonyl imines **4a-4c**, with however moderate success (Table 3). The reaction is highly dependent on the substituent bulkiness: When relatively small substituents (R^1 = H or Me) are used low diastereo- and enantioselectivities are observed whereas moving to bulkier *i*Pr group good diastereo (*dr* = 9:1) and enantioselectivity (82% *ee*) are obtained. When substituted *N*-sulfonyl imines **4b** and **4c** (entries 5 and 6) were used, low diastereoselectivities and moderate *ees* have been reached.

Table 3. Reaction scope.[a]

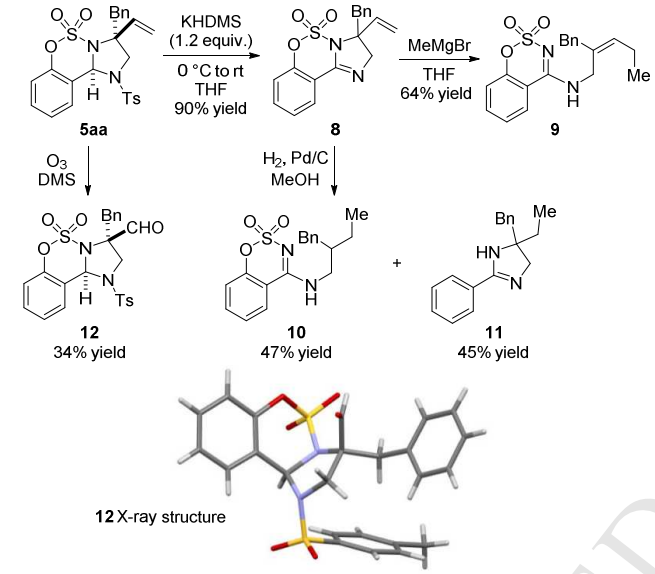


Entry	R^1	R^2	Product	Yield[b] (%)	*dr*[c]	*ee*[d] (%)
1	Bn	H	**5aa**	85	3:1	90 (99)[e]
2	Me	H	**5ca**	84	2:1	40
3	H	H	**5da**	86	1:1	13
4	*i*Pr	H	**5ba**	83	9:1	82
5	Bn	4-Br	**5ab**	90	2:1	65
6	Bn	3-Cl	**5ac**	88	2:1	64

[a] Reaction conditions: Unless otherwise noted, reactions were conducted with aziridines **3** (0.13 mmol) and imines **4** (0.16 mmol) under $Pd_2(dba)_3{\cdot}CHCl_3$ (2.5 mol%) catalyst, ligand (*S*)-**L2** (12 mol%) and AcOH (10 mol%) in toluene (1.5 mL) at –30 °C for 12 h. [b] Isolated yield after purification on column chromatography. [c] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [d] Enantiomeric excesses were determined by HPLC on a chiral stationary phase. [e] After recrystallization in a CH_2Cl_2/pentane system.

Post-transformations of aminals ***5***

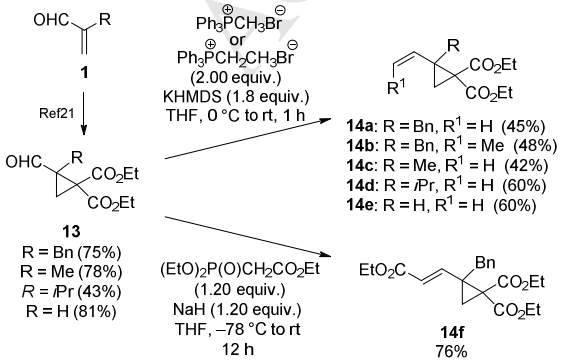
Aminals **5** can also be considered as potential synthetic platforms as illustrated in scheme 9. In the presence of KHMDS (1.2 equiv.), the corresponding compound **8** was cleanly obtained in 90% yield through the elimination of the tosylate group. This compound could further be transformed by addition of MeMgBr: interestingly the acyclic aminal product **9** was obtained in 64% yield through an S_N2' reaction. When compound **8** was subjected to hydrogenation conditions, two products could be isolated. In both products, the vinylic double bond is reduced and this expected reduction is accompanied by both the reduction of C(IV)–N bond (47% yield, compound **10**) and the reduction of the aromatic C–O bond (45% yield, compound **11**). Moreover, under reductive ozonolysis conditions, aldehyde **12** was isolated in 34% yield and its structure was unambiguously confirmed by X-ray analysis.[20]



Scheme 9. Post-transformation of aminal **5aa**.

Vinylcyclopropanes as zwitterionic precursors

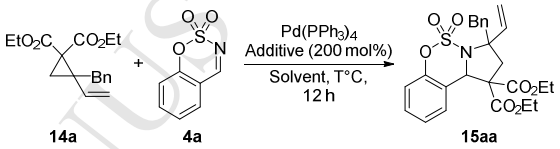
2-Substituted vinylcyclopropanes **14** can also be easily obtained from the corresponding α-substituted enals **1** under organocatalytic reactions,[21] and we were thus keen to use them in Pd-catalyzed (3+2)-cycloadditions (Scheme 10).[22,23] It is worth mentioning that to the best of our knowledge 2-substituted vinylcyclopropanes (R ≠ H) have not been used in Pd-catalyzed (3+2)-cycloadditions yet.[24] Aldehydes **13** have been obtained in 43-81% yields.[21] Further Wittig or HWE reactions lead to the 2-substituted vinylcyclopropanes **14** in good yields (42-76%).



Scheme 10. Synthesis of 2-substituted vinylcyclopropanes **14a-f**.

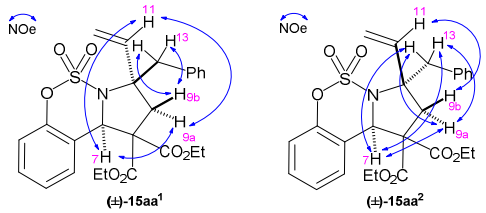
Vinylcyclopropane **14a** was next engaged in a model reaction with *N*-sulfonyl imine **4a** in the presence of $Pd(PPh_3)_4$ (Table 4). In the absence of any additive, the reaction led to the expected (3+2)-cycloaddition in good yields, however in the complete absence of diastereoselectivity, whatever the solvent used (THF, DMF or toluene). No impact on the yield or the diastereoselectivity could be observed when decreasing the temperature to –30 °C (entries 4-5). The use of LiCl (200 mol%) as an additive was also unproductive either at room temperature or at –30 °C (entries 6-7, 9). Diastereoselectivity could be finally only slightly improved to 1:3 by using TBACl (200 mol%) at –30 °C in toluene (entry 10). These results are in sharp contrast to those observed with vinylaziridines where high diastereoselectivities have been generally observed (Scheme 4). Moreover, the diastereomers (±)-**15aa**[1] and (±)-**15aa**[2] could be separated by column chromatographic and their relative configuration could be thus successfully assigned by NOESY experiments (Scheme 11).[25]

Table 4. Pd-catalyzed (3+2)-cycloaddition reactions with 2-substituted vinylcyclopropane **14a** and cyclic *N*-sulfonyl imine **4a**[a]



Entry	Solvent	T °C	Additive	Yield[b] (%)	*dr*[c]
1	**THF**	**rt**	**–**	**90**	**1:1**
2	DMF	rt	–	87	1:1
3	toluene	rt	–	85	1:1
4	THF	–30	–	85	1:1
5	toluene	–30	–	84	1:1
6	THF	rt	LiCl	82	1:1
7	toluene	rt	LiCl	83	1:1
8	toluene	rt	TBACl	83	1:1
9	toluene	–30	LiCl	85	1:1
10	**toluene**	**–30**	**TBACl**	**88**	**1:3**

[a] Reaction conditions: Unless otherwise noted, reactions were conducted with vinylcyclopropane **14a** (0.13 mmol) and imine **4a** (0.16 mmol) under $Pd(PPh_3)_4$ (10 mol%) catalyst and additive (200 mol%) in solvent (1.5 mL) at T °C for 12 h. [b] Isolated yield after purification on column chromatography. [c] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture.



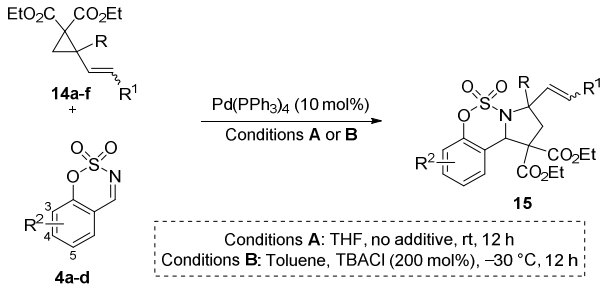
Scheme 11. Relative configuration of (±)-**15aa**[1] and (±)-**15aa**[2] *via* NOESY experiments.[25]

The scope of the reaction was next investigated using several substituted vinylcyclopropanes **14a-14f** and *N*-sulfonyl imines **4a-4d** and the reactions have been tested either in the absence (conditions A: THF, rt) or in the presence of TBACl (conditions B: toluene, –30 °C); Results are summarized in table 5.

In general, the reaction outcomes are very good delivering the expected compounds with very high conversions and yields (entries 1-9, 13). As previously observed, no diastereoselectivity is obtained: conditions B exhibiting a marginal effect. The reaction was also very sensitive towards the bulkiness of the

tetrasubstituted vinylcyclopropanes as illustrated when R = *i*Pr (entries 11 and 12). Curiously, cyclic *N*-sulfonyl imine **4d** substituted at the position 5 with a *t*Bu group did react very well to give pyrrolidine **15ad** when conditions A were employed (entry 13); however switching to conditions B, no conversion could be observed (entry 14). When the terminal vinylic position on the cyclopropane partner was substituted (R^1 = Me or CO_2Et), the (3+2)-cycloaddition process was somehow reluctant (entries 15-18, pyrrolidines **15ba** and **15fa**). Indeed, in these particular cases, only vinylcyclopropane **14f** (R = Bn, R^1 = CO_2Et) sluggishly reacts with unsubstituted cyclic *N*-sulfonyl imine **4a** to give the product in moderate conversion and low yield (60% and 37% respectively) (entry 17).

