Novel Catalytic Bromolactonization of Alkenoic Acids Using Iodobenzene and Oxone®

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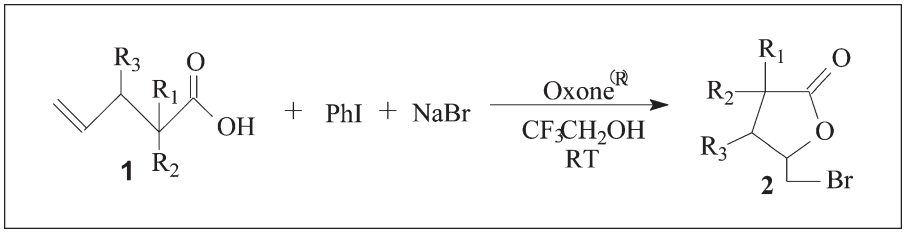
Received April 10, 2010
DOI 10.1002/jhet.617
Published online 22 February 2011 in Wiley Online Library (wileyonlinelibrary.com).



The novel catalytic reaction for bromolactonization of alkenoic acids is reported. When iodobenzene is used as recyclable catalyst in combination with Oxone® as terminal oxidant, the cyclization of various 4-pentenoic acids with sodium bromide is easily carried out in CF_3CH_2OH at room temperature and giving five-membered bromolactones in good yields.

J. Heterocyclic Chem., **48**, 695 (2011).

INTRODUCTION

Halolactonization serves as an important key reaction in a variety of syntheses and has been studied extensively [1]. Usually, alkenoic acids are used to construct lactones in the reaction, which includes an electrophilic addition of molecular halogens on the double bond, and then following an intramolecular nucleophilic cyclization [2]. Molecular iodine is a nontoxic and easy to handle solid, the iodolactonization is the most widespread applied halolactonization. However, because molecular bromine is a toxic, difficult to handle, low-boiling lachrymatory liquid, and also a strong oxidant, the bromolactonization has some restrictions [3]. To improve bromolactonization, *N*-bromosuccinimide in combination with catalysts were used in place of molecular bromine had been successful [4]; the complexes of bis(2,6-disubstitutedpyridine)bromonium triflates and dibromodiarylselenium (IV) species were also used as the efficient sources of positive bromine for bromolactonization [5]; NaBr and H_2O_2 with catalytic selenoxide, arylseleninic acids, and organotellurides were found to be preferred in the reactions [6]; Braddock *et al.* [7] reported a convenient method for the bromolactonization of 4-pentenoic acid using hypervalent iodine reagent (diacetoxyiodo)-benzene and lithium bromide.

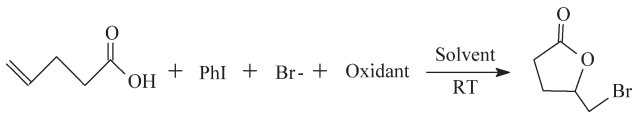
Recently, the catalytic utilization of hypervalent iodine reagents is increasing in importance, with the growing interest in the development of environmentally benign synthetic transformations [8]. In these catalytic reactions, a catalytic amount of iodoarene together with a stoichiometric oxidant are used. Usually, iodobenzene (PhI) is the most utilized iodoarene, *m*-chloroperbenzoic acid, and Oxone® ($KHSO_4{\cdot}2KHSO_5{\cdot}K_2SO_4$) are often used as the terminal oxidants. In the catalytic reaction, the oxidant generates the hypervalent iodine reagent *in situ*, and after the oxidative transformation, the reduced iodoarene is reoxidized.

Using catalytic hypervalent iodine reagents, some new lactonizations have been reported: Liu and Tan [9] investigated the iodobenzene-catalyzed iodolactonization of alkenes in which sodium perborate monohydrate as stoichiometric oxidant was used; Braddock *et al.* [10] demonstrated that suitably *ortho*-substituted iodobenzenes can catalyze the intramolecular bromolactonization of alkenes. Very recently, we found an efficient catalytic sulfonyloxylactonization of alkenoic acids using hypervalent iodine reagent [11]. To extend the catalytic cyclization scope, we have investigated the catalytic halolactonization of alkenoic acids. Herein, we would like to report the novel catalytic bromolactonization of alkenoic acids with iodobenzene as catalyst and Oxone® as terminal oxidant.

