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Selective Oxidation of Alcohols Using the 1:1 Complex of *N*-Bromosuccinimide and Tetrabutylammonium Iodide

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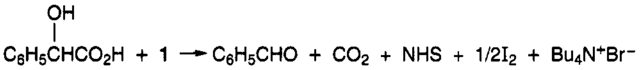
The reaction of alcohols with *N*-iodosuccinimide (NIS) to form the corresponding alkyl hypoiodites,[1−3] which break down in a variety of ways to form stable products, is a well-studied reaction. However, the NIS reagent is expensive to make and is not very selective in its oxidizing ability. NIS reacts[2] readily with primary, secondary, and tertiary alcohols as well as 1,2-diols, 1,4-diols, and α-hydroxycarboxylic acids. In this paper, we introduce the 1:1 complex **1**,[4] prepared by mixing equal molar amounts of *N*-bromosuccinimide (NBS) and tetrabutylammonium iodide, as a selective oxidizing agent of alcohols. When the complex **1** is prepared there is evidence[4] that the most electronegative halogen, the bromine atom, becomes the anion while the other halogen, the iodine, is attached to the nitrogen of succinimide forming NIS as part of the complex. An equilibrium[5] in solution ($\text{NBS} + \text{I}^- \leftrightarrows \text{NS}^- + \text{BrI} \leftrightarrows \text{NIS} + \text{Br}^-$) has been suggested as a source of the NIS. The resulting product contains a complex which is able to produce hypoiodites with certain hydroxy groups and is much more selective in its oxidizing abilities than is NIS itself. Table 1 outlines the selective nature of the oxidation of alcohols with the complex 1. Reactions were conducted in acetonitrile with irradiation. The 150-W bulbs heated the mixtures to reflux during the reactions and no other heat was added. Irradiations of reactions with 1 which were kept below 20 °C gave reaction percentages of products that were very low. Reactions with 1 which were not heated and not irradiated gave essentially no product yields. NIS reaction percentages are given first for comparison with reactions performed with the complex **1**, with and without the addition of silver nitrate. When silver nitrate was added a precipitate of silver bromide was formed, presumably releasing the NIS from the complex and the resulting oxidizing agent was NIS and not the complex. The complex **1** was inactive toward nonbenzylic primary, secondary, and tertiary alcohols but easily oxidized benzyl alcohols, 1,2-diols, and α-hydroxy carboxylic acids. The reaction of mandelic acid with **1** is shown below. The products of the oxidations of *meso*-hydrobenzoin, mandelic acid, pinacol, and α-hydroxyisobutyric acid by **1** indicate intermediate hypoiodite[3] activity during the reaction.

$$\text{NBS} + \text{Bu}_4\text{N}^+\ \text{I}^- \rightarrow \text{1:1 complex } \mathbf{1}$$



$$\text{C}_6\text{H}_5\text{CH(OH)CO}_2\text{H} + \mathbf{1} \rightarrow \text{C}_6\text{H}_5\text{CHO} + \text{CO}_2 + \text{NHS} + 1/2\text{I}_2 + \text{Bu}_4\text{N}^+\text{Br}^-$$

The results of competitive reactions involving the complex **1**, benzyl alcohol, and several of the alcohols which were unreactive with **1** are listed in Table 2. Comparison competitive reactions were also run with NIS. The competitive reactions with **1** give strong evidence of the selective oxidizing ability of the complex containing *N*-iodosuccinimide.

Several experiments were conducted using about 10−20 times the usual amounts of complex **1** and alcohols. Two experiments are described. Benzyl alcohol was oxidized with **1** under these conditions producing a GC yield of 89% benzaldehyde. Workup of the reaction produced 81% crude benzaldehyde which gave 77% yield of an orange-red 2,4-dinitrophenylhydrazine precipitate. A large competitive oxidation of benzyl alcohol and 3-ethyl-3-pentanol with complex **1** produced a GC yield of 65−69% benzaldehyde and no 3-pentanone with an isolated yield of 55% of the 2,4-dinitrophenylhydrazone product.

Experimental Section

Analyses given in Tables 1 and 2 were performed by GC. Liquid chemicals used in the reaction mixtures and the standard GC mixtures all had greater than 99.5% purity as determined by gas chromatographic analysis. The acetonitrile solvent was spectroscopically pure and was used as purchased. GC analyses were done on 6 ft × 0.25 in. copper columns of 10% SE-30, 7% SE-30 and 3% Carbowax 20M, and 10% Carbowax 20M. The NBS and NIS were used as purchased and titrated with thiosulfate to give 97.5−99.0% active halogen. The tetrabutylammonium iodide was used as purchased. Irradiation of reaction mixtures was effected with a GE Projector Spot 150-W, 1310-V tungsten lamp.

