Bromodecarboxylation of Arylpropiolic Acids with Oxone® and Sodium Bromide

Kee-Jung Lee,* Keun Wan Lim, and Dae Yoon Chi†

Department of Industrial Chemistry, Hanyang University, Seoul 133-791, Korea
†Department of Chemistry, Inha University, Inchon 402-751, Korea
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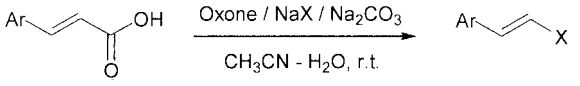
There is a considerable current interest in the synthesis of 1-haloalkynes due to their uses as the versatile intermediates in organic synthesis,[1] in the design of molecular materials,[2] and in the preparation of biocidal agents.[3] Major synthetic routes to 1-haloalkynes are usually via the halogenation of metal acetylides,[4] dehydrohalogenation of 1,1-dihaloolefins,[5] oxidative halogenation of terminal alkynes,[6] and halodecarboxylation of acetylenic acids.[7]

In previous paper,[8] we showed that sodium bromide combined with an oxidation reagent such as Oxone® generates in situ hypobromous acid and serves as an effective bromodecarboxylation reagent of various α,β-ethylenic acids bearing aryl at β-carbon in aqueous acetonitrile (Scheme 1). In the course of our study to extend the scope of the Oxone®/NaBr reagent in organic synthesis, we have found that this reagent facilitates the bromodecarboxylation of arylpropiolic acids very efficiently under the similar conditions. We report herein a facile and bench-frienldy method for the bromodecarboxylation of propiolic acids containing phenyl or thienyl groups with Oxone®/NaBr.

Recent reports have dealt with the use of potassium hydrogen persulfate ($KHSO_5$), which is commercially available as Oxone®[9] and can be used for the oxidation of alkenes,[9] arenes,[10] amines,[11] imines,[12] sulfides,[13] selenides,[14] α-amino acids,[15] acetals,[16] and for carbonyl regeneration from thioacetals,[17] oximes[18] and nitroalkanes.[19] Moreover, the use of Oxone® and aqueous sodium halide was reported as a convenient halogenating reagent to achieve oxidation of α,β-enones,[20] bromination of pyrimidines,[21] and halogenation of toluene.[9]

The acetylenic acids studied were either commercially available or prepared by literature method.[22] Thus reaction of phenylpropiolic acid (3 mmol) with sodium bromide (6 mmol), sodium carbonate (3 mmol) and Oxone® (2.4 mmol) in 30 mL of acetonitrile/water (1 : 1 v/v) at room temperature was clean and complete in 5 min (TLC), leading to 1-bromophenylacetylene in 96% isolated yield (Table 1). The reaction has been extended to various ring-substituted phenylpropiolic acids and 2-thienylpropiolic acid. As can be seen from Table 1, except in the cases of *p*-nitrophenylpropiolic acid and thienylpropiolic acid, the yields of 1-bromoacetylenes are excellent to quantitative within 5 min.[23] Analogous chlorodecarboxylation of phenylpropiolic acid using sodium chloride afforded 1-chlorophenylacetylene in 35% yield, however, iododecarboxylation did not proceed at all even if electron-rich 4-methoxyphenylpropiolic acid was subjected.



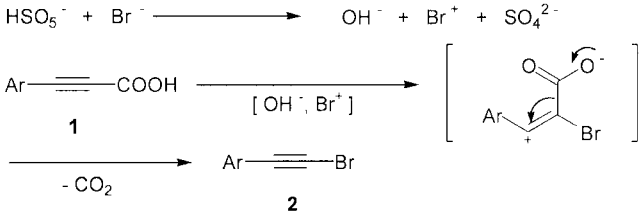
Scheme 1

*Corresponding Author. e-mail: leekj@hanyang.ac.kr; Fax: +82-2-2298-4101

Table 1. Bromodecarboxylation of Ar-C≡C-CO_2H (**1**) to Ar-C≡C-Br (**2**) with Oxone® and NaBr

Product No.	Ar	Reaction Time (min)	Yield[a] (%)
2a	C_6H_5	5	96
2b	4-ClC_6H_4	5	96
2c	4-BrC_6H_4	5	96
2d	4-FC_6H_4	5	96
2e	4-MeC_6H_4	5	98
2f	4-$MeOC_6H_4$	5	98
2g	4-$O_2NC_6H_4$	24[b]	0
2h	2-thienyl[c]	10	54

[a]Yields of isolated products. All compounds were characterized by IR, ^1H, ^{13}C NMR and mass spectra. [b]Hours. 92% of starting acid was recovered. [c]Oxidation of sulfur atom was not observed.



