Rh(II)-catalysed room temperature aziridination of homoallyl-carbamates†

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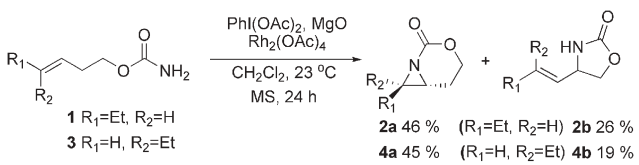
Rhodium(II) catalysts and PhIO in benzene convert homoallylic carbamates into the corresponding aziridines at room temperature.

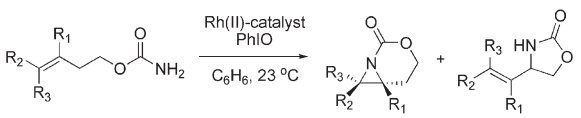
There has been a recent resurgence of interest in transition metal-catalysed amination reactions and it is now possible to effect efficient and highly selective 1,5- or 1,6-CH insertions under mild conditions using carbamate or sulfamate ester precursors respectively.[1] Du Bois' recent total syntheses of tetrodotoxin and manzacidin A[2] serve as excellent illustrations of what can be achieved using this new synthetic tool. Aziridination has also developed at a fast pace, with homoallyl-sulfamate esters being excellent precursors for this transformation.[3] Padwa,[3d,e] Rojas[4] and Lebel[5] have all reported studies on the catalytic aziridination and subsequent ring opening of allylic carbamates but the equivalent aziridination and ring opening of homoallyl-carbamates has been somewhat overlooked. Lebel *et al.* attempted this transformation on two substrates, but they found that 1,5-CH insertion was the only reaction pathway on one example and the second gave equal amounts of CH-insertion and aziridination. In this communication we wish to report reaction conditions for the room temperature aziridination of homoallylic carbamates, along with studies on regioselective aziridine-ring openings.

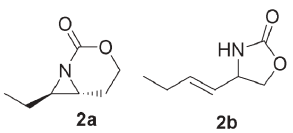
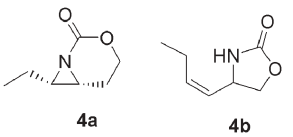
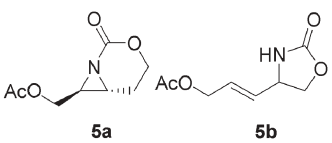
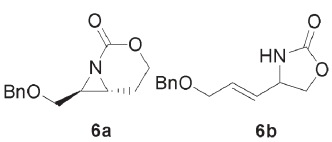
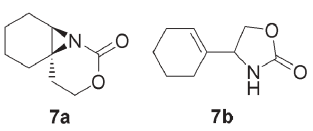
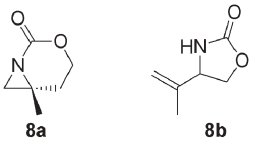
We first prepared the *E*- and *Z*-homoallyl-carbamates **1** and **3**, from the corresponding alcohols according to the procedure of Kocovsky,[6] and then subjected them to the previously developed CH-insertion conditions of Du Bois ($Rh_2(OAc)_4$, $PhI(OAc)_2$, CH_2Cl_2) (Scheme 1). Encouragingly, aziridination was favoured over the competing CH-insertion reaction pathway, and the transformation was stereospecific. We next examined the use of Padwa's iodosylbenzene-based conditions ($Rh_2(OAc)_4$, PhIO, CH_2Cl_2) that had been developed for aziridination of allylic carbamates, but no significant improvement was observed. During further optimization studies we found that replacing CH_2Cl_2 with benzene led to a significant improvement in aziridination (entries 1 and 5, Table 1) and these conditions were used on a range of other homoallyl-carbamates. We were pleased to see that the expected aziridines were formed as the major products in all cases (entries 9, 12, 14, 16, Table 1). The stereochemistry of the aziridine products was determined from the magnitude of the vicinal coupling constant between the two aziridine protons in the ^{1}H NMR spectrum.[7] We did not observe any aziridination under thermal



Scheme 1

Table 1 Rh(II)-mediated aziridination of homoallyl-carbamates[a]



Entry	Catalyst	% Yield	Products
1	$Rh_2(OAc)_4$	68 : 14	 **2a** **2b**
2	$Rh_2(Oct)_4$	71 : 6	
3	Rh_2(*S*-TBSP)$_4$	66 : 12	
4	Rh_2(*S*-MEOX)$_4$	0 : 40	
5	$Rh_2(OAc)_4$	58 : 18	 **4a** **4b**
6	$Rh_2(Oct)_4$	70 : 13	
7	Rh_2(*S*-TBSP)$_4$	71 : 13	
8	Rh_2(*S*-MEOX)$_4$	31 : 30	
9	$Rh_2(OAc)_4$	39 : 17	 **5a** **5b**
10	Rh_2(*S*-TBSP)$_4$	78 : 0	
11	Rh_2(*S*-MEOX)$_4$	0 : 33	
12	$Rh_2(OAc)_4$	31 : 8	 **6a** **6b**
13	Rh_2(*S*-TBSP)$_4$	66 : 0	
14	$Rh_2(OAc)_4$	26 : 5	 **7a** **7b**
15	Rh_2(*S*-TBSP)$_4$	60 : 0	
16	$Rh_2(OAc)_4$	35 : 5	 **8a** **8b**

[a] 2 equiv. PhIO, 0.05 equiv. Rh(II)-catalyst in benzene at 23 °C over 3 Å mol. sieves for 24 h.

