CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201103435

An Approach to the Regioselective Diamination of Conjugated Di- and Trienes

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The direct addition of two nitrogen groups onto 1,3-butadienes constitutes a convenient approach toward higher functionalized dinitrogenated molecules.[1] This reaction has been developed by using a series of metal promoters and can proceed with different regioselectivity depending on the reaction conditions.[2] In a pioneering demonstration, Sharpless et al. reported the use of stoichiometric amounts of bisimidoselenium compounds for the 1,2-diamination of 1,3-dienes.[3] In the area of palladium chemistry, Bäckvall et al. introduced a regioselective 1,4-addition reaction,[4,5] while Lloyd-Jones, Booker-Milburn, and Bar demonstrated that the related 1,2-addition can be carried out under catalytic conditions with ureas as the nitrogen source.[6,7] An elegant body of work by Shi et al. demonstrated that diaziridinones and related nitrogen sources can be employed in the regioselective 1,2-diamination of conjugated butadienes and hexatrienes under palladium and copper catalysis, respectively.[8,9]

Very recently, we discovered an unprecedented intermolecular diamination of styrenes by using either a combination of iodosobenzene diacetate ($PhI(OAc)_2$) and bistosylimide (Ts_2NH), in a 1:2 ratio, or a new hypervalent iodine(III) reagent, $PhI(OAc)(NTs_2)$, in combination with an additional equivalent of Ts_2NH.[10] In general, hypervalent iodine(III) reagents are known to effectively oxidize organic molecules[11] and can be used for the construction of carbon–nitrogen bonds under attractive metal-free conditions.[12] The unprecedented ability of the new I^{III} reagent $PhI(OAc)(NTs_2)$ in diamination reactions prompted us to investigate the related diamination reactions of conjugated dienes and trienes under metal-free conditions, pursuing different regio- and stereoselectivity. The initial results of this study are reported herein and include examples of selective 1,4-diamination reactions of conjugated dienes.

By applying the conditions from the diamination of styrenes[10] to 1-phenyl butadiene (**1a**), the regioselective 1,2-diamination of the terminal alkene was accomplished in high yield (Table 1). The reaction can be conducted readily at room temperature without requiring an inert atmosphere or the use of dry solvents. Several different bisimido sources were examined in this transformation, all of which provided good yields of the corresponding diamination products **2**, although a slightly better result was obtained with Ts_2NH (Table 1, entries 1–6) and this nitrogen source was subsequently employed for further reactions. If Ms_2NH (Ms = mesyl) was used as the nitrogen source, preformation of the reactive I^{III}–N species was required to achieve a good yield (Table 1, entries 3 vs. 4).

Unexpectedly, if the reaction was performed with a mixture of the *E*- and *Z*-stereoisomers of **1a**, a similar result to reactions with geometrically pure starting materials was obtained and the final product was again the (*E*)-configured vicinal diamine **2a** (Table 1, entries 7 and 8). This apparent tolerance for geometric mixtures was found to be a general feature of the reaction. Thus, substrates **1b**–**d**, with different *para* substituents on the arene, were prepared as mixtures of (*E*)- and (*Z*)-isomers and submitted to the same reaction conditions (Table 1, entries 9–12). The products with exclusively the *E* configuration at the remaining double bond were again obtained for both bistosylimide and bismesylimide as the nitrogen source. Finally, a mixture of (*E*)- and (*Z*)-1-(2-naphthyl)-1,3-butadiene **1e** was separated and both stereoisomers were independently submitted to the diamination reaction. As expected, the identical product (*E*)-**2e** was obtained from both reactions with very similar yields (Table 1, entries 13 and 14).

