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Synthesis of highly substituted pyrrolidines via palladium-catalyzed cyclization of 5-vinyloxazolidinones and activated alkenes

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Abstract

N-Tosyl-5,5-divinyloxazolidin-2-one undergoes a palladium-catalyzed decarboxylative cyclization across a range of electrophilic alkenes to give the corresponding pyrrolidine derivatives bearing two contiguous quaternary centres. Alkenes bearing two electron-withdrawing groups are required; pyrrolidines were not formed from mono-activated alkenes. Bulky, electron-rich phosphines promote pyrrolidine formation with less highly electrophilic, doubly activated alkenes, and a dramatic improvement is observed in the presence of iodide.

1. Introduction

Pyrrolidine-containing compounds display a wide variety of biological activities.[1] Pyrrolidines have also been used extensively in chiral ligands and auxiliaries for asymmetric synthesis,[2] and as highly effective scaffolds for the development of organocatalysts.[3] Because of this, the synthesis of the pyrrolidine ring system has been the subject of much research. We were interested in developing a one-pot synthesis of pyrrolidines based on [3+2] cycloaddition of an activated alkene with a 1,3-dipole (Fig. 1, path a) as an alternative to the more commonly used addition of azomethine ylides to activated alkenes[4] (Fig. 1, path b).

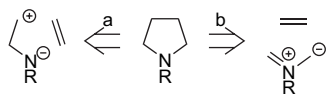

Figure 1. Construction of the pyrrolidine ring via [3+2] cycloaddition.

In fact, this approach to the construction of the pyrrolidine ring by cyclization across a carbon–carbon double bond to form the N–C1 and C2–C3 bonds has been accomplished previously using a range of different enophiles. These include the base-promoted addition of β-chloro-amines to enones;[5] addition of allylic amines across electron-rich alkenes mediated by palladium(II)[6] or across acrylates mediated by base;[7] formation of 3-exomethylenepyrrolidines by cyclization of propargylic amines across electron poor alkenes mediated by base,[8] copper (I)[9] or palladium (0);[10] Lewis acid mediated cyclization of α-amino aldehydes across allyl silanes[11] or tandem Knoevenagel reaction of α-amino aldehydes followed by cyclization of the resulting highly electron-deficient allylic amines across enol ethers.[12]

We have reported[13–15] the decarboxylative carbonylation of 5-vinyloxazolidin-2-ones **1** as a stereocontrolled route to piperidines **2** and have used this reaction as the key step in the synthesis of polyhydroxylated piperidines such as deoxymannojirimycin and mannolactam.[16] This reaction is proposed to proceed via a π-allyl palladium(II) cation such as **3**, which can be regarded, after loss of CO_2, as an equivalent of the 1,3-dipole **4** (Fig. 2). This suggested the possibility of cycloaddition to suitably activated electrophilic alkenes, which would lead to pyrrolidines. In fact, 2-vinylaziridines **5** (R^1=alkyl) have been shown to

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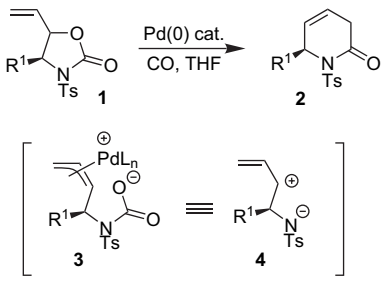


Figure 2. Decarboxylative carbonylation of 5-vinyloxazolidin-2-ones via a 1,3-dipole equivalent.

undergo palladium-catalyzed ring-opening cyclization with a range of heterocumulenes such as carbodiimides, isothiocyanates and isocyanates to give the corresponding five-membered heterocycles **6** (Fig. 3),[17] and this reaction has been used as the basis for an enantioselective synthesis of imidazolidinones using a chiral palladium catalyst.[18] Yamamoto has reported the synthesis of pyrrolidines **7** by palladium-catalyzed addition of *N*-tosyl-2-vinylaziridines **5** (R^1=Ts) to highly electrophilic alkenes[19] and, since Ibuka has shown that *N*-sulfonyl-5-vinyloxazolidin-2-ones **8** are readily converted to the corresponding vinylaziridines **9** by palladium-catalyzed decarboxylation,[20] this suggests that the more easily synthesized oxazolidinones might be used in place of aziridines for the preparation of pyrrolidine derivatives. In a similar way, Takemoto has reported the use of *N*-sulfonyloxazolidinones in place of the corresponding aziridines in a palladium-catalyzed synthesis of γ-amino alcohols.[21]

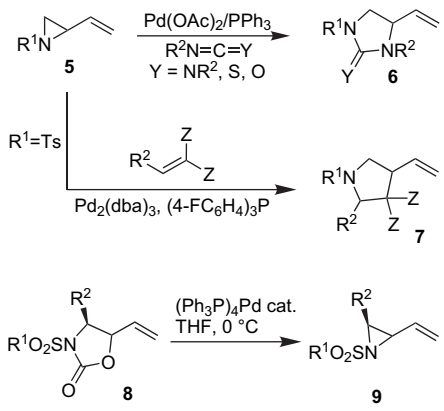


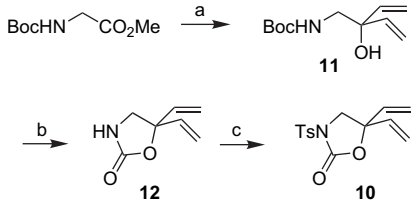
Figure 3. Palladium-catalyzed reactions involving vinylaziridines.

