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Oxidant- and additive-free simple synthesis of 1,1,2-triiodostyrenes by one-pot decaroboxylative iodination of propiolic acids



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ABSTRACT

A metal- and oxidant-free facile synthesis of a range of 1,1,2-triiodostryrene derivatives has been developed which utilizes a simple decarboxylative triiodination of propiolic acids using molecular iodine and sodium acetate in a one-pot manner. Electron-withdrawing or donating substituents in the aryl rings display marginal influence on the course of the reaction. Mechanistic investigation reveals that the reaction proceeds via a mono-iodo alkyne derivative which subsequently adds an iodine molecule to provide the title compounds. On the other hand, $\beta_i\beta$ -diarylacrylic acids, under identical conditions undergo only decarboxylative mono-iodinaion to provide 1,1-diaryl-2-iodoalkenes, which do not undergo further iodination. The scope of the latter reaction was also examined.

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Introduction

Haloalkenes represent an important class of building blocks in organic synthesis ranging from natural products to functional molecules [1]. These have gained much prominence largely due to developments in metal-catalyzed cross-coupling reactions for the creation of carbon-carbon and carbon-hetero bond formation. As a result, a large number of methodologies have been developed for rapid access to haloalkenes [2]. Polyhaloalkenes serve similarly as step-economic means for poly-functionalization of alkene derivatives related to the preparation of materials of optical and electronic interest [3]. Due to greater reactivity, the vinyl polyiodides and polybromides have seen majority of the applications and thus, several methodologies have been developed for the synthesis of such kind of alkenes. The terminal acetylenes have remained the major source since well-defined and elegant halogenation techniques employing iodine and an oxidant such as PhI (OAc)₂ [4] Oxone [5], and DMSO [6] have been developed. The classical Hunsdiecker-type decarboxylative halogenation of propiolic acids is an important methodology [7,8] for traceless conversion for direct access to vinyl monohalides and dihalides (halogen = Cl, Br, I). A recent achievement is the oxidative tribromination of phenyl propiolic acids [9]. Triiodination of phenyl propiolic acid with I₂O₅ as oxidant has been observed as a side reaction during preparation of triiodo ketones from aryl propiolic acids [10]. Though considerable progress has been made, many of these methods employ expensive metal catalysts and/or hazardous oxidants or reagents (Scheme 1).

Thus, need for the development of a simple route for the synthesis of triiodo styrenes employing easily available precursors and simple reagents is of importance. Herein, we describe an oxidant-, additive, and metal-free synthesis of triiodostyrenes by decarboxylative triiodination of phenyl propiolic acid, in continuation of our interest on iodine-mediated transformations [11].

Results and discussion

When the decarboxylative iodination of phenyl propiolic acid was attempted using two equivalents each of iodine and sodium acetate using acetonitrile as solvent, little conversion took place and a mixture of inseparable products formed [entry 1, Table 1]. Increasing the equivalence of iodine to three did not accelerate the conversion much at room temperature while under refluxing conditions, a complex mixture of products formed. On the other hand, when six equivalents of iodine was used together with two equivalents of sodium acetate (entry 3) at room temperature, a slow but steady conversion took place and the desired product 2 was obtained in 87% yield within 16 h. Use of two equivalents of base seemed to be optimal, since when the equivalents were reduced to one (entry 4), or one and a half (entry 5) lower yields were obtained. Similarly, with further addition of base (3/4 equiv., entry 6, 7) little improvement of yield was noticed. Attempts to reduce the reaction time by refluxing in acetonitrile indeed





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(a) Earlier work



CO₂H



Scheme 1. Previous and present work.

