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# Organic reactions in water: an efficient one-pot synthesis of acyloxiranes from Baylis–Hillman adducts using hypervalent iodine☆

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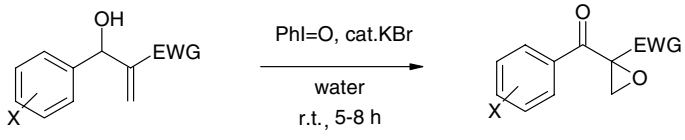
**Abstract**—Treatment of Baylis–Hillman adducts with iodosobenzene (PhI=O) in the presence of a catalytic amount of KBr in water at room temperature afforded the corresponding acyloxiranes in good yields.


Hypervalent iodine reagents have attracted considerable attention in organic synthesis due to their interesting activity, ready availability and easy handling[1] whilst organoiodine(III) reagents have been employed to carry out useful transformations. We have recently applied diacetoxyiodobenzene (DIB) to the preparation of isoxazolines from activated alkenes by treatment with aldoximes.[2] In continuation of our work on the application of hypervalent iodine reagents to organic synthesis, we now report the use of iodosobenzene (PhI=O) for the preparation of acyloxiranes from the Baylis–Hillman adducts **1**.

Baylis–Hillman adducts, 3-hydroxy-2-methylene alkanoates and 3-hydroxy-2-methylene-alkanenitriles are useful precursors in synthesis.[3] During our work[2a,4] on the reactions of these adducts we have observed that treatment of these compounds **1** with iodosobenzene in the presence of a catalytic amount of KBr in water at room temperature produced the corresponding acyloxiranes **2** (Scheme 1).

It is known that, (i) iodosobenzene can oxidize secondary alcohols including allylic alcohols to the corresponding keto compounds[5] and, (ii) electron deficient enones can undergo epoxidation with this reagent.[6] Thus, Baylis–Hillman adducts containing the necessary structural requirements, that is, an allylic hydroxyl group and an electron-withdrawing group at the requisite positions were considered for single-step conversion into their corresponding acyloxiranes.




**1** **2**

EWG = -$COOCH_3$, -CN

X = -$NO_2$, -$CF_3$, -Cl, -$OCH_3$

56–85%

**Scheme 1.**

*Keywords*: Baylis–Hillman adducts; Hypervalent iodine; PhI=O; Acyloxiranes; Aqueous medium.
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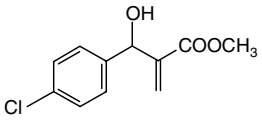
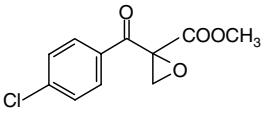
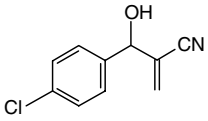
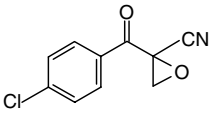
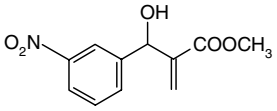
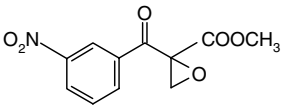
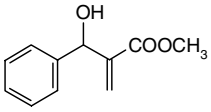
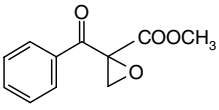
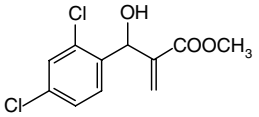
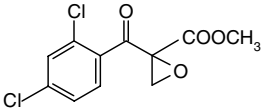
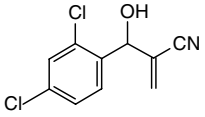
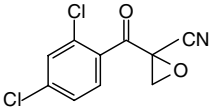
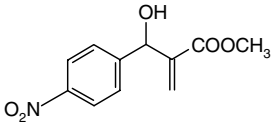
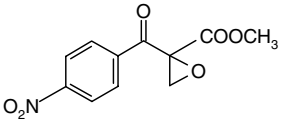
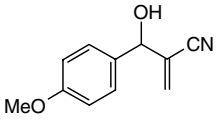
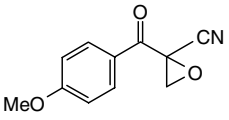
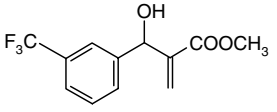
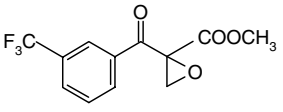
**Table 1.** Preparation of acyloxiranes from Baylis–Hillman adducts using PhI=O activated by KBr[a]

