Stereoselective synthesis of (*Z*)-β-arylvinyl bromides from *anti*-2,3-dibromo-3-arylpropanoic acids

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A novel method for the stereoselective synthesis of (*Z*)-*β*-arylvinyl bromides in excellent yields by debrominative decarboxylation of *anti*-2,3-dibromo-3-arylpropanoic acids using NaN_3 was developed. This facile transformation was achieved under room temperature for 1–2 h.

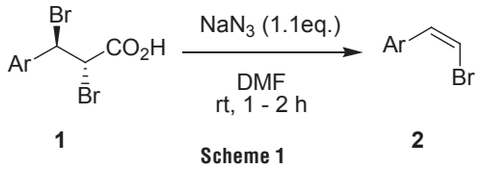
Keywords: stereoselective synthesis, (*Z*)-*β*-arylvinyl bromide, decarboxylation, NaN_3

(*Z*)-*β*-Arylvinyl bromides are versatile precursors in many useful organic transformations including the Stille,[1] Suzuki,[2,3] Ulmann,[4] and Sonogashira[5,6] couplings, as well as the Buchwald[7] methodology for stereospecific synthesis of substituted alkenes. Some efficient methods for the synthesis of stereoseletive (*Z*)-*β*-arylvinyl bromides have been reported. The most common include Wittig olefination of an aldehyde with bromomethylene triphenylphosphoran,[8–11] boron–bromine or silicon–bromine exchange of vinyl boronates (boronic acids)[12,13] or vinylsilanes,[14] hydroboration-protonolysis of haloalkynes,[15,16] palladium-catalysed reductive removal of one bromide from 1,1-dibromo-1-alkenes by tributyltin hydride,[17,18] Julia olefination between aromatic aldehydes and α-bromomethyl sulfones,[19] and debrominative decarboxylation of cinnamic and acrylic acids dibromides.[20–28] Among these reports, debrominative decarboxylation of cinnamic acid dibromides using a variety of bases in different organic solvents might be the most effective, which deserves attention because the starting substrates are readily available and the procedure is very convenient. Our group has described a rapid method for an efficient and stereoselective synthesis of (*Z*)-*β*-arylvinyl bromides from the corresponding 2,3-dibromoalkanoic acids using a Et_3N/DMF system under microwave irradiation.[25,26] Functionalised (*Z*)-*β*-arylvinyl bromides can be also formed by using an one-pot synthetic strategy under the same decarboxylation system.[27] We also demonstrated that stereoselective (*Z*)-4-(2-bromovinyl)benzenesulfonamides could be afforded by microwave-induced simultaneous debrominative decarboxylation and sulfamation of *anti*-2,3-dibromo-3-(4-chlorosulfonylphenyl)propanoic acid using a diverse range of alkyl and aryl amines.[28] Ranu and co-authors found that basic ionic liquid, [bmIm]OH could be an effective promoter for the debrominative decarboxylation.[29] However, heating, microwave irradiation or excess organic amines were needed in most reports.

Besides organic base, NaN_3 might be an effective decarboxylation reagent. We have developed an one-pot method for the preparation of 4-aryl-1H-1,2,3-triazoles from *anti*-3-aryl-2,3-dibromopropanoic acids and NaN_3 catalysed by $Pd_2(dba)_3$ and Xantphos in moderate to high yields,[30] where the debrominative decarboxylation of *anti*-3-aryl-2,3-dibromopropanoic acids by NaN_3 giving the (*Z*)-*β*-arylvinyl bromides played a key role in the two-step transformation. However, the (*Z*)-*β*-arylvinyl bromide intermediates were not isolated in this report.