Table 5. Reaction scope with vinylcyclopropanes **14a-f**.



14 (R, R^1): Bn, H (**14a**); Bn, Me (**14b**); Me, H (**14c**); *i*Pr, H (**14d**); H, H (**14e**); Bn, CO_2Et (**14f**); **4** (R^2): H (**4a**); 4-Br (**4b**); 3-Cl (**4c**); 5-*t*Bu (**4d**)

Entry	R	R^1	R^2	Conditions/ Conversion[a] (%)	Product (Yield[b] %)	*dr*[c]
1	Bn	H	H	**A** / 100%	**15aa** (90)	1:1
2	Bn	H	H	**B** / 100%	**15aa** (88)	1:3
3	Me	H	H	**A** / 100%	**15ca** (92)	1:1
4	Me	H	H	**B** / 100%	**15ca** (90)	1:1
5	H	H	H	**A** / 100%	**15ea** (91)	1:1
6	H	H	H	**B** / 100%	**15ea** (89)	1:1
7	Bn	H	3-Cl	**A** / 100%	**15ac** (89)	1:1
8	Bn	H	3-Cl	**B** / 80%	**15ac** (68)	1:1
9	Bn	H	4-Br	**A** / 70%	**15ab** (66)	1:1
10	Bn	H	4-Br	**B** / 40%	**15ab** (<10)	9:1
11	*i*Pr	H	H	**A** / 20%	**15da** (14)	>20:1
12	*i*Pr	H	H	**B** / 0%	**15da** (–)	–
13	Bn	H	5-*t*Bu	**A** / 100%	**15ad** (95)	1:1
14	Bn	H	5-*t*Bu	**B** / 0%	**15ad** (–)	–
15	Bn	Me	H	**A** / 0%	**15ba** (–)	–
16	Bn	Me	H	**B** / 0%	**15ba** (–)	–
17	Bn	CO_2Et	H	**A** / 60%	**15fa** (37)	3:1
18	Bn	CO_2Et	H	**B** / 0%	**15fa** (–)	–

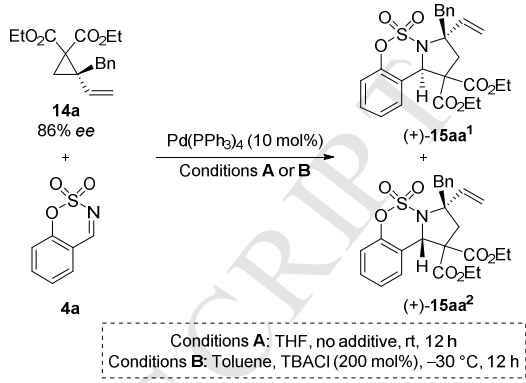
[a] Conversion determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [b] Isolated yield after purification on column chromatography. [c] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture.

The low observed diastereoselectivities prompted us to study the (3+2)-cycloaddition of enantioenriched vinylcyclopropane **14a** (86% *ee*). In the absence of any additive (Table 6, conditions A), a 1:1 mixture of the two diastereomers of **15aa** was obtained in 90% yield and, as one could expected, each diastereomer was recovered with a slight erosion on the initial enantiomeric excess (Table 6, entry 1). Under 'equilibrating' conditions B (*i.e.* TBACl, toluene, –30 °C), a 1:3 mixture of the two diastereomers was obtained and as a consequence, the major diastereomer was obtained in reduced *ee* (30%).[26]

Mechanistic discussion

The obtention of imidazolidines **5** and pyrrolidines **15**, as illustrated in scheme 12, results from three consecutive reactions. The π-allyl palladium **A** is first formed (Scheme 12, step a), resulting in the liberation of the nucleophile X^- (X^- = TsN^- in the case of vinylaziridines **3** or X^- = $(EtO_2C)_2C^-$ in the case of vinylcyclopropanes **14**). It should also be emphasized that in the presence of chiral ligand **L*** the ionization could occur in either a matched or mismatched fashion to give either $\mathbf{A^1}$ and/or $\mathbf{A^2}$. Moreover, $\mathbf{A^1}$ and $\mathbf{A^2}$ could be in equilibrium through a π–σ–π isomerization of the π-allyl palladium depending on the reaction conditions (X^- nature, palladium source, ligand, additives…).

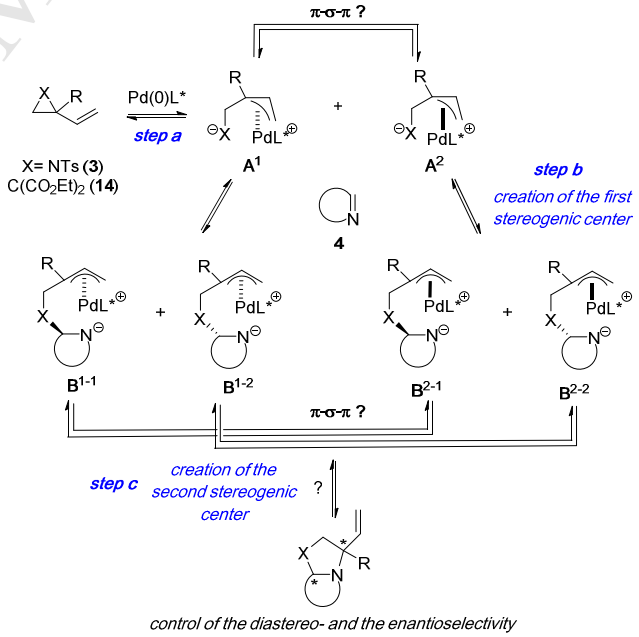
Table 6. Trials from chiral vinylcyclopropane **14a**.



Entry	Conditions	*dr*[a]	*ee*[b] dia 1 %	*ee*[b] dia 2 %	Yield[c] %
1	**A**	1:1	81	78	90
2	**B**	1:3	86	30	92

[a] Diastereomeric ratios (*dr*) were determined on the basis of ^{1}H NMR analysis of crude reaction mixture. [b] Enantiomeric excesses (*ee*) were determined by HPLC on a chiral stationary phase. [c] Isolated yield after purification on column chromatography.

Scheme 12. Mechanism proposal.



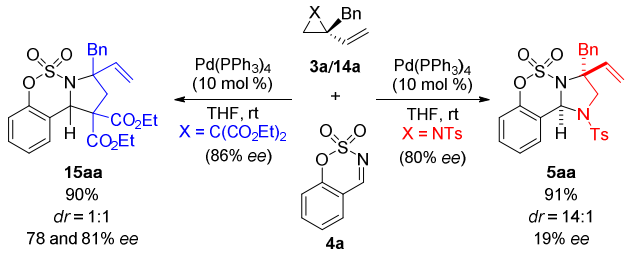
The attack of the nucleophile X^- to the *N*-sulfonyl imine **4** next enables the formation of the zwitterionic intermediates **B** (Scheme 12, step b). This **A** → **B** reaction also results in the creation of the first stereogenic center. The chiral ligand could indeed directly control the facial selectivity of the addition but the reaction could also be unselective leading to a mixture of four potential epimeric π-allyl palladium complexes $\mathbf{B^{1\text{-}1}}$, $\mathbf{B^{1\text{-}2}}$, $\mathbf{B^{2\text{-}1}}$ and $\mathbf{B^{2\text{-}2}}$. These four intermediates are anyway potentially in equilibrium through π–σ–π interconversions and/or through a reversible addition.

The third step is the cyclization, *i.e.* the intramolecular attack of the sulfonyl-amidate to the π-allyl palladium, thus generating the second, tetrasubstituted, stereogenic center (Scheme 12, step c). According to the Curtin-Hammett principle, this cyclization could be ideally stereocontrolled to give the diastereo- and enantio-enriched imidazolidines **5** or pyrolidines **15**.

In our mechanistic scenario, two π–σ–π isomerizations are potentially occurring: are they both effective? What is the influence of the coordination of the X^- to the palladium in the π–σ–π isomerizations?

As observed in control experiments (Scheme 13), the nature of the leaving group X^- [TsN^- *vs* $(EtO_2C)_2C^-$] has a dramatic influence on the stereochemical outcome of the reaction. When starting from enantiomeric enriched vinylcyclopropane **14a** (X^- = $(EtO_2C)_2C^-$, 86% *ee*), pyrrolidine **15aa** is obtained as a 1:1 mixture of the two diastereomers and a slight erosion of the chirality (78 and 81% *ee*), whereas starting with vinylaziridine **3a** (X^- = TsN^-, 80% *ee*), the corresponding imidazolidine **5aa** is isolated in excellent diastereoselectivity (*dr* = 14:1) and a dramatic drop of the enantioselectivity (19% *ee*).

Scheme 13. Control experiments: Influence of the leaving group in the diastereoselectivity outcome.

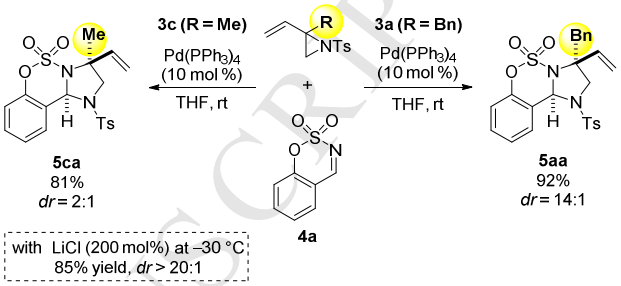


It thus appears that limited π–σ–π isomerizations occur with cyclopropanes **14** in these reaction conditions.[26] This result is rather surprising since DYKAT (3+2)-cycloadditions of vinylcyclopropanes have been described elsewhere in high diastereo- and enantioselectivities.[23,27] Nonetheless, it should be emphasized that, to the best of our knowledge, all reported examples describe the use of non-substituted vinylcyclopropanes (R = H). The use of various additives (LiCl, TBACl) was found, in our hands, to be unsuccessful to dramatically change the diastereoselectivity outcome.

