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Convenient and stereoselective synthesis of (*Z*)-1-bromo-1-alkenes by microwave-induced reaction

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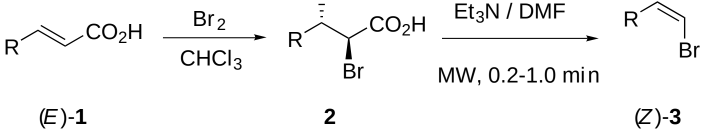
Abstract—(*Z*)-1-Bromo-1-alkenes were stereoselectively prepared in high yields in a short reaction time (0.2–1.0 min) by microwave irradiation of the corresponding 2,3-dibromoalkanoic acids in DMF in the presence of triethylamine. © 2001 Elsevier Science Ltd. All rights reserved.

(*Z*)-1-Bromo-1-alkenes are an important synthetic intermediate for stereospecific synthesis of substituted alkenes. A variety of methods have been reported for the stereocontrolled preparation of (*Z*)-1-bromo-1-alkenes, including Wittig-type reaction,[1] metal–halogen exchange of metalloalkenes,[2] hydroboration–protonolysis of haloalkynes,[3] palladium-catalyzed hydrogenolysis of 1,1-dibromo-1-alkenes by tributyltin hydride,[4] reduction of 1-haloalkynes with diimine,[5] transformation of ketones using an appropriate acetyl halide in a strongly acidic solvent,[6] SmI_2-mediated β-elimination of *O*-acetyl dihalo alcohols,[7] and debrominative decarboxylation of cinnamic and acrylic acid dibromides.[8] Debrominative decarboxylation of brominated α,β-unsaturated carboxylic acids[8] might be one of the most useful methods for a synthesis of (*Z*)-1-bromo-1-alkenes since the starting α,β-unsaturated acids are readily available and the procedure is very simple. However, the yields are low in the case of aliphatic (*Z*)-1-bromoalkenes and (*Z*)-β-bromostyrene carrying *ortho*- and *para*-nitro-substituents even if an improved procedure using triethylamine and DMF solvent was used in these reactions.[8i] Recently, we found that microwave irradiation in the reported improved procedure resulted in highly selective formation of (Z)-1-bromo-1-alkenes with excellent yields. In this communication, we report a convenient method for an efficient and stereoselective synthesis of (*Z*)-1-bromo-1-alkenes by microwave irradiation of 2,3-dibromoalkanoic acids with a short reaction time.

Microwave-induced rate acceleration technology is becoming a powerful tool in organic synthesis.[9] We also reported a microwave-induced reaction for a stereoselective synthesis of (*E*)-β-arylvinyl halides from α,β-unsaturated carboxylic acids.[10] Therefore, we can successfully achieve a highly stereoselective synthesis of both (*E*)- and (*Z*)-vinyl bromides, starting from the same α,β-unsaturated carboxylic acids, by using a microwave irradiation technique.

2,3-Dibromoalkanoic acids (**2**) were readily obtained by bromination of the corresponding *trans*-α,β-unsaturated carboxylic acids ((*E*)-**1**) in $CHCl_3$ at rt to 60°C or by bromination of (*E*)-**1** in $CHCl_3$ under irradiation with a tungsten lump. Microwave irradiation of *anti*-2,3-dibromoalkanoic acids (**2**), in DMF solution containing 1.05 equiv. of triethylamine for 0.2–1.0 min,



Scheme 1.

Keywords: (*Z*)-vinyl bromide; α,β-unsaturated carboxylic acids; decarboxylation; microwave irradiation.

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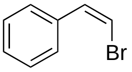
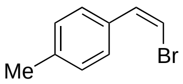
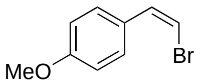
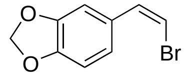
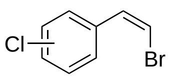
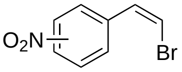
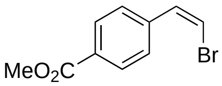
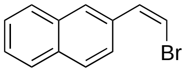
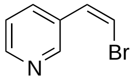
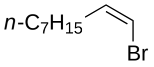
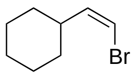
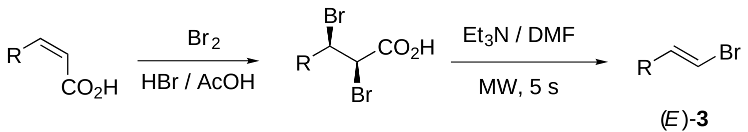
gave the corresponding (*Z*)-vinyl bromides ((*Z*)-**3**) in excellent yields and high (*Z*)-selectivities (Scheme 1). The yields of (*Z*)-**3** and the ratios of (*Z*) and (*E*) are summarized in Table 1.

Table 1. Stereoselective synthesis of (*Z*)-vinyl bromides (**3**) by microwave irradiation of 2,3-dibromoalkanoic acids (**2**)

Entry	R of **2**	Product (**3**)	MW (min)	Yield of **3** (%)[a)]	*Z*/*E*[b)]
1	C_6H_5		0.5	95	>99 / 1
2	4-$CH_3C_6H_4$		0.5	98	98 / 2
3	4-$CH_3OC_6H_4$		0.5	95	75 / 25
4	3,4-$OCH_2OC_6H_3$		0.5	99	95 / 5
5	4-ClC_6H_4		1.0	96	>99.5 / 0.5
6	2-ClC_6H_4		1.0	94	98 / 2
7	4-$NO_2C_6H_4$		1.0	98	>99.5 / 0.5
8	3-$NO_2C_6H_4$		1.0	99	>99.9 / 0.1
9	2-$NO_2C_6H_4$		1.0	96	>99.5 / 0.5
10	4-$CH_3O_2CC_6H_4$		1.0	99	>99.9 / 0.1
11	2-Naphthyl		0.5	96	>99.5 / 0.5
12	3-Pyridyl		1.0	73	>99.9 / 0.1
13	*n*-C_7H_{15}		0.2	91	>99.9 / 0.1
14	*c*-C_6H_{11}		0.2	82	>99.9 / 0.1

a) Isolated yields.

b) Determined by ^{1}H NMR.



