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Iodination of Activated 1-Hetero-1,3-dienes

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Abstract: 1-Hetero-1,3-dienes activated by nitrogen, oxygen or sulfur react with bis(pyridine)-iodonium(I) tetrafluoroborate (IPy_2BF_4) to give 3-iodofunctionalized 1-hetero-1,3-dienes in good yields. The reaction takes place in a single one-pot procedure at room temperature under mild conditions.

Cycloaddition reactions of heterodienes have been shown to be of great potential in heterocyclic chemistry.[1] This synthetic potential is enhanced if the starting reagents bear a halogen atom, since this can take part in subsequent processes. In particular, vinyl iodides are an interesting group of compounds due to their valuable participation as synthetic intermediates in many useful transformations through either ionic[2] or radical[3] pathways. There have been a few methods described to obtain chlorine and bromine heterodiene derivatives - one of them involves thermolytic elimination of sulfur and hydrogen halides from α,α-dihalosulfides and carbon-carbon double bond formation;[4] azabutadiene derivatives can be halogenated with N-chlorosuccinimide or N-bromosuccinimide;[5] and 2-haloenones are prepared from enones using phenylselenium chloride or bromide[6] - but not any systematic procedure to prepare the corresponding iodine compounds. In fact, the only described precedent is the formation of α,β-unsaturated-α-iodo-aldehydes from oxidation of α-ynol-iodine complexes with pyridinium dichromate.[7] However, the scope of this reaction is very limited by the nature of the starting product which restricts its use in 2-iodoacrylaldehyde preparation.

In the course of our investigations on the photochemistry of 4-amino-1-aza-1,3-butadienes, we found it of interest to study the behavior of iodofunctionalized alkenimines. Due to the lack of a procedure to prepare these iodinated compounds, it was necessary to develop a method. Taking into account our experience in iodination reactions with bis(pyridine)iodonium(I) tetrafluoroborate (IPy_2BF_4),[8] we carried out the first attempts with this electrophilic reagent. This kind of reaction often take place in the presence of an acid to neutralize pyridine and liberate the iodinating agent. However, in the present case, the iminic nature of the starting products determines the absence of acid to prevent imine decomposition. Thus, the treatment of 4-amino-1-aza-1,3-dienes with IPy_2BF_4 in dichloromethane at room temperature during three hours allows the

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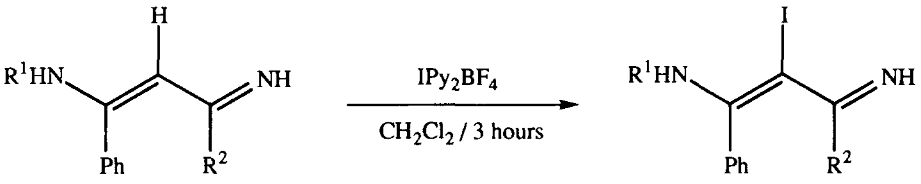
preparation of 4-amino-3-iodo-1-aza-1,3-dienes in good to nearly quantitative yields in a clean process (Scheme 1). All compounds were full characterized by their spectroscopic data (^1H and ^{13}C NMR, and IR) and mass spectrometry.



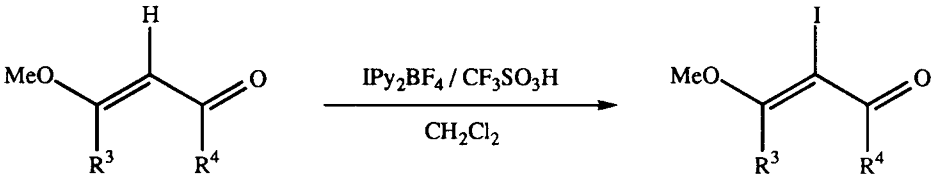
1 **2**

Azadiene **1**	R^1	R^2	Iodoazadiene 2	Yield (%)
1a	Ph	Ph	**2a**	83
1b	Ph	4-Tol	**2b**	89
1c	4-Tol	Ph	**2c**	94
1d	4-Tol	4-Tol	**2d**	91
1e	2-Tol	4-Tol	**2e**	86

Scheme 1

The obtained results prompted us to study the reactions of IPy_2BF_4 with other heterodienes. Initially, 4-methoxy-1-oxa-1,3-dienes were assayed. These dienes seem less reactives in these processes than the above described and it was necessary to add two equivalents of an acid to promote the reaction. Tetrafluoroboric acid was initially used but we have found that triflic acid improves the yield and the reaction rate of formation of the corresponding 3-iodo conjugated enone and acrylate derivatives. In order to avoid the possible undesirable side polymerizations, a solution of IPy_2BF_4 and triflic acid was prepared in dichloromethane at 0 °C, and then, the heterodiene was added and the mixture was allowed to warm to room temperature and stirred (Scheme 2). The regioselectivity observed for iodination of **3a** and **3b** is noteworthy, where only one of the two olefinic hydrogens is substituted leading, exclusively, to the 3-isomer.

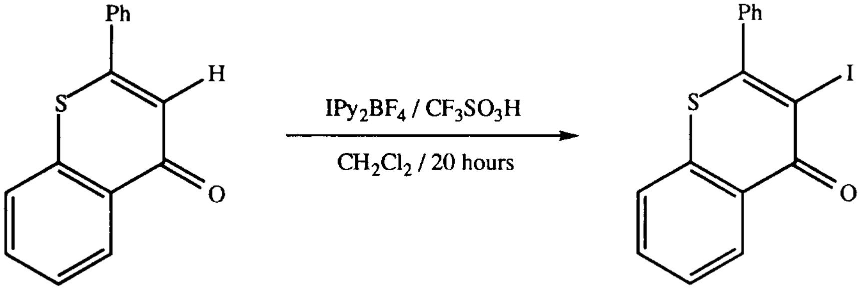
Later, the oxadiene **5** (Scheme 3), which is activated by sulfur, was allowed to react with a mixture of IPy_2BF_4 and triflic acid in dichloromethane, in the aforementioned conditions, to yield the expected iodinated product at the 3 position.



3 **4**

Oxadiene **3**	R^3	R^4	Reaction time (h)	Iodooxadiene **4**	Yield (%)
3a	H	Me	18	**4a**	62
3b	H	MeO	18	**4b**	65
3c	$-CH_2O-$		24	**4c**	54

Scheme 2



5 6 (58 %)

Scheme 3

In summary, we have described the first method for the direct iodination of 1-hetero-1,3-dienes activated by nitrogen, oxygen or sulfur. These iodinated compounds are of great interest due to their potential use. The reaction is regiospecific and occurs at the carbon placed at 3. Like heteroatom, we have used nitrogen and oxygen, but the obtained results allow us to assert that this reaction should have a wide scope. The mildness of the reaction conditions is also noteworthy as well as the good yields achieved in this simple and clean one-pot procedure.

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