In choosing a suitable dipolarophile, we were guided by the extensive reports of palladium-catalyzed tandem additions of a range of nucleophile/electrophile combinations to highly electron-deficient alkylidene malonate derivatives.[22] Balme has reported the synthesis of exomethylene tetrahydrofurans and pyrrolidines by palladium-mediated cyclization of propargylic alcohols and amines across alkylidene malonates[23] and has extended this to three-component couplings terminated by metal-catalyzed arylation to give benzylidene pyrrolidines from propargylic amines.[10b,f] Yamamoto has used the palladium-catalyzed addition of vinyloxiranes to alkylidene malonates to form tetrahydrofurans[24] and has reported an enantioselective variant based on the generation of similar hydroxyalkyl π-allyl palladium cationic intermediates from hydroxyalkyl allyl carbonates using Trost's chiral ligand.[25]

We have reported[26] our preliminary investigation on the synthesis of highly substituted pyrrolidines via palladium-catalyzed decarboxylative [3+2] cycloaddition of 5,5-divinyl *N*-tosyloxazolidinones across alkylidene malonate derivatives and herein present the full details of this work. Recently, Tunge has reported the very closely analogous decarboxylative cyclization of 6-vinyloxazinanones with alkylidene malonates to give the corresponding vinylpiperidines.[27]

2. Results and discussion

As the synthesis of pyrrolidines **7** from vinylaziridines **5** is reported to occur with low diastereoselectivity,[19] we chose to use the achiral 5,5-divinyloxazolidinone **10**, which avoids this issue as long as the two electron-withdrawing groups on the alkene are identical. Oxazolidinone **10** was prepared in three steps from *N*-Boc glycine methyl ester (Scheme 1). Treatment of the amino ester with excess vinyl magnesium bromide gave the bisallylic alcohol **11**, which, without purification, was cyclized to the oxazolidinone **12** by treatment with potassium *tert*-butoxide. Tosylation of the oxazolidinone nitrogen produced **10** in good yield.



Scheme 1. *Reagents and conditions*: (a) $CH_2CHMgBr$ (2.5 equiv), THF, −78 °C to 20 °C, 4 h; (b) KO^{t}Bu, THF, 0 °C, 3 h, 45% for two steps; (c) NaH, THF, 0 °C, then TsCl, 90%.

The benzylidene Meldrum's acid derivative **13a** was used to investigate the optimum conditions for the reaction. We were pleased to find that treatment of the oxazolidinone **10** with palladium tetrakis(triphenylphosphine) (10 mol %) followed by the alkene **13a** at 40 °C gave the corresponding pyrrolidine **14a** albeit in low yield (23%, Table 1, entry 1). In our work on carbonylation of *N*-tosyl 5-vinyloxazolidinones we found that a reduction in the phosphine/palladium ratio was tolerated such that yields were essentially unchanged when just one phosphine per palladium was used.[28] The results in Table 1 (entries 1−5) show that this is true here also. The yield of pyrrolidine **14a** was essentially unchanged as the phosphorus/palladium ratio was reduced from 4:1 to 1:1, although no reaction was observed when triphenylphosphine was omitted altogether. It can also be seen that the yields are relatively independent of the nature of the palladium precursor: $Pd(PPh_3)_4$ (entry 1), $Pd_2(dba)_3$ plus PPh_3 (entry 5) and $Pd_2(dba)_3\cdot CHCl_3$ plus PPh_3 (entries 2−4) all giving similar yields of pyrrolidinone (Scheme 2).

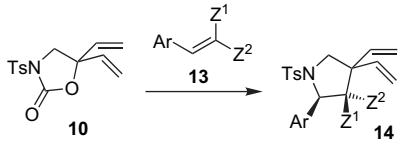
A range of phosphines of varying steric and electronic properties were screened (entries 6−11). Tributylphosphine and the

Table 1
Palladium-catalyzed decarboxylative cyclization of 5,5-divinyloxazolidin-2-one **10** with Michael acceptors **13** (Scheme 2)

