

Synthetic Methods

An Intermolecular Palladium-Catalyzed Diamination of Unactivated Alkenes**

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Dedicated to Professor José Barluenga on the occasion of his 70th birthday

1,2-Diamines represent a functional group in organic chemistry, which commonly is not conceived in a direct manner, but rather through a combination of several synthetic steps.^[1] An attractive route to vicinal diamines consists of the direct oxidative transformation of alkenes.^[1d,2–7] Recently, this reaction has been investigated intensively using palladium catalysts.^[3,4] While the diamination of butadienes and related processes involving allylic and homoallylic C–H activation events^[5] have been developed to a large extent, the corresponding direct oxidation of alkenes has only become available for intramolecular processes.^[6,7] We report herein the first general intermolecular 1,2-diamination of unactivated alkenes employing high-oxidation-state palladium catalysis.^[8,9]

Initial attempts to realize an intermolecular diamination tried to make use of the privileged role of phthalimide as a nitrogen source in palladium-catalyzed oxidation chemistry.^[10,11] However, it quickly became evident that for the present case this compound is not suited in combination with several nitrogen-based oxidants such as N-bromosuccinimide (NBS), chloramine-T, N-fluorobis(phenylsulfonyl)imide, or hypervalent iodo derivatives. In contrast to phthalimide, the use of saccharin as the nitrogen source led to the long-sought break-through (Table 1), when working with 1-octene as alkene in the presence of iodobenzene dicarboxylates as oxidants.^[12] The reaction was developed on a 1 mmol scale for preparative reasons, and the alkene was the limiting agent. Attempts to work with saccharin as the only nitrogen source were not productive (Table 1; entries 1 and 2) and with a palladium dichloride catalyst led exclusively to enamide formation.^[13] This outcome verifies saccharin as an efficient nitrogen source for aminopalladation. If a further 1.5 equivalents of bistosylimide are added, this is selectively incorporated into the products as the second nitrogen source. This

Table 1: Optimization of the intermolecular diamination.

Entry	Pd ^{II} Salt	Equiv HNTos ₂	Oxidant R =	Conversion [%] ^[a]
1 ^[b]	Pd(OAc) ₂	0	Me	n.d. ^[c]
2 ^[b]	[Pd(NCMe) ₂ Cl ₂]	0	Me	68 ^[d]
3	Pd(OAc) ₂	1.5	Me	n.d.
4	[Pd(O ₂ CCF ₃) ₂]	1.5	Me	n.d.
5	[Pd(NCMe) ₂ Cl ₂]	1.5	Me	37
6 ^[e]	[Pd(NCMe) ₂ Cl ₂]	1.5	Me	n.d.
7	[Pd(NCMe) ₂ Cl ₂]	1.3	tBu	60
8	[Pd(NCPh) ₂ Cl ₂]	1.3	tBu	95 (74) ^[f]
9 ^[g]	[Pd(NCPh) ₂ Cl ₂]	1.3	tBu	95 (74) ^[f]
10 ^[h]	[Pd(NCPh) ₂ Cl ₂]	1.3	tBu	95 (74) ^[f]
11	No Pd Salt	1.3	tBu	0

[a] Estimated from the ¹H NMR spectrum of the crude reaction mixture. [b] Reaction with 2 equivalents of saccharin. [c] n.d. = not determined, less than 5% conversion. [d] Enamide product. [e] In the presence of 2 equivalents of NaOAc. [f] Yield of isolated product in parentheses. [g] Reaction at room temperature. [h] With 5 mol% catalyst. Tos = toluene-4-sulfonyl.

reaction again requires bis(acetonitrile)palladium dichloride as the catalyst source (Table 1; entry 5), while related acetate and trifluoroacetate salts are completely unreactive (Table 1; entries 3 and 4). Aminoacetoxylation products as known for reactions with phthalimide^[11a] were not obtained at all. Addition of a base was found to inhibit the reaction completely (Table 1; entry 6). Yields can be further increased upon changing iodobenzene diacetate for iodobenzene dipivalate and by use of the benzonitrile complex [Pd-(NCPh)₂Cl₂] (Table 1; entries 7 and 8). Finally, the catalyst loading and the amount of bistosylimide can be decreased to 5 mol% and 1.3 equivalents, respectively, and the temperature lowered to room temperature (Table 1; entries 9 and 10). No conversion takes place in the absence of the palladium salt (Table 1; entry 11).

A series of terminal alkenes is converted into the corresponding diamines under these reaction conditions with saccharin and bistosylimide as nitrogen sources. All of these reactions proceed with high chemoselectivity and complete regioselectivity. Representative examples are depicted in Table 2.

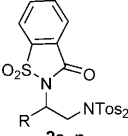
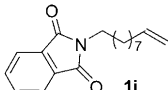

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Table 2: Intermolecular palladium-catalyzed diamination of alkenes.^[a]

$\text{R}-\text{CH}=\text{CH}_2$ <p>1a–n</p>		$\text{Pd}(\text{NCPH})_2\text{Cl}_2 \text{ (5 mol\%)} \\ \text{Saccharin (1.1 equiv)} \\ \text{HNTos}_2 \text{ (1.3 equiv)} \\ \text{PhI}(\text{O}_2\text{CtBu})_2 \text{ (1.1 equiv)} \\ \text{CH}_2\text{Cl}_2, \text{RT, 3–16 h}$	 <p>2a–n</p>	
Entry	Alkene	Product	Yield [%] ^[b]	
1	1-octene (1a)	2a : $n=4$	74	
2	1-hexene (1b)	2b : $n=2$	73	
3	1-decene (1c)	2c : $n=6$	76	
4	1-duodecene (1d)	2d : $n=8$	87	
5 ^[b]	4-phenylbutene (1e)	2e	82	
6 ^[b]	vinylcyclohexane (1f)	2f	78	
7 ^[b,c]	3-methylhexene (1g)	2g/2g'	93 ^[d]	
8	$\text{MeO}_2\text{C}-\text{CH}_2-\text{CH}=\text{CH}_2$ (1h)	2h	72	
9	 (1i)	2i	67	
10	11-bromoundecene (1j)	2j	94	
11	7-bromoheptene (1k)	2k	87	
12	7-azidoheptene (1l)	2l	90	
13	 (1m)	2m	35	
14	2-allyl diethylmalonate (1n)	2n	40	