The situation appears more complex with vinylaziridines **3**. When using bulky R-substituents, such as benzyl, the imidazolidine **5aa** was obtained in 92% yield with a 14:1 diastereoselectivity whereas in the presence of smaller groups (R = Me, H) very low diastereoselectivity is observed (*dr* = 2:1 when R = Me, Scheme 14). In the latter case, the use of LiCl or TBACl (200 mol%) was necessary to obtain a good diastereoselectivity control (*dr* > 20:1). With bulky substituents the cyclization (Scheme 12, step c) could be slow, enabling the π–σ–π isomerization and a good diastereoselectiviy. With smaller substituents (R = Me, H), the cyclization could be faster, and in this case, an additive (such as LiCl or TBACl) is required to promote a rapid π–σ–π isomerization of the π-allyl palladium and ensure a good diastereoselective outcome.

Based on the observation of the erosion of the enantioselectivity in the reaction with enantiomerically enriched vinylaziridine **3a** (80% *ee*) (Scheme 13), the reaction in the presence of chiral catalysts was thus investigated. With various chiral ligands, catalytic and asymmetric reactions have been attempted leading to the expected imidazolidines in high yields, high enantioselectivities albeit in poor diastereoselectivities. Even in the presence of 10 mol% of AcOH, an efficient known additive to promote the π–σ–π isomerization of π-allyl palladium complexes,[2b] the diastereoselectivity remains moderate (Table 3, entry 1). Interestingly, additives known to promote π–σ–π isomerizations could have divergent issues: the use of TBACl (200 mol%) ensures a good diastereoselectivity (*dr* = 20:1) but no enantioselectivity (Table 2, entry 6), whereas acetic acid has no effect on the *dr* outcome (*dr* = 3:1) but allows a 90% *ee* (Table 2, entry 8). It thus appears that in our current reaction conditions, we are not able to efficiently manage the two π–σ–π isomerization events in order to control both diastereo- and enantioselectivity outcomes at once.

Scheme 14. R groups steric effect on the 2-substituted vinylaziridines **3a** and **3c**.



3. Conclusion

In conclusion, we have developed a synthetically practical and useful protocol to allow the synthesis of several imidazolidines **5** and pyrrolidines **15** bearing a tetrasubstituted carbon. The method goes through a Pd-catalyzed (3+2)-cycloaddition reaction, via zwitterionic π-allyl palladium intermediates, in the presence of cyclic *N*-sulfonyl imines with either vinylaziridines or vinylcyclopropanes. Divergent and interesting behaviors were observed depending on the leaving group bore by the vinylic substrate (NTs *vs* malonate). In the former case, excellent reaction outcomes were accompanied by high diastereoselectivities thanks to a rapid π–σ–π isomerization of π-allyl palladium complexes. In the case of recalcitrant substrates (*i.e.* less encumbered ones, for which moderate-to-low *dr* were first obtained) the addition of additives such as TBACl or LiCl was favorable to promote such 'equilibria' and considerably improve the diastereoselectivities. Seeking to develop a DYKAT process, chiral ligands were tried; unfortunately, good enantioselectivity was followed by a substantial drop on the diastereoselectivity even if additives were used. On the other hand, moving to vinylcyclopropane substrates, the π–σ–π isomerization of π-allyl palladium complexes seems somehow trickier and very limited and the chirality of the substrates was almost completely transferred to the products at the expense of the diastereoselectivity. The method proposed within this study affords a quite simple procedure to prepare several imidazolidines (and analogues through derivatization) as well as pyrrolidines richly functionalized and bearing a tetrasubstituted carbon. Currently, work is ongoing on the combination of other vinylic substrates with palladium-catalysis in order to propose novel versatile compounds through cycloaddition reactions.

4. Experimental section

4.1. General information

Unless otherwise specified, all commercial products and reagents were used as purchased. Reactions were carried out in round-

bottom flasks and schlenks equipped with a magnetic stirring bar under argon atmosphere. Analytical thin-layer chromatography (TLC) of all reactions was performed on silica gel 60 F254 TLC plates. Visualization of the developed chromatogram was performed by UV absorbance (254nm), using *p*-anisaldehyde and/or $KMNO_4$. Flash chromatography was carried out on silica gel 60 Å (35-70 nm) and Biotage Isolera™ Flash Purification System. FT-IR spectra were recorded with a Perkin-Elmer Spectrum 1000; absorptions are given in wave numbers (cm^{-1}). ^1H (400 MHz), ^{13}C (100 MHz), NMR spectra were recorded with a Bruker Ultra Shield 400 Plus. ^1H chemical shifts are reported in delta (δ) units in parts per million (ppm) relative to the singlet at 7.26 ppm for d-chloroform (residual $CHCl_3$). ^{13}C chemical shifts are reported in ppm relative to the central line of the triplet at 77.0 ppm for d-chloroform. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; and br, broad and combinations thereof. All coupling constants (J values) are reported in Hertz (Hz). Enantiomeric excesses were measured on a Shimadzu® LC 20A HPLC with a UV/visible detector at 254nm and 210nm. Optical rotations were measured with a Bellingham + Stanley® ADP 440 Polarimeter or a Perkin Elmer® Polarimeter with a sodium lamp at 589nm. Low resolutions mass spectra were recorded on a Waters QTof-I spectrometer using electrospray ionization. High resolution mass spectra were obtained using the mass spectrometers operated by the "Laboratoire de Mesures Physiques of the University of Montpellier". THF was dried by distillation over sodium metal and benzophenone under argon.

4.2. General procedures

*4.2.1 Racemic synthesis of compounds **5***

Compounds **3**, **4** and **5** were synthesized according to a described methodology.[14] Analytical data were identical in all respects to those previously reported.[14]

*4.2.2 Synthesis of chiral ligands **L9** and **L22***

*2,6-di-tert-butyl-N,N-dimethyl-8,9,10,11,12,13,14,15-octahydrodinaphtho[2,1-d:1',2'-f][1,3,2]dioxaphosphepin-4-amine (**L9**)*

(*R*)-(+)-5,5',6,6',7,7',8,8'-octahydro-3,3'-di-*tert*-butyl-1,1'-bi-2-naphthol, dipotassium salt (150 mg, 0.31 mmol) was partitioned between chloroform and saturated aqueous NH_4Cl, the aqueous phase was extracted 3 times with $CHCl_3$. The combined organic layers was dried over anhydrous $MgSO_4$, filtered, and concentrated. The residue was mixed with $P(NMe_2)_3$ (73 µL, 0.4 mmol) in dry toluene (2 mL) at room temperature under argon atmosphere. The reaction mixture was warmed to 100 °C, and stirred overnight. After reaction completion (TLC monitoring), the solvent was removed in vacuum and the residue was directly purified by silica-gel column chromatography using pentane (100%) to pentane/AcOEt (9:1). The expected fractions were combined and the solvent was removed under reduced pressure to afford pale yellow oil (30 mg, 20% yield). Rf = 0.70 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^1H NMR (400 MHz, $CDCl_3$): δ 7.03 (s, 1H), 6.98 (s, 1H), 2.83-2.68 (m, 5H), 2.48-2.32 (m, 6H), 2.20-1.96 (m, 3H), 1.78-1.65 (m, 6H), 1.59-1.52 (m, 2H), 1.44 (s, 9H), 1.38 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.1 (d, J = 1.0 Hz), 145.8 (d, J = 1.0 Hz), 138.2 (d, J = 3.0 Hz), 137.2, 134.7 (d, J = 1.0 Hz), 134.1 (d, J = 1.0 Hz), 132.2 (d, J = 1.0 Hz), 131.2 (d, J = 1.0 Hz), 130.7 (d, J = 6.0 Hz), 129.8 (d, J = 3.0 Hz), 126.9 (d, J = 3.0 Hz), 126.9 (d, J = 2.0 Hz), 34.6 (d, J = 1.0 Hz), 34.6 (d, J = 1.0 Hz), 31.2, 31.1, 30.6 (6C), 29.6, 29.5, 27.4, 27.0, 23.3, 23.2, 23.1, 22.9 ppm; ^{32}P NMR (400 MHz, $CDCl_3$): δ 140.7 ppm; $[\alpha]_D$ = –222.2 (*c* 1.35, $CHCl_3$); FTIR neat (cm^{-1}): 2928, 2864, 1418, 1270, 1224, 1207, 976, 955, 873, 843, 805, 780, 750, 687; HRMS-TOF (+) calculated for $C_{30}H_{43}NO_2P$ (m/z): $[M+H]^+$: calculated: 480.3031, found: 480.3031; MS (ESI+): m/z 480.30 (100, $[M+H]^+$)

(1S,2S,4S)-1-(2-(diphenylphosphanyl)benzyl)-2-((R)-hydroxy(quinolin-4-yl)methyl)-5-vinylquinuclidin-1-ium (**L22**)

