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Iodobenzene-catalysed iodolactonisation using sodium perborate monohydrate as oxidant

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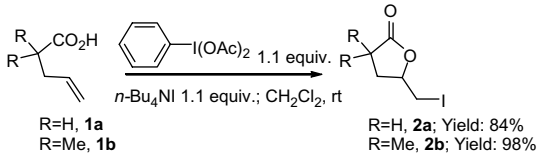
Abstract—A convenient approach has been developed for iodolactonisation using iodobenzene as catalyst. The active reagent was generated in situ with tetra-*n*-butylammonium iodide (TBAI) and hypervalent iodine reagent, diacetoxyiodobenzene (PIDA). PIDA, in turn, was generated in situ using a catalytic amount of iodobenzene with sodium perborate monohydrate as the stoichiometric oxidant. A variety of olefinic acids including δ-pentenoic acids, δ-pentynoic acids and δ-hexynoic acid gave high yields of lactones using this methodology.

Besides being mild oxidants, there are many impressive reactions, including C–C and C–X bond formations, that can be performed using hypervalent iodine reagents.[1] It is now possible to promote certain transformations using catalytic amounts of iodine reagents, in combination with stoichiometric oxidants.[2] It was demonstrated by Kita and Ochiai that *m*-chloroperbenzoic acid (*m*CPBA) was an effective oxidant for the in situ re-generation of the active hypervalent iodine(III) reagent.[3,4] It was also reported that peracetic acid, sodium perborate, $NaIO_4$ and CrO_3 were unsuitable as the stoichiometric oxidants.[3b] Recently, *N*-bromosuccinimide (NBS) was used with a catalytic amount of *o*-substituted amidyl iodobenzene for the bromination of alkenes.[5]

The chemistry of hypervalent iodine(I) reagents is relatively less explored. Diacetyloxyiodate(I) has been shown to promote oxidative phenolic coupling[6] and the iodoacetoxylation and azidoiodination of alkenes.[7] Polymer-bound diazidoiodate(I) was developed as a safe alternative to IN_3. The reagent was not deactivated after extensive washing of the resin with solvent. Formation of the ionic diacetyloxyiodate(I) was proposed as an intermediate during the preparation of this reagent.[8]

Halolactonisation is widely used to construct lactones from olefinic carboxylic acids.[9] We were keen to develop a convenient approach which would also provide a platform for the development of a catalytic version. We found that hypervalent diacetyloxyiodate(I), under mild conditions, can promote iodolactonisation (Scheme 1). This reagent can be prepared from a mixture of diacetoxyiodobenzene (PIDA) and tetra-*n*-butylammonium iodide (TBAI) in a 1:1 molar ratio. The iodolactonisation reaction of pent-4-enoic acid **1a** and 2,2-dimethylpent-4-enoic acid **1b** proceeded smoothly at room temperature with diacetyloxyiodate(I). Excellent yields of 84% and 98% were obtained, respectively, after 1 h. In the absence of TBAI, the reaction did not progress, even with heating.

When a 1:1 mixture of PIDA and TBAI was observed using ^1H NMR experiments, a new peak (s, δ 1.91 ppm) appeared and gradually replaced the Ac group (s, δ 1.99 ppm) of PIDA (see Supplementary data). An equal amount of iodobenzene was also detected downfield. This new singlet was not assigned to acetyl hypoiodite (IOAc) as it is known to have a



Scheme 1. Iodolactonisation actived by hypervalent diacetyloxyiodate(I).

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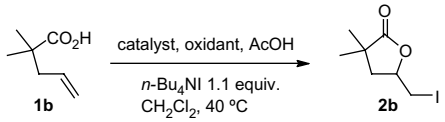
chemical shift of 2.19 ppm.[10] The generation of molecular iodine was also excluded as a possibility after a simple starch test was conducted. The iodo group on lactones **2a**–**b** is derived from TBAI. A catalytic version of this reaction is, thus, possible if we could regenerate PIDA in situ.

To investigate the catalytic version, we reduced the amount of PIDA and added a stoichiometric amount of a co-oxidant. With 10 mol % of PIDA, several oxidants including *m*CPBA were used as the oxidant (Table 1, entries 1–3) for the iodolactonisation of 2,2-dimethylpent-4-enoic acid **1b**. A moderate yield of 16% was obtained when *m*CPBA was used (entry 1). It was an unsuitable oxidant as it may also oxidise the olefin. Several side-products were observed. Sodium perborate in acetic acid was shown to oxidise iodobenzene to PIDA.[11] We found that sodium perborate monohydrate ($NaBO_3{\cdot}H_2O$) was the ideal oxidant for the iodolactonisation, giving the product cleanly. With an increased amount of acetic acid (3 equiv), the yield was improved to 64% (entry 3).

The reaction worked well even when the catalyst, PIDA was replaced with iodobenzene (entry 4). Increasing the amount of acetic acid to 5 equiv, only 5 mol % of iodobenzene was required to obtain a yield of 83% (entry 6). The catalyst amount could be reduced to 1 mol % but the yield became unacceptable. When no catalyst (PhI) was used, only a trace amount of the product was observed. Increasing the amount of TBAI did not affect the reaction at all. Other solvents such as THF, CH_3CN, $ClCH_2CH_2Cl$ were also useful for this reaction but the best result was obtained with CH_2Cl_2. This reaction also worked when TBAI was replaced with NaI (entry 9). Based on these results, we proposed a plausible catalytic cycle (Scheme 2).

