Platinum(II)-catalyzed intermolecular hydroamination of monosubstituted allenes with secondary alkylamines†

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A 1 : 1 mixture of (dppf)PtCl2 and AgOTf (5 mol%) catalyzed the intermolecular hydroamination of monosubstituted allenes with secondary alkylamines at 80 °C to form allyllic amines in good yield with selective formation of the E-diastereomer.

The transition metal-catalyzed addition of the N–H bond of an amine across a C–C multiple bond represents an attractive and atom economical approach to the synthesis of functionalized amines. Despite prolonged effort in this area, many of the possible permutations of catalytic hydroamination remain poorly developed. As one example, the intermolecular hydroamination of allenes with alkylamines remains problematic, which is unfortunate as this transformation represents a potentially expedient approach to the synthesis of allyllic amines. Group IV complexes catalyze the intermolecular hydroamination of allenes with alkylamines at elevated temperatures but form imines rather than allyllic amines. Palladium(II) complexes catalyze the intermolecular hydroamination of allenes with alkylamines, but these transformations are of extremely limited scope. More recently, cationic gold(1) phosphine4 and cyclic (alkyl)(amino)carbene5,6 complexes have been applied to the intermolecular hydroamination of allenes with secondary alkylamines. However, the former method was restricted to morpholine as a nucleophile while the latter required forcing conditions (130–165 °C) with monosubstituted allenes and/or simple dialkyl amines. Here we report an effective Pt(II)-catalyzed protocol for the intermolecular hydroamination of monosubstituted allenes with secondary alkylamines.

We have previously employed neutral platinum(II) mono(phosphine) complexes as catalysts for the intramolecular hydroamination of unactivated allenes with secondary alkylamines. Furthermore, Panunzi et al. have shown that alkylamines react with the platinum(II) π-allene complex (PPh3)PtCl2(η2-H2C=C=CMe2) to form zwitterionic platinum σ-alkenyl complexes (PPh3)PtCl2(η1-Me2C=CCH2NR3) that react with HCl to form allyllic ammonium chloride salts. Together these steps constitute a potential catalytic cycle for allene hydroamination. For these reasons, we targeted neutral platinum mono(phosphine) complexes as catalysts for the intermolecular hydroamination of allenes with alkylamines. Initial experiments were encouraging, and treatment of benzyl n-butyl amine with dimethyl 2,3-butadienylmalonate (1; 2 equiv.) catalyzed by a 1 : 1 mixture of PtCl2 and P(t-Bu)2biphenyl (5 mol%) in dioxane at 80 °C for 24 h led to isolation of allyllic amine 2a in 65% yield as a 4.7 : 1 mixture of E-Z isomers (eqn (1)). Unfortunately, subsequent modification of ligand led to no improvement in either the yield or the diastereoselectivity of hydroamination.

As an alternative to neutral mono(phosphine) complexes, we targeted cationic platinum bis(phosphine) complexes as catalysts for allene hydroamination. Although ultimately successful, an initial experiment employing benzyl n-butyl amine, 1 (2 equiv.), and a catalytic 1 : 1 mixture of (dppp)PtCl2 [dppp = 1,3-bis(diphenylphosphino)propane] and AgOTf led to no detectable formation of 2a (Table 1, entry 1). The effect of the natural bite angle ($\beta_1$) of a bidentate phosphine ligand on the efficiency and/or selectivity of transition metal-catalyzed transformations is well documented.10 For this reason, we evaluated the efficiency of platinum-catalyzed conversion of 1 to 2a as a function of phosphine bite angle. The effect was dramatic, and the yield of 2a increased from 0% to 88% as $\beta_1$ increased from 91° to $\geq 108^\circ$,11 although the E-Z selectivity followed no discernable trend (Table 1, entries 1–7). From this group of complexes, we targeted (dppf)PtCl2 [dppf = 1,1'-bis(diphenylphosphino)ferrocene] and (Nixanthphos)PtCl2 [Nixanthphos = 4,6-bis(diphenylphosphino)phenoxazine] for further evaluation, owing to the favorable combination of yield and diastereoselectivity realized with these precatalysts. Optimization with respect to solvent revealed that toluene provided higher yield of 2a without significant deterioration of diastereoselectivity (Table 1, entries 10 and 11).12

