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A Unique and Highly Efficient Method for Catalytic Olefin Aziridination

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Methods for the selective functionalization of unsaturated hydrocarbons through catalytic oxidation reactions are indispensable tools for chemical synthesis.[1] Olefin dihydroxylation and epoxidation rank foremost among such processes, having been advanced to exceptional levels of efficiency and product control.[2,3] Intensive efforts to develop protocols of comparable utility for the direct amination or aziridination of alkenes are motivated by the prevalence of nitrogen-containing functional groups in natural and synthetic products.[4−6] We describe herein a highly effective and broadly applicable method for the preparation of aziridines using a sulfamate ester, a Rh-carboxamide catalyst, and an inexpensive terminal oxidant (Figure 1).[7] Reactions are performed with limiting amounts of alkene substrate, conditions considered optimal but found to be atypical for previously reported metal-catalyzed aziridination strategies. In addition, the alkoxysulfonyl moiety serves as a convenient amine protecting group and may be readily excised from the aziridine ring-opened products. The operational simplicity of the aziridination protocol and the practical import of the alkoxysulfonylated aziridines should establish this method as a useful innovation for synthesis.

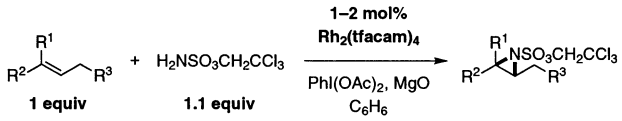
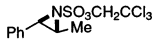
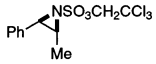
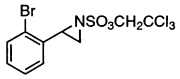
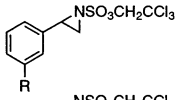
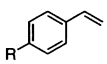
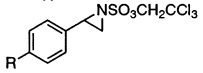
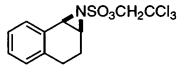
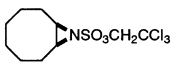
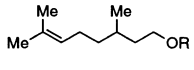
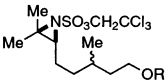
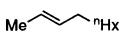
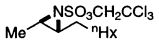
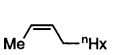
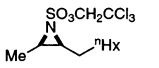
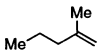
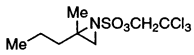


Figure 1. Rh-catalyzed alkene aziridination.

Early efforts in our lab demonstrated the unique reactivity of sulfamate esters, $PhI(OAc)_2$, and catalytic amounts ($\leq$2 mol %) of $Rh_2(OAc)_4$ for intramolecular C−H insertion reactions.[8] Concurrent with these studies, we had found that identical conditions could promote intramolecular alkene aziridination with exceptional efficiency.[9] The overall utility of this process being limited to homoallyl sulfamates, however, we wished to delineate protocols for intermolecular *N*-atom transfer to olefins. Accordingly, the crystalline trichloroethylsulfamate ester, $H_2NSO_3CH_2CCl_3$ **1**, was identified as an optimal nitrogen source because of its ease of preparation and its inability to undergo intramolecular C−H insertion. Also considered was the potential to excise the trichloroethoxysulfonyl group from the product under mild reductive conditions (e.g., Zn).[10]

A series of exploratory reactions with **1** and different dinuclear Rh^{2+} catalysts (2−5 mol %), including $Rh_2(OAc)_4$, $Rh_2(O_2CCPh_3)_4$, $Rh_2(acam)_4$, and $Rh_2(tfacam)_4$ (tfacam = CF_3CONH), showed the latter to be particularly effective for aziridination of *trans*-β-methylstyrene.[11] With a limiting amount of olefin and a slight excess of **1**, $PhI(OAc)_2$, and MgO, ^{1}H NMR analysis of the unpurified reaction mixture revealed only the desired product and small amounts of unreacted starting material. Subsequently, we have found that the same reaction can be performed with 1 mol % $Rh_2(tfacam)_4$ at 0.5 M in substrate to afford the *trans*-aziridine in 85% isolated yield (entry 1, Table 1).[12] These conditions are general for almost all of the substrates that have been tested to date.[13] The tetratrifluoroacetamide Rh-catalyst appears to be optimally tuned for this aziridination process and displays a strong bias for π-bond functionalization over σ-C−H insertion (entries 8−11).[7,8,14] Other tetracarboxamide complexes that have been sampled under our reaction conditions (e.g., $Rh_2(acam)_4$, $Rh_2(MEOX)_4$) are rapidly decomposed and give only trace amounts of product.

Table 1. Alkene Aziridination with Catalytic $Rh_2(tfacam)_4$

Entry	Substrate	Product		Yield[a]
1				85
2				85
3				79
4			R = H = NO_2	95 95
5			R = Me = Cl = NO_2	91 88 71
6				65[b]
7				82[c]
8			R = TBS = Ac	72[c] 72[c]
9				57[d]
10				72
11				72[c]
12				84

[a] All reactions were conducted at 0 °C in C_6H_6 with 1 mol % $Rh_2(tfacam)_4$, 0.5 mmol of olefin, and 0.55 mmol of **1** at 0.5 M [olefin] with the exception of entries 7, 8, 9, and 11. [b] Isolated yield is reduced due to product instability on SiO_2. [c] Performed with 2 mol % $Rh_2(tfacam)_4$. [d] Performed at 1.0 M [olefin] concentration.