(*Z*)-**1** **4** (*E*)-**3**

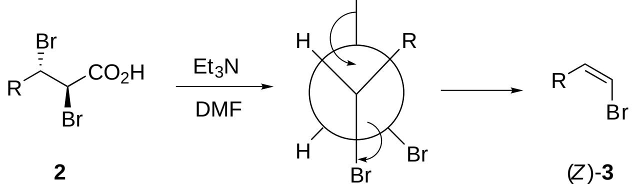
[R= C_6H_5: 95%, *E* / *Z* = 99 / 1]

Scheme 2.

These results indicate that the present microwave-induced reaction can be used for the synthesis of both aromatic and aliphatic (*Z*)-1-bromo-1-alkenes. Cinnamic acid dibromides carrying electron-donating or electron-withdrawing groups could be converted into the corresponding (*Z*)-β-bromostyrenes in excellent yields with high stereoselectivities (entries 2–10). It is noteworthy that the yields of (*Z*)-β-bromostyrenes carrying nitro groups (entries 7–9) and those of aliphatic (*Z*)-1-bromo-1-alkenes (entries 13 and 14) increased to 82–98%, although even an improved method of debrominative decarboxylation in DMF at 80°C gave those vinyl bromides in 41–61% yield.[8i] The stereoselectivity of *Z*/*E* was lowered to 75% only in the case of *p*-methoxyphenyl vinyl bromide (entry 3). However, all of the results in Table 1 indicate that the yields and *Z*/*E* stereoselectivities by the present method are quite higher than those of previous procedures.[8i,8j]

The present microwave-induced method can be applied to a synthesis of (*E*)-vinyl bromides. Microwave irradiation of *syn*-2,3-dibromoalkanoic acids (**4**), prepared by bromination of *cis*-α,β-unsaturated acids ((*Z*)-**1**),[11] for 5 s under the same conditions as those for **2** furnished (*E*)-vinyl bromide ((*E*)-**3**) stereoselectively in 95% yield (Scheme 2). These results show that the present debrominative decarboxylation by microwave irradiation proceeds in a highly stereospecific manner from either *anti*- or *syn*-2,3-dibromoalkanoic acid.

Two proposed reaction pathways for the present debrominative decarboxylations are shown in Schemes 3 and 4. Most of the reactions probably proceed via *trans*-β-elimination involving simultaneous loss of carbon dioxide and bromide ion to give (*Z*)-vinyl bromides (Scheme 3). On the other hand, in the case of 3-*p*-anisyl-2,3-dibromopropanoic acid, a unimolecular elimination process of bromide ion to give relatively stable carbocations **A** and **B** may be involved. Elimination of carbon dioxide from **A** and **B** would give (*Z*)- and (*E*)-vinyl bromide, respectively, with a preferential formation of (*Z*)-isomer (Scheme 4).



Scheme 3.

The typical experimental procedure is as follows: A mixture of cinnamic acid dibromide (1 mmol) and triethylamine (1.05 mmol) was added to 2 ml of DMF. The mixture was kept inside a microwave oven operated at 2450 MHz (Toshiba, ER-V11, 200 W) and was irradiated for 0.5 min without any stirring. The reaction mixture was then removed from the oven and cooled to room temperature. Water and ether were added to the reaction mixture and the organic layer was separated. The aqueous layer was extracted with ether. The combined organic layers were washed with water and brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave almost pure (*Z*)-β-bromostyrene in 95% yield (*Z*/*E* >99/1). Large scale reaction using 20 mmol of cinnamic acid dibromide also proceeded in the same way to give (*Z*)-β-bromostyrene in 95% yield (*Z*/*E* >99/1).

In conclusion, we have developed a rapid and convenient method for an efficient and stereoselective synthesis of (*Z*)-1-bromo-1-alkenes from the corresponding 2,3-dibromoalkanoic acids using a triethylamine/DMF system under microwave irradiation. The present debrominative decarboxylation of dibrominated cinnamic and acrylic acids using microwave irradiation was found to have significant advantages over existing procedures.

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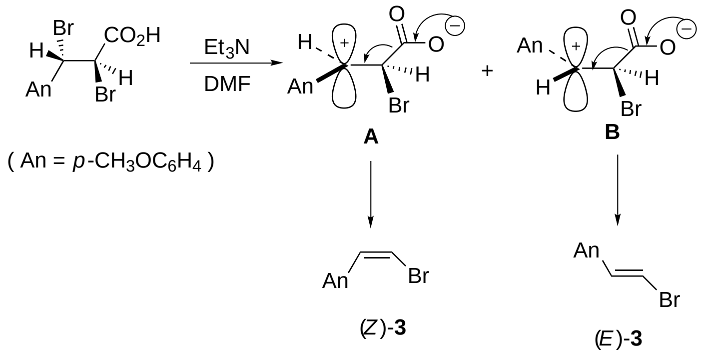

Scheme 4.

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