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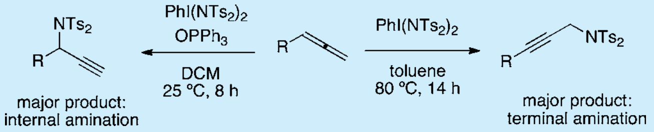
Hypervalent Iodine Mediated Oxidative Amination of Allenes

Nibadita Purkait,[†] Sota Okumura,[†] José A. Souto,[†] and Kilian Muñiz*,[†,‡]

[†]Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans 16, 43007 Tarragona, Spain
[‡]Catalan Institution for Research and Advanced Studies (ICREA), Pg. Lluís Companys 23, 08010 Barcelona, Spain

Supporting Information

ABSTRACT: An oxidative amination of allenes using a single hypervalent iodine reagent is reported. The reaction proceeds very efficiently for monosubstituted allenes and leads to formation of the corresponding propargylic amines, either as the internal or as the terminal amine. The respective reaction outcome could be influenced in favor of the former product by addition of triphenylphosphine oxide to the iodine(III) reagent.



We have recently been interested in the development of new oxidative amination reactions of unsaturated hydrocarbons using conceptually new hypervalent iodine reagents such as **1** with transferable nitrogen groups.[1,2] The *portefeuille* of metal-free aminative transformations using this reagent include diamination reactions of alkenes[3] and 1,3-butadienes,[4] allylic amination reactions,[5] the C−H amination of terminal acetylenes,[6] and the conversion of silyl enol ethers into α-aminated ketones[2] (Figure 1). Within our aim to further explore the potential of such amination reactions, we turned our attention to allenes.

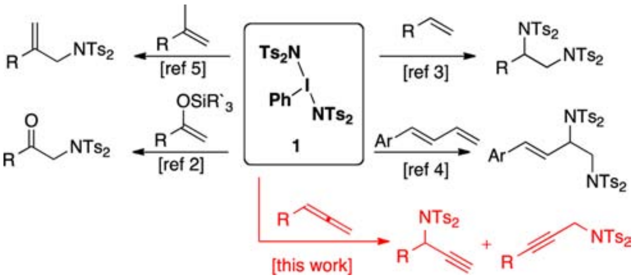


Figure 1. Iodine(III)-promoted amination reactions of hydrocarbon substrates with reagent **1**.

Allenes constitute the simplest class of cumulenes, and due to their inherent unsaturation over three consecutive carbon atoms they provide a comparably higher reactivity than alkenes or alkynes.[7,8] As a result, recent years have witnessed a rapid growth in the synthetic development of new allene transformation reactions.[7,9]

Despite the unique reactivity pattern of allenes, we are aware of only a single report of their use as substrates in hypervalent iodine mediated oxidation.[10] In 1992, Moriarty reported the oxygenation of polarized 1-alkoxyallenes to carbonyl products within a clean oxidation reaction.[11,12] We herein report our efforts to develop a new oxidative amination reaction of allenes based on the hypervalent iodine reagent **1**.