Consequently, the corresponding internal 1,3-butadiene **1f**, as a mixture of its (1*E*,3*E*)- and (1*E*,3*Z*)-isomers, also led to a single product **2f** (Table 1, entry 15). The expected (*E*)-geometry and *trans* stereochemistry of **2f** were confirmed by X-ray analysis (Figure 1).[13] Replacing the methyl substituent with an electron-demanding ester functionality allows invertion of the regioselectivity of the reaction to the other double bond of the conjugated system (Figure 1). Nevertheless, the reaction remains selective in favor of a vicinal diamination and the stereoselectivity in **2g** also remains *trans* (Table 1, entries 16 and 17, Figure 1), even though the overall reaction rate diminishes and the reaction requires an increase in temperature and an excess of the diamination reagent to reach full conversion. It is interesting

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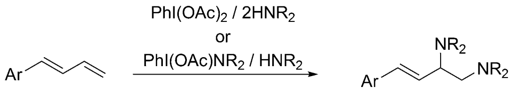
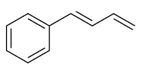
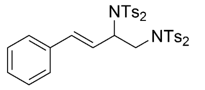
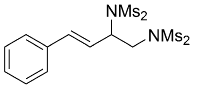
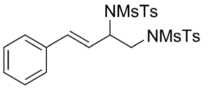
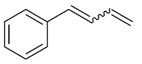
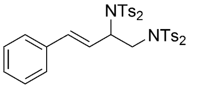
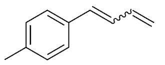
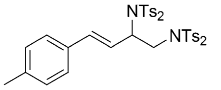
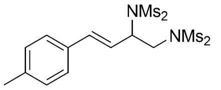
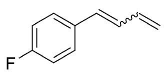
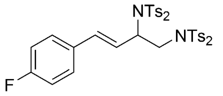
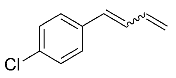
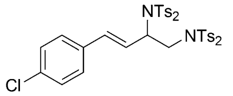
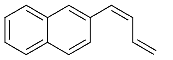
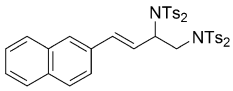
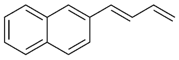
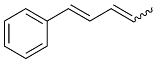
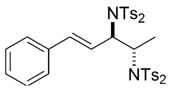
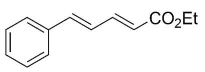
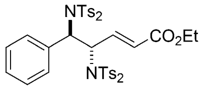
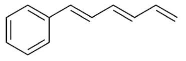
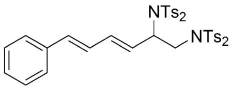
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201103435.

Table 1. Vicinal diamination of 1-aryl-substituted butadienes.



Entry	Substrate		R_2NH	Product		Conditions[a]	Yield [%][b]
1		**1a**	Ts_2NH		**2a**	A	73
2						B	75
3			Ms_2NH		**2aa**	A	35
4						B	66
5			MsTsNH		**2ab**	A	62
6						B	64
7		**1a** (*E*/*Z*=1:1.4)	Ts_2NH		**2a**	A	72
8						B	71
9		**1b** (*E*/*Z*=1:1.5)	Ts_2NH		**2b**	A	40
10			Ms_2NH		**2ba**	B	59
11		**1c** (*E*/*Z*=1:1.5)	Ts_2NH		**2c**	A	72
12		**1d** (*E*/*Z*=1:1.7)	Ts_2NH		**2d**	A	73
13		(*Z*)-**1e**	Ts_2NH		**2e**	A	65
14		(*E*)-**1e**				A	67
15		**1f** (*E*/*Z*=1:1.4)	Ts_2NH		**2f**	A	71
16[c]		**1g**	Ts_2NH		**2g**	A	23[e]
17[c]						B[d]	64
18		**1h**	Ts_2NH		**2h**	A	61
19						B	65

[a] Conditions A: butadiene (0.5 mmol), $PhI(OAc)_2$ (0.6 mmol), bissulfonylimide R_2NH (1.2 mmol), CH_2Cl_2 (1.5 mL), RT, 12 h. Conditions B: butadiene (0.5 mmol), $PhI(OAc)(NR_2)$ (0.6 mmol), R_2NH (0.6 mmol), CH_2Cl_2 (1.5 mL), RT, 12 h. [b] Isolated yield after column chromatography. [c] Relative stereochemistry of the product was confirmed by X-ray analysis. [d] Double the amount of $PhI(OAc)(NR_2)$ and R_2NH (1.2 mmol) was used at 50 °C for 48 h to achieve full conversion. [e] Starting material (45 %) was recovered.