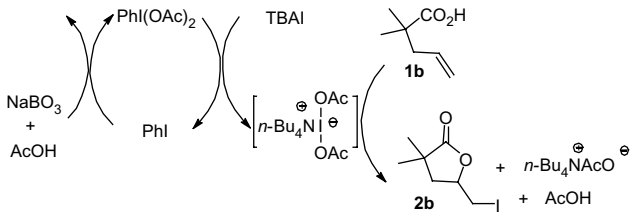
A series of δ-pentenoic acids were subjected to the optimised conditions for iodolactonisation using 5 mol % of iodobenzene (Table 2). Complete conversions were observed and lactones **2a** and **2c**–**g** were obtained in excellent isolated yields. The 5-*exo-trig* ring-closing reaction was preferred and the other possible regioisomer from a 6-*endo-trig* closure was not observed. No exocyclic olefin due to elimination was observed in any of the reactions. For the α-substituted acids, a mixture of two diastereoisomers was obtained. NOE experiments showed that *syn* lactones were the major isomers (Table 2, entries 2–4). Similarly, **2f** and **2g** were obtained in 5:1 ratio in favour of the *syn* lactone.

Table 1. Iodobenzene catalysed iodolactonisation



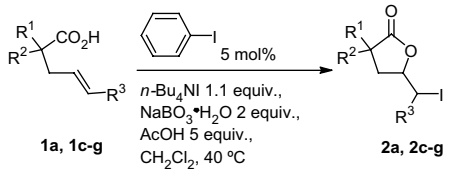
Entry	Oxidant (equiv)	Catalyst (equiv)	AcOH (equiv)	Time (h)	Yield[a] (%)
1	*m*CPBA (1.5)[b]	PIDA (0.1)	1	1	16
2	$NaBO_3{\cdot}H_2O$ (5)	PIDA (0.1)	1	21	46
3	$NaBO_3{\cdot}H_2O$ (5)	PIDA (0.1)	3	12	64
4	$NaBO_3{\cdot}H_2O$ (5)	PhI (0.1)	3	10	68
5	$NaBO_3{\cdot}H_2O$ (2)	PhI (0.1)	5	10	81
6	$NaBO_3{\cdot}H_2O$ (2)	PhI (0.05)	5	10	83
7	$NaBO_3{\cdot}H_2O$ (2)	PhI (0.01)	5	10	28
8	$NaBO_3{\cdot}H_2O$ (2)	0	5	10	Trace
9[c]	$NaBO_3{\cdot}H_2O$ (7)	PhI (0.1)	5	23	56

[a] Isolated yield.
[b] Unpurified *m*CPBA, rt.
[c] NaI (5 equiv) instead of TBAI; DMF as solvent.



Scheme 2. Proposed catalytic cycle.

Table 2. Iodolactonisation of δ-pentenoic acids



Entry	1	R^1	R^2	R^3	Time (h)	2	Yield[a] (%)
1	**1a**	H	H	H	22	**2a**	80
2	**1c**	Bn	H	H	12	**2c**	97 (dr 2:1)
3	**1d**	Et	H	H	10	**2d**	81 (dr 3:2)
4	**1e**	Me	H	H	13	**2e**	84 (dr 2:1)[b]
5	**1f**	H	H	Me	11	**2f**	87 (dr 5:1)[c]
6	**1g**	H	H	Et	19	**2g**	83 (dr 5:1)

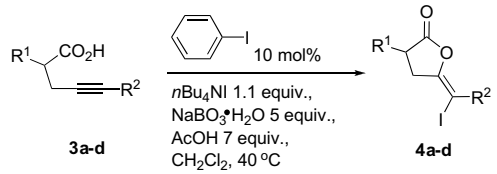
[a] Isolated yield.
[b] 3 equiv oxidant used.
[c] 5 equiv oxidant used.

This protocol was also used to prepare iodoenol lactones **4a**–**d** from δ-pentynoic acids **3a**–**c** and δ-hexynoic acid **3d** (Table 3). Haloenol lactones were previously synthesised as potential inhibitors of serine proteases and glutathione *S*-transferases.[12] The 5-*exo-dig* reaction was favoured and is also highly diastereoselective; only the *E* olefins **4a**–**c** were formed. While complete conversions were observed, the instability of these iodoenol lactones led to lower than expected yields.

When (*E*)-hex-3-enoic acid **5** was subjected to the same conditions, the 5-*endo-trig* lactone was obtained (Scheme 3). The iodo group was eliminated under the reaction conditions to provide α,β-unsaturated lactone **6** in an excellent yield (Scheme 3).

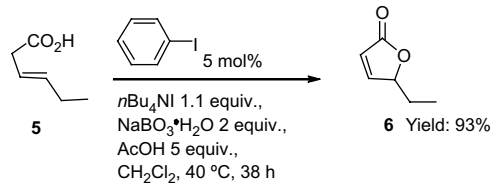
In conclusion, we have developed a new approach to iodolactonisation using iodobenzene as catalyst. The active reagent was identified as diacetyloxyiodate(I)

Table 3. Iodolactonisation of various alkynes



Entry	3	R^1	R^2	Time (h)	4	Yield[a] (%)
1	**3a**	H	H	4	**4a**	72
2	**3b**	Et	H	3	**4b**	83
3	**3c**	Bn	H	3	**4c**	57
4	**3d**	H	Me	4	**4d**	70

[a] Isolated yield.



Scheme 3. Iodolactonisation followed by elimination of iodo group.

and was generated in situ with hypervalent iodine reagent, PIDA. PIDA, in turn, was generated in situ using a catalytic amount of iodobenzene and sodium perborate as the stoichiometric oxidant. A variety of olefinic acids gave high yields of lactones using this methodology. This study should provide a platform for the possible development of a catalytic, asymmetric iodolactonisation reaction.

Acknowledgements

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Supplementary data

Experimental procedures, characterisation and spectroscopic data (PDF). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.09.078.

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