| Entry | Reactant **1** | Product **2** | Time (h) | Isolated yield (%)[b] |
|---|---|---|---|---|
| a |  |  | 6 | 81 |
| b |  |  | 5 | 80 |
| c |  |  | 6 | 70 |
| d |  |  | 6 | 85 |
| e |  |  | 5 | 64 |
| f |  |  | 5 | 56 |
| g |  |  | 8 | 78 |
| h |  |  | 6 | 65 |
| i |  |  | 1.6 | 72 |

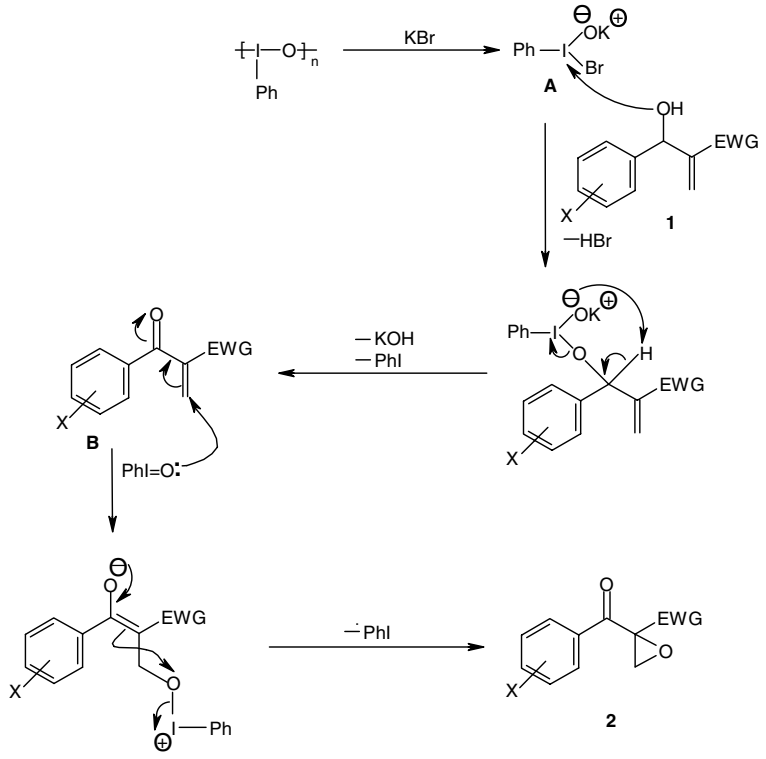
[a] The structures of the products were established from their spectral ($^1$H NMR and MS) data.
[b] A minor amount (~5%) of the parent aldehydes from which the Baylis–Hillman adducts were prepared was also obtained.

A series of acyloxiranes was prepared[7] from Baylis–Hillman adducts **1** with an ester or a nitrile substituent (Table 1). These adducts containing an electron-donating or electron-withdrawing group on the aromatic ring underwent the conversion smoothly. The structures of the products were established from their spectral ($^1$H NMR and MS) data.[7] Previously this conversion has been carried out[8] using NaOCl but this method involves the possibilities of further oxidation of the acyloxiranes to acids. In the present case, minor amounts of the parent aldehyde (≈5%) from which the Baylis–Hillman adducts were prepared were also obtained.

Initially, we used iodosobenzene by itself for oxidation of the Baylis–Hillman adducts **1** but no products were formed. However, when KBr or LiBr was added[5] to this reagent in water its activity increased significantly and the corresponding acyloxiranes **2** were formed.