We chose phenyl allene **2a** as a standard substrate for an exploration on the oxidation behavior of several hypervalent iodine reagents. Attempts to realize oxygenation reactions using (diacetoxy)iodobenzene $PhI(OAc)_2$ or iodosobenzene PhIO led to no conversion of the allene, while bis(trifluoroacetoxy)iodobenzene $PhI(O_2CCF_3)_2$ or Koser's reagent PhI(OH)OTs led to either degradation or formation of a complex mixture of products, respectively.[13] Gratifyingly, use of the preformed reagent bis(ditosylimido)iodobenzene $PhI(NTs_2)_2$ **1** enabled the realization of a new oxidative amination of allene **2a** (Table 1). An initial reaction between **1** and **2a** in dichloroethane at elevated temperature gave the two regioisomeric products **3a** and **4a** in a 63:37 ratio (entry 1). The presence of free bistosylimide enhanced this ratio to 4:1, while the presence of base did not change the initial outcome (entries 2,3). Attempts to combine bistosylimide with (diacetoxy)iodobenzene, Koser's reagent, or iodosobenzene led to no conversion (entries 4−6), while use of the preformed compound $PhI(NTs_2)(OAc)$[3a,b] resulted in uncontrolled decomposition of the allene (entry 7). A reaction between **1** and **2a** in toluene at 80 °C resulted in a good yield of 62% with a reversal in regioselectivity in favor of product **4a** (entry 8). Other solvents such as acetonitrile, ethyl acetate, and chloroform showed related reaction outcomes as initially obtained (entries 9−11 vs entry 1), while hexane did not promote any reactivity (entry 12). Introduction of base completely shut down the reaction (entry 13). Finally, an improved selectivity in favor of **3a** could be obtained from a room temperature reaction in dichloromethane (entry 14). With triphenylphosphine oxide as an additive, the ratio between **3a** and **4a** was further enhanced to a synthetically useful 92:8 (entry 15), while a smaller or more bulky phosphine did have less effect (entries 16,17).

Under the optimized conditions, a series of different allenes undergo oxidative amination either with reagent **1** or with the reagent combination **1**-$OPPh_3$. For the sake of comparison, the respective reaction outcome of the two conditions is listed for every individual substrate (Table 2, entries 1−20). For reactions with reagent **1** (procedure **A**), lower selectivities are

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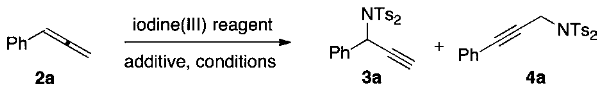
Table 1. Optimization of Reaction Conditions for the Amination of Allene 2a with Iodine(III) Reagents[a]



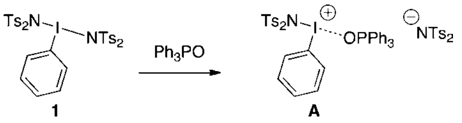
entry	reagent (equiv)	additive (equiv)	conditions	yield (%)[b]	ratio **3a**:**4a**[c]
1	$PhI(NTs_2)_2$ (1.1)	–	1,2-DCE, 80 °C, 12 h	60	63:37
2	$PhI(NTs_2)_2$ (1.1)	$HNTs_2$ (1.0)	1,2-DCE, 80 °C, 12 h	55	80:20
3	$PhI(NTs_2)_2$ (1.1)	$HNTs_2/K_2CO_3$ (1.0)	1,2-DCE, 80 °C, 14 h	60	67:33
4	$PhI(OAc)_2$ (1.1)	$HNTs_2$ (1.0)	1,2-DCE, 80 °C, 13 h	s.m.[d]	–
5	PhI(OH)(OTs) (1.1)	$HNTs_2$ (1.0)	1,2-DCE, 80 °C, 13 h	s.m.	–
6	PhIO (1.1)	$HNTs_2$ (1.0)	1,2-DCE, 80 °C, 13 h	s.m.	–
7	$PhI(NTs_2)(OAc)$ (1.1)	–	1,2-DCE, 80 °C, 13 h	dec.	–
8	**$PhI(NTs_2)_2$ (1.1)**	–	**toluene, 80 °C, 14 h**	**62**	**22:78**
9	$PhI(NTs_2)_2$ (1.1)	–	MeCN, 80 °C, 12 h	60	72:28
10	$PhI(NTs_2)_2$ (1.1)	–	EtOAc, 80 °C, 12 h	58	72:28
11	$PhI(NTs_2)_2$ (1.1)	–	$CHCl_3$, 60 °C, 12 h	61	67:33
12	$PhI(NTs_2)_2$ (1.1)	–	hexane, 60 °C, 14 h	s.m.	–
13	$PhI(NTs_2)_2$ (1.1)	K_2CO_3 (1.0)	toluene, 80 °C, 12 h	s.m.	–
14	$PhI(NTs_2)_2$ (1.1)	–	DCM, 25 °C, 14 h	62	85:15
15	**$PhI(NTs_2)_2$ (1.1)**	**$OPPh_3$ (1.1)**	**DCM, 25 °C, 8 h**	**78**	**92:8**
16	$PhI(NTs_2)_2$ (1.1)	$OPPh_2Xyl$ (1.1)	DCM, 25 °C, 8 h	76	84:16
17	$PhI(NTs_2)_2$ (1.1)	$OPPh_2Me$ (1.1)	DCM, 25 °C, 8 h	72	82:18