Preparation[4,5] of the Tetrabutylammonium Iodide/*N*-Bromosuccinimide Complex 1. A mixture of 2.213 g (5.99 mmol) of tetrabutylammonium iodide, 50 mL of dry acetone, and 50 mL of anhydrous ether was stirred in a 500 mL round-bottomed flask. When the tetrabutylammonium iodide had dissolved completely 1.082 g (6.08 mmol) of NBS was added and the mixture was stirred until all of the NBS dissolved. An additional amount of anhydrous ether was added (about 200 mL) until a white precipitate formed. The mixture was placed in a freezer for 3 h-, and 50 mL of cold ether was then added to the mixture to precipitate more crystals. The mixture was kept in the freezer overnight (15 h)-, and the crystals (2.72 g, 83.0%, mp 104−106 °C) were collected by vacuum filtration. Active iodine titration (thiosulfate) gave 98.0% activity.

Oxidation of *meso*-Hydrobenzoin with Complex 1. A 25-mL reaction mixture was prepared containing 1.147 g (10.19 mmol) of chlorobenzene (internal standard) and 1.065 g (4.97 mmol) of *meso*-hydrobenzoin in acetonitrile. Five mL of the reaction mixture which contained 0.548 g (1.00 mmol) of complex **1** was stirred and irradiated. Samples were analyzed at various intervals giving percentage yields of benzaldehyde of 65 (15 min), 74 (30 min), 90 (70 min), and 94 (100 min). Thiosulfate titration gave a 93% yield of molecular iodine.

Oxidation of Benzyl Alcohol with Complex 1. **(a)** Five mL of an acetonitrile solution containing 0.220 g (2.04 mmol) of

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Table 1

alcohol	ox products	NIS (%)	complex **1** (%)	$AgNO_3$/**1** (%)
3-ethyl-3-pentanol	iodoethane	96–98	0	78–85
	3-pentanone	98–99	0	55–60
2-methyl-2-propanol	iodomethane	67–72	0	49–58
	acetone	61–65	0	55–59
1-pentanol	pentanal	0–1	0	1–4
	2-methylTHF	92–94	0	81–84
1-butanol	butanal	0–1	0	0–1
	THF	60–65	0	48–51
2-methyl-1-phenyl-1-propanol	benzaldehyde	80–87	0	78–82
	isobutyrophenone	4–9	0	4–11
benzyl alcohol	benzaldehyde	85–92	85–95	79–86
4-methylbenzyl alcohol	*p*-tolualdehyde	82–89	85–92	77–85
meso-hydrobenzoin	benzaldehyde	92–96	90–97	88–94
mandelic acid	benzaldehyde	93–99	96–99	91–93
pinacol	acetone	96–99	82–87	92–95
α-hydroxyisobutyric acid	acetone	91–98	88–91	85–88

Table 2

alcohol mixture	oxidation products	NIS (%)	complex **1** (%)
benzyl alcohol and pinacol	benzaldehyde and acetone	7–9	52–55
		70–73	47–50
benzyl alcohol and 3-ethyl-3-pentanol	benzaldehyde and 3-pentanone	58–60	67–72
		60–62	0–2
benzyl alcohol and 1-pentanol	benzaldehyde and 2-methylTHF	66–73	69–72
		31–33	0
benzyl alcohol and 2-methyl-2-propanol	benzaldehyde and acetone	not done	81–88
			0
benzyl alcohol and 1-butanol	benzaldehyde and THF	74–81	67–74
		21–25	0
benzyl alcohol and cyclopentanol	benzaldehyde and 5-iodopentanal	not done	60–62
			0

benzyl alcohol and 0.225 g (1.98 mmol) of chlorobenzene (internal standard) was added to 1.095 g (2.00 mmol) of complex **1**. The mixture was irradiated and stirred. Percentage yields of benzaldehyde by gas chromatographic analysis were 67 (5 min), 75 (15 min), and 95 (30 min). Thiosulfate titration gave 97% yield of molecular iodine.

(b) A 50-mL acetonitrile solution of 2.59 g (24.0 mmol) benzyl alcohol and 16.82 g (30.7 mmol) complex **1** was irradiated with stirring for 1 h. GC analysis yielded 89% benzaldehyde. Workup of the reaction mixture produced a crude benzaldehyde product (2.12 g, 81%) which was converted with 2,4-dinitrophenylhydrazine to a 2,4-dinitrophenylhydrazone precipitate, 5.04 g (77%), mp 233–236 °C (lit.[6] mp 237 °C).