The mechanism of the reaction may involve[5] depolymerization of iodosobenzene by the additon of KBr to form the highly reactive intermediate **A**. This intermediate reacts with the hydroxyl group of Baylis–Hillman adduct **1** to form the enone **B**. Iodosobenzene then attacks[6] the enone **B** to produce the acyloxirane **2** (Scheme 2).

In conclusion, we have developed an efficient process for the synthesis of acyloxiranes from Baylis–Hillman adducts using iodosobenzene activated by a catalytic amount of KBr in water at room temperature. Iodosobenzene has been utilized here for twofold oxidation of a *secondary* alcohol of a Baylis–Hillman adduct




**Scheme 2.**

followed by subsequent epoxidation of the generated enone in the one-pot synthesis of an acyloxirane.

## Acknowledgements

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7. General procedure for the preparation of acyloxiranes: To a stirred mixture of the Baylis–Hillman adduct (1 mmol) and KBr (0.2 mmol) in water (2 ml), PhI=O (2.2 mmol) was added at room temperature. Stirring was continued and the reaction was monitored by TLC. After completion, the reaction mixture was extracted with ethyl acetate ($3 \times 5$ ml), the combined organics washed with brine ($3 \times 5$ ml) and then dried over anhydrous $Na_2SO_4$. The extract was filtered and the filtrate was concentrated under vacuum. The residue was purified by column chromatography over silica gel (EtOAc/*n*-hexane) to afford the pure acyloxirane. The spectral ($^1$H NMR and MS) and analytical data of new acyloxiranes are given below. The remaining products are known.[8]
Compound **2c**: $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ 8.82 (1H, d, $J = 2.0$ Hz), 8.46 (1H, dd, $J = 8.0$, 2.0 Hz), 8.31 (1H, dd, $J = 8.0$, 2.0 Hz), 7.71 (1H, t, $J = 8.0$ Hz), 3.83 (3H, s), 3.47 (1H, d, $J = 6.0$ Hz), 3.22 (1H, d, $J = 6.0$ Hz); EIMS: *m*/*z* 251 ($M^{+\cdot}$); Anal. Calcd for $C_{11}H_9NO_6$: C, 52.59; H, 3.59; N, 5.58. Found: C, 52.74; H, 3.62; N, 5.53.
Compound **2e**: $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ 7.73 (1H, d, $J = 8.0$ Hz), 7.48 (1H, d, $J = 2.0$ Hz), 7.36 (1H, dd, $J = 8.0$, 2.0 Hz), 3.82 (3H, s), 3.43 (1H, d, $J = 6.0$ Hz), 3.12 (1H, d, $J = 6.0$ Hz); EIMS: *m*/*z* 278, 276, 274 ($M^{+\cdot}$); Anal. Calcd for $C_{11}H_8Cl_2O_4$: C 48.00; H, 2.91. Found: C, 48.31; H, 2.84.
Compound **2f**: $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ 7.56–7.33 (3H, m), 3.55 (1H, d, $J = 6.0$ Hz), 3.21 (1H, d, $J = 6.0$ Hz): EIMS: *m*/*z* 245, 243, 241 ($M^{+\cdot}$); Anal. Calcd for $C_{10}H_5Cl_2NO_2$: C, 49.59; H, 2.07; N, 5.79. Found: C, 49.82; H, 2.11; N, 5.63.
Compound **2i**: $^1$H NMR ($CDCl_3$, 200 MHz): $\delta$ 8.28 (1H, d, $J = 2.0$ Hz), 8.19 (1H, dd, $J = 8.0$, 2.0 Hz), 7.90 (1H, dd, $J = 8.0$, 2.0 Hz), 7.64 (1H, t, $J = 8.0$ Hz), 3.79 (3H, s), 3.40 (1H, d, $J = 6.0$ Hz), 3.21 (1H, d, $J = 6.0$ Hz); EIMS: *m*/*z* 274 ($M^{+\cdot}$); Anal. Calcd for $C_{12}H_9F_3O_4$: C, 52.56; H, 3.29. Found: C, 52.76; H, 3.20.
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