Entry	Michael acceptor	Phosphine	P:Pd[a]	Additive	Product	Yield[b]
1	**13a**	PPh_3	4[c]	—	**14a**	23[d]
2	**13a**	PPh_3	4	—	**14a**	24[d]
3	**13a**	PPh_3	2	—	**14a**	21[d]
4	**13a**	PPh_3	1	—	**14a**	23[d]
5	**13a**	PPh_3	1[e]	—	**14a**	18[d]
6	**13a**	Bu_3P	4	—	**14a**	0
7	**13a**	TMPP[f]	4	—	**14a**	35
8	**13a**	dppb	4	—	**14a**	0
9	**13a**	dppf	4	—	**14a**	0
10	**13a**	2-Ph(C_6H_4)PCy_2 (**15a**)	4	—	**14a**	36
11	**13a**	2-Ph(C_6H_4)P^tBu_2 (**15b**)	4	—	**14a**	11
12	**13a**	PPh_3	4	Bu_4NF	**14a**	0
13	**13a**	PPh_3	4	Bu_4NCl	**14a**	0
14	**13a**	PPh_3	4	Bu_4NBr	**14a**	67
15	**13a**	PPh_3	4	Bu_4NI	**14a**	77
16	**13a**	PPh_3	4	Bu_4NOAc	**14a**	42
17	**13b**	PPh_3	1	—	**14b**	38
18	**13b**	PPh_3	1	Bu_4NI	**14b**	60
19	**13b**	PPh_3	4	Bu_4NI	**14b**	63
20	**13b**	PPh_3	4	Bu_4NI	**14b**	78[g]
21	**13c**	PPh_3	1	—	**14c**	65
22	**13c**	PPh_3	4	Bu_4NI	**14c**	62
23	**13c**	PPh_3	4	Bu_4NI	**14c**	73[g]
24	**13c**	2-Ph(C_6H_4)PCy_2 (**15a**)	4	Bu_4NI	**14c**	72
25	**13d**	PPh_3	1	—	**14d**	95
26	**13d**	PPh_3	4	Bu_4NI	**14d**	68
27	**13d**	PPh_3	4	Bu_4NI	**14d**	35[g]
28	**13e**	PPh_3	1	—	**14e**	97
29	**13e**	PPh_3	4	Bu_4NI	**14e**	84
30	**13e**	PPh_3	4	Bu_4NI	**14e**	53[g]
31	**13f**	PPh_3	1	—	**14f**	82
32	**13f**	PPh_3	4	Bu_4NI	**14f**	58
33	**13f**	PPh_3	4	Bu_4NI	**14f**	43[g]

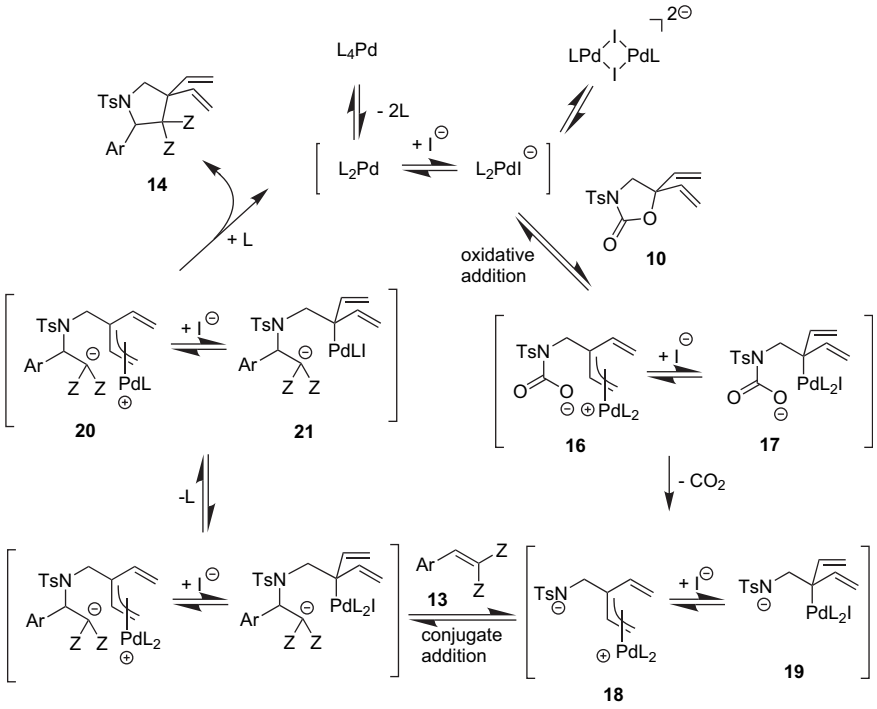
[a] Ratio of phosphorus/palladium in catalyst used.
[b] Isolated yield.
[c] $Pd(PPh_3)_4$ (10 mol %) was used in this case.
[d] NMR yield, see Section 3 for details.
[e] $Pd_2(dba)_3$ (5 mol %) was used in this case.
[f] TMPP=trimethylolpropane phosphite.
[g] Reaction time was 18 h in this case.

chelating diphosphines dppb and dppf gave no product (the oxazolidinone was the major component visible in the NMR of the crude product mixture). Improvements in the yield of pyrrolidine were observed using the phosphite TMPP (entry 7) and the bulky electron-rich 2-(dicyclohexylphosphino)biphenyl **15a** (entry 10), introduced by Buchwald[29] for amination reactions. The even more bulky 2-(di-*tert*-butylphosphino)biphenyl **15b** gave a poorer result (entry 11). Although the improvements in yield were encouraging, the relatively high cost of TMPP and **15a** in comparison to triphenylphosphine makes these less attractive.