[a] Conditions: substrate **2** (0.2 mmol), iodine(III) reagent (0.22 mmol, 1.1 equiv), additive (0.2 mmol, entries 2–6 or 0.22 mmol, entry 14). [b] Isolated yield after purification. [c] Determined from integration of the ^1H NMR reaction crude. [d] s.m. = recovered starting material, dec. = decomposed material only.

usually obtained. For the cases of the 1-aryl allenes **2a,d,e,k** the corresponding internal propargyl amine **4** is obtained as the major product, while an equimolar product composition or a slight excess in favor of the terminal propargyl amine **3** is obtained for the other substrates **2b,c,f,g,h,i**. For the aliphatic allenes **2l,m** the internal propargyl amines are formed either with preference (entry 23) or as the single oxidation product **4l** (entry 22). A synthetically useful excess of the terminal propargyl amine **3** is generated from the reagent combination **1**-$OPPh_3$ (procedure **B**). In these cases, selectivities in favor of 4:1 to 32:1 for the corresponding amines **3** could be achieved. The constitution of these compounds was unambiguously assured from X-ray structural analyses of compounds **3b**, **3c**, and **3g**.[13]

Due to respective electronic or steric reasons, compounds **2e,k** constitute an exception as they continue to provide the corresponding terminal amines **4e,k** with complete selectivity (*vide intra*). The exact effect from the addition of triphenylphosphine oxide to the hypervalent iodine reagent **1** requires further detailed studies. A ^{31}P NMR spectrum of an equimolar mixture of **1** and Ph_3PO reveals the formation of a single new compound at $\delta = 33.5$ ppm.[13] We currently assign this signal to a newly formed complex **A** (Scheme 1), which should contain a slightly less electrophilic iodine center than the parent compound **1**. For the latter reagent a dissociation had been established to take place in solution generating free bistosylimide and cationic $PhI(NTs_2)^+$.[2]