Employment of (dppf)PtCl2 or (Nixanthphos)PtCl2 as precatalysts allowed for the efficient hydroamination of allene 1 with a range of secondary alkylamines. The former generally provided superior yields and reaction of 1 with benzyl methyl amine, di-n-butyl amine, diethyl amine, morpholine, piperidine, or pyrrolidine catalyzed by a 1 : 1 mixture of (dppf)PtCl2 and AgOTf in toluene at 80 °C led to isolation of the corresponding allyllic amines 2b–2g in $\geq 78\%$ yield with $\geq 7.6 : 1$ E-Z diastereoselectivity (Table 2, entries 1–6). Alternatively, reaction of 1 with dibenzyl amine catalyzed by (Nixanthphos)PtCl2·AgOTf...
led to isolation of 2h in 66% yield as a 6.9 : 1 mixture of E-Z diastereomers (Table 2, entry 7). In addition, a number of aliphatic and aromatic monosubstituted allenes including n-octyl-, cyclohexyl-, benzyl-, phenyl-, and 2-naphthylallene underwent efficient hydroamination with benzyl n-butyl amine in the presence of (dppp)PtCl₂·AgOTf to form the corresponding allylic amines 2i–2m in good yield with ≥ 15 : 1 E-Z diastereoselectivity (Table 2, entries 8–12). Neither 1,1- nor 1,3-disubstituted allenes underwent efficient intermolecular hydroamination with benzyl n-butyl amine under these conditions.

Guided by the precedents of Panunzi et al.⁸,¹² and others¹³–¹⁶ we propose a mechanism for the platinum-catalyzed hydroamination of allenes with secondary alkylamines initiated by chloride abstraction from (P-P)PtCl₂ with AgOTf to initially form the cationic platinum amine complex I (Scheme 1).¹⁴ Displacement of the amine ligand of I with free amine would form cationic platinum π-allene complexes II. Although a number of platinum(ii) π-allene complexes are known,¹⁵,¹⁶ complexes of monosubstituted allenes are not among them and hence, the preferred binding mode of monosubstituted allenes to Pt(ii) is not known. However, platinum π-allene complexes are known to undergo intramolecular exchange of all four possible allene π-faces, presumably via an η¹-allene intermediate or transition state.¹⁵,¹⁷ Therefore, preferential outer-sphere addition of amine to the unsubstituted allene terminus of platinum π-allene isomer cis-II would lead to selective formation of platinum σ-alkenyl complex (Z)-III. A control experiment ruled out Z-E isomerization of the allylic amine under reaction conditions.⁹ Protonolysis of the Pt-C bond of (Z)-III could occur through a number of pathways. As one possibility, deprotonation of the ammonium moiety of (Z)-III with free amine followed by intermolecular protonolysis of the Pt-C bond of the resulting neutral

σ-alkenyl complex IV with ammonium salt would release allylic amine 2 with regeneration of I (Scheme 1).

In summary, we have developed a platinum(ii)-catalyzed protocol for the intermolecular hydroamination of monosubstituted allenes with secondary alkylamines to form allylic amines in good yield with selective formation of the E-diastereomer. We are currently working toward the development of more general and more effective hydroamination protocols that employ alkylamines as nucleophiles.

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Notes and references

† Experimental procedure: a suspension of (dpff)PtCl₂ (8.2 mg, 0.010 mmol), AgOTf (2.6 mg, 0.010 mmol), ferrocene (3.7 mg, 0.020 mmol; internal standard), benzyl n-butyl amine (36 µL, 33 mg, 0.20 mmol) and 1 (74 mg, 0.40 mmol) in toluene (0.4 mL) was heated at 80 °C for 24 h. Column chromatography of the crude reaction mixture (SiO₂ pretreated with Et₃N; hexanes–EtOAc = 9 : 1) gave 2a (pale yellow oil, 56 mg, 81%) as a 10 : 1 mixture of E and Z diastereomers.
§ Control experiments ruled out the significant contribution of acid- or silver-catalyzed pathways to the intermolecular hydroamination of 1 and benzyl n-butyl amine (see ESI†).
* Treatment of a 3.9 : 1 E-Z mixture of 2b with a catalytic 1 : 1 mixture of (dpff)PtCl₂ and AgOTf in toluene at 80 °C for 24 h led to no detectable change in the E/Z ratio.