Scheme 2. *Reagents and conditions*: $Pd_2(dba)_3 \cdot CHCl_3$ (5 mol %), PPh_3, **13** (1.5 equiv), additive (2.0 equiv), THF, 40 °C, 2 h.

The influence of added halide and acetate ions was then examined using triphenylphosphine as the ligand (entries 12–16). Both fluoride and chloride ions inhibited the reaction and none of the pyrrolidine was observed (entries 12 and 13). A dramatic improvement was observed when tetrabutylammonium



Scheme 3. Proposed catalytic cycle.

bromide was used (67%, entry 14) and this was increased further still with iodide (77%, entry 15). Acetate ions also promoted the reaction, but to a lesser extent than either bromide or iodide (42%, entry 16).

Having established the effective reaction conditions, we then investigated a variety of different electron-deficient coupling partners. The 3-cyanochromone **13b** behaved in a similar way to the Meldrum's acid derivative **13a** in that cyclization occurred to give the corresponding pyrrolidine **14b** in moderate yield (38%, entry 17). In the presence of iodide, the yield was improved to 60% (entry 18) and use of a P:Pd ratio of 4 gave a slightly better yield than a ratio of 1 (63%, entry 19). The best yield (78%) was obtained by extending the reaction time to 18 h (entry 20). The use of a more electrophilic alkene, ethyl *E*-2-cyanocinnamate **13c** gave the pyrrolidine **14c** in 65% yield, essentially as a single diastereoisomer (entry 21). In this case the addition of iodide produced an almost identical yield (62%, entry 22) with a reaction time of 2 h, but this was improved (73%, entry 23) after 18 h. The yield was not further increased by using the bulky phosphine **15a** (72%, entry 24). The stereochemistry of the pyrrolidine **14c** was assigned on the basis of comparison of the chemical shift of the pyrrolidine 2-proton (5.51 ppm), which was much closer to the value (5.76 ppm) in the Meldrum's acid derived product **14a** in which the 2-H is *syn* to an ester than to that of the corresponding malononitrile-derived products **14d–f** (5.18–4.97 ppm), in which the 2-H is necessarily *syn* to a nitrile group. The stereochemical outcome can be explained on the basis of minimizing the steric interaction between the phenyl ring and the substituents (CO_2Et and CN) on the 3-position of the pyrrolidine but would also arise if the cyclization occurred by a concerted *syn*-addition across the dipolarophile.

The more highly activated arylidene malononitrile derivatives **13d–f** gave excellent yields of the corresponding pyrrolidines **14d–f** (entries 25, 28, 31) and in these cases the addition of iodide led to lower yields (entries 26, 29, 32), which dropped even further with prolonged reaction times (entries 27, 30, 33). The benzylidene malononitrile **13d** was recovered unchanged after treatment with tetrabutylammonium iodide in THF either in the presence or absence of $Pd_2(dba)_3$ and triphenylphosphine. The reason for the detrimental effect of iodide in these cases is unclear but probably involves further reactions of the initially formed pyrrolidine on extended reaction times.

Attempts to use less activated Michael acceptors such as ethyl cinnamate, ethyl acrylate, acrylonitrile, maleic anhydride, phenyl vinyl sulfone, β-nitrostyrene and dimethyl acetylenedicarboxylate were all unsuccessful.

A possible catalytic cycle is shown in Scheme 3. Failure of the reaction when chelating diphosphines dppb and dppf were used suggests that at some stage of the mechanism palladium carries only one phosphine ligand. This may also be supported by the success of the reaction even when the phosphorus/palladium ratio is reduced from 4:1 to 1:1 and also by the improvement when the very bulky phosphine **15a** was used, since this ligand favours mono-phosphine π-allyl palladium(II) complexes.[30] Electron-rich phosphines, such as **15a** are expected to accelerate the rate of the oxidative addition step and bulky ligands facilitate reductive elimination.[29,31] Halide ions are well known to affect the outcomes of transition metal-catalyzed processes, including reactions involving π-allyl palladium(II) species.[32] Acceleration of the oxidative addition step to form a π-allyl palladium(II) intermediate may result from the increased nucleophilicity of $(Ph_3P)_nPdX^-$

species.[32] Halide ions are known to add to π-allyl palladium(II) cations to set up an equilibrium with the corresponding η^1-bonded allyl complexes.[32] In this case, decarboxylation of the π-allyl cation **16** may be slow due to a favourable intramolecular interaction between the palladium and the carbamate anion. Iodide-induced conversion of **16** into the σ-allyl **17** may facilitate the subsequent decarboxylation by disrupting this interaction. In a similar way, the conjugate addition of the π-allyl cation **18** to the electrophile **13** may be retarded by stabilization of the amide anion by palladium; this interaction would also be reduced by formation of the corresponding σ-allyl complex **19**. It is likely that the final, cyclization step occurs from a π-allyl cation, such as **20**, rather than the less electrophilic σ-allyl **21**. In our case, iodide proved to be the most effective halide additive, and this was especially evident in reactions of less reactive alkenes (**13a–c**) and chloride ions were found to inhibit the present reaction completely (Table 1, entry 13). Given the improvement found using the bulky electron-rich phosphine **15a** and iodide, steric factors may be important, either in favouring ligand dissociation or dissociation of coordinated carbamate oxygen (from a species such as **16**), which will facilitate decarboxylation or reductive elimination in the cyclization step.