To a suspension of cinchonidine (0.189 g, 0.64 mmol) in dry and degassed toluene (4 mL) was added the (2-(chloromethyl)phenyl)diphenylphosphane[28] (0.300 g, 0.97 mmol). This mixture was stirred at reflux for 2 h under argon atmosphere. The solution was cooled to rt, poured into 50 mL of diethyl ether and filtered. A white solid was obtained (220 mg, 57% yield). M.p.: 109.5-115.7 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.98 (d, J = 4.4 Hz, 1H), 8.34 (ddd, J = 7.9, 4.5 and 1.6 Hz, 1H), 8.29 (d, J = 7.0 Hz, 1H), 8.16 (ddd, J = 10.7, 8.5 and 1.4 Hz, 2H), 7.91 (d, J = 4.5 Hz, 1H), 7.82 (ddd, J = 8.5, 6.9 and 1.2 Hz, 1H), 7.67-7.62 (m, 2H), 7.59 (ddd, J = 7.6, 7.6 and 1.2 Hz, 1H), 7.52-7.17 (m, 12H), 6.85 (d, J = 6.9 Hz, 1H), 6.63 (dd, J = 12.3 and 2.1 Hz, 1H), 5.71-5.58 (m, 2H), 5.38 (ddt, J = 12.3, 11.1 and 3.1 Hz, 1H), 4.87-4.82 (m, 2H), 4.09-4.05 (m, 1H), 3.66-3.42 (m, 3H), 2.76-2.70 (m, 1H), 2.43-2.35 (m, 3H), 1.99-1.93 (m, 1H), 1.75-1.68 (m, 1H) ppm; ^{31}P NMR (400 MHz, $CDCl_3$): δ –16.7 ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.2, 148.4, 145.8, 140.2 (d, J = 15.0 Hz), 137.4, 136.7 (d, J = 9.0 Hz), 136.0 (d, J = 2.0 Hz), 135.7 (d, J = 5.0 Hz), 134.7 (d, J = 9.0 Hz), 133.8 (d, J = 27.0 Hz), 133.9, 133.7, 133.4, 133.2, 130.6, 130.5, 129.9, 129.4, 129.2, 129.0, 129.0 (d, J = 1.0 Hz), 128.9, 128.2, 127.0, 125.2, 124.9, 122.8, 120.4, 115.9, 71.9, 62.9, 61.6 (d, J = 13.0 Hz), 61.2 (d, J = 21.0 Hz), 50.9, 38.1, 26.6, 24.8, 21.2 ppm; $[\alpha]_D$ = +21.7 (*c* 1.29, $CHCl_3$); FTIR neat (cm^{-1}): 3051, 1591, 1508, 1457, 1434, 1325, 1091, 1065, 1028, 923, 882, 858, 801, 744, 696; HRMS-TOF (+) calculated for $C_{38}H_{38}N_2OP$ (m/z): $[M+H]^+$: calculated : 569.2722, found: 569.2724; MS (ESI+): m/z 569.27 (100, $[M+H]^+$)

*4.2.3 Asymmetric synthesis of compounds **5***

*(3S,10bR)-3-benzyl-1-tosyl-3-vinyl-1,2,3,10b tetrahydrobenzo[e] imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5aa**)*

Representative procedure 1

In a flame-dried 10 mL flask equipped with a stir bar was charged with the $Pd_2(dba)_3.CHCl_3$ (3.4 mg, 0.0033 mmol.) and the ligand ((*S*)-**L2**) (5.9 mg, 0.0156 mmol.). Then 1.4 mL of dried toluene was added, this mixture was stirred at room temperature 10 min. A stock solution of acid acetic in dried toluene was added [100 µL of THF containing acetic acid (0.76 µL, 0.0132 mmol)] to the mixture. After 10 min of stirring the catalyst solution was poured dropwise to a flame dried flask containing the vinylaziridine **3a** (41 mg, 0.13 mmol) and the cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) at –30 °C. This solution was stirred at this temperature for 12 h. The reaction was quenched with 1M HCl (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The expected compound was isolated by silica gel chromatography using pentane (100 %) to pentane/AcOEt (7:3) as eluent. The solvent was removed under reduced pressure and afford a white solid (59 mg, 90% yield). Analytical data were identical in all respects to those previously reported in the literature.[12] Chiral HPLC: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 20.94 min and t_{R2} = 26.84 min; *dr*: 3:1 (determined by ^1H NMR of the crude product; up to > 20:1 by recrystallization); *ee*: 90% (up to > 99% by recrystallization); $[\alpha]_D$ = –34.1 (*c* 0.82, $CHCl_3$)

*(3R,10bS)-3-benzyl-8-bromo-1-tosyl-3-vinyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5ab**)*

The title compound was prepared according to the *representative procedure 1* from the corresponding vinylaziridine **3a** (41 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4b** (42 mg, 0.16 mmol) using (*R*)-**L2** as ligand to give a white solid (68.0 mg, 90% yield). Analytical data were identical in all respects to those previously reported in the literature.[14] Chiral HPLC: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 15.87 min and t_{R2} = 21.31 min; *dr*: 2:1 (determined by ^{1}H NMR of the crude product); *ee*: 65%

*(3S,10bR)-3-benzyl-7-chloro-1-tosyl-3-vinyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5ac**)*

The title compound was prepared according to the *representative procedure 1* from the corresponding vinylaziridine **3a** (41 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4c** (34 mg, 0.16 mmol) using (*R*)-**L2** as ligand to give a white solid (61.4 mg, 88% yield). Analytical data were identical in all respects to those previously reported in the literature.[14] Chiral HPLC: analytical column CHIRALCEL® AD column (250 x 4.6 mm); *n*hexane/*i*PrOH 98:2, 1.0 mL/min, 25 °C): dia 1: t_{R1} = 23.09 min and t_{R2} = 32.10 min; dia 2: t_{R1} = 20.59 min and t_{R2} = 26.69 min; *dr*: 2:1 (determined by ^{1}H NMR of the crude product); *ee*: 64%

*(3R,10bS)-3-isopropyl-1-tosyl-3-vinyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5ba**)*

The title compound was prepared according to the *representative procedure 1* from the corresponding vinylaziridine **3b** (35 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) using (*R*)-**L2** as ligand to give a white solid (51.7 mg, 88% yield). Analytical data were identical in all respects to those previously reported in the literature.[14] Chiral HPLC: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 14.34 min and t_{R2} = 17.90 min; *dr*: 9:1 (determined by ^{1}H NMR of the crude product); *ee*: 82%; $[\alpha]_D$ = –53.1 (*c* 0.98, $CHCl_3$)

*(3S,10bR)-3-methyl-1-tosyl-3-vinyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5ca**)*

The title compound was prepared according to the *representative procedure 1* from the corresponding vinylaziridine **3c** (31 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) using (*S*)-**L2** as ligand to give a white solid (48.7 mg, 88% yield). Analytical data were identical in all respects to those previously reported in the literature.[14] Chiral HPLC: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 33.31 min and t_{R2} = 38.28 min; *dr*: 2:1 (determined by ^{1}H NMR of the crude product); *ee*: 40%

*(3R,10bR)-1-tosyl-3-vinyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**5da**)*

The title compound was prepared according to the *representative procedure 1* from the corresponding vinylaziridine **3d** (29 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) using (*R*)-**L2** as ligand to give a white solid (51.0 mg, 90% yield). Analytical data were identical in all respects to those previously reported in the literature.[14] Chiral HPLC: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 42.98 min and t_{R2} = 48.93 min; *dr*: 1/1 (determined by ^{1}H NMR of the crude product); *ee*: 13%

*4.2.4 Post-transformation of compound **5aa***

*3-benzyl-3-vinyl-2,3-dihydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine 5,5-dioxide (**8**)*

In a flame-dried 10 mL flask equipped with a stir bar was charged with the imidazolidine **5aa** (105 mg, 0.21 mmol) and 2.0 mL of dried THF. Then a solution of KHMDS 0.5M in toluene was added dropwise (500 µL, 0.25 mmol) at 0 °C. The mixture was warmed up to room temperature and stirred for 2 h. The reaction was quenched with saturated aqueous NH_4Cl solution (5 mL), and the resulting mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine (15 mL) and dried over anhydrous $MgSO_4$. Filtration and evaporation under vacuum furnished the crude product, which was purified by column chromatography using pentane/AcOEt (9:1 to 6:4) as eluent. The expected fractions were combined and the solvent was removed under vacuum to afford colorless oil (64 mg, 89% yield). Rf = 0.5 (eluent: pentane/AcOEt 8:2, UV and KMNO4 staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 7.8 and 1.6 Hz, 1H), 7.56 (ddd, *J* = 8.3, 7.4 and 1.7 Hz, 1H), 7.34-7.17 (m, 7H), 6.40 (dd, *J* = 17.4 and 10.8 Hz, 1H), 5.49 (d, *J* = 17.5 Hz, 1H), 5.46 (d, *J* = 10.8 Hz, 1H), 4.20 (d, *J* = 15.9 Hz, 1H), 3.99 (d, *J* = 15.8 Hz, 1H), 3.64 (d, *J* = 13.9 Hz, 1H), 3.14 (d, *J* = 13.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.2, 151.1, 137.6, 134.7, 134.0, 130.8 (2C), 128.4 (2C), 128.0, 127.1, 126.6, 118.6, 117.6, 115.1, 72.4, 64.0, 41.1 ppm; FTIR neat (cm^{-1}): 2929, 1651, 1460, 1388, 1344, 1202, 1176, 854, 788, 760, 655; HRMS-ASAP (+) calculated for $C_{18}H_{17}N_2O_3S$ (m/z): $[M+H]^+$: calculated : 341.0960, found: 341.0963; MS (ESI+): m/z 341.09 (100, $[M+H]^+$)

*(Z)-4-((2-benzylpent-2-en-1-yl)amino)benzo[e][1,2,3]oxathiazine 2,2-dioxide (**9**)*