to compare this unprecedented reactivity with the established metal-catalyzed *syn*-diamination as it provides complementary regio- and stereoselectivity for cases related to **1a** and **1g**.[8a]

Finally, the selective diamination of a conjugated triene was also found to be feasible. In a similar manner to the case of 1-aryl-substituted 1,3-butadienes, the (1*E*,3*E*)-1-phenyl-1,3,5-hexatriene **1h** underwent regioselective terminal oxidation to the vicinal 1,2-diamination product **2h** (Table 1, entries 18 and 19).

The observed selective formation of vicinal diamines was found to be the consequence of the aromatic substituent in substrates **1a**–**g**. When investigating 1,3-butadiene, the simplest substrate, the oxidation was technically challenging and was best carried out with an excess of butadiene as the feedstock and by using the oxidant as the limiting factor. As a result, reactions in the presence of the preformed iodine(III) reagents $PhI(OAc)(NTs_2)$, $PhI(OAc)(NMs_2)$, and PhI(OAc)(NTsMs) were superior to the in situ conditions (Table 2, entries 1–5). The products were obtained as mixtures of 1,2- and 1,4-diamines. Importantly, for substituted butadienes, exclusively 1,4-diamination occurs (Figure 2). This is a noteworthy feature of these reactions as selective 1,4-diamination represents an unsolved challenge in the area. For example, 2-methyl butadiene leads to an 84 % overall yield of two isomers, which are isolated in a 2:1 ratio (Table 2, entry 6). 2,3-Dimethyl butadiene gives a 1:1 mixture of two isomeric 1,4-oxidation products (Table 2, entry 7, Figure 2), whereas the rigid substrate **1l** leads to selective product formation (Table 2, entry 8). Performing this reaction with preformed $PhI(OAc)(NTs_2)$ allowed the reaction to be run on a 10 mmol scale (Table 2, entry 9). Importantly, oxidation of the conjugated hexatriene **1m** led to unprecedented 1,6-diamination product **2m** in very good yield (Table 2, entry 10).

A mechanistic scenario for the observed diamination reactions is reminiscent of that for the related diamination of styrenes.[10] It starts with an electrophilic interaction between the sterically more accessible double bond of the butadiene and the hypervalent iodine center (Scheme 1). The resulting

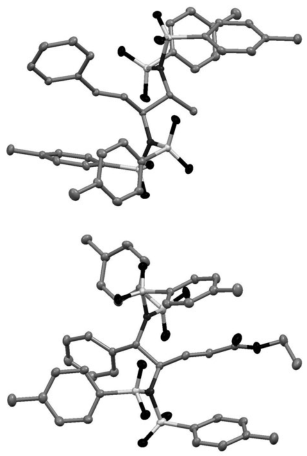


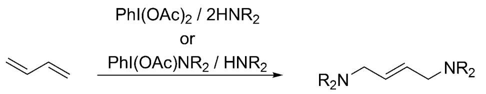
Figure 1. X-ray structures of 1,2-diamination products **2f** (top) and **2g** (bottom).[13]

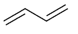
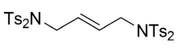
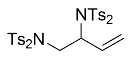
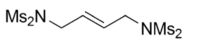
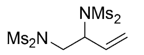
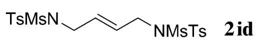
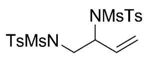
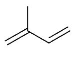
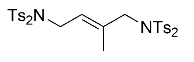
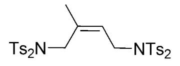
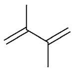
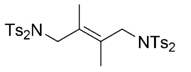
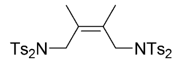
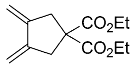
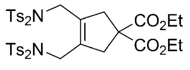
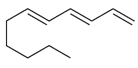
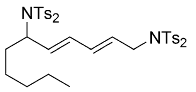
three-membered ring intermediate **A** undergoes regioselective opening by the bissulfonimide anion at the less hindered position. The resulting allylic iodine(III) intermediate **B** undergoes protolytic loss of acetic acid to form **C**, followed by loss of iodobenzene. The subsequent allylic intermediate **D** explains the independence from the original double-bond geometry observed in the product.[14] It then combines with bissulfonimide, the positioning of which will depend on the electronic situation. For aryl substituents, 1,2-diamination results in the formation of the more stable styrene derivatives, whereas terminal addition, leading to 1,4-diamination products, results from reduced steric hindrance. For nonterminal butadienes, such as **1f**, the same steps give a related racemic intermediate **B′**, which leads to an allylic intermediate **D′**, for which the final *anti*-stereochemistry arrives from a C−N bond formation that is guided by the existing stereocenter.[15]

