

# Benzylic and Allylic Oxidations with Bis(trifluoroacetoxyiodo)benzene and *tert*-Butyl Hydroperoxide

Mustafa Catir, Hamdullah Kilic\*

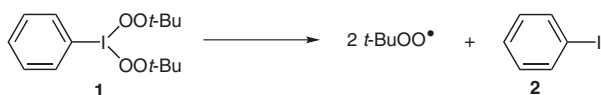
Faculty of Sciences, Department of Chemistry, Ataturk University, 25240 Erzurum, Turkey  
Fax +90(442)2360948; E-mail: hkilic@atauni.edu.tr

Received 29 December 2010

**Abstract:** Oxidation of benzylic and allylic substrates with a bis(trifluoroacetoxyiodo)benzene/*tert*-butyl hydroperoxide system to the corresponding  $\alpha,\beta$ -unsaturated enones was investigated. The scope and reaction mechanism are discussed.

**Key words:** hydrocarbons, hypervalent iodine, *tert*-butyl hydroperoxide, radical reaction, oxidation, ketones

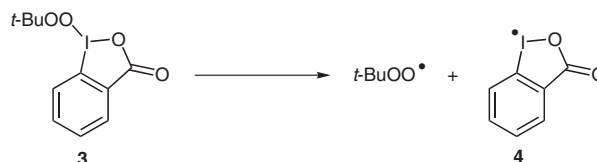
Although a variety of new reagents of iodine(III) and iodine(V) has been developed and received considerable attention in recent years, little is known about peroxyiodanes.<sup>1</sup> This is due the fact that such compounds have a high tendency to decompose and thus they are not isolable. For example, treatment of phenyliodane oxide with *tert*-butyl hydroperoxide (TBHP) was reported to give in situ generated labile bis(*tert*-butylperoxy)(phenyl)- $\lambda^3$ -iodane (**1**), which decomposes homolytically at  $-80\text{ }^\circ\text{C}$  to give iodobenzene (**2**) and *tert*-butyloxidanyl (Equation 1).<sup>2</sup> Plesnicar and Russell reported the first synthesis of bis(benzoylperoxy)(phenyl)- $\lambda^3$ -iodane as a labile amorphous solid from the reaction of phenyliodane oxide with perbenzoic acid.<sup>3</sup>



Equation 1

Ochiai and coworkers found that the Lewis acid catalyzed ligand exchange of 1-hydroxy-1,2-benziodoxol-3(1*H*)-one with TBHP in chloroform affords the crystalline (alkylperoxy)iodane, 1-(*tert*-butylperoxy)-1 $\lambda^3$ ,2-benziodoxol-3(1*H*)-one (**3**), which is stable in the solid state but gradually decomposes in solution at ambient temperature to give *tert*-butyloxidanyl and [9-I-2] iodanyl radical **4** through homolytic cleavage of the hypervalent iodine(III)–peroxy bond (Equation 2).<sup>4</sup>

The *tert*-butylperoxy and iodanyl radicals, shown to be efficient radical oxidants, are responsible for the oxidation of sulfides, secondary and tertiary amines and amides, benzyl and allyl ethers, and phenols to the corresponding oxygenated product.<sup>5</sup>



Equation 2

Recently, we described the conversion of aromatic substrates that have no phenolic hydroxy or amino substituents to their corresponding quinones by the system comprising bis(trifluoroacetoxyiodo)benzene (PIFA, **5**, Figure 1) and TBHP.<sup>6</sup> Based on the successful oxidation results obtained using PIFA/TBHP, we reasoned that this system ought to oxidize benzylic and allylic substrates to the corresponding  $\alpha,\beta$ -unsaturated enones since it generates *tert*-butyloxidanyl and shares many of the chemical features of **3**, and thus may exhibit high oxidant efficiency comparable with results using **3** as oxidant. Herein, we report the conversion of a series of benzylic and allylic substrates with PIFA/TBHP into the corresponding  $\alpha,\beta$ -unsaturated enones under mild conditions. The oxidation system is found to be generally versatile with benzylic and allylic substrates under optimized reaction conditions.