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As highlighted in Table 1, aziridine formation proceeds in good yield with a range of structurally and electronically disparate alkenes. Importantly, aziridination is stereospecific with *trans*- and *cis*-β-methylstyrene and *trans*- and *cis*-2-decene substrates (entries 1, 2 and 9, 10). Such findings intimate a mechanism involving electrophilic Rh-nitrene transfer. This conclusion is supported further through a competition experiment between *p*-methyl and *p*-nitrostyrene, which shows that the former, electron-rich alkene is consumed preferentially. A similar reactivity trend is observed with nonstyrenyl olefins where the degree of π-bond substitution is found to influence reaction rates and, in some cases, product yields.

Alkoxysulfonylated aziridines perform as effective substrates in nucleophilic ring-opening reactions (Figure 2). Under ambient conditions, the styrenyl derivative **2** couples selectively and in high yield with PhSH, NaN_3, or $BnNH_2$. Addition of N_3^- or H_2O to trisubstituted aziridine **3** furnishes the corresponding *N*-alkoxysulfonylated aliphatic amines with similar efficacy. In general, the observed reactivity trends for both **2** and **3** seem to mirror those of analogous *N*-sulfonylated compounds.[6] We have found that removal

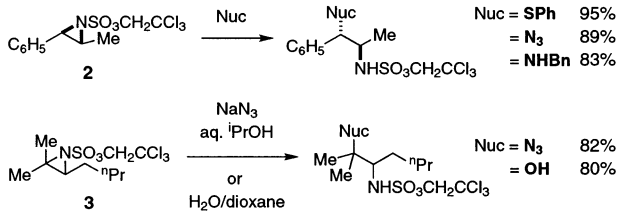
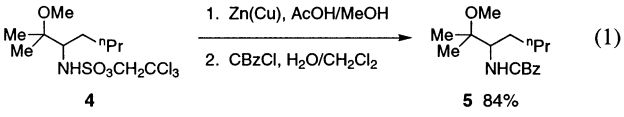


Figure 2. Addition reactions with alkoxysulfonyl aziridines.

of the alkoxysulfonyl group from aziridine-opened products is readily accomplished with Zn(Cu) in AcOH/MeOH followed by mild acid treatment (eq 1).[10] By employing these conditions, the amine hydrochloride salt is isolated in >95% purity. Conversion of this material to carbamate **5** facilitates subsequent purification by chromatography and yields the desired CBz-amine in 84% for the two-step sequence. The effectiveness of Zn(Cu) for sulfamate ester cleavage and generation of the free amine is an important and distinguishing feature of our aziridination method.



(1)

Sulfamate esters other than **1** as well as certain phosphoramidates function as competent nitrogen sources under our catalytic aziridination conditions (Figure 3). These reagents make possible

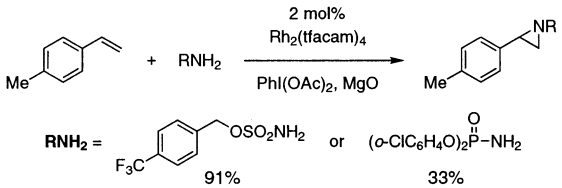


Figure 3. Olefin aziridination using modified RNH_2 agents.

the application of alternative strategies for *N*-deprotection following aziridine ring opening (e.g., H_2/Pd−C, acid catalysis).[15] Our preliminary findings indicate that reaction performance is highly responsive to steric and electronic modifications of the nitrogen source. Additionally, these disparate *N*-atom sources may prove useful for influencing product selectivity in asymmetric aziridination reactions. Such investigations are currently in progress along with continued efforts to examine the mechanism of this unique aziridination process.

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Supporting Information Available: Experimental details and analytical data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) Rh_2(tfacam)$_4$ is easily prepared from $Rh_2(OAc)_4$ and used without purification (see the Supporting Information for details). This complex has been synthesized previously, see: Dennis, A. M.; Korp, J. D.; Bernal, I.; Howard, R. A.; Bear, J. L. *Inorg. Chem.* **1983**, *22*, 1522−1529.
(12) Although reactions are generally performed in C_6H_6, CH_2Cl_2 and C_6H_5Cl can be used with little diminution in product yields.
(13) Reaction of the electron-deficient alkene, methyl *trans*-cinnamate (1 equiv), gives 54% of the desired aziridine using 4 mol % Rh_2(tfacam)$_4$ (C_6H_5Cl, −40 → 25 °C); see the Supporting Information for details. This yield compares favorably to a prior report for methyl cinnamate aziridination with 10 mol % $CuPF_6$, PhI═O, and RSO_2NH_2; see ref 5h.
(14) The only exceptions that we have found to date are cyclohexene and cyclopentene, which give ~1:1 and 2:1 mixtures of both the desired aziridine and the allylic insertion product, respectively.
(15) As an example, we have found that 1 atm H_2 (AcOH) is sufficient to cleave reductively the *p*-(trifluoromethyl)benzyloxysulfonyl group.

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