The failure of reactions using less electrophilic alkenes suggests that the nucleophilicity of the nitrogen-based anion is important. While the strongly electron-withdrawing tosyl group assists in the decarboxylation step by stabilizing the resulting anion on nitrogen, this same stabilization will reduce the nucleophilicity of the anion and slow down the subsequent conjugate addition step. It may therefore be useful to explore less powerfully electron-withdrawing substituents on nitrogen. Indeed, Yamamoto has recently reported a very effective intermolecular aminoallylation of activated alkenes using allyl carbamates in which the nitrogen atom bears a less electron-withdrawing alkoxycarbonyl group.[33]

In summary, we have developed an effective palladium-catalyzed cyclization of the 5,5-divinyloxazolidinone **10** across a range of electron-deficient alkenes. Iodide promotes the reaction with less highly activated electrophiles and the cyclization generates pyrrolidines **14** bearing two contiguous quaternary carbon atoms in good yields.

3. Experimental

3.1. General

Melting points were determined on a Linkham TC92 hot stage and are uncorrected. Infrared spectra were recorded on a Nicolet 20 PCIR instrument. Mass spectra were recorded on Micromass Autospec M and Kratos MS80 RF spectrometers in electron impact (EI) mode. ^{1}H NMR spectra were recorded on Bruker WM 300 (300 MHz), JEOL LA 500 (500 MHz) and Bruker AMX 500 (500 MHz) spectrometers at ambient temperature. ^{13}C NMR was recorded on Bruker WM 300 (75 MHz) and JEOL LA 500 (125 MHz) spectrometers at ambient temperature. Thin layer chromatography was performed on EM reagent 0.25 mm silica gel 60-F plates. Flash column chromatography was performed on Fluorochem LC3025 silica gel (40–63 μm). All reactions were carried out under an atmosphere of nitrogen in pre-dried glassware unless otherwise stated. Where necessary, solvents were dried prior to use. Dichloromethane was distilled from calcium hydride under nitrogen immediately prior to use. Ethanol was distilled from magnesium under nitrogen and stored over 4 Å molecular sieves. Ether and tetrahydrofuran were distilled from sodium/benzophenone ketyl immediately prior to use. All chemicals were purchased from the Aldrich, Fluka, Sigma, Strem or Lancaster chemical companies and were used as supplied except where indicated. The benzylidene Meldrum's acid derivative **13a** was prepared as previously described.[34]

3.2. 5,5-Divinyloxazolidin-2-one *12*

To a stirred solution of *N*-(*tert*-butoxycarbonyl)glycine methyl ester (10.06 g, 53.2 mmol) in THF (500 mL) was added vinyl magnesium bromide (212 mL, 1 M solution in THF, 212 mmol) dropwise and the mixture was stirred at room temperature for 2 h. The reaction was quenched with saturated aqueous ammonium chloride (100 mL) and the mixture was extracted with EtOAc (3×100 mL). The combined organic layers were washed with brine (2×100 mL), dried ($MgSO_4$), filtered and the solvent removed under reduced pressure to give the crude bisallylic alcohol **11** as a light brown oil (10.89 g), which was used without further purification.

For the crude product **11**: δ_H (300 MHz, $CDCl_3$) 5.88 (2H, dd, J=10.7, 17.3 Hz, C*H*=CH$_2$), 5.41 (2H, d, J=17.3 Hz, CH=CH_2), 5.20 (2H, d, J=10.7 Hz, CH=CH_2), 3.25 (2H, d, J=6.2 Hz, NCH_2), 1.43 (9H, s, ^{t}Bu).

To a stirred solution of the bisallylic alcohol **11** (10.89 g, 51.1 mmol) in THF (500 mL) at 0 °C was added KO^{t}Bu (6.87 g, 61.3 mmol) and the reaction mixture was stirred for 15 h. The solvent was removed under reduced pressure and the residue dissolved in ethyl acetate. The solution was washed with brine until the brine layer was clear. The organic layer was dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (petrol/EtOAc, 1:1) to give the oxazolidinone **12** as a light brown oil (3.33 g, 45% over two steps). δ_H (300 MHz, $CDCl_3$): 6.18 (1H, br s, N*H*), 5.88 (2H, dd, J=10.7, 17.1 Hz, C*H*=CH$_2$), 5.35 (2H, d, J=17.1 Hz, HC=C*H*H), 5.24 (2H, d, J=10.7 Hz, HC=CH*H*), 3.49 (2H, s, NCH_2); δ_C (75 MHz, $CDCl_3$): 159.2, 136.8, 116.2, 83.5, 50.6; ν_{max}/cm^{-1} (film): 3292, 2989, 1754; *m*/*z* (EI$^+$): 140 (M$^+$, 11%), 112 (20), 98 (8), 94 (24), 83 (77), 68 (54), 55 (90), 43 (19), 39 (100). Anal. Calcd for $C_7H_9NO_2$: C, 60.42; H, 6.52; N, 10.07%, found: C, 60.96; H, 6.45; N, 9.62%.