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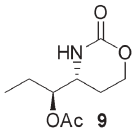
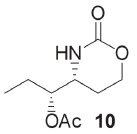
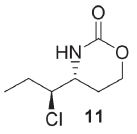
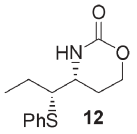
† Electronic supplementary information (ESI) available: Experimental procedures and analytical data for all new compounds. See DOI: 10.1039/b611662k

Table 2 Nucleophilic ring openings of aziridines

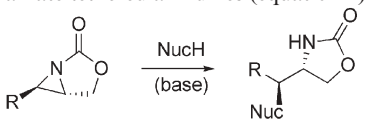
Entry	Starting Material	Conditions	% Yield	Product
1	**2a**	HOAc, THF	88	 **9**
2	**4a**	HOAc, THF	74	 **10**
3	**2a**	HCl, 1,4-dioxan, H_2O	62	 **11**
4	**4a**	PhSH, CH_2Cl_2	91	 **12**

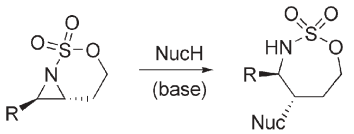
conditions (40–80 °C) in the absence of the Rh(II) catalyst, thus proving that this is a metal-catalysed process, and this is contrary to Padwa's observations in the allylic carbamate series.[3d,e]

We speculated that the heterogeneous nature of the reaction conditions contributed to the variability in isolated yield of the aziridines. In order to test this hypothesis we examined the use of $Rh_2(Oct)_4$ and $Rh_2(S\text{-TBSP})_4$ as catalysts due to their improved solubility in benzene.‡ Pleasingly, both catalysts gave reproducibly good yields of aziridines (entries 2, 3, 6, 7, Table 1), but $Rh_2(S\text{-TBSP})_4$ proved to be the better catalyst over a wider range of substrates (entries 3, 7, 10, 13, 15, Table 1). Enantiomeric excesses of between 1 and 23% were observed in the reactions using $Rh_2(S\text{-TBSP})_4$ and $Rh_2(S\text{-MEOX})_4$ as catalysts (please see supporting information for individual values), and work is underway to try and improve the asymmetric induction in these transformations. It is interesting to note that during our catalyst screen, we found that $Rh_2(S\text{-MEOX})_4$ tended to catalyse the competitive 1,5-CH-insertion reaction (entries 4 and 11, Table 1), thus demonstrating that the nature of the ligand is crucial in controlling the chemoselectivity of the reaction. Although most di- and tri-substituted alkenes underwent aziridination, we did find that terminal alkenes were generally poor substrates (*e.g.* entry 16, Table 1) and that α,β-unsaturated ketones failed to cyclise under any form of Rh(II)-catalysis.

In order to assess their future synthetic potential, a selection of the previously formed aziridines was exposed to a range of hetero-atom nucleophiles, and the results are summarized in Table 2.

Complete regioselectivity was observed in all ring-opening reactions, and stereochemical integrity was maintained during the course of the reactions. The regioselectivity observed in the [4,1,0]-carbamate-tethered aziridine ring opening reactions was the same as that observed for the related [3,1,0]-carbamate-tethered aziridine series (equation 1),[8,3d] but is complementary to that observed for [4,1,0]-sulfamate tethered aziridines (equation 2).[1b,e,3c]

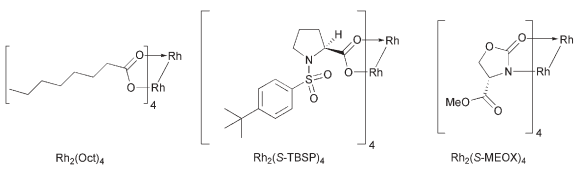

(1)


(2)

Our efforts are now directed towards the development of enantioselective variants of these transformations, and the results of these studies will be reported in due course.

Notes and references

‡ The commercially available catalysts $Rh_2(Oct)_4$, $Rh_2(S\text{-TBSP})_4$ and $Rh_2(S\text{-MEOX})_4$ have the following structures:



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7 As with other reported aziridine products, the *trans*-isomers have smaller coupling constants (J = 3–3.5 Hz) than the corresponding *cis*-isomers (J = 5–5.5 Hz).

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