In a flame-dried 2 mL flask equipped with a stir bar was charged with the sulfamate **8** (12 mg, 0.035 mmol) and 0.2 mL of dried THF. Then a solution of MeMgBr 3M in Et_2O was added dropwise (35 µL, 0.11 mmol) at 0 °C. The mixture was warmed up to room temperature and stirred overnight. The reaction was quenched with saturated aqueous NH_4Cl (5 mL), and the resulting mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine (15 mL), and dried over anhydrous $MgSO_4$. Filtration and evaporation under vacuum furnished the crude product, which was purified by column chromatography using pentane/AcOEt (9:1 to 6:4) as eluent. The expected fractions were combined and the solvent was removed under vacuum to afford 8 mg of white solid (yield: 64%). m.p.: 138.7-143.9 °C; Rf = 0.3 (eluent: pentane/AcOEt 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (ddd, *J* = 8.4, 7.4 and 1.5 Hz, 1H), 7.35-7.19 (m, 6H), 7.09 (dd, *J* = 7.6 and 0.8 Hz, 1H), 6.49 (dd, *J* = 7.9 and 1.5 Hz, 1H), 5.71 (t, *J* = 7.3 Hz, 1H), 5.47 (brs, 1H), 4.17 (d, *J* = 5.0 Hz, 2H), 3.47 (s, 2H), 2.24-2.17 (m, 2H), 1.06 (t, *J* = 7.5 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 153.5, 140.0, 136.4, 135.3, 131.0, 129.2 (2C), 128.6 (2C), 126.8, 124.7, 123.5, 119.6, 112.0, 44.1, 42.1, 21.5, 14.3 ppm; FTIR neat (cm^{-1}): 3340, 2962, 1598, 1576, 1529, 1334, 1185, 1152, 1111, 1047, 918, 857, 768, 737, 682; HRMS-TOF (+) calculated for $C_{19}H_{21}N_2O_3S$ (m/z): $[M+H]^+$: calculated : 357.1273, found: 357.1276; MS (ESI+): m/z 357.13 (100, $[M+H]^+$)

*4-((2-benzylbutyl)amino)benzo[e][1,2,3]oxathiazine 2,2-dioxide (**10**) + 4-benzyl-4-ethyl-2-phenyl-4,5-dihydro-1H-imidazole (**11**)*

In a round bottom flask was put the sulfamate **8** (34 mg, 0.1 mmol) and the MeOH at room temperature. Several vacuum/argon cycles were performed in the flask prior to the

addition of the Pd/C (10 wt%). The argon atmosphere was replaced by H_2 and the suspension was stirred for 12 h at room temperature. After reaction completion (TLC control), the catalyst was filtered off with a syringe filter, and the filter was rinsed several times with the solvent. Then, the solvent was removed under vacuum. The crude product (1:1 mixture of **10** and **11**) was purified by column chromatography using pentane/AcOEt (9:1 to 0:10) as eluent. The expected fractions for each compound were combined and the solvent was removed under vacuum to afford **10** as colorless oil (16 mg, 47% yield) and **11** as colorless oil (12 mg, 45% yield). Combined yield: 92% Product **10**: Rf = 0.4 (eluent: pentane/AcOEt 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (ddd, J = 8.4, 7.4 and 1.5 Hz, 1H), 7.35-7.22 (m, 5H), 7.19 (dd, J = 8.4 and 1.2 Hz, 1H), 7.11 (ddd, J = 8.1, 7.3 and 1.6 Hz, 1H), 6.59 (dd, J = 8.0 and 1.5 Hz, 1H), 5.76 (brs, 1H), 3.76 (ddd, J = 13.9, 6.6 and 4.3 Hz, 1H), 3.28 (ddd, J = 13.9, 8.7 and 4.4 Hz, 1H), 2.97 (dd, J = 13.9 and 4.7 Hz, 1H), 2.50 (dd, J = 13.9 and 8.6 Hz, 1H), 2.11-2.09 (m, 1H), 1.52-1.45 (m, 2H), 1.04 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.0, 153.4, 140.6, 135.3, 129.2 (2C), 129.0 (2C), 126.5, 124.7, 123.7, 119.6, 112.0, 46.5, 41.2, 40.1, 26.1, 11.3 ppm; FTIR neat (cm^{-1}): 3363, 2927, 1598, 1568, 1533, 1348, 1186, 1165, 1110, 856, 746, 680; HRMS-TOF (+) calculated for $C_{18}H_{21}N_2O_3S$ (m/z): $[M+H]^+$: calculated: 345.1273, found: 345.1275; MS (ESI$^+$): m/z 345.13 (100, $[M+H]^+$). Product **11**: R_f = 0.4 (eluent: AcOEt 100%, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.18 (m, 10H), 3.71 (d, J = 12.0 Hz, 1H), 3.62 (d, J = 14.2 Hz, 1H), 3.47 (d, J = 12.0 Hz, 1H), 2.73 (d, J = 14.2 Hz, 1H), 2.42 (dq, J = 14.4 and 7.4 Hz, 1H), 1.67 (dq, J = 14.4 and 7.3 Hz, 1H), 1.00 (t, J = 7.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.8, 153.5, 140.0, 136.4, 135.3, 131.0, 129.2 (2C), 128.6 (2C), 126.8, 124.7, 123.5, 119.6, 112.0, 44.1, 42.1, 21.5, 14.3 ppm; FTIR neat (cm^{-1}): 3215, 2926, 1610, 1516, 1485, 1282, 1252, 1052, 1035, 915, 731, 704; HRMS-TOF (+) calculated for $C_{18}H_{21}N_2$ (m/z): $[M+H]^+$: calculated: 265.1705, found: 265.1711; MS (ESI+): m/z 265.17 (100, $[M+H]^+$)

*3-benzyl-1-tosyl-1,2,3,10b-tetrahydrobenzo[e]imidazo[1,2-c][1,2,3]oxathiazine-3-carbaldehyde 5,5-dioxide (**12**)*

Imidazolidine **5aa** (50 mg, 0.1 mmol) was dissolved in CH_2Cl_2/MeOH (5:1, 5 mL), and the solution was cooled to –78 °C. Ozone was bubbled through the cooled solution until a blue color was obtained (~5 min). Argon was then bubbled through for 10 min., and then methyl sulfide (37µL, 0.5 mmol) was added. The reaction was allowed to warm to room temperature and stir overnight. The solvent was removed under reduced pressure and the crude was recrystallized using a AcOEt/pentane system to afford white crystal (17 mg, 34% yield). m.p.: 159.5-162.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.89(s, 1H), 7.86-7.84 (m, 2H), 7.56 (dt, J = 7.9 and 1.3 Hz, 1H), 7.43-7.37 (m, 3H), 7.29-7.23 (m, 4H), 6.99-6.96 (m, 3H), 6.64 (s, 1H), 3.86 (d, J = 12.8 Hz, 1H), 3.76 (d, J = 12.9 Hz, 1H), 3.35 (d, J = 14.3 Hz, 1H), 2.70 (d, J = 14.3 Hz, 1H), 2.50 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.7, 149.7, 145.5, 134.0, 133.0, 131.5, 130.5 (2C), 130.2 (2C), 128.9 (2C), 128.0 (2C), 127.8, 127.7, 126.5, 118.3, 118.0, 77.5, 73.0, 49.4, 39.9, 21.7 ppm; FTIR neat (cm^{-1}): 3070, 1735, 1596, 1454, 1407, 1353, 1204, 1166, 1089, 1024, 983, 890, 829, 756, 729, 667; HRMS-TOF (+) calculated for $C_{24}H_{23}N_2O_6S_2$ (m/z): $[M+H]^+$: calculated: 499.0998, found: 499.1006; MS (ESI+): m/z 499.10 (100, $[M+H]^+$)

*4.2.5 Synthesis of compounds **13***

Compounds **13a-d** were synthesized according to a described methodology.[21] Analytical data were identical in all respects to those previously reported.[21]

*4.2.6 Synthesis of compounds **14a-f***

*Diethyl 2-benzyl-2-vinylcyclopropane-1,1-dicarboxylate (**14a**)*

Representative procedure 2

KHMDS in toluene (0.5 M, 11.8 mL, 5.92 mmol) was added to an ice-cooled (0 ˚C) solution of methyltriphenylphosphonium bromide (2.35 g, 6.60 mmol) in THF (18 mL). After 15 min of stirring, a solution of the corresponding aldehyde (1.0 g, 3.30 mmol) in THF (10 mL plus 2 × 1 mL rinse) was added, and the mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine (15 mL), and dried over anhydrous $MgSO_4$. Filtration and evaporation under vacuum furnished the crude product, which was purified by column chromatography using pentane/AcOEt (9.8:0.2 to 7.5:2.5) as eluent. The expected fractions were combined and the solvent was removed under vacuum to afford 450 mg of colorless oil (yield: 45 %). Rf = 0.70 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.16 (m, 5H), 5.76 (dd, J = 17.1 and 10.5 Hz, 1H), 5.06 (dd, J = 10.6 and 0.8 Hz, 1H), 4.97 (dd, J = 17.2 and 0.8 Hz, 1H), 4.21-4.12 (m, 4H), 3.22 (d, J = 15.5 Hz, 1H), 3.02 (d, J = 15.5 Hz, 1H), 1.91 (d, J = 5.4 Hz, 1H), 1.79 (d, J = 5.4 Hz, 1H), 1.25 (td, J = 7.2 and 6.1 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 167.4, 138.6, 136.3, 128.9 (2C), 128.1 (2C), 126.1, 117.3, 61.6, 61.4, 40.9, 38.3, 36.9, 23.3, 14.1, 14.1 ppm; FTIR neat (cm^{-1}): 2981, 1719, 1369, 1297, 1248, 1215, 1097, 1023, 921, 861, 721, 697; HRMS-TOF (+) calculated for $C_{18}H_{23}O_4$ (m/z): $[M+H]^+$: calculated: 303.1596, found: 303.1599; MS (ESI+): m/z 303.16 (100, $[M+H]^+$) ; $[\alpha]_D$ = +17.4 (*c* 1.15, $CHCl_3$, (*S*)-isomer, 86% *ee*)

*Diethyl (Z)-2-benzyl-2-(prop-1-en-1-yl)cyclopropane-1,1-dicarboxylate (**14b**)*