Table 1			
Optimization of the	conversion 1	→ 2	

Entry	Reagents (eqv)	Conditions	% 2
1	I ₂ (2equiv) /NaOAc (2)	MeCN, rt, 16 h	Mixture of
2	I ₂ (3) /NaOAC (2)	MeCN, rt to reflux, 6 h	products Mixture of products
3	I ₂ (6)/ NaOAc (2)	MeCN, rt, 16 h	87
4	I ₂ (6)/ NaOAc (1)	MeCN, rt, 16 h	61
5	I ₂ (6)/ NaOAc (1.5)	MeCN, rt, 16 h	78
6	I ₂ (6)/ NaOAc (3)	MeCN, rt, 16 h	84
7	I ₂ (6)/ NaOAc (4)	MeCN, rt, 16 h	88
8	I ₂ (6)/NaOAc (2)	MeCN, reflux, 2 h	65
9	I ₂ (9)/NaOAc (2)	MeCN, reflux, 2 h	72
10	I ₂ (6)/ KOAc (2)	MeCN, rt, 16 h	84
11	$I_2/n-Bu_4N^+OAc^-(2)$	MeCN, rt, 16 h	79
12	I ₂ (6)/ K ₂ CO ₃ (2)	MeCN, rt, 16 h	77
13	I ₂ (6)/ Cs ₂ CO ₃ (2)	MeCN, rt, 16 h	74
14	I ₂ (6)/ NaOAc (2)	DMSO, rt, 16 h	60
15	I ₂ (6)/ NaOAc (2)	DMSO,50 °C, 16 h	71
16	I ₂ (6)/ NaOAc (2)	DMSO, 90 °C, 8 h	Complex mixture
17	I ₂ (6)/ NaOAc (2)	MeOH, rt, 16 h	60
18	NIS (6)/ NaOAC (2)	MeCN, rt, 16 h	3 (62%)

resulted in accelerated conversion but a lower yield of the product 2 (65%) was obtained within two hours (entry 8). Increasing the loading of iodie to nine equivalent, somewhat improved the yield of 2 to 72% (entry 9). But purification of the product was a little more challenging. Changing the base from sodium acetate to potassium acetate or tetrabutylammonium acetate did not significantly alter the course of the reaction (entries 10 and 11). More or less similar conversion was noticed when potassium carbonate (entry 12) or cesium carbonate (entry 13) were also used as bases. Similarly, when the solvent was changed to DMSO, little drop in yield was observed under otherwise analogous conditions (entry 14). Attempts to optimize the conditions by heating at 50 °C were

marginally successful (entry 15). However, further increase of temperature (entry 16) proved to be deleterious when the desired product was not seen at all; the fate being formation of a dark mixture of several products. When methanol was used as solvent, the conversion was somewhat lower (entry 17, 60%) at room temperature which marginally improved on refluxing (70%). The starting material was recovered (10–15%) in both the cases. Interestingly, when *N*-iodosuccinimide was used as the iodinating agent (entry 18) only Hunsdiecker-type decarboxylative mono-iodination took place even when six equivalents of the reagent was used. Thus, the entry 3 was accepted as the optimised condition for the study of scope and limitation of the reaction $1 \rightarrow 2$ (Scheme 2).

The reaction proceeds well with substrates having one methyl substituent at para-, ortho- or meta positions (**2b-d**, Fig. 1) or two such substituent (**2e**, **f**) with little difference in yields. Similar results were also obtained with methoxy-substituted iodoarenes resulting in compounds (**2g-i**). Moreover, electron withdrawing substituents such as fluorine (**2j-l**), chlorine (**2m**, **n**), nitro (**2o**, **p**) and trifluoromethyl (**2q**, **r**) also behaved analogously in terms of rate and yield of product in each case. The 1-naphthyl ring system (**2s**) and the hetero-aromatic derivative (**2t**) were prepared in good yields under analogous conditions. Thus, the reaction appears to tolerate a good variety of electron donating and withdrawing systems as well as applicable to polyaromatic and heteroaromatic substrates.



Scheme 2. Mechanistic studies.



Fig. 1. Substrate scope of the eaction $1 \rightarrow 2$.