Scheme 1. Reaction between Iodine Complex 1 and Ph_3PO



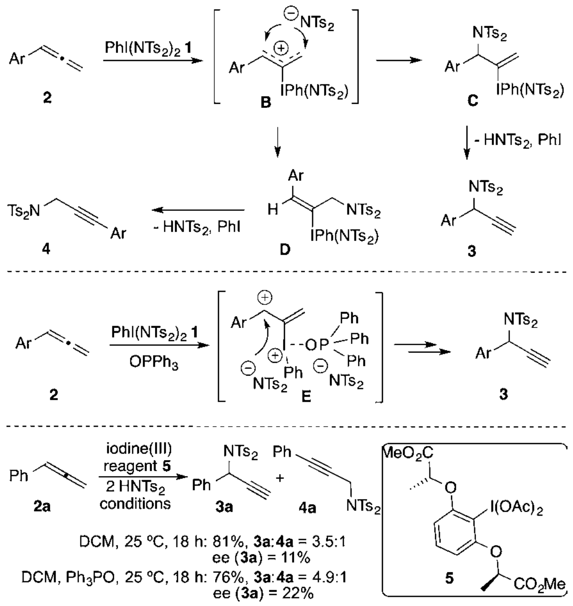
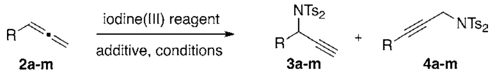
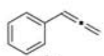
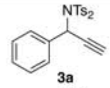
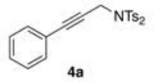
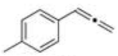
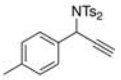
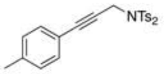
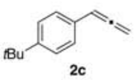
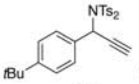
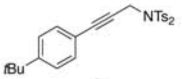
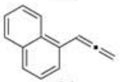
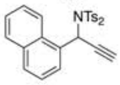
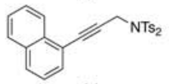
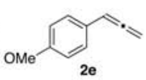
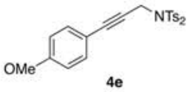
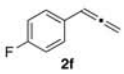
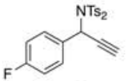
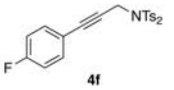
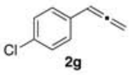
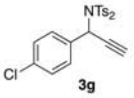
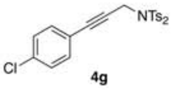
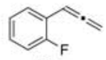
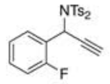
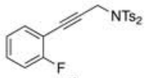
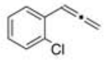
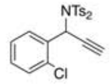
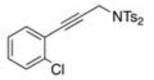
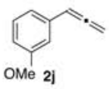
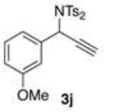
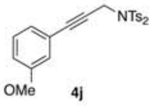
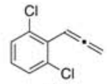
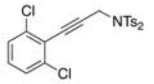
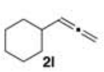
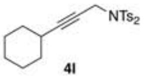
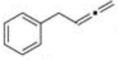
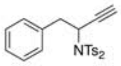


Figure 2. Iodine(III)-promoted amination reactions of hydrocarbon substrates with reagent **1**.

The formation of such a species **A** should then account for the observed difference in the product formation. We propose the following mechanistic context to be involved in the observed amination of allenes (Figure 2). The reaction is initiated by interaction between the allene substrate **2** and the hypervalent iodine reagent **1**. This reaction should direct the electrophilic iodine(III) to the 2-terminus of the allene to generate a cationic intermediate **B**. A related regioselectivity is commonly observed for electrophilic metal complexes[9b,h] and iodonium reagents.[12] Nucleophilic addition at the benzylic position will provide the amination intermediate **C**, from which a reductive β-elimination[14,15] will release the reduced iodine(I) species and generate the acetylene, thus arriving at

Table 2. Scope of the Amination of Allenes with Iodine(III) Reagent 1



entry	substrate	conditions[a]	products		ratio 3:4[b]	yield [%][c]
1 2	 2a	A B	 3a	 4a	1:4 12:1	62 78
3 4	 2b	A B	 3b	 4b	2:1 16:1	64 80
5 6	 2c	A B	 3c	 4c	1:1 32:1	85 88
7 8	 2d	A B	 3d	 4d	1:10 5:1	85 82
9 10	 2e	A B		 4e	0:100 0:100	63 72
11 12	 2f	A B	 3f	 4f	2:1 6:1	66 72
13 14	 2g	A B	 3g	 4g	2:1 9:1	75 79
15 16	 2h	A B	 3h	 4h	1:1 4:1	58 61
17 18	 2i	A B	 3i	 4i	1:1 5:1	75 78
19 20	 2j	A B	 3j	 4j	2:1 12:1	69 67
21	 2k	A[d]		 4k	0:100	31
22	 2l	A[e]		 4l	0:100	68
23	 2m	A	 3m	 4m	1:3	70

[a] Conditions **A**: substrate **2** (0.2 mmol), reagent **1** (0.22 mmol, 1.1 equiv), toluene, 80 °C, 8–14 h. Conditions **B**: substrate **2** (0.2 mmol), reagent **1** (0.22 mmol, 1.1 equiv), Ph_3PO (0.22 mmol, 1.1 equiv), dichloromethane, 25 °C, 10–24 h. [b] Determined from integration of the ^{1}H-NMR reaction crude. [c] Isolated yield after purification. [d] 100 °C, 48h; 59% recovered starting material. [e] 1,2-Dichloroethane as solvent.