Oxidation of 3-Ethyl-3-pentanol with Complex 1. A reaction mixture was prepared in a 25-mL volumetric flask by adding 0.866 g (5.52 mmol) of bromobenzene (internal standard) and 0.583 g (5.02 mmol) of 3-ethyl-3-pentanol to acetonitrile. Five mL of the reaction mixture containing 0.173 g (1.10 mmol) of bromobenzene and 0.117 g (1.00 mmol) of 3-ethyl-3-pentanol was added to 0.560 g (1.10 mmol) of complex **1**. The mixture was stirred and irradiated with GC samples taken at intervals. No iodoethane or 3-pentanone peaks were detected after 90 min. Ninety-three percent of the starting alcohol was found to remain on GC analysis.

Oxidation of 3-Ethyl-3-pentanol with a Mixture of Complex 1 and Silver Nitrate. To 0.550 g (1.005 mmol) of complex **1** and 0.176 g (1.04 mmol) of silver nitrate was added 5 mL of an acetonitrile reaction mixture containing 0.173 g (1.10 mmol) of bromobenzene (internal standard) and 0.117 g (1.00 mmol) of 3-ethyl-3-pentanol. The mixture was stirred and irradiated and analyzed by GC. Percentage yields were 58 (20 min), 59 (45 min), 61 (60 min), 62 (90 min) of iodoethane and 72 (20 min), 77 (45 min), 79 (60 min), 78 (90 min) 3-pentanone.

Competitive Oxidation of a Mixture of Benzyl Alcohol and Pinacol with Complex 1. Five mL of a reaction mixture containing 0.216 g (1.99 mmol) of benzyl alcohol, 0.236 g (2.00 mmol) of pinacol, and 0.205 g (1.89 mmol) of chlorobenzene in acetonitrile was added to 0.870 g (1.589 mmol) of complex **1**. The mixture was stirred and irradiated, and samples were taken at intervals. Percentage yields as determined by GC were 49 (8 min), 51 (28 min), 57 (47 min), 55 (64 min), and 66 (160 min) benzaldehyde and 53 (8 min), 53 (28 min), 49 (47 min), 47 (64 min), and 48 (160 min) acetone.

Competitive Oxidation of a Mixture of Benzyl Alcohol and 3-Ethyl-3-pentanol with Complex 1. (a) Five mL of a reaction mixture containing 0.108 g (1.00 mmol) of benzyl alcohol, 0.120 g (1.04 mmol) of 3-ethyl-3-pentanol, and 0.103 g (0.944 mmol) of chlorobenzene in acetonitrile was added to 0.438 g (0.800 mmol) of complex **1**. The mixture was stirred and irradiated, and samples were taken at intervals. GC analysis gave percent yields of 50 (5 min), 56 (25 min), 62 (45 min), 68 (64 min), and 70 (90 min) benzaldehyde while no peaks of iodoethane or 3-pentanone were found during the run.

(b) A 100 mL acetonitrile mixture of 5.401 g (46.5 mmol) of 3-ethyl-3-pentanol, 5.271 g (48.6 mmol) of benzyl alcohol, and 21.145 g (38.6 mmol) of complex **1** was irradiated and stirred for 2 h. Analysis by GC gave a benzaldehyde yield of 65–69% with no 3-pentanone peaks found. Workup of the reaction gave 9.92 g of crude mixture (benzyl alcohol, benzaldehyde, and 3-ethyl-3-pentanol) which produced 7.60 g (55%), mp 234–236 °C (lit.[6] 237 °C), of 2,4-dinitrophenylhydrazone.

Competitive Oxidation of a Mixture of Benzyl Alcohol and 3-Ethyl-3-pentanol with NIS. Five mL of an acetonitrile reaction mixture containing 0.216 g (1.99 mmol) of benzyl alcohol, 0.232 g (2.00 mmol) of 3-ethyl-3-pentanol, and 0.098 g (0.898 mmol) of chlorobenzene was added to 0.362 g (1.61 mmol) of *N*-iodosuccinimide. The mixture was stirred and irradiated. GC samples were taken at intervals. The yields were 54% (24 min), 56% (43 min), and 60% (63 min) benzaldehyde and 55% (24 min), 61% (43 min), and 62% (63 min) 3-pentanone. The iodoethane peaks were not monitored.

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