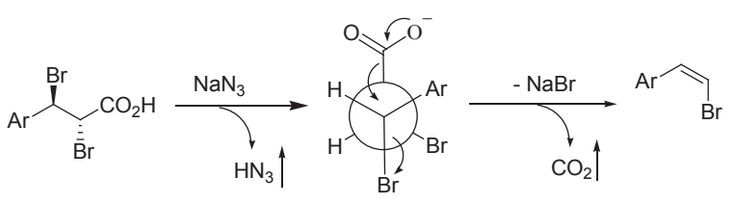
We now describe the use of NaN_3/DMF system for the synthesis of stereoselective (*Z*)-*β*-arylvinyl bromides **2** by debrominative decarboxylation of *anti*-2,3-dibromo-3-arylpropanoic acids **1** at room temperature (Scheme 1). This method might be an alternative to the previous report due to its convenience, excellent yields and mild reaction condition without the use of either microwave irradiation or excess organic amines.

A possible mechanism for this conversion is shown in Scheme 2. The mild condition and high efficiency should be attributed to the release of HN_3 from the system by alkalisation of $-CO_2H$ during the formation of intermediates **A**, which favours the reaction equilibrium shifting, hence, promoting the following debrominative decarboxylation process.



1 **2**

Scheme 1



1 **A** **2**

Scheme 2

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Results and discussion

Our initial attempt began with the debrominative decarboxylation of *anti*-2,3-dibromo-3-arylpropanoic acid **1a**. The experiment was carried out with **1a** (1 mmol), NaN_3 (1.1 mmol) in DMF. The reaction mixture was stirred at room temperature for 1 h. The expected product **2a** was afforded in 94% yield (Table 1, entry 1). Various solvents were examined to optimise the yield and stereoselectivity of **2**. It was found that CH_2Cl_2 and THF were less satisfactory as solvents than DMF. While DMF turned out to be the most effective solvent for the stereocontrolled preparation of (*Z*)-*β*-arylvinyl bromides, the dropwise addition of compound **1** in DMF to the suspension of NaN_3 in DMF was also necessary for the reaction efficiency. Other dibromo-3-arylpropanoic acids besides **1a** were employed successfully using the same conditions for 1–2 h (entries 2–8). This reaction system proved to be applicable for aromatic ring bearing both electron-donating groups such as Me (entry 2) and electron-withdrawing groups like F, Cl, Br and CO_2Me, affording products **2b**–**g** in 80–94% yields (entries 3–7). The steric hindrances of the substituents like Cl on the *ortho*-position of the aromatic ring (entry 6) did not alter the efficiency of the reaction. Interestingly, *anti*-2,3-dibromo-3-(4-(chlorosulfonylphenyl)propanoic acid **1h** could smoothly convert to the corresponding (*Z*)-4-(2-bromovinyl) benzenesulfonyl azide **2h** in a high yield of 95% when 2.2 equiv. of NaN_3 was used (entry 8).

Table 1 Synthesis of (*Z*)-*β*-arylvinyl bromides **2** using NaN_3/DMF system

Entry	Ar		Product	Time/h	Yield of **2**/% [a,b]
1	C_6H_5	**1a**	**2a**	1	94
2	4-Me-C_6H_4	**1b**	**2b**	1	97
3	4-F-C_6H_4	**1c**	**2c**	2	94
4	4-Cl-C_6H_4	**1d**	**2d**	1.5	93
5	4-Br-C_6H_4	**1e**	**2e**	1.5	95
6	2-Cl-C_6H_4	**1f**	**2f**	2	91
7	4-MeO_2C-C_6H_4	**1g**	**2g**	2	92
8[c]	4-ClO_2S-C_6H_4	**1h**	**2h**	2	95

[a]Isolated yields based on *anti*-2,3-dibromo-3-arylpropanoic acids **1**.
[b]*Z*/*E*>98%, determined by ^1H NMR.
[c]2.2 equiv. of NaN_3 was used.

Experimental

Melting points were recorded using a WRS-1B digital melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded using Bruker DPX-400 spectrometer in $CDCl_3$ with $SiMe_4$ as an internal standard. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with HuanghaiGF$_{254}$ silica gel coated plates. Column chromatography was carried out using 300–400 mesh silica gel at medium pressure.

