

Zn-Catalyzed Direct Synthesis of 3-Iodo-1,3-dienes from α -Allenols [†]

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Abstract: We wish to report herein a new protocol that allows one to obtain 3-iodo-1,3-dienes through a sustainable process starting from α -allenols. In this new synthetic route, zinc (II) derivatives are used as metallic promoter, which are an inexpensive and environmentally friendly species.

Keywords: allenes; 3-iodo-1,3-dienes and zinc

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1. Introduction

In recent years, the chemistry of allenes has attracted the attention of many chemists giving rise to numerous studies. The presence of a cumulated diene in the structure of the allene compound allows for the selective synthesis of different functionalized organic molecules [1–3].

Allenes are the starting point of a large number of synthetic routes, due to the possibility of having four substituents in its structure. Furthermore, both the electronic density and the reactivity of each carbon of the allenes can be modulated as a function of the substitution. Besides, the inherent axial chirality allows the stereoselective synthesis of optically active allenes and the transfer of chirality from the allenes to the final product.

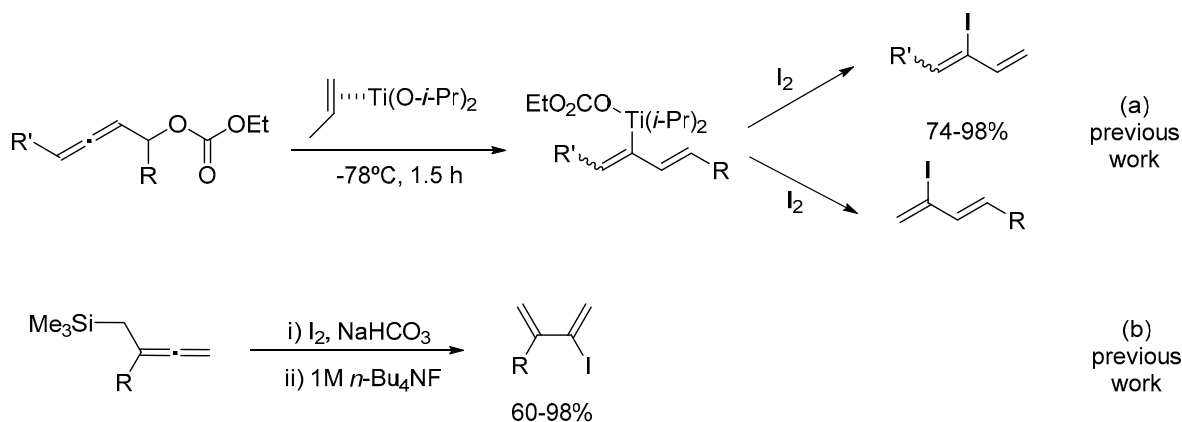
On the other hand, iododienes are interesting species for organic chemistry because of their wide reactivity. These compounds are precursors in Diels–Alder reactions [4], palladium-catalyzed reactions [5] such as Stille [6], Negishi [7], and Sonogashira [8] and carbonylation cross-couplings [9,10], solvolysis [11,12], and metalation reactions [8].

In the literature there are several methods of synthesis of iododienes from allenes. Okamoto et al. described the oxidative addition of (η^2 -propene)Ti(O-*i*-Pr)₂ to α -allenyl carbonates to form titanium complexes that by reacting with molecular iodine resulted in 2-iodo-1,3-dienes (Scheme 1a) [13]. Nishimaya et al. observed the formation of 2-iodo-1,3-butadiene by treatment of 1-trimethylsilyl-2,3-butadiene with I₂ and tetra-*n*-butylammonium fluoride (TBAF) (Scheme 1b) [9].