3.3. 3-(para-Toluenesulfonyl)-5,5-divinyloxazolidin-2-one *10*

To a suspension of sodium hydride (1.153 g, 60% dispersion in oil, 28.8 mmol) in THF (14 mL) and DMF (36 mL) at 0 °C were added 5,5-vinyloxazolidin-2-one **12** (2.005 g, 14.4 mmol) and *p*-toluenesulfonyl chloride (3.571 g, 18.7 mmol) and the mixture was stirred overnight. The reaction

mixture was cooled to −78 °C, quenched with saturated ammonium chloride (50 mL) and extracted with ether (2×75 mL). The combined organic layers were washed with hydrochloric acid (50 mL, 2.0 M), saturated aqueous sodium hydrogen carbonate (50 mL), water (50 mL) and brine (100 mL), dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure. The crude mixture was purified by flash column chromatography (petrol/EtOAc, 19:1, 9:1, 4:1) to give the oxazolidinone **10** as a white solid (2.188 g, 90%); mp 85–87 °C; δ_H (300 MHz, $CDCl_3$): 7.95 (2H, d, J=8.3 Hz, two of $MeC_6H_4SO_2$), 7.41 (2H, d, J=8.3 Hz, two of $MeC_6H_4SO_2$), 5.91 (2H, dd, J=17.2, 10.8 Hz, C*H*=CH_2), 5.43 (2H, d, J=17.2 Hz, HC=C*H*H), 5.36 (2H, d, J=10.8 Hz, HC=CH*H*), 3.95 (s, 2H, NCH_2), 2.48 (s, 3H, CH_3); δ_C (75 MHz, $CDCl_3$): 151.3, 146.2, 135.4, 134.3, 130.3, 128.6, 118.3, 81.9, 54.2, 22.1; ν_{max}/cm^{-1} (KBr): 2923, 1776, 1363, 1169; *m/z* (EI^+): 229 (M^+−64, 36%), 174 (8), 157 (6), 149 (83), 139 (30), 119 (11), 108 (19), 91 (100), 79 (21), 65 (66), 56 (87), 39 (24). Anal. Calcd for $C_{14}H_{15}NO_4S$: C, 57.32; H, 5.15; N, 4.77%, found: C, 57.40; H, 5.16; N, 4.78%.

3.4. Typical procedure for palladium-catalyzed pyrrolidine formation

$Pd_2(dba)_3\cdot CHCl_3$ (41.4 mg, 0.04 mmol) was added to a stirred solution of the oxazolidinone **10** (234 mg, 0.8 mmol), phosphine (0.08–0.32 mmol, depending on the reaction) and tetrabutylammonium salt (1.6 mmol, added in some cases, see table) in THF (10 mL). The mixture was stirred at 40 °C for 20 min and then a solution of the electrophilic alkene **13** (1.2 mmol) in THF (4 mL) was added dropwise. The resulting solution was stirred for 2 h, filtered through a plug of Celite, washed with dichloromethane and the solvent was removed under reduced pressure. Purification by flash column chromatography (SiO_2) eluting with petrol/EtOAc (5:1) gave the pyrrolidine **14**.

For the initial comparative study of $Pd(PPh_3)_4$ and $Pd_2(dba)_3$ with varying amounts of PPh_3, yields were measured by ^1H NMR as follows: the crude product was filtered through Celite, washed with CH_2Cl_2 (30 mL) and then the solvent was removed under reduced pressure. The resulting oil was dissolved in $CDCl_3$ (2.0 mL). Two hundred and fifty microlitres of this solution was placed into an NMR tube and 250 μL of a solution of 1,3-dinitrobenzene [0.8 mmol in $CDCl_3$ (2.0 mL)] was added. The resulting mixture was diluted with $CDCl_3$ and the ^1H NMR spectrum was recorded. The NMR yield was calculated from the relative integrals of the signals from 1,3-dinitrobenzene (δ 9.00, 1H, H-2; δ 8.50, 2H, H-4) and the pyrrolidine product **14a** (δ 5.18–5.04, 3H, vinyl-H; δ 4.51, 1H, H-5; δ 4.02, 1H, H-5). In the case of Table 1, entry 5, purification of the product resulted in an isolated yield of 18%, close to the NMR yield of 23%.