KHMDS in toluene (0.5 M, 5.9 mL, 2.95 mmol) was added to an ice-cooled (0 ˚C) solution of ethyltriphenylphosphonium bromide (1.22 g, 3.26 mmol) in THF (9 mL). After 15 min of stirring, a solution of the corresponding aldehyde (500 mg, 1.63 mmol) in THF (6 mL plus 2 × 1 mL rinse) was added, and the mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine (15 mL), and dried over anhydrous $MgSO_4$. Filtration and evaporation under vacuum furnished the crude product, which was purified by column chromatography using Pentane/AcOEt (9.8:0.2 to 8:2) as eluent. The expected fractions were combined and the solvent was removed under vacuum to afford 240 mg of colorless oil (yield: 48 %). Rf = 0.70 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.18 (m, 5H), 5.54 (dq, J = 10.8 and 7.1 Hz, 1H), 5.35 (dq, J = 10.8 and 1.8 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 4.19-4.12 (m, 2H), 3.13 (d, J = 14.1 Hz, 1H), 2.64 (d, J = 14.0 Hz, 1H), 1.86 (d, J = 5.0 Hz, 1H), 1.76 (d, J = 5.0 Hz, 1H), 1.45 (dd, J = 7.1 and 1.8 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 167.9, 138.6, 130.2, 129.4 (2C), 128.0 (2C), 127.7, 126.2, 61.5, 61.3, 39.8, 39.8, 36.0, 25.8, 14.1, 14.1, 13.76 ppm; FTIR neat (cm^{-1}): 2981, 1722, 1445, 1368, 1302, 1212, 1202, 1098, 1020, 862, 723, 698; HRMS-TOF (+) calculated for $C_{19}H_{25}O_4$ (m/z): $[M+Na]^+$: calculated: 317.1753, found: 317.1754; MS (ESI+): m/z 317.18 (100, $[M+Na]^+$)

*Diethyl 2-methyl-2-vinylcyclopropane-1,1-dicarboxylate (**14c**)*

The title compound was prepared according to the *representative procedure 2* from the corresponding aldehyde (1.1 g, 4.82 mmol)

to give colorless oil (456 mg, yield: 42 %). Rf = 0.80 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^1H NMR (400 MHz, $CDCl_3$): δ 5.84 (dd, J = 17.6 and 10.8 Hz, 1H), 5.18 (dd, J = 17.6 and 1.2 Hz, 1H), 5.13 (dd, J = 10.8 and 1.2 Hz, 1H), 4.26-4.13 (m, 4H), 1.76 (d, J = 5.2 Hz, 1H), 1.60 (d, J = 5.3 Hz, 1H), 1.35 (s, 3H), 1.27 (dt, J = 13.4 and 7.2 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 168.1, 138.5, 115.4, 61.5, 61.4, 40.9, 33.6, 26.0, 17.8, 14.1, 14.1 ppm; FTIR neat (cm^{-1}): 2982, 1721, 1447, 1368, 1298, 1227, 1174, 1104, 1002, 914, 862, 781; HRMS-TOF (+) calculated for $C_{12}H_{19}O_4$ (m/z): $[M+Na]^+$: calculated: 227.1283, found: 227.1284; MS (ESI+): m/z 227.13 (100, $[M+Na]^+$)

*Diethyl 2-isopropyl-2-vinylcyclopropane-1,1-dicarboxylate (**14d**)*
The title compound was prepared according to the *representative procedure 2* from the corresponding aldehyde (0.330 mg, 1.30 mmol) to give colorless oil (200 mg, yield: 60 %). Rf = 0.80 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^1H NMR (400 MHz, $CDCl_3$): δ 5.96 (dd, J = 17.1 and 10.4 Hz, 1H), 5.19 (dd, J = 10.4 and 1.5 Hz, 1H), 5.05 (dd, J = 17.1 and 1.5 Hz, 1H), 4.24-4.07 (m, 4H), 1.87-1.80 (m, 2H), 1.47 (dd, J = 5.1 and 1.2 Hz, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H), 0.99 (d, J = 6.9 Hz, 3H), 0.90 (d, J = 6.9 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 167.5, 132.5, 118.7, 61.4, 61.1, 44.5, 41.0, 30.9, 30.1, 22.9, 19.9, 19.1, 14.1, 14.1 ppm; FTIR neat (cm^{-1}): 2965, 1721, 1446, 1369, 1291, 1232, 1213, 1164, 1124, 1098, 1051, 1030, 994, 920, 860, 802; HRMS-TOF (+) calculated for $C_{14}H_{23}O_4$ (m/z): $[M+Na]^+$: calculated : 255.1596, found: 255.1598; MS (ESI+): m/z 255.16 (100, $[M+Na]^+$)

*Diethyl 2-vinylcyclopropane-1,1-dicarboxylate (**14e**)*
The title compound was prepared according to the *representative procedure 2* from the corresponding aldehyde (0.500 mg, 1.30 mmol) to give colorless oil (300 mg, yield: 60 %). Analytical data were identical in all respects to those previously reported in the literature.[29] R_f = 0.70 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining).

*Diethyl (E)-2-benzyl-2-(3-ethoxy-3-oxoprop-1-en-1-yl) cyclopropane-1,1-dicarboxylate (**14f**)*
In a flame dried round bottom flask was charged the phosphonate (236 µL, 1.18 mmol) with 3 mL of dried THF. To this solution was poured the NaH (28 mg, 1.18 mmol). The mixture was cooled at –78 °C and a solution of the corresponding aldehyde (300 mg, 0.99 mmol) in THF (2 mL plus 2 × 0.5 mL rinse) was added. The mixture was stirred for 1h min at –78 °C, then allowed to warm up to rt and stirred overnight. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), and the resulting mixture was extracted with AcOEt (3 × 20 mL). The combined organic layers were washed with brine (15 mL), and dried over anhydrous Na_2SO_4. Filtration and evaporation under vacuum furnished the crude product, which was purified by column chromatography using pentane/AcOEt (9.8:0.2 to 8:2) as eluent. The expected fractions were combined and the solvent was removed under vacuum to afford a colorless oil (280 mg, yield: 76%). Rf = 0.45 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^1H NMR (400 MHz, $CDCl_3$): δ 7.28-7.16 (m, 5H), 6.78 (d, J = 15.7 Hz, 1H), 5.71 (d, J = 15.7 Hz, 1H), 4.23-4.09 (m, 6H), 3.28 (d, J = 16.1 Hz, 1H), 3.05 (d, J = 16.1 Hz, 1H), 1.95-1.92 (m, 2H), 1.19-1.28 (m, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.6, 167.0, 165.8, 146.8, 137.6, 128.5 (2C), 128.4 (2C), 126.3, 123.0, 62.0, 61.8, 60.5, 41.8, 36.3, 36.2, 25.0, 14.1, 14.0, 14.0 ppm; FTIR neat (cm^{-1}): 2982, 1716, 1647, 1369, 1253, 1174, 1097, 1030, 984, 860, 729, 698; HRMS-TOF (+) calculated for $C_{21}H_{27}O_6$ (m/z): $[M+Na]^+$: calculated : 375.1808, found: 375.1807; MS (ESI+): m/z 375.18 (100, $[M+Na]^+$)

*4.2.7 Synthesis of compounds **15***

*Diethyl 3-benzyl-3-vinyl-2,3-dihydrobenzo[e]pyrrolo[1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide (**15aa^1** and **15aa^2**)*

Representative procedure A
A flame-dried 10 mL flask equipped with a stir bar was charged with vinylcyclopropane **14a** (32 mg, 0.13 mmol), the $Pd(PPh_3)_4$ (15 mg, 0.013 mmol.) and the cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol). Then 1.5 mL of dried THF was added, the yellow mixture was stirred at room temperature for 12 h. The reaction was quenched with 1M HCl (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. Expected compounds were isolated by silica gel chromatography using pentane (100%) to pentane/AcOEt (7:3) as eluent. The solvent was removed under reduced pressure and afford two colorless oils (**15aa^1**: 29 mg, **15aa^2**: 28 mg, combined yield: 90%); *dr*: 1:1 (determined by ^1H NMR of the crude product)

Representative procedure B
A flame-dried 10 mL flask equipped with a stir bar was charged with vinylcyclopropane **14a** (32 mg, 0.13 mmol), the $Pd(PPh_3)_4$ (15 mg, 0.013 mmol.) the cyclic *N*-sulfonylimine **4a** (29 mg, 0.16 mmol). and TBACl (72 mg, 0.26 mmol). Then 1.5 mL of dried Toluene was added at –30 °C and the yellow mixture was stirred at this temperature for 12 h. The reaction was quenched with 1M HCl (2 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 5 mL), the combined organic layers were washed with brine (5 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. Expected compounds were isolated by silica gel chromatography using pentane (100%) to pentane/AcOEt (7:3) as eluent. The solvent was removed under reduced pressure and afford two colorless oils (**15aa^1**: 14 mg, **15aa^2**: 42 mg, combined yield: 88%); *dr*: 1:3 (determined by ^1H NMR of the crude product). Rf **15aa^1** = 0.32 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); Rf **15aa^2** = 0.28 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^1H NMR (400 MHz, $CDCl_3$) **15aa^1**: δ 7.43 (d, J = 8.3 Hz, 1H), 7.32-7.20 (m, 6H), 7.13 (td, J = 7.6 and 1.4 Hz, 1H), 7.03 (dd, J = 8.4 and 1.5 Hz, 1H), 6.18 (dd, J = 17.3 and 10.9 Hz, 1H), 5.50 (s, 1H), 5.36 (d, J = 10.8, 1H), 5.07 (d, J = 17.3, 1H), 4.38-4.21 (m, 2H), 3.90-3.70 (m, 2H), 3.58 (d, J = 13.6 Hz, 1H), 3.42 (d, J = 13.6 Hz, 1H), 2.89 (d, J = 14.2 Hz, 1H), 2.49 (d, J = 14.2 Hz, 1H), 1.30 (t, J = 7.2, 3H), 0.82 (t, J = 7.2, 3H) ppm. **15aa^2**: δ 7.27-7.35 (m, 6H), 7.21 (d, J = 8.3 Hz, 1H), 7.10 (td, J = 7.6 and 1.4 Hz, 1H), 7.01 (dd, J = 8.4 and 1.5 Hz, 1H), 6.50 (dd, J = 17.5 and 11.1 Hz, 1H), 5.45 (s, 1H), 5.22 (d, J = 11.1, 1H), 5.17 (d, J = 17.5, 1H), 4.25 (q, J = 7.1 Hz, 2H), 3.81 (q, J = 7.1 Hz, 2H), 3.40 (d, J = 13.6 Hz, 1H), 3.22 (d, J = 13.6 Hz, 1H), 2.88 (d, J = 14.2 Hz, 1H), 2.73 (d, J = 14.2 Hz, 1H), 1.28 (t, J = 7.2, 3H), 0.94 (t, J = 7.2, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) **15aa^1**: δ 169.9, 168.7, 150.3, 137.4, 136.1, 131.0 (2C), 129.4, 128.0 (2C), 127.4, 126.8, 125.0, 120.4, 118.3, 117.6, 71.0, 65.8, 62.6, 62.0, 61.7, 44.3, 40.0, 14.0, 13.3 ppm. **15aa^2**: δ 169.3, 168.1, 150.8, 140.1, 135.4, 131.3 (2C), 129.3, 128.3 (2C), 127.1, 126.9, 124.9, 120.7, 118.6, 114.8, 71.8, 67.0, 62.7, 62.6, 61.9, 44.4, 42.5, 13.9, 13.4 ppm; FTIR neat (cm^{-1}): **15aa^1**: 2982, 1729, 1489, 1454, 1382, 1263, 1194, 1173, 1102, 1056, 1031, 935, 840, 783, 757, 702. **15aa^2**: 2984, 1730, 1488, 1454, 1388, 1263, 1195, 1176, 1102, 925, 892, 850, 825, 783, 755, 705; HRMS-TOF (+) calculated for $C_{25}H_{28}NO_7S$ (m/z): $[M+H]^+$: calculated : 486.1586, found: 486.1590; MS (ESI+): m/z 486.15 (100, $[M+H]^+$); Chiral HPLC **15aa^1**: analytical