Table 1 shows the results of the catalytic bromolactonization of 4-pentenoic acid with 0.1 equiv. of iodobenzene at room temperature for 24 h, which indicates that the yields of 5-(bromomethyl)-γ-butyrolactone mainly depend on solvents and CF_3CH_2OH is the most effective one (entries 4, 8–11). As a suitable oxidant, Oxone® is the most preferred (entries 1–4). NaBr, KBr, and NH_4Br

Table 1

Results of the catalytic bromolactonization of 4-pentenoic acid with 0.1 equiv. of iodobenzene.



Entry	Br^- (1.5 equiv.)	Oxidant (1.0 equiv.)	Solvent	Yield (%)[a]
1	NaBr	$NaBO_3 \cdot 4H_2O$	CF_3CH_2OH	15
2	NaBr	*m*CPBA	CF_3CH_2OH	74
3	NaBr	$K_2S_2O_8$	CF_3CH_2OH	18
4	NaBr	Oxone®	CF_3CH_2OH	82
5	LiBr	Oxone®	CF_3CH_2OH	64
6	KBr	Oxone®	CF_3CH_2OH	80
7	NH_4Br	Oxone®	CF_3CH_2OH	75
8	NaBr	Oxone®	CH_2Cl_2	54
9	NaBr	Oxone®	THF	39
10	NaBr	Oxone®	CH_3CN	14
11	NaBr	Oxone®	DMF	23

[a] Isolated yield.

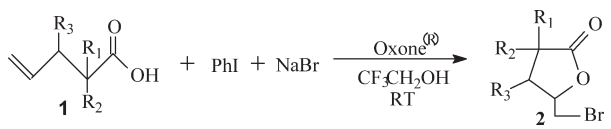
are efficient sources of bromine anion and usually NaBr is the best choice (entries 4–7).

Under the optimum reaction conditions, the reactions of a series of 4-pentenoic acids (1) with equal equivalent of Oxone®, 1.5 equiv. of NaBr, and 0.1 equiv. of iodobenzene in CF_3CH_2OH for 24 h are investigated (Scheme 1), the results are summarized in Table 2.

It is shown from Table 2 that most reactions provide good to excellent yields of five-membered bromolactones (entries 1–4). When 2-cyclopentene-1-acetic acid (1e) is used in the reaction, the corresponding product is in middle yield due to the restrictive effect of the ring (entry 5). Similar treatment of 3-butenoic acid and trans-3-hexenoic acid, the reactions only obtain the unsaturated lactones not the desired bromolactones (entries 6 and 7). It is found by ^{1}H-NMR technique that the desired five-membered lactones and four-membered lactones are first formed, which then transformed into the unsaturated lactones during workup procedure by elimination. Efforts for preparation of the sex-membered lactone of 6-bromomethyltetrahydropyran-2-one using 5-hexenoic acid are partially successful, and the desired product is separated in only 27% of yield, which is much lower than that of five-membered bromolactones.

Koser *et al*. [12] in 1988 reported a lactonization using the hypervalent iodine reagent, [hydroxyl ((bis(phenyloxy)phosphoryl)oxy)iodo]benzene, and they found when 2-methyl-4-pentenoic acid was treated with the hypervalent iodine reagent, the product was a mixture of diastereomers, the ratios varied from 1.2 to 1.4:1. In our reaction protocol, we find when **1b** is used, the corresponding product is also a mixture of diastereomers by examination of the ^{1}H-NMR spectra of bromolactones, the ratio is 2:1; while 3-methyl-4-pentenoic acid (1c) is treated in the reaction, the ratio for the obtained mixture of diastereomers is 58:42.

Scheme 1



The proposed mechanism for the catalytic cycle of bromolactonization is depicted in Scheme 2, which includes the electrophilic addition of hypervalent iodine reagent on the double bond, then an intramolecular nucleophilic cyclization is happened, and another nucleophilic bromolactonization is followed. The reduced by-product of PhI is regenerated into hypervalent iodine reagent by the oxidation of Oxone® and used in the cycle.