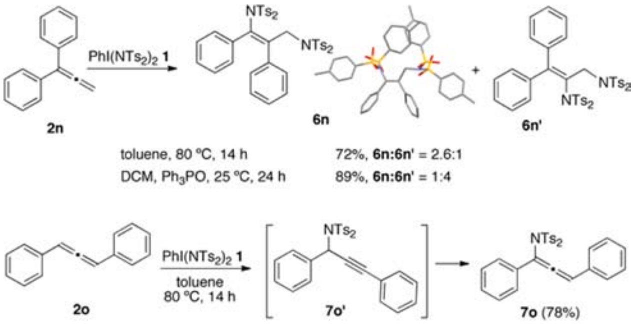
product **3**. In contrast, a terminal amination reaction at stage **B** will generate the regioisomeric intermediate **D**, which would consequently eliminate to the internal product **4**. Obviously under thermal conditions and particularly for reactions in toluene, which should be prone to proceed within a solvent cage, these two pathways are expected to be of related efficiency. In contrast, for the cases of **2e,k** the benzylic cation **B** receives stabilization by either electronic (**2e**)[13] or steric (**2k**) shielding, respectively, and thus reacts exclusively through the substitution pathway at the terminal carbon to yield **4e,k** as the exclusive products.

The regioselectivity can be greatly influenced by a room temperature process with **1**-$OPPh_3$ in dichloromethane as solvent. In this case, allenes **2** convert into an intermediate **E**, in which the nucleophilic addition pathway to the terminal carbon is sterically disfavored due to the presence of the bulky phosphine oxide substituent providing higher selectivity in favor of the terminal propargylic amines **3**.

This mechanistic proposal also explains the low enantioselectivity that was observed for reactions with a chiral iodine reagent **5**.[16] For amination of **2a**, product **3a** was obtained with 11 and 22% ee, respectively (Figure 2). Obviously, this reagent is not capable of efficiently differentiating the enantiotopic faces at the cationic stage **B**.

Finally, the oxidative amination of two diphenylated allenes was briefly explored. For 1,1-diphenyl allene **2n**, the two regioisomeric diamination products **6n** and **6n′** were obtained (Scheme 2). In agreement with the mechanistic proposal from Figure 2, the reaction requires proceeding through an intermediate related to **D**, as a potential amination at the other allene terminus would provide a very labile dibenzylic-allylic imine.[13] From the related intermediate, direct C–N coupling through reductive elimination of iodobenzene will provide **6n′**, while a 1,2-phenyl shift will provide the migratory product **6n**, the structure of which was assured from X-ray analysis.[13] A thermal reaction in toluene favors phenyl migration to diamination product **5n** as the major product, while the presence of triphenylphosphine oxide in dichloromethane provides preferential direct reductive amination to **6n′**. Final formation of the enimine moiety of both products can be rationalized from a direct three-center-four-electron reductive amination of the intermediary vinyl iodine(III)[17] or nucleophilic vinylic attack.[18] The exclusive formation of the aminated allene **7o** can be explained by the prototropic rearrangement of the expected propargyl amine **7o′** in the presence of the acidic bistosylimide byproduct.

Scheme 2. Reaction between Iodine Complex 1 and Higher-Substituted Allenes 2n,o



In summary, we have explored oxidative amination reactions of allenes. This study revealed that a new reagent combination of bis(ditosylimido)iodobenzene $PhI(NTs_2)_2$ **1** and triphenylphosphine oxide is capable of generating a series of terminal propargylic amines from 1-aryl allenes with good regioselectivities under mild conditions. This work expands the synthetic potential of oxidative amination of unsaturated hydrocarbons by hypervalent iodine(III) reagents, which now also includes the class of allenes.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental description, characterization of new compounds and data on X-ray structure determination for compounds **3b,c,g** and **6n**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: kmuniz@iciq.es.

Notes

The authors declare no competing financial interest.

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