*3.4.1. 8,8-Dimethyl-1-phenyl-2-(para-toluenesulfonyl)-4,4-divinyl-7,9-dioxa-2-azaspiro[4.5]decane-6,10-dione **14a***

White solid; mp 144–146 °C; δ_H (300 MHz, $CDCl_3$): 7.58 (2H, d, J=8.4 Hz, Ar*H*), 7.30–7.15 (7H, m, Ar*H*), 5.76 (1H, s, NC*H*), 5.72 (1H, dd, J=17.4, 11.1 Hz, C*H*=CH_2), 5.62 (1H, dd, J=17.1, 10.5 Hz, C*H*=CH_2), 5.39 (1H, d, J=11.1 Hz, CH=CH*H*), 5.18 (1H, d, J=17.4, CH=C*H*H), 5.13 (1H, d, J=17.1 Hz, CH=C*H*H), 5.04 (1H, d, J=10.5 Hz, CH=CH*H*), 4.51 (1H, d, J=10.9 Hz, NCH_2), 4.02 (1H, d, J=10.9 Hz, NCH_2), 2.41 (3H, s, ArCH_3), 1.51 (3H, s, CH_3), 0.89 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$): 165.2, 163.0, 143.8, 136.9, 136.4, 135.3, 133.9, 129.7, 129.5, 128.8, 128.3, 128.1, 120.0, 117.4, 105.6, 71.44, 68.1, 58.1, 56.9, 30.4, 28.3, 21.7; ν_{max}/cm^{-1} (KBr): 2924, 1774, 1742; *m/z* (EI^+): 482 (M^+, 55%), 449 (50), 349 (96), 305 (100), 261 (54); found: (M^+) 482.1623, $C_{23}H_{28}NO_6S$ requires: 482.1637.

*3.4.2. 1,2,3,3a,4,9a-Hexahydro-4-oxo-1-(para-toluenesulfonyl)-3,3-divinylchromeno[2,3-b]pyrrole-3a-carbonitrile **14b***

White solid; mp 145–148 °C; δ_H (300 MHz, $CDCl_3$): 7.80–7.70 (3H, m, Ar*H*), 7.50 (1H, apparent t, J=7.8 Hz, Ar*H*), 7.29 (2H, d, J=7.8 Hz, Ar*H*), 7.02 (1H, t, J=7.8 Hz, Ar*H*), 6.94 (1H, d, J=8.4 Hz, Ar*H*), 6.17 (1H, dd, J=17.4, 10.8 Hz, C*H*=CH_2), 6.08 (1H, s, NC*H*), 5.69 (1H, dd, J=17.4, 10.8 Hz, C*H*=CH_2), 5.33 (1H, d, J=10.8 Hz, CH=CH*H*), 5.09 (1H, d, J=17.4 Hz, CH=C*H*H), 5.06 (1H, d, J=17.4 Hz, CH=C*H*H), 4.93 (1H, d, J=10.8 Hz, CH=CH*H*), 3.74 (1H, d, J=9.6 Hz, NCH_2), 3.60 (1H, d, J=9.6 Hz, NCH_2), 2.36 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$): 182.8, 159.3, 145.1, 138.2, 135.3, 135.2, 134.2, 130.3, 128.2, 128.0, 127.7, 123.6, 120.1, 119.8, 119.2, 114.7, 91.33, 60.3, 57.0, 54.2, 21.8; ν_{max}/cm^{-1} (KBr): 2247, 1638, 1644; *m/z* (EI^+): 421 (M^+, 20%), 208 (50); found: (M^++H) 421.1230, $C_{23}H_{21}N_2O_4S$ requires: 421.1222.

*3.4.3. 1-(para-Toluenesulfonyl)-3-cyano-3-ethoxycarbonyl-2-phenyl-5,5-divinylpyrrolidine **14c***

White prisms; mp 102–103 °C; δ_H (300 MHz, $CDCl_3$): 7.40 (2H, d, J=6.6 Hz, Ar*H*), 7.30–7.10 (7H, m, Ar*H*), 6.24 (1H, dd, J=17.4, 10.8 Hz, C*H*=CH_2), 5.52 (1H, dd, J=17.1, 10.8 Hz, C*H*=CH_2), 5.51 (1H, s, NC*H*), 5.45 (1H, d, J=10.8 Hz, CH=CH*H*), 5.38 (1H, d, J=17.1 Hz, CH=C*H*H), 5.28 (2H, m, CH=CH_2), 4.15 (1H, d, J=11.5 Hz, NCH_2), 4.25–4.00 (2H, m, OCH_2CH$_3$), 3.95 (1H, d, J=11.5 Hz, NCH_2), 2.31 (3H, s, ArCH_3), 1.18 (3H, t, J=7.1 Hz, OCH$_2$CH_3); δ_C (125 MHz, $CDCl_3$): 163.7, 144.1, 136.6, 135.2, 134.9, 133.7, 129.8, 129.2, 128.8, 128.4, 127.7, 120.0, 119.9, 115.4, 66.8, 65.1, 63.9, 56.4, 55.7, 21.5, 14.4; ν_{max}/cm^{-1} (KBr): 2244, 1745, 1342, 1270, 1164, 1095, 1000; *m/z* (EI^+): 450 (M^+, 8%), 295 (95), 118 (100), 91 (65); found: (M^+) 450.1607, $C_{25}H_{26}N_2O_4S$ requires: 450.1613.