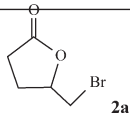
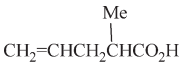
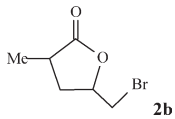
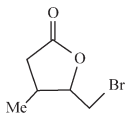
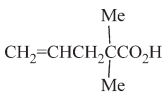
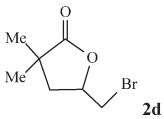
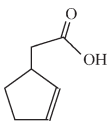
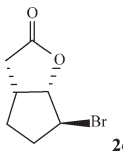
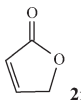
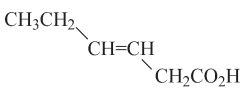
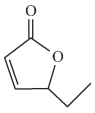
In summery, we have successfully developed an efficient catalytic bromolactonization of alkenoic acids using catalyst of PhI and Oxone® as terminal oxidants, which has some advantages such as mild reaction conditions, simple procedure, and good yields for five-membered bromolactones. Furthermore, the scope of catalytic use of hypervalent iodine reagents in organic synthesis could be extended.

EXPERIMENTAL

General procedure for the catalytic bromolactonization of alkenoic acids.. To CF_3CH_2OH (2 mL), alkenoic acid **1** (0.3 mmol), Oxone® (0.3 mmol), sodium bromide (0.45 mmol), and iodobenzene (0.03 mmol) are added. The mixture is stirred at room temperature for 24 h and then separated on a

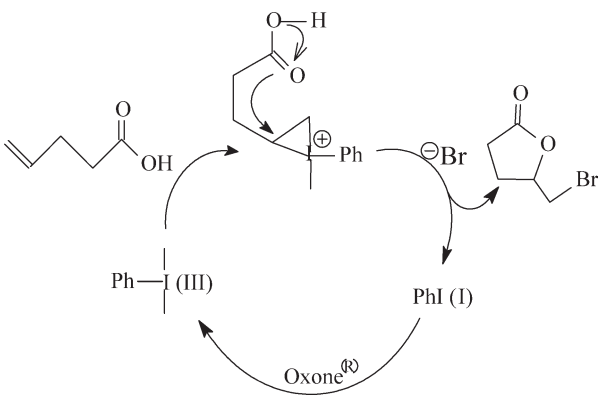
Table 2

Results of the catalytic bromolactonization of alkenoic acids.

Entry	Alkenoic acids (1)	Bromolactones (2)	Yield (%)[a]
1	$CH_2=CH(CH_2)_2CO_2H$ **1a**	 **2a**	82
2	 **1b**	 **2b**	96
3	 **1c**	 **2c**	95
4	 **1d**	 **2d**	95
5	 **1e**	 **2e**	63
6	$CH_2=CHCH_2CO_2H$ **1f**	 **2f**	23
7	 **1g**	 **2g**	38

[a] Isolated yield.

Scheme 2



silica gel plate using (3:2 hexane-ethyl acetate) as eluent to give **2** in good to excellent yields.

5-(Bromomethyl)-γ-butyrolactone (2a). Oil [7]. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.78–4.73 (m, 1H), 3.59–3.52 (m, 2H), 2.69–2.63 (m, 1H), 2.61–2.54 (m, 1H), 2.49–2.42 (m, 1H), 2.15–2.11 (m, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): 176.1, 77.9, 34.0, 28.3, 26.2. IR (film): ν = 2962, 1777, 1168, 1023, 917 cm^{-1}. MS (EI, *m*/*z*, %): 179 (13), 181 (14), 99 (100).