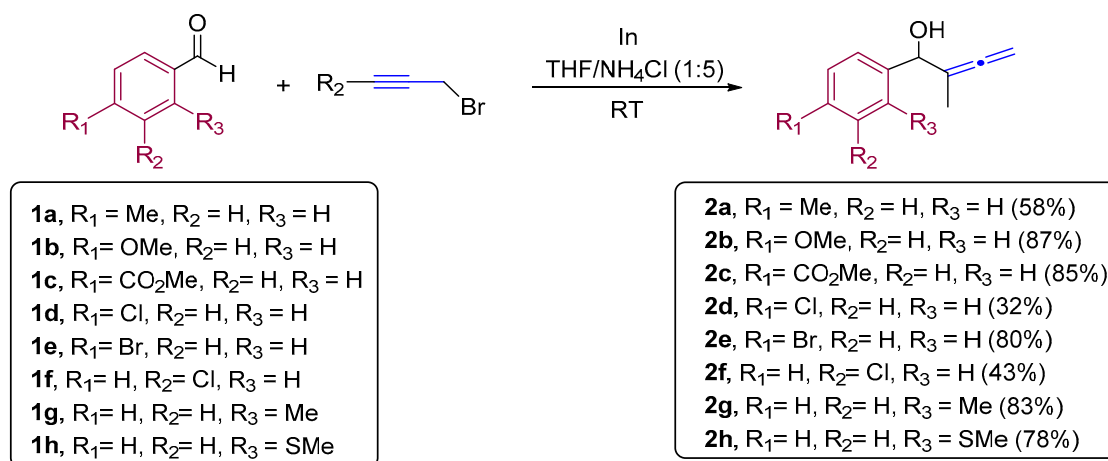
Based on these precedents, the main aim of this project is the development of a new synthetic method that allows one to obtain 3-iodo-1,3-dienes directly from α -allenols through a sustainable process.

First, the allenylation reaction was carried out on the aldehydes **1** (Scheme 2). Experiments were performed according to previous conditions developed in our research group [14,15]. Barbier-type conditions [16] were used where aldehydes **1** reacted with differently substituted propargyl bromides, using indium and a THF/NH₄Cl mixture (1:5)

as a metal promoter and solvent, respectively. In this way, α -allenols **2** were prepared with total regioselectivity.

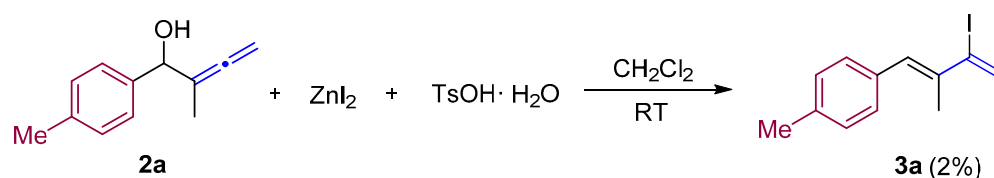


Scheme 1. Previous reports on the synthesis of iododienes from allenes [9,13].



Scheme 2. Synthesis of α -allenols [14,15].

Once the starting materials were synthesized, allenol **2a** was selected as model substrate. Initial experiments were performed though the reaction of **2a** with ZnI₂ and *p*-toluenesulfonic acid monohydrate in dichloromethane (Scheme 3), which provided the 3-iodo-1,3-diene **3a** as the only reaction product.



Scheme 3. Synthesis of 3-iodo-1,3-diene **3a**.

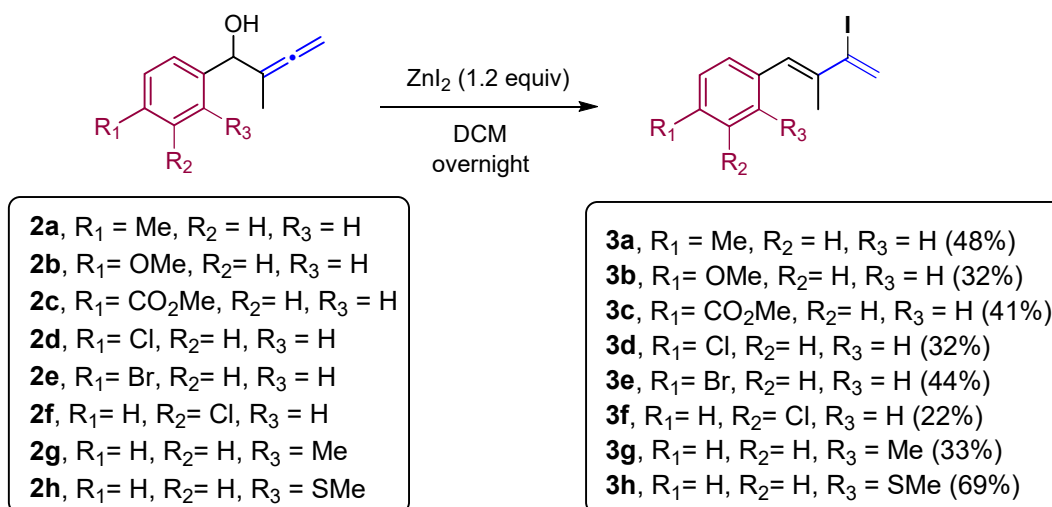
This reactivity involving addition of the iodine atom and double bond rearrangement was surprising, because it was expected to obtain the corresponding dihydrofuran through the well-developed metal-catalyzed oxycyclization of α -allenols [17].