[a] Reactions on a 1 mmol scale. [b] Yield of isolated product. [c] With 10 mol% of catalyst, 1.5 equivalents of oxidant, 2 equivalents of bisulfonimide. [d] 3:2 ratio of diastereomers. HNSacc = saccharin.

At the outset, the oxidation of simple alkenes with hydrocarbon substituents including a 3,3-disubstitution pattern were investigated, all of which led to regio and chemo-selective diamination reactions in good yields (Table 2; entries 1–6). Enamide formation is less than 15% in all cases, which demonstrates that the competing β -hydride elimination pathways are efficiently disabled under the chosen oxidation conditions.^[8] The chiral 3-methylhexene **1g** is converted into a 3:2-mixture of the two corresponding diastereomeric diamines **2g/2g'** in high yield (Table 2; entry 7). Common functional groups, such as esters, amides, halogenides, azides, and sulfones are all tolerated under these reaction conditions (Table 2; entries 8–13). Finally, the allyl

malonate **1n** gives rise to the corresponding diamine **2n** with acceptable yield (Table 2; entry 14). These examples constitute the first palladium-catalyzed intermolecular diamination of simple alkenes and the first to use commercially available nitrogen sources^[14] for the construction of noncyclic vicinal diamine derivatives. The catalyst loading of 5–10 mol% remains relatively high, but compares well with respect to related alkene oxidation reactions.^[9,11] Internal alkenes do not react under these conditions.

All products **2a–n** display spectroscopic data in agreement with the expected vicinal diamine motif, this was unambiguously confirmed by an X-ray structure determination of derivative **2f** (Figure 1).

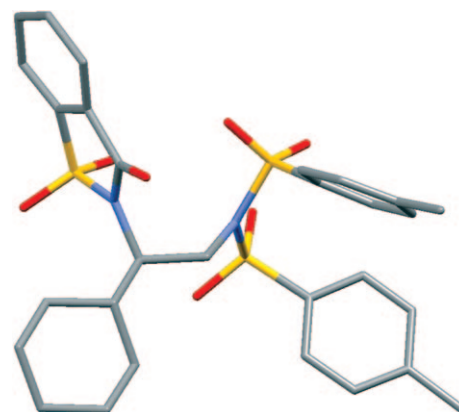
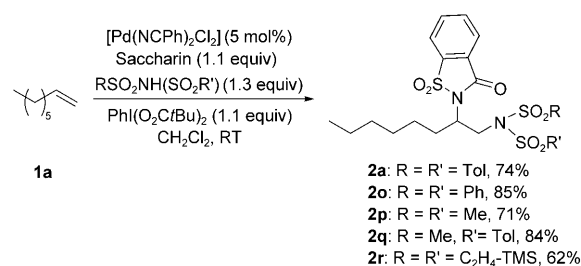


Figure 1. X-ray structure of **2f** C gray, N blue, O red, S yellow.

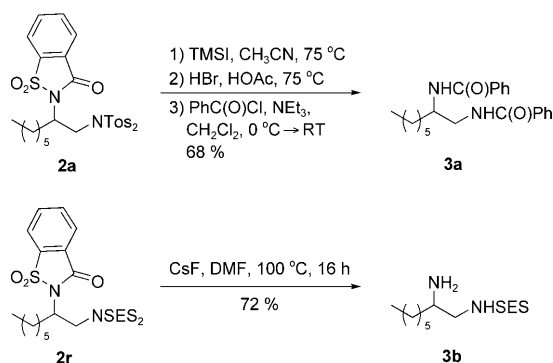
The reaction can also be conducted with bisulfonimides other than bistosylimide. Scheme 1 shows some examples of imides of the type $(\text{RSO}_2)_2\text{NH}$ in the vicinal diamination of 1-octene.



Scheme 1. Regioselective diamination of 1-octene with different bisulfonimides as the nitrogen source; TMS = trimethylsilyl, Tol = tolyl.

For the standard product **2a**, the deprotection of the two amino groups proceeds under acidic conditions (Scheme 2), and the free diamine was converted into the bisbenzoylamide **3a** to allow for a suitable confirmation of identity. Interestingly, treatment of the di-SES-derivative **2r** with an excess of cesium fluoride, not only leads to selective removal of one of the SES groups,^[15] but complete removal of the saccharin group to give the free primary amine **3b** was accomplished.

To conclude, we have developed the first palladium-catalyzed intermolecular diamination of non-activated termi-



Scheme 2. Deprotection of the diamination products **2a** and **2r**. SES = 2-trimethylsilylethyl.

nal alkenes. The reaction employs two commercially available nitrogen sources and proceeds with complete regioselectivity under very mild conditions. In contrast to earlier alkene diamination reactions,^[1,2,5,6] the current method no longer requires any intramolecular reaction steps. We are currently investigating the extension of this reaction to other classes of alkenes and nitrogen sources.

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