column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 19.07 min and t_{R2} = 26.06 min (*ee*: 81% with *procedure A* and 86% with *procedure B*); Chiral HPLC **15aa[2]**: analytical column CHIRALCEL® IC column (250 x 4.6 mm); *n*hexane/*i*PrOH 97:3, 1.0 mL/min, 25 °C): t_{R1} = 24.49 min and t_{R2} = 30.82 min (*ee*: 78% with *procedure A* and 30% with *procedure B*); $[\alpha]_D$ **15aa[1]** = +38.7 (*c* 0.62, $CHCl_3$, 81% *ee*); $[\alpha]_D$ **15aa[2]**= +15.5 (*c* 1.55, $CHCl_3$, 78% *ee*)

*Diethyl 3-benzyl-8-bromo-3-vinyl-2,3-dihydrobenzo[e]pyrrolo [1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide **(15ab)***

The title compound was prepared according to the *representative Procedure A* from the corresponding vinylcyclopropane **14a** (32 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4b** (42 mg, 0.16 mmol) to give colorless oil (48.4 mg, 66%). *dr*: 1:1 (determined by ^{1}H NMR of the crude product); Rf = 0.40 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.19 (m, 15H), 7.11-7.09 (m, 1H), 6.47 (dd, *J* = 17.5 and 11.1 Hz, 1H), 6.17 (dd, *J* = 17.2 and 10.9 Hz, 1H), 5.42 (s, 1H), 5.37 (d, *J* = 11.0 Hz, 1H), 5.33 (s, 1H), 5.23 (d, *J* = 11.1 Hz, 1H), 5.16 (d, *J* = 17.5 Hz, 1H), 5.07 (d, *J* = 17.3 Hz, 1H), 4.38-4.22 (m, 4H), 3.95-3.75 (m, 4H), 3.57 (d, *J* = 13.5 Hz, 1H), 3.41 (d, *J* = 13.6 Hz, 1H), 3.38 (d, *J* = 14.0 Hz, 1H), 3.20 (d, *J* = 13.8 Hz, 1H), 2.91-2.86 (m, 2H), 2.72 (d, *J* = 14.0 Hz, 1H), 2.48 (d, *J* = 14.1 Hz, 1H), 1.29 (dt, *J* = 9.1 and 7.2 Hz, 6H), 0.99 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 169.1, 168.5, 167.9, 151.1, 150.6, 139.9, 137.3, 136.0, 135.2, 131.3 (2C), 131.0 (2C), 130.2, 130.0, 128.8, 128.4 (2C), 128.2, 128.2, 128.1, 128.1 (2C), 122.3, 122.1, 121.9, 121.5, 119.9, 119.5, 117.8, 115.0, 72.1, 71.2, 66.8, 65.6, 62.8, 62.8, 62.6, 62.2, 62.1, 61.7, 44.5, 44.2, 42.4, 39.8, 14.0, 13.9, 13.5, 13.5 ppm; FTIR neat (cm^{-1}): 2983, 1730, 1604, 1482, 1388, 1261, 1195, 1177, 1096, 909, 861, 786, 755, 732, 703; HRMS-TOF (+) calculated for $C_{25}H_{27}NO_7SBr$ (m/z): $[M+H]^+$: calculated: 564.0692, found: 564.0690; MS (ESI+): m/z 564.07 (100, $[M+H]^+$)

*Diethyl 3-benzyl-7-chloro-3-vinyl-2,3-dihydrobenzo[e]pyrrolo [1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide **(15ac)***

The title compound was prepared according to the *representative procedure A or B* from the corresponding vinylcyclopropane **14a** (32 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4c** (34 mg, 0.16 mmol) to give colorless oil (*A*: 60 mg, 89%; *B*: 46 mg, 68%). *dr*: 1:1 (determined by ^{1}H NMR of the crude product); Rf = 0.28 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.22 (m, 13H), 7.14-7.11 (m, 1H), 7.36 (dt, *J* = 18.1 and 8.0 Hz, 2H), 6.49 (dd, *J* = 17.5 and 11.1 Hz, 1H), 6.18 (dd, *J* = 17.2 and 10.8 Hz, 1H), 5.51 (s, 1H), 5.40 (s, 1H), 5.38 (d, *J* = 10.8 Hz, 1H), 5.24 (d, *J* = 11.0 Hz, 1H), 5.18 (d, *J* = 17.5 Hz, 1H), 5.08 (d, *J* = 17.3 Hz, 1H), 4.39-4.22 (m, 4H), 3.92-3.73 (m, 4H), 3.59 (d, *J* = 13.6 Hz, 1H), 3.42 (d, *J* = 13.6 Hz, 1H), 3.40 (d, *J* = 14.0 Hz, 1H), 3.21 (d, *J* = 13.8 Hz, 1H), 2.93-2.88 (m, 2H), 2.73 (d, *J* = 14.1 Hz, 1H), 2.50 (d, *J* = 14.1 Hz, 1H), 1.29 (dt, *J* = 10.5 and 7.1 Hz, 6H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 169.1, 168.5, 167.9, 146.9, 146.4, 139.9, 137.3, 136.0, 135.2, 131.3 (2C), 131.0 (2C), 130.2, 130.0, 128.4 (2C), 128.1 (2C), 127.2, 126.9, 125.7, 125.2, 125.1, 125.0, 123.7, 123.4, 122.8, 122.3, 117.8, 115.0, 72.2, 71.3, 67.1, 65.9, 62.8, 62.8, 62.8, 62.2, 62.0, 61.9, 44.5, 44.2, 42.7, 40.1, 14.0, 13.9, 13.4, 13.4 ppm; FTIR neat (cm^{-1}): 2983, 1730, 1447, 1390, 1264, 1196, 1178, 1147, 1072, 926, 854, 756, 731, 704; HRMS-TOF (+) calculated for $C_{25}H_{27}NO_7SCl$ (m/z): $[M+H]^+$: calculated: 520.1197, found: 520.1199; MS (ESI+): m/z 520.12 (100, $[M+H]^+$)

*Diethyl 3-benzyl-9-(tert-butyl)-3-vinyl-2,3-dihydrobenzo[e] pyrrolo[1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide **(15ad)***

The title compound was prepared according to the *representative procedure A* from the corresponding vinylcyclopropane **14a** (32 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4d** (38 mg, 0.16 mmol) to give colorless oil (66.9 mg, 95%). *dr*: 1:1 (determined by ^{1}H NMR of the crude product); Rf = 0.50 (eluent: Pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46 (m, 1H), 7.36-7.22 (m, 13H), 6.95 (d, *J* = 8.8 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.50 (dd, *J* = 17.5 and 11.1 Hz, 1H), 6.18 (dd, *J* = 17.4 and 10.8 Hz, 1H), 5.48 (s, 1H), 5.43 (s, 1H), 5.36 (d, *J* = 10.9 Hz, 1H), 5.21 (d, *J* = 11.1 Hz, 1H), 5.16 (d, *J* = 17.5 Hz, 1H), 5.09 (d, *J* = 17.3 Hz, 1H), 4.38-4.17 (m, 4H), 3.89-3.65 (m, 4H), 3.54 (d, *J* = 13.5 Hz, 1H), 3.44 (d, *J* = 13.6 Hz, 1H), 3.39 (d, *J* = 13.8 Hz, 1H), 3.21 (d, *J* = 13.8 Hz, 1H), 2.92 (d, *J* = 14.2 Hz, 1H), 2.86 (d, *J* = 14.1 Hz, 1H), 2.71 (d, *J* = 14.1 Hz, 1H), 2.55 (d, *J* = 14.1 Hz, 1H), 1.31 (dt, *J* = 13.4 and 7.2 Hz, 6H), 1.26 (s, 9H), 1.23(s, 9H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.75 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 169.5, 168.9, 168.3, 148.4, 148.0, 148.0, 147.9, 140.4, 137.4, 136.1, 135.4, 131.3 (2C), 131.0 (2C), 128.3 (2C), 128.0 (2C), 127.1, 126.8, 126.3, 126.2, 124.3, 123.8, 119.9, 119.6, 117.9, 117.6, 117.6, 117.6, 114.7, 114.7, 71.8, 71.0, 67.2, 66.0, 62.9, 62.7, 61.9, 61.8, 44.4, 44.2, 42.6, 40.0, 34.6, 34.5, 31.2 (3C), 31.2 (3C), 14.0, 14.0, 13.4, 13.3 ppm; FTIR neat (cm^{-1}): 2965, 1731, 1496, 1384, 1368, 1261, 1179, 1121, 1099, 1060, 860, 730, 705; HRMS-TOF (+) calculated for $C_{29}H_{36}NO_7S$ (m/z): $[M+H]^+$: calculated: 542.2212, found: 542.2213; MS (ESI+): m/z 542.22 (100, $[M+H]^+$)