2-Methyl-5-(bromomethyl)-γ-butyrolactone (2b). Oil [13]. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.78–4.73 (**2b$_1$**) and 4.61–4.55 (**2b$_2$**) (m, 1H), 3.60–3.57 (**2b$_1$**) and 3.54–3.50 (**2b$_2$**) (m, 2H), 2.86–2.81 (**2b$_1$**) and 2.78–2.71 (**2b$_2$**) (m, 1H), 2.66–2.60 (**2b$_1$**) and 2.44–2.38 (**2b$_2$**) (m, 1H), 2.13–2.07 (**2b$_1$**) and 1.75–1.68 (**2b$_2$**) (m, 1H), 1.31 (d, *J* = 7.0 Hz, 3H), ^{13}C-NMR (125 MHz, $CDCl_3$): 179.1, 178.4, 75.9, 75.8, 35.6, 35.5, 34.0, 33.8, 33.7,

33.5, 16.1, 15.0. IR (film): ν = 2975, 1775, 1182, 1157, 1016, 927 cm^{-1}. MS (EI, *m*/*z*, %): 193 (100), 195 (93).

3-Methyl-5-(bromomethyl)-γ-butyrolactone (2c). Oil [14]. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.72–4.69 (**2c$_1$**) and 4.30–4.27 (**2c$_2$**) (m, 1H), 3.63–3.44 (m, 2H), 2.84–2.50 (m, 2H), 2.34 (dd, *J* = 17.0, 3.5 Hz, **2c$_1$**) and 2.25 (dd, *J* = 18.0, 8.0 Hz, **2c$_2$**) (1H), 1.23 (d, *J* = 7.0 Hz, **2c$_1$**) and 1.17 (d, *J* = 7.0 Hz, **2c$_2$**) (3H). ^{13}C-NMR (125 MHz, $CDCl_3$): 175.6, 175.3, 84.5, 80.9, 37.2, 36.6, 34.1, 34.0, 32.5, 32.3, 28.6, 19.6, 18.3, 13.0. IR (film): ν = 2969, 1781, 1156, 998, 940 cm^{-1}. MS (EI, *m*/*z*, %): 193 (12), 195 (13), 71 (100).

2, 2-Dimethyl-5-(bromomethyl)-γ-butyrolactone (2d). Oil [15]. ^{1}H-NMR (500 MHz, $CDCl_3$): 4.67–4.61 (m, 1H), 3.57 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.50 (dd, *J* = 11.0, 6.5 Hz, 1H), 2.28 (dd, *J* = 13.0, 6.5 Hz, 1H), 1.94 (dd, *J* = 13.0, 10.0 Hz, 1H), 1.30 (s, 3H), 1.10 (s, 3H), 0.89 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$): 180.9, 74.6, 41.9, 40.5, 33.6, 24.9 (d, *J* = 3.8 Hz). IR (film): ν = 2971, 1773, 1206, 1139, 1111, 1026, 915 cm^{-1}. MS (EI, *m*/*z*, %): 207 (100), 209 (96).

6-Bromohexahydrocyclopenta[b]furan-2-one (2e). Oil [10]. ^{1}H-NMR (500 MHz, $CDCl_3$): 5.08 (d, *J* = 6.0 Hz, 1H), 4.54 (d, *J* = 4.0 Hz, 1H), 3.19–3.14 (m, 1H), 2.88 (dd, *J* = 18.5, 10.0 Hz, 1H), 2.50–2.00 (m, 4H), 1.63–1.58 (m, 1H). ^{13}C-NMR (125 MHz, $CDCl_3$): 176.4, 90.5, 52.8, 36.0, 35.9, 33.1, 31.3. IR (film): ν = 2968, 1778, 1159, 1014, 875. MS (EI, *m*/*z*, %): 205 (5), 207 (4), 79 (100).

2(5H)-Furanone (2f). Oil [16]. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.61–7.59 (m, 1H), 6.19–6.17 (m, 1H), 4.93–4.92 (m, 2H). IR (film): ν = 3100, 1780, 1750, 1600, 1450, 1350, 1330, 1150, 1090, 1030 cm^{-1}.

5-Ethyl-2(5H)-Furanone (2g). Oil [16]. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.47–7.45 (m, 1H), 6.14–6.12 (m, 1H), 5.03–5.00 (m, 1H), 1.88–1.82 (m, 1H), 1.77–1.70 (m, 1H), 1.02 (t, *J* = 1.9 Hz, 3H). IR (film): ν = 3110, 2995, 1810, 1260, 1170, 1150, 1110, 920 cm^{-1}.

Acknowledgment. Financial support from the Natural Science Foundation of China (Project 21072176) is greatly appreciated.

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