However, the yield was very low and the reaction conditions were optimized (see Table 1). The highest yield of the product was achieved by employing 1.2 equiv. of ZnI₂ at room temperature in dichloromethane without the presence of *p*-toluenesulfonic acid (Table 1, entry 4).

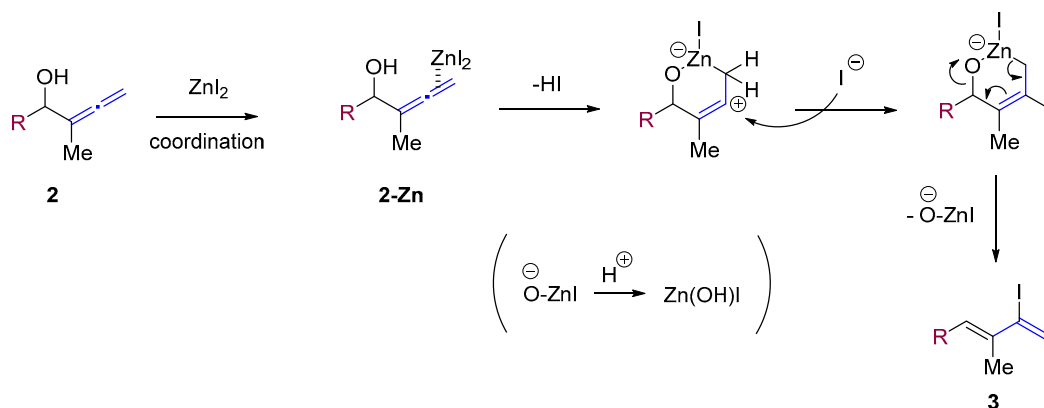
Table 1. Optimization of reaction conditions for the formation of 3-iodo-1,3-dienes **3**.

Entry	ZnI ₂ (Equiv.)	TsOH·H ₂ O (Equiv.)	Yield (%)
1	0.025	0.025	2
2	0.1	0.1	33
3	1.2	0.1	37
4	1.2	-	48

The scope of the reaction was explored in different α -allenols giving rise to the corresponding 3-iodo-1,3-dienes **3a–h** in reasonable yields (22–69%) and good (*E*)-diastereoselectivity (Scheme 4). It should be noted that in products **3a** and **3b** the reaction temperature had to be increased to 80 °C to consume the starting material.

**Scheme 4.** Preparation of 3-iodo-1,3-dienes **3a–h**.

A possible pathway for the generation of 3-iodo-1,3-dienes **3** from α -allenols **2** is outlined in Scheme 5. It is assumed that the initial step is the coordination of the zinc salt to the terminal double bond of the allene to give the corresponding complex **2-Zn**. Subsequently, the loss of HI occurs followed by an addition of an iodine atom. Final elimination of the hydroxyl group of the former α -allenol assisted by Zn generated the iodo-diene.

**Scheme 5.** Possible mechanism for the formation of 3-iodo-1,3-dienes **3**.

2. Experimental Section

General methods: ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance-300 spectrometer. NMR spectra were recorded in C_6D_6 , except otherwise stated. Chemical shifts are given in ppm relative to TMS (^1H , 0.00 ppm), or C_6D_6 (^1H , 7.16 ppm; ^{13}C , 128.0 ppm). Low and high resolution mass spectra were taken on an AGILENT 6520 Accurate-Mass QTOF LC/MS spectrometer using the electrospray mode (ES) unless otherwise stated. IR spectra were recorded on a Bruker Tensor 27 spectrometer. All commercially available compounds were used without further purification.

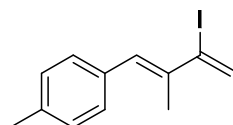
2.1. General Procedure for the Preparation of α -Allenols **2a–h**

These precursors were readily obtained as described in the literature [14,15].