Towards understanding the mechanistic possibilities, it was observed that probably the reaction proceeds through the intermediate formation [12] of the decarboxylative iodination product **3** since the later delivered the triiodo compound **2** when separately treated with iodine (five equiv.) under analogous conditions. The diiodination of 3 may proceed through an open-cation 4 or the cyclic iodonium ion 5 [14]. However, when the ß,ß-disubstituted iodoalkene 7, prepared from the decarboxylative iodination of ßphenylcinnamic acid, under analogous conditions did not undergo further iodination even with six equivalent iodine. Thus, the presence of a further cation- stabilizing phenyl group has little influence and the reaction may involve other pathways also. It is possible that the addition perhaps proceeds under steric control. The possibility of involvement of radicals also looks remote based on the fact that when the reaction was conducted in the presence of radical quencher like TEMPO or BHT, the reaction proceeded similarly but in somewhat reduced yields.

We further investigated for the scope and optimization of conditions of the transformation $\mathbf{6} \rightarrow \mathbf{7}$ (Scheme 3) in view of a similar report [13]. Although the reaction was first observed as a side reaction, it appeared that, this was the condition of choice since attempted searches for use of lesser equivalents of iodine and base (entries 2–8, Table 2), shorter reaction time (entry 9), change of base to KOAc/K₂CO₃ (entries 10, 11) and use of DCM as solvent (entry 12) all proved to be somewhat less effective for the synthesis of **7**. Thus, the use of excess iodine seems to be crucial. The conver-



Scheme 3. Formation of compound 7 from 6.

Та	ble	2	
-			

Optimization	of the	conversion	6	\rightarrow	7.
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Entry	Reagents (eqv)	Conditions	% 7
1	I ₂ (6equiv) /NaOAc (2)	MeCN, rt. 16 h	81%
2	I_2 (1equiv) /NaOAc (1)	MeCN, rt, 5 h	Trace
3	I ₂ (1equiv) /NaOAc (1)	MeCN, rt, 16 h	15
4	I ₂ (2equiv) /NaOAc (1)	MeCN, rt, 16 h	22
5	I ₂ (3equiv) /NaOAc (1)	MeCN, rt, 16 h	27
6	I ₂ (4equiv) /NaOAc (1)	MeCN, rt, 16 h	32
7	I ₂ (4equiv) /NaOAc (2)	MeCN, rt, 16 h	57
8	I ₂ (5equiv) /NaOAc (2)	MeCN, rt, 16 h	68
9	I ₂ (6equiv) /NaOAc (2)	MeCN, reflux, 6 h	53
10	I ₂ (6equiv) /KOAc (2)	MeCN, rt, 16 h	72
11	I_2 (6equiv) / K_2CO_3 (2)	MeCN, rt, 16 h	69
12	I ₂ (6equiv) /NaOAc (2)	CH ₂ Cl ₂ , rt, 16 h	71

Table 3

Substrate scope for the conversion 6 to 7.



sion has previously been attempted [13] in substrates having an obligatory methoxy substituent in either of the phenyl rings. However, under the presently developed conditions, substrates containing substituents such as methyl, methoxy, chlorine, fluorine or a *tert*-butyl group as well as unsubstituted phenyl ring (compounds **6a–I**, Table 3) all proceeded with more or less equal ease and similar yields under the optimised conditions. Moreover, the substrate **6i** containing a methyl substitution in place of the second aryl ring also behaved analogously. The substrates may be considered important in view of the possibility of further functionalization through metal catalyzed cross-coupling reactions [15].

Conclusion

In conclusion, a simple synthesis of 1,1,2-triiodostyrenes has been developed by decarobxylative iodination of using molecular iodine and a simple base. The reaction tolerates the presence of both electron withdrawing and electron donating functional groups. An interesting extension is the preparation of the ß,ßdiaryliodoalkenes **7a-i** of potential applications. The methodology may thus complement the existing literature and hence find applications.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.152378.

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