(Z)-β-arylvinyl bromides **(2)***; general procedure*

To a stirred suspension of NaN_3 (1.1 mmol) in DMF (3 mL) was added dropwise **1** (1 mmol) in DMF (3 mL). After stirring the reaction mixture for 1–2 h at room temperature, it was diluted with Et_2O (20 mL) and then with water (20 mL). The mixture was stirred for an additional 30 min at room temperature and two layers were separated. The aqueous layer was extracted with Et_2O (10 mL). The combined ether layers were washed three times with water (30 mL) in order to remove the DMF as much as possible and dried over anhydrous Na_2SO_4. Evaporation of the solvent gave the crude product, which was subjected to column chromatography (silica gel, EtOAc : petroleum ether = 1 : 9) to afford **2** in yields of 91–97%. The structure of **2a–g** were fully consistent with the previous report,[14,22,26] except for product **2h**, the structure of which was confirmed by its ^1H NMR and ^{13}C NMR data.

(Z)-β-Bromostyrene **(2a)**:[14,26] Colourless oil; IR (neat) 1611, 1594, 1488, 928, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.43 (1H, d, *J* = 8.2 Hz), 7.07 (1H, d, *J* = 8.2 Hz), 731–7.40 (3H, m), 7.66–7.69 (2H, m).

(Z)-β-Bromo-4-methylstyrene **(2b)**:[22,26] Colourless oil; IR (neat) 1603, 1557, 1490, 945 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.36 (3H, s), 6.36 (1H, d, *J* = 7.9 Hz), 7.02 (1H, d, *J* = 7.9 Hz), 7.17 (2H, d, *J* = 7.9 Hz), 7.58 (2H, d, *J* = 7.9 Hz).

(Z)-β-Bromo-4-fluorostyrene **(2c)**:[26] Colourless oil; IR (neat) 1609, 1510, 1327, 1230 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.38 (1H, d, *J* = 8.2 Hz), 6.97–7.07 (3H, m), 7.61–7.67 (2H, m).

(Z)-β-Bromo-4-chlorostyrene **(2d)**:[26] Colourless oil; IR (neat) 1616, 1580, 1490, 1010, 725 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.45 (1H, d, *J* = 7.9 Hz), 7.12 (1H, d, *J* = 7.9 Hz), 7.34 (2H, d, *J* = 8.2 Hz), 7.62 (2H, d, *J* = 8.2 Hz).

(Z)-β-Bromo-4-bromostyrene **(2e)**:[26] Colourless oil; IR (neat) 1616, 1575, 1495, 1013 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.45 (1H, d, *J* = 8.2 Hz), 6.98 (1H, d, *J* = 8.2 Hz), 7.48 (2H, d, *J* = 8.6 Hz), 7.54 (2H, d, *J* = 8.6 Hz).

(Z)-β-Bromo-2-chlorostyrene **(2f)**:[26] Colourless oil; IR (neat) 1616, 1589, 1461, 1435, 949 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 6.59 (1H, d, *J* = 8.2 Hz), 7.23–7.31 (3H, m), 7.37–7.44 (1H, m), 7.80–7.84 (1H, m).

(Z)-Methyl-4-(β-bromovinyl)benzoate **(2g)**:[26] M.p. 43–44 °C (hexane, lit: 43–44 °C); IR (film) 1716, 1605, 1579, 961 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.93 (3H, m), 7.56 (1H, d, *J* = 8.2 Hz), 7.12 (1H, d, *J* = 8.2 Hz), 7.74 (2H, d, *J* = 8.6 Hz), 8.04 (2H, d, *J* = 8.6 Hz).

(Z)-4-(β-Bromovinyl)benzenesulfonyl azide **(2h)**: Light yellow liquid. IR (KBr): 2128, 1601, 1479, 1369, 1173 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.70 (1H, d, *J* = 8.3 Hz), 7.16 (1H, d, *J* = 8.3 Hz), 7.89 (2H, d, *J* = 8.5 Hz), 7.96 (2H, d, *J* = 8.5 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): δ 111.06, 127.45, 129.92, 130.56, 137.48, 141.43.

Conclusion

In conclusion, we have developed a new method for the synthesis of (*Z*)-*β*-arylvinyl bromides by debrominative decarboxylation of *anti*-2,3-dibromo-3-arylpropanoic acids using NaN_3/DMF system under mild conditions.