*Diethyl 3-benzyl-8-bromo-3-vinyl-2,3-dihydrobenzo[e]pyrrolo [1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide **(15ca)***

The title compound was prepared according to the *representative procedure A or B* from the corresponding vinylcyclopropane **14c** (29 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) to give white solid (*A*: 49 mg, 92%; *B*: 48 mg, 90%). m.p.: 76.5-85.7 °C; *dr*: 1:1 (determined by ^{1}H NMR of the crude product); Rf = 0.30 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (dt, *J* = 7.9 and 1.2 Hz, 1H), 7.36 (dt, *J* = 7.9 and 1.2 Hz, 1H), 7.32-7.27 (m, 2H), 7.17-7.11 (m, 2H), 7.01 (d, *J* = 1.2 Hz, 1H), 6.99 (d, *J* = 1.2 Hz, 1H), 6.30 (dd, *J* = 17.5 and 10.8 Hz, 1H), 6.05 (dd, *J* = 17.2 and 10.7 Hz, 1H), 5.74 (s, 1H), 5.69 (s, 1H), 5.34-5.18 (m, 4H), 4.41-4.28 (m, 4H), 4.00-3.86 (m, 4H), 2.83 (d, *J* = 13.8 Hz, 1H), 2.74 (d, *J* = 13.6 Hz, 1H), 2.68 (d, *J* = 13.6 Hz, 1H), 2.43 (d, *J* = 13.6 Hz, 1H), 1.76 (s, 3H), 1.68 (s, 3H), 1.34 (td, *J* = 7.2 and 4.8 Hz, 6H), 0.97 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 169.6, 168.2, 167.9, 150.7, 150.4, 141.7, 140.0, 129.5, 129.5, 127.6, 127.4, 124.8, 124.8, 120.1, 120.0, 118.6, 118.5, 67.4, 66.3 (2C), 65.8, 62.7, 62.6, 62.3, 62.3, 62.2, 62.0, 47.7, 45.7, 24.9, 24.1, 14.0, 14.0, 13.5, 13.4 ppm; FTIR neat (cm^{-1}): 2989, 1723, 1455, 1390, 1374, 1267, 1186, 1164, 1039, 929, 892, 850, 818, 797, 766, 756, 721, 705; HRMS-TOF (+) calculated for $C_{19}H_{24}NO_7S$ (m/z): $[M+H]^+$: calculated : 410.1273, found: 410.1275; MS (ESI+): m/z 410.13 (100, $[M+H]^+$)

*Diethyl 3-isopropyl-3-vinyl-2,3-dihydrobenzo[e]pyrrolo[1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide **(15da)***

The title compound was prepared according to the *representative procedure A* from the corresponding vinylcyclopropane **14d** (33 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16

mmol) to give white solid (8 mg, 14%). m.p.: 77.2-81.7 °C; *dr* > 20:1 (determined by ^{1}H NMR of the crude product); Rf = 0.30 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30-7.28 (m, 1H), 7.20-7.18 (m, 1H), 7.13-7.09 (m, 1H), 7.00 (dd, *J* = 8.2 and 1.2 Hz, 1H), 6.33 (dd, *J* = 17.5 and 11.1 Hz, 1H), 5.59 (s, 1H), 5.20 (d, *J* = 11.2, 1H), 5.18 (d, *J* = 17.6 Hz, 1H), 4.39 (dq, *J* = 7.1 and 1.8 Hz, 2H), 3.85 (q, *J* = 7.1 Hz, 2H), 2.82 (d, *J* = 14.1 Hz, 1H), 2.69 (d, *J* = 14.1 Hz, 1H), 2.52-2.45 (m, 1H), 1.37 (t, *J* = 7.2, 3H), 1.14 (d, *J* = 6.7, 3H), 0.97-0.92 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 167.1, 150.8, 137.5, 129.1, 126.5, 124.8, 121.1, 118.7, 115.2, 76.2, 67.5, 62.9, 62.5, 61.8, 37.4, 35.1, 18.2, 17.1, 14.0, 13.4 ppm; FTIR neat (cm^{-1}): 2981, 1731, 1455, 1386, 1253, 1196, 1176, 1102, 1002, 850, 824, 783, 756; HRMS-TOF (+) calculated for $C_{21}H_{28}NO_7S$ (m/z): $[M+H]^+$: calculated: 438.1586, found: 438.1587; MS (ESI+): m/z 438.16 (100, $[M+H]^+$)

*Diethyl 3-vinyl-2,3-dihydrobenzo[e]pyrrolo[1,2-c][1,2,3] oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide (**15ea**)*

The title compound was prepared according to the *representative procedure A or B* from the corresponding vinylcyclopropane **14e** (28 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) to give white solid (*A*: 46.8 mg, 91%; *B*: 45.7 mg, 89%). m.p.: 67.2-70.6 °C; *dr*: 1:1 (determined by ^{1}H NMR of the crude product); Rf = 0.28 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54-7.51 (m, 1H), 7.46-7.44 (m, 1H), 7.33-7.27 (m, 2H), 7.18-7.13 (m, 2H), 7.03-7.00 (m, 2H), 6.14 (ddd, *J* = 17.1, 10.1 and 8.7 Hz, 1H), 5.92 (s, 1H), 5.87 (ddd, *J* = 17.2, 10.0 and 6.8 Hz, 1H), 5.45 (s, 1H), 5.40 (d, *J* = 17.3 Hz, 1H), 5.32 (d, *J* = 17.0 Hz, 1H), 5.27-5.23 (m, 2H), 4.92 (ddd, *J* = 9.7, 7.2 and 6.7 Hz, 1H), 4.41-4.25 (m, 5H), 3.99-3.66 (m, 4H), 2.80-2.65 (m, 3H), 2.18 (dd, *J* = 13.5 and 9.7 Hz, 1H), 1.33 (dt, *J* = 16.9 and 7.1 Hz, 6H), 0.94 (td, *J* = 7.4 and 3.7 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 169.1, 168.3, 168.1, 151.0, 150.4, 137.0, 136.2, 129.7, 129.6, 128.3, 127.8, 125.4, 124.8, 120.4, 119.7, 119.0, 117.8, 67.1, 66.7, 65.2, 64.8, 62.7, 62.5, 62.4, 62.1, 61.8, 40.0, 39.6, 14.0, 14.0, 13.5, 13.4 ppm; FTIR neat (cm^{-1}): 2986, 1714, 1491, 1458, 1392, 1277, 1196, 1180, 1108, 1056, 928, 857, 793, 776, 757, 715; HRMS-TOF (+) calculated for $C_{18}H_{22}NO_7S$ (m/z): $[M+H]^+$: calculated: 396.1117, found: 396.1119; MS (ESI+): m/z 396.11 (100, $[M+H]^+$)

*Diethyl (E)-3-benzyl-3-(3-ethoxy-3-oxoprop-1-en-1-yl)-2,3-dihydrobenzo[e]pyrrolo[1,2-c][1,2,3]oxathiazine-1,1(10bH)-dicarboxylate 5,5-dioxide (**15fa**)*

The title compound was prepared according to the *representative procedure A* from the corresponding vinylcyclopropane **14f** (49 mg, 0.13 mmol) and cyclic *N*-sulfonyl imine **4a** (29 mg, 0.16 mmol) to give white solid (26.8 mg, 37%). m.p.: 93.6-98.7 °C; *dr*: 3:1 (determined by ^{1}H NMR of the crude product); Rf = 0.30 (eluent: pentane/Et_2O 8:2, UV and $KMNO_4$ staining); Major dia: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 16.0 Hz, 1H), 7.36-7.27 (m, 7H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.04 (dd, *J* = 8.1 and 0.8 Hz, 1H), 5.96 (d, *J* = 16.0 Hz, 1H), 5.39 (s, 1H), 4.27-4.18 (m, 4H), 3.83-3.67 (m, 2H), 3.48 (d, *J* = 13.7 Hz, 1H), 3.22 (d, *J* = 13.7 Hz, 1H), 2.93 (d, *J* = 14.3 Hz, 1H), 2.69 (d, *J* = 14.2 Hz, 1H), 1.31-1.25 (m, 6H), 0.92 (t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 167.8, 166.0, 150.6, 149.4, 134.4, 131.3 (2C), 129.4, 128.6 (2C), 127.5, 127.2, 125.2, 121.0, 120.5, 118.7, 70.8, 67.1, 62.7, 62.1, 60.6, 44.4, 43.1, 14.2, 13.9, 14.0, 13.4 ppm; FTIR neat (cm^{-1}): 2982, 1721, 1454, 1390, 1264, 1178, 1103, 1034, 892, 851, 826, 792, 756, 704; HRMS-TOF (+) calculated for $C_{28}H_{32}NO_9S$ (m/z): $[M+H]^+$: calculated: 558.1798, found: 558.1801; MS (ESI+): m/z 558.18 (100, $[M+H]^+$)

Dedication

In honor of Prof. Leon Ghosez, a fantastic mentor, for his commitment with Tetrahedron.

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Supplementary data

Supplementary material related to this article can be found at [insert DOI url for website].

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