The synthetic utility of the obtained products was investigated in two preliminary transformations. First, simple treatment with potassium hydroxide allows for selective removal of one sulfonyl group from each N atom in products **2aa** and **2ia** (Scheme 2). The product **4** can be further manipulated through a metathesis reaction to yield γ,δ-diamino acid derivative **5**, which could not be accessed directly from diamination of the corresponding butadiene (Scheme 2).

In summary, we have described unprecedented diamination reactions of butadienes and hexatrienes. These reactions employ easily accessible hypervalent iodine(III) reagents under robust conditions. The reactions represent the first examples of the metal-free diamination of butadienes and extend this oxidation methodology to the highly attractive 1,4 installation of two nitrogen atoms within a single step.

Table 2. 1,4-Diamination of butadienes.



Entry	Substrate		R$_2$NH	Product(s)				Conditions[a]	Yield [%][b]
1[c]		**1i**	Ts$_2$NH		**2i**		**2ia**	A	25 (1:1.3)
2[c]								B	73 (1:1.3)[d]
3[c]			Ms$_2$NH		**2ib**		**2ic**	B	20 (1:1.4)
4[c]								B[e]	81 (1:1.4)
5[c]			MsTsNH		**2id**		**2ie**	B	71 (1:1.3)
6[f]		**1j**	Ts$_2$NH		**2j**		**2ja**	A	84 (2:1)
7[g]		**1k**	Ts$_2$NH		**2k**		**2ka**	A	82 (1:1)
8		**1l**	Ts$_2$NH		**2l**			A	81
9								B[h]	80
10		**1m**	Ts$_2$NH		**2m**			A	60

[a] Conditions A: butadiene (0.5 mmol), PhI(OAc)$_2$ (0.6 mmol), bissulfonylimide R$_2$NH (1.2 mmol), CH$_2$Cl$_2$ (1.5 mL), RT, 18 h. Conditions B: butadiene (0.5 mmol), PhI(OAc)(NR$_2$) (0.6 mmol), R$_2$NH (0.6 mmol), CH$_2$Cl$_2$ (1.5 mL), RT, 18 h. [b] Isolated yield after column chromatography. [c] With an excess of condensed 1,3-butadiene, the yield is based on the I^{III} reagent. [d] NMR spectroscopic ratio of the two regioisomers. [e] Reaction was performed at 40 °C for 48 h. [f] Stereochemistry of the product was determined by NOESY experiments. [g] Stereochemistry of the product was confirmed by X-ray analysis.[13] [h] Reaction was performed on a 10 mmol scale.

Experimental Section

Representative example of the diamination of butadienes by using the preformed reagent PhI(OAc)(NR$_2$): A suspension of PhI(OAc)(NR$_2$) (0.6 mmol) and the bissulfonylimide (0.6 mmol) in dichloromethane (1 mL) was stirred for 5 min. A solution of the butadiene (0.5 mmol) in dichloromethane (0.5 mL) was then added through a syringe. The mixture was stirred at the indicated temperature for 12 h. The resulting mixture was purified by silica gel column chromatography (ethyl acetate/hexane) to afford the products as white solids.