*3.4.4. 1-(para-Toluenesulfonyl)-3,3-dicyano-2-phenyl-5,5-divinylpyrrolidine **14d***

White prisms; mp 99–101 °C; δ_H (300 MHz, $CDCl_3$): 7.40–7.10 (9H, m, Ar*H*), 6.04 (1H, dd, J=17.4, 10.8 Hz, C*H*=CH_2), 5.96 (1H, dd, J=17.4, 10.8 Hz, C*H*=CH_2), 5.67 (1H, d, J=17.4 Hz, CH=C*H*H), 5.62 (1H, d, J=10.8 Hz, CH=CH*H*), 5.55 (1H, d, J=10.8 Hz, CH=CH*H*), 5.40 (1H, d, J=17.4 Hz, CH=C*H*H), 5.05 (1H, s, NC*H*), 4.45 (1H, d, J=11.7 Hz, NCH_2), 3.80 (1H, d, J=11.7 Hz, NCH_2), 2.32 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$): 143.0, 134.7, 133.4,

130.7, 130.5, 129.7, 129.5, 128.6, 128.3, 127.2, 126.8, 126.1, 120.9, 120.3, 67.9, 54.5, 52.7, 52.3, 21.7; ν_{max}/cm^{-1} (KBr): 2359, 2339, 1345, 1166; *m/z* (EI^+): 403 (M^+, 45%), 248 (27), 118 (100), 91 (60); found: (M^+) 403.1372, $C_{23}H_{21}N_3O_2S$ requires: 403.1354.

3.4.5. 1-(para-Toluenesulfonyl)-3,3-dicyano-2-(4-methoxyphenyl)-5,5-divinylpyrrolidine ***14e***

White prisms; mp 98–99 °C; δ_H (300 MHz, $CDCl_3$) 7.40 (2H, d, *J*=8.4 Hz, Ar*H*), 7.04–7.02 (4H, m, Ar*H*), 6.75 (2H, d, *J*=8.7 Hz, Ar*H*), 6.04 (1H, dd, *J*=17.4, 10.8 Hz, C*H*=CH_2), 5.95 (1H, dd, *J*=17.1, 10.8 Hz, C*H*=CH_2), 5.65 (1H, d, *J*=17.1 Hz, CH=C*H*H), 5.61 (1H, d, *J*=10.8 Hz, CH=CH*H*), 5.54 (1H, d, *J*=10.8 Hz, CH=CH*H*), 5.40 (1H, d, *J*=17.4 Hz, CH=C*H*H), 4.97 (1H, s, NC*H*), 4.31 (1H, d, *J*=11.8 Hz, NCH_2), 3.82 (1H, d, *J*=11.8 Hz, NCH_2), 3.69 (3H, s, OCH_3), 2.32 (3H, s, ArCH_3); δ_C (125 MHz, $CDCl_3$) 165.2, 161.1, 144.7, 133.2, 132.3, 129.4, 128.8, 127.7, 124.4, 124.0, 122.4, 121.8, 114.9, 113.8, 69.2, 55.9, 55.7, 54.4, 53.8, 21.9; ν_{max}/cm^{-1} (KBr): 2225, 1513, 1278, 1180; *m/z* (EI^+): 433 (M^+, 50%), 278 (59), 184 (41), 148 (100), 121 (38), 91 (41); found: (M^+) 433.1472, $C_{24}H_{23}N_3O_3S$ requires: 433.1460.

3.4.6. 1-(para-Toluenesulfonyl)-3,3-dicyano-2-(2-furyl)-5,5-divinylpyrrolidine ***14f***

White prisms; mp 102–104 °C; δ_H (300 MHz, $CDCl_3$): 7.45 (2H, d, *J*=8.1 Hz, Ar*H*), 7.30–7.20 (3H, m, Ar*H*), 6.44 (1H, d, *J*=3.3 Hz, Ar*H*), 6.32 (1H, dd, *J*=3.3, 1.8 Hz, Ar*H*), 6.07 (1H, dd, *J*=17.4, 10.8 Hz, C*H*=CH_2), 5.97 (1H, dd, *J*=17.4, 10.5 Hz, C*H*=CH_2), 5.64 (1H, d, *J*=17.4 Hz, CH=C*H*H), 5.64 (1H, d, *J*=10.5 Hz, CH=CH*H*), 5.55 (1H, d, *J*=10.8 Hz, CH=CH*H*), 5.41 (1H, d, *J*=17.4 Hz, CH=C*H*H), 5.18 (1H, s, NC*H*), 4.21 (1H, d, *J*=11.4 Hz, NCH_2), 3.82 (1H, d, *J*=11.4 Hz, NCH_2), 2.37 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$): 144.9, 144.3, 135.6, 132.7, 131.9, 130.2, 129.7, 127.3, 122.0, 121.7, 112.7, 111.4, 111.3, 111.0, 62.9, 55.8, 52.8, 51.3, 21.6; ν_{max}/cm^{-1} (KBr): 2356, 2339, 1357, 1164; *m/z* (EI^+): 393 (M^+, 7%), 238 (22), 108 (100), 91 (29); found: (M^+) 393.1152, $C_{21}H_{19}N_3O_3S$ requires: 393.1147.

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