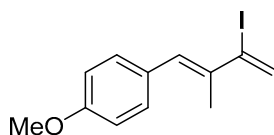
2.2. General Procedure for the Preparation of 3-Iodo-1,3-dienes **3a–h**

ZnI_2 (1.2 mmol) was added to a well stirred solution of α -allenol (1 mmol) in CH_2Cl_2 (10 mL). After the disappearance of the starting material (TLC) the mixture was filtered through a short pad of celite, washed with CH_2Cl_2 , and then concentrated under reduced pressure to give the product.

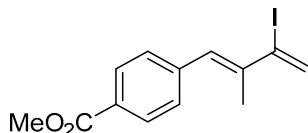
Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure compounds **3**. It should be noted that in products **3a** and **3b** the reaction temperature had to be increased to 80 °C to consume the starting material.



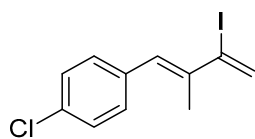
3-iodo-1,3-diene 3a. From 40 mg (0.23 mmol) of allenol **2a**, and after chromatography of the residue using hexanes/ethyl acetate (60:1) as the eluent gave compound **3a** (31 mg, 48%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 °C): δ = 6.95 (s, 1H), 6.88 (d, 2H, J = 6.0 Hz), 6.78 (d, 2H, J = 6.1 Hz), 5.87 (d, 1H, J = 3.2 Hz), 5.70 (d, 1H, J = 3.0 Hz), 1.94 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (75 MHz C_6D_6 , 25 °C): δ = 137.0, 136.5, 136.3 (CH), 134.8, 129.6 (2CH_{Ar}), 129.2 (2CH_{Ar}), 126.3 (CH₂), 114.6, 21.1 (CH₃), 15.6 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3051, 2898, 553.



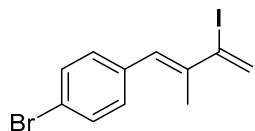
3-iodo-1,3-diene 3b. From 100 mg (0.53 mmol) of allenol **2b**, and after chromatography of the residue using hexanes/ethyl acetate (60:1) as the eluent gave compound **3b** (50 mg, 32%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 °C): δ = 7.08 (s, 1H), 7.04 (d, 2H, J = 8.4 Hz), 6.72 (d, 2H, J = 8.8 Hz), 6.04 (d, 1H, J = 1.5 Hz), 5.87 (d, 1H, J = 1.6 Hz), 3.28 (s, 3H), 1.87 (d, 3H, J = 1.1 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 °C): δ = 159.3, 136.0 (CH), 135.6, 131.0 (2CH_{Ar}), 130.0, 128.5 (2CH_{Ar}), 126.0 (CH₂), 114.9, 54.7 (CH₃), 15.7 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3079, 2854, 554.



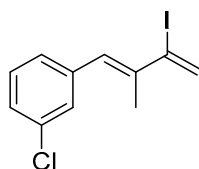
3-iodo-1,3-diene 3c. From 100 mg (0.46 mmol) of allenol **2c**, and after chromatography of the residue using hexanes/ethyl acetate (13:1) as the eluent gave compound **3c** (62 mg, 41%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 °C): δ = 8.06 (m, 2H), 7.16 (s, 1H), 6.93 (m, 2H), 6.00 (d, 1H, J = 1.7 Hz), 5.85 (d, 1H, J = 1.7 Hz), 3.51 (s, 3H), 1.69 (d, 3H, J = 1.1 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 °C): δ = 166.4, 142.0, 138.7, 135.1 (CH), 129.8 (2CH_{Ar}), 129.4 (2CH_{Ar}), 129.1, 127.7 (CH₂), 113.6, 51.6 (CH₃), 15.6 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3001, 2854, 760, 548.



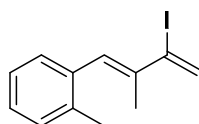
3-iodo-1,3-diene 3d. From 75 mg (0.39 mmol) of allenol **2d**, and after chromatography of the residue using hexanes/ethyl acetate (60:1) as the eluent gave compound **3d** (38 mg, 32%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ 7.03 (d, 2H, J = 8.5 Hz), 6.85 (s, 1H), 6.71 (d, 2H, J = 8.2 Hz), 5.99 (d, 1H, J = 1.6 Hz), 5.84 (d, 1H, J = 1.7 Hz), 1.67 (d, 3H, J = 1.2 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 137.6, 135.9, 134.9 (CH), 131.2, 130.8 (2CH_{Ar}), 128.6 (2CH_{Ar}), 126.9 (CH₂), 113.8, 15.5 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3047, 2937, 1095, 564.



