

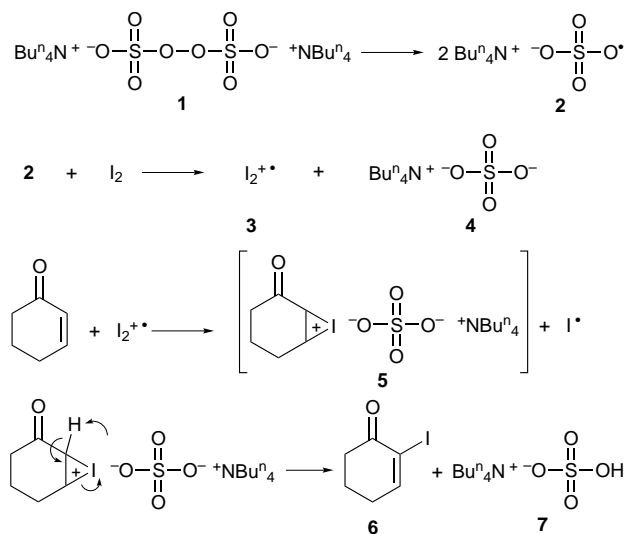
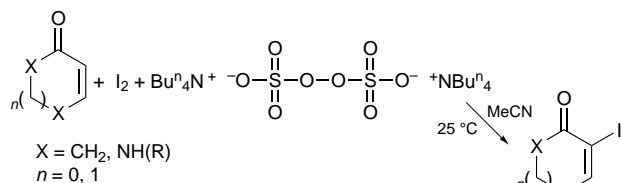
Novel α -iodination of functionalized ketones with iodine mediated by bis(tetra-*n*-butylammonium) peroxydisulfate

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α,β -Unsaturated ketones, β -keto esters and uracil derivatives react with iodine in the presence of bis(tetra-*n*-butylammonium) peroxydisulfate under mild conditions in MeCN at 25 °C to give the corresponding α -iodinated products in good yields.

α -Haloenones and α -halo ketones are highly reactive and versatile intermediates for the generation of α -carbon substituted enones¹ and ketones.² α -Halo ketones have been well studied and documented, but only a few reports on the preparation of α -iodoenones have been reported, which employ iodine-ceric ammonium nitrate³ and I₂-pyridine-CCl₄.⁴ The reactivity of α -iodine is higher, especially in transition metal mediated reactions, than the corresponding bromo or chloro derivatives, while functionalization of the 5-position of uracils or uridines is important for the synthesis of chemotherapeutic agents⁵ and synthetic oligonucleotide probes.⁶ Bis(tetra-*n*-butylammonium) peroxydisulfate **1** has been successfully prepared and turns out to be a useful source of tetra-*n*-butylammonium sulfate radical **2**,^{7†} which is readily convertible to sulfate anion by one electron transfer from a substrate. Working on the supposition that activation of iodine by **2** might be possible, various enones, ketones, and uracils were examined in the reaction system.



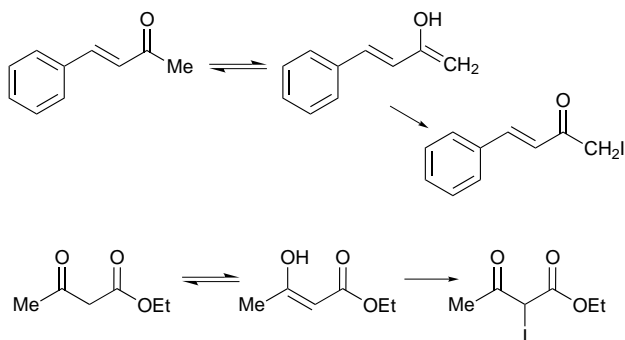
We have found that α,β -unsaturated ketones, β -keto esters and uracil derivatives reacted with I₂ in the presence of **1** to give the corresponding α -iodo α,β -unsaturated ketones, α -iodo β -keto esters and 5-iodouracil products respectively in good yields (Scheme 1).

An example of the procedure is as follows. A solution of cyclohex-2-ene-1-one (1.0 mmol, 1.0 equiv.) in 5 ml of dried MeCN was added at room temperature to a solution of bis(tetra-*n*-butylammonium) peroxydisulfate (1.0 mmol, 1.0 equiv.) and I₂ (1.0 mmol, 1.0 equiv.) in 5 ml of dried MeCN. The reaction mixture was monitored by thin layer chromatography with stirring at room temperature. When the reaction was completed,

Table 1 α -Iodinations with I₂ and bis(tetra-*n*-butylammonium) peroxydisulfate in MeCN at 25 °C

Entry	Reactant	I ₂ /equiv.	1 equiv.	t/h	Solvent	Product	Yield (%) ^a
1		0.5	0.5	5	MeCN		48
2		0.5	1.0	5	MeCN		60
3		1.0	0.5	5	MeCN		54
4		1.0	1.0	5	CCl ₄		25
5		1.0	1.0	5	CH ₂ Cl ₂		65
6		1.0	1.0	5	CHCl ₃		34
7		1.0	1.0	5	MeCN		85
8		1.0	1.0	3.5	MeCN		83
9		1.0	1.0	24	MeCN		95
10		1.0	1.0	2	MeCN		90
11		1.0	1.0	1	MeCN		72
12		1.0	1.0	3.5	MeCN		75
13		1.0	1.0	12	MeCN		82

^a Isolated yield; purified by column chromatography.



Scheme 3

the mixture was poured into 10% aqueous sodium bisulfate (30 ml) and extracted with ethyl acetate (30 ml \times 3). The organic layer was washed with H₂O (40 ml \times 3) and dried over anhydrous MgSO₄. After filtration and concentration under reduced pressure, the residue was purified by flash column chromatography (silica gel 230–400 mesh, EtOAc–*n*-hexane, 1 : 10, v/v) to give 2-iodocyclohex-2-en-1-one (85%). All the products were identified by their ¹H NMR and/or ¹³C NMR and mass spectra.

Optimization of the iodinations indicates that 1 equiv. each of substrate, iodine and **1** affords the best results. The results obtained are summarized in Table 1.

The reaction mechanism is not clear. It appears to be initiated by cleavage of **1** to give **2**.^{7†} The sulfate radical **2** may react with I₂ to form a cationic iodine radical **3** and the sulfate anion **4**. The cyclic enone then reacts with **3** to form an iodine-bridged intermediate **5**. A sulfate anion **4** may abstract the α -proton from intermediate **5** to form the products **6** and **7**,[‡] as shown in Scheme 2.

It is of interest that α,β -unsaturated methyl ketones gave the methyl-iodinated products (95%, entry 9) instead of iodination at the double bond, and a β -keto ester afforded an α -iodinated

product (90%, entry 10). These reactions appears to proceed via their enol forms (Scheme 3).

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Footnotes

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† Bis(tetra-*n*-butylammonium) peroxydisulfate was prepared from 2.0 equiv. of tetra-*n*-butylammonium hydrogen sulfate and 1.0 equiv. of potassium peroxydisulfate in water at room temperature. It was extracted with CH₂Cl₂, dried over anhydrous MgSO₄ and then concentrated to give **1**, which was dried under vacuum for one day.

‡ In the iodination of cyclohex-2-en-1-one, **7** was isolated in 80% and its identity confirmed; mp 170–172 °C (*Aldrich Catalogue Hand Book of Fine Chemicals*, 1996–1997, mp 171–173 °C).

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