Scheme 2

A plausible mechanism of the bromodecarboxylation is shown in Scheme 2 based on the literature. The oxidation of bromide ion by peroxymonosulfate ion would give the hypobromite ion[24] and subsequent bromination at carbon-carbon triple bond followed by decarboxylation would afford 1-bromophenylacetylene.[7d]

In conclusion, we have shown that a facile bromodecarboxylation of arylpropiolic acids can be carried out using a mixture of Oxone® and sodium bromide, thus further widening the scope of the Hunsdiecker-Cristol reaction.[25] The described procedure is safe and economically and environmentally advantageous over reported methods.

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23. *General procedure for the bromodecarboxylation of arylpropiolic acids*: Sodium bromide (6 mmol, 0.62 g) and sodium carbonate (3 mmol, 0.32 g) was added to a stirred solution of arylpropiolic acid (3 mmol) in 30 mL of CH_3CN-H_2O (1 : 1 v/v), and then followed by the addition of Oxone® (2.4 mmol, 1.48 g) all at once. Reactions were monitored by thin-layer chromatography and stirred at r.t. for 5 to 10 min. The reaction mixture was quenched with aqueous sodium thiosulfate, and extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by chromatography on a silica gel column and eluted with hexane-EtOAc 10 : 1 to give the products.
The spectral and analytical data of products are as follows:
2a: Liquid.[5d] ^{1}H NMR ($CDCl_3$): δ 7.29-7.45 (m, 5H). ^{13}C NMR ($CDCl_3$): δ 49.7, 80.0, 122.6, 128.3, 128.6, 131.9. EIMS m/z (rel intensity, %): 182 and 180 (M^+, 100), 101 (50), 75 (30). IR (neat) cm^{-1}: 3060, 2198, 1689, 1596, 1479, 1436, 1211, 1172, 1067, 1025, 753.
2b: mp 87-89° (Lit.[5a] 88-90°). ^{1}H NMR ($CDCl_3$): δ 7.28 (d, 2H, J = 8.8 Hz), 7.37 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$): δ 51.0, 78.9, 121.1, 128.7, 133.2, 134.8. EIMS m/z (%): 218 (M^-, 24), 216 (M^+, 100), 214 (M^+, 78), 135 (25), 99 (42), 74 (31). IR (KBr) cm^{-1}: 3060, 2186, 1487, 1394, 1083, 1013, 827, 504.
2c: mp 93-96° (Lit.[5a] 96-97°) ^{1}H NMR ($CDCl_3$): δ 7.30 (d, 2H, J = 8.6 Hz), 7.44 (d, 2H, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$): d 51.2, 79.0, 121.6, 123.0, 131.6, 133.4. EIMS m/z (%): 262 (M^+, 48), 260 (M^+, 100), 258 (M^-, 52), 181 (20), 179 (21), 100 (33), 74 (33). IR (KBr) cm^{-1}: 2920, 2194, 1483, 1390, 1064, 1009, 819, 508.
2d: Liquid. ^{1}H NMR ($CDCl_3$): δ 7.03 (m, 2H), 7.41 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 49.5, 79.0, 115.5, 123.5, 133.9, 164.3. EIMS m/z (%): 200 (M^+, 100), 198 (M^+, 99), 119 (46), 99 (31). IR (neat) cm^{-1}: 2916, 2185, 1596, 1506, 1234, 1157, 833, 726, 528.
2e: Liquid (Lit.[5a] bp 97-98°/14 Torr). ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 3H), 7.11 (d, 2H, J = 8.0 Hz), 7.34 (d, 2H, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$): δ 21.6, 48.7, 80.1, 119.6, 129.1, 131.8, 138.9. EIMS m/z (%): 196 (M^+, 69), 194 (M^+, 71), 115 (100), 89 (10). IR (neat) cm^{-1}: 2914, 2198, 1696, 1509, 1181, 819, 522.
2f: Liquid (Lit.[5a] mp 39-41°) ^{1}H NMR ($CDCl_3$): δ 3.82 (s, 3H), 6.88 (d, 2H, J = 8.8 Hz), 7.34 (d, 2H, J = 8.8 Hz). ^{13}C NMR ($CDCl_3$): δ 55.3, 87.2, 89.2, 113.7, 124.8, 130.3, 160.0. EIMS m/z (%): 212 (M^-, 95), 210 (M^-, 100), 197 (62), 195 (62), 169 (34), 167 (34), 88 (29). IR (neat) cm^{-1}: 2908, 2154, 1569, 1477, 1277, 1231, 1154, 831, 554.
2h: Liquid. ^{1}H NMR ($CDCl_3$): δ 7.02 (dd, 1H, J = 5.2 and 3.7 Hz), 7.43 (dd, 1H, J = 3.7 and 1.2 Hz), 7.45 (dd, 1H, J = 5.2 and 1.2 Hz). ^{13}C NMR ($CDCl_3$): δ 90.6, 117.9, 126.7, 128.5, 131.1, 139.8. EIMS m/z (%): 188 (M^-, 100), 186 (M^-, 99), 107 (29), 81 (18). IR (neat) cm^{-1}: 2920, 1413, 1234, 757, 699.
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