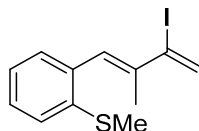
3-iodo-1,3-diene 3e. From 50 mg (0.21 mmol) of allenol **2e**, and after chromatography of the residue using hexanes/ethyl acetate (16:1) as the eluent gave compound **3e** (32 mg, 44%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 7.53 (d, 2H, J = 8.5 Hz), 7.50 (s, 1H), 6.98 (d, 2H, J = 8.2 Hz), 6.33 (d, 1H, J = 1.6 Hz), 6.18 (d, 1H, J = 1.7 Hz), 1.00 (d, 3H, J = 1.2 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 137.7, 136.3, 134.9 (CH), 131.5 (2CH_{Ar}), 131.0 (2CH_{Ar}), 127.0 (CH₂), 121.5, 113.8, 15.4 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3047, 2900, 1100, 528.



3-iodo-1,3-diene 3f. From 100 mg (0.51 mmol) of allenol **2f**, and after chromatography of the residue using hexanes as the eluent gave compound **3f** (35 mg, 22%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 7.04 (m, 1H), 6.99 (ddd, 1H, J = 7.5, 2.6, 1.0 Hz), 6.77 (m, 3H), 5.95 (d, 1H, J = 1.6 Hz), 5.82 (d, 1H, J = 1.7 Hz), 1.64 (d, 3H, J = 1.1 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 139.4, 138.3, 134.6 (CH), 134.4, 129.6 (CH), 129.4 (CH), 127.5 (CH), 127.3 (CH), 127.1 (CH₂), 113.5, 15.4 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3052, 2958, 1073, 601.



3-iodo-1,3-diene 3g. From 100 mg (0.57 mmol) of allenol **2g**, and after chromatography of the residue using hexanes as the eluent gave compound **3g** (54 mg, 33%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 7.09 (s, 1H), 7.00 (m, 4H), 6.03 (d, 1H, J = 1.5 Hz), 5.87 (d, 1H, J = 1.7 Hz), 2.07 (s, 3H), 1.71 (d, 3H, J = 1.1 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 136.9, 136.8, 136.7 (CH), 130.2 (CH_{Ar}), 129.3 (CH_{Ar}), 128.0, 127.7 (CH_{Ar}), 126.5 (CH₂), 125.7 (CH_{Ar}), 114.4, 19.9 (CH₃), 15.2 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3039, 2906, 587.



3-iodo-1,3-diene 3h. From 50 mg (0.24 mmol) of allenol **2h**, and after chromatography of the residue using hexanes/ethyl acetate (12:1) as the eluent gave compound **3h** (53 mg, 69%) as a yellow oil; ^1H NMR (300 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 7.42 (s, 1H), 7.24 (m, 1H), 7.02 (m, 3H), 6.15 (m, 1H), 5.94 (d, 1H, J = 1.7 Hz), 1.99 (s, 3H), 1.81 (d, 3H, J = 1.1 Hz); ^{13}C NMR (75 MHz, C_6D_6 , 25 $^\circ\text{C}$): δ = 139.5, 137.6, 136.2, 135.2 (CH), 129.7 (CH_{Ar}), 128.1 (CH_{Ar}), 126.7 (CH₂), 125.4 (CH_{Ar}), 124.4 (CH_{Ar}), 113.7, 15.4 (CH₃), 15.1 (CH₃); IR (CHCl₃, cm^{-1}): ν = 3100, 2252, 524.

3. Conclusions

In conclusion, we present the controlled preparation of 3-iodo-1,3-dienes, directly from allenes through the coordination of the zinc salt to the double terminal bond of the allene by a subtle variation of the substituents.

Author Contributions: M.T.-P. and B.P. planned and conducted experiments. M.T.-P. and B.P. analyzed the data for the compounds and compiled most of the Supplementary Information. T.M.d.C. analyzed data to support the mechanistic proposal. P.A. designed and directed the project. M.T.-P. wrote the manuscript. T.M.d.C. and P.A. contributed to discussion. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

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