Acknowledgements

The authors thank the Fundación ICIQ, the Consolider INTECAT 2010 (Project CSD2006–0003), and the Fonds der Chemischen Industrie for financial support, and Dr. E. C. Escudero, Dr. M. Martínez, and Dr. E. Martin for the crystal structure analyses. A.L. is a doc-

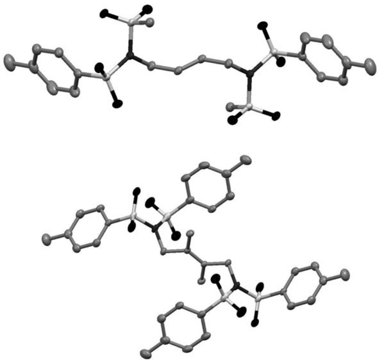
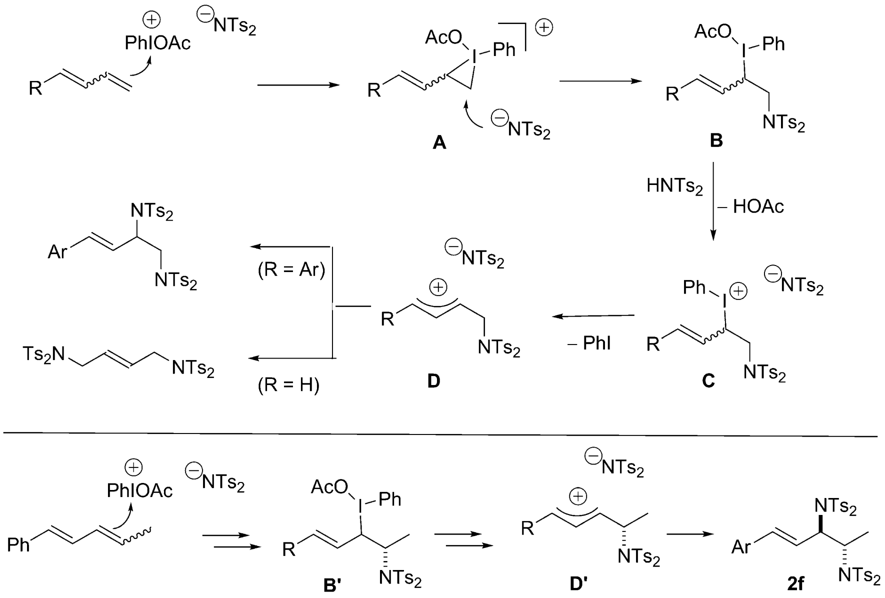
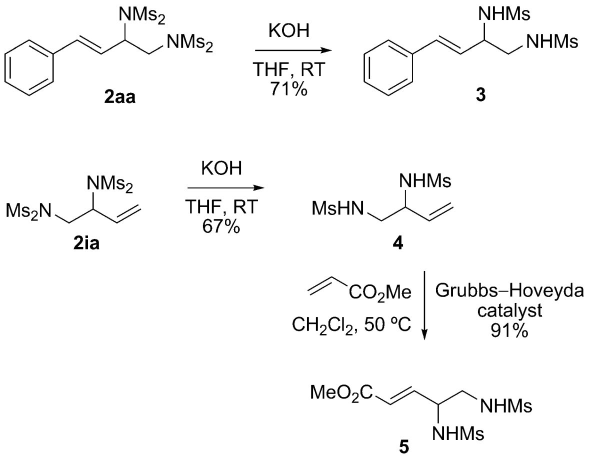


Figure 2. X-ray structures of 1,4-diamination products **2id** (top) and (*E*)-**2k** (bottom).[13]



Scheme 1. Mechanistic pathways for the 1,2- and 1,4-diamination reactions.



Scheme 2. Transformations of the diamination products.

toral student on leave from Strasbourg University and thanks the French MESR for a predoctoral fellowship.

Keywords: amines · amination · butadienes · diamination · iodine · oxidation

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[14] Furthermore, this provides the reason that attempts to find an enantioselective reaction by using a chiral iodine(III) derivative have so far met with no success. For example, a previously employed reagent derived from lactic acid leads to only a 4% *ee* in the diamination of **1a**.

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Received: November 1, 2011
Revised: December 18, 2011