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References

1 P. Espinet and A.M. Echavarren, *Angew. Chem. Int. Ed*., 2004, **43**, 4704.
2 N. Miyaura and A. Suzuki, *Chem. Rev*., 1995, **95**, 2457.
3 J.H. Li, J.L. Li, D.P. Wang, S.F. Pi, Y.X. Xie, M.B. Zhang and X.C. Hu, *J. Org. Chem*., 2007, **72**, 2053.
4 Q. Liao, Y.X. Wang, L.Y. Zhang and C.J. Xi, *J. Org. Chem*., 2009, **74**, 6371.
5 E. Negishi and L. Anastasia, *Chem. Rev*., 2003, **103**, 1979.
6 D. Saha, T. Chatterjee, M. Mukherjee and B.C. Ranu, *J. Org. Chem*., 2012, **77**, 9379.
7 L. Jiang, G.E. Job, A. Klapars and S.L. Buchwald, *Org. Lett*., 2003, **5**, 3667.
8 R.H. Smithers, *J. Org. Chem*., 1978, **43**, 2833.
9 M. Matsumoto and K. Kuroda, *Tetrahedron Lett*., 1980, **21**, 4021.
10 G. Stork and K. Zhao, *Tetrahedron Lett*., 1989, **30**, 2173.
11 X.P. Zhang and M. Schlosser, *Tetrahedron Lett*., 1993, **34**, 1925.
12 C. Morrill and R.H. Grubbs, *J. Org. Chem*., 2003, **65**, 6031.
13 N.A. Petasis and I.A. Zavialov, *Tetrahedron Lett*., 1996, **37**, 567.
14 R.B. Miller and G. McGarvey, *J. Org. Chem*., 1978, **43**, 4424.

15 H.C. Brown, C.D. Blue, D.J. Nelson and N.G. Bhat, *J. Org. Chem*., 1989, **54**, 6064.
16 H.C. Brown, C. Subrahmanyam, T. Hanaoka, N. Ravindran, D.H. Bowman, S. Misumi, M.K. Unni, V. Somayaji and N.G. Bhat, *J. Org. Chem*., 1989, **54**, 6068.
17 J. Uenishi, R. Kawahama, Y. Shiga and O. Yonemitsu, *Tetrahedron Lett*., 1996, 37, 6759.
18 J. Uenishi, R. Kawahama, O. Yonemitsu and J. Tsuji, *J. Org. Chem*., 1998, **63**, 8965.
19 M.E. Lebrun, P.L. Marquand and C. Berthelette, *J. Org. Chem*., 2006, **71**, 2009.
20 J.E. Grovenstein and D.E. Lee, *J. Am. Chem. Soc*., 1953, **75**, 2639.
21 S.J. Cristol and W.P. Norris, *J. Am. Chem. Soc*., 1953, **75**, 2645.
22 L.A. Paquette, W.E. Fristad, D.S. Dime and T.R. Bailey, *J. Org. Chem*., 1980, **45**, 3017.
23 E.D. Matveeva, A.S. Erin and A.L. Kurz, *Russ. J. Org. Chem*., 1997, **33**, 1065.
24 S.H. Kim, H.X. Wei, S. Willis and G. Li, *Synth. Commun*., 1999, **29**, 4179.
25 C.X. Kuang, H. Senboku and M. Tokuda, *Tetrahedron Lett*., 2001, **42**, 3893.
26 C.X. Kuang, Q. Yang, H. Senboku and M. Tokuda, *Tetrahedron*, 2005, **61**, 4043.
27 Y.B. Jiang and C.X. Kuang, *Synth. Commun*., 2009, **39**, 4298.
28 W.S. Zhang, C.X. Kuang and Q. Yang, *Z. Naturforsch*., 2009, **64b**, 292.
29 B.C. Ranu, S. Banerjee and J. Gupta, *Synth. Commun*., 2007, **37**, 2869.
30 W.S. Zhang, C.X. Kuang and Q. Yang, *Synthesis*, 2010, 283.