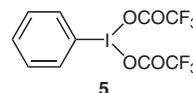
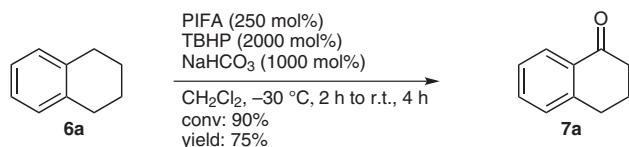


Figure 1

The benzylic substrate **6a** was used as the model substrate to test the reactivity (% conversion of the benzylic substrate **6a**) of the PIFA/TBHP system. In the absence of either PIFA or TBHP, the benzylic substrate **6a** remained unchanged even after two hours exposure to the oxidation conditions, implying that both components are essential for the oxidation. The results for the benzylic and allylic substrates are shown in Table 1 for the best set of oxidation conditions determined in Scheme 1. Our initial experiments focused on the oxidation of tetraline (**6a**) to  $\alpha$ -tetralone<sup>7</sup> (**7a**) by PIFA and anhydrous TBHP in dichloromethane at  $-30\text{ }^\circ\text{C}$  (Scheme 1). The release of oxygen gas in the course of the reaction was very slow at this temperature. The mixture was stirred for two hours at this temperature, and then the temperature was allowed to increase slowly to room temperature. Analysis of the crude reaction mixture based on the  $^1\text{H}$  NMR spectrum recorded

after complete consumption of PIFA indicated the formation of **7a**, iodobenzene (**2**), and unreacted starting material **6a** along with unidentified compounds. However, when the reaction was conducted at room temperature little conversion of tetraline (**6a**) into  $\alpha$ -tetralone (**7a**) occurred as determined by  $^1\text{H}$  NMR analysis of the crude mixture, indicating that the reactive intermediate is quenched before the reaction.

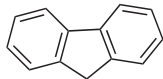
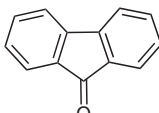
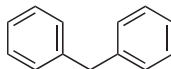
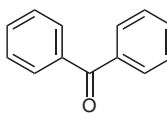
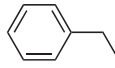
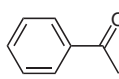
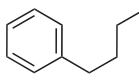
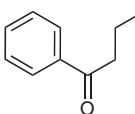
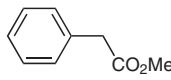
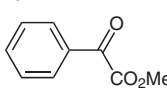
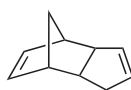
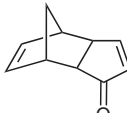
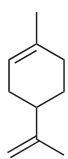
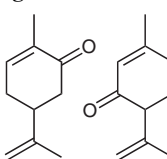
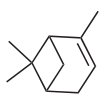
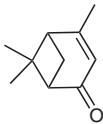

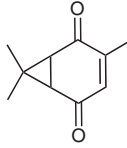


**Scheme 1** Oxidation of tetraline

The optimized reaction conditions<sup>8</sup> (Scheme 1) were then applied to the set of benzylic and allylic substrates **6b–l** (Table 1), to assess structural effects on the reactivity of the present system. Depending on the structure of benzylic and allylic substrates **6b–l**, the conversions varies from 15% to 99%. Fluorene (**6b**) containing a doubly activated benzylic position was easily oxidized to fluorenone<sup>9</sup> (**7b**) in 80% yield (entry 1). Diphenylmethane (**6c**) was oxidized to benzophenone<sup>10</sup> (**7c**) under the same conditions in 63% chemical yield (entry 2). The oxidations of ethyl benzene (**6d**) and *n*-butylbenzene (**6e**) gave acetophenone (**7d**) and butyrophenone<sup>10</sup> (**7e**), respectively. Methyl 2-phenylacetate (**6f**) with an electron-withdrawing group was oxidized to  $\alpha$ -keto ester<sup>11</sup> **7f** at low conversion. To determine the oxidation potential of the present system the oxidation of other compounds with allylic C–H bonds, dicyclopentadiene **6g**, limonene (**6h**),  $\alpha$ -pinene (**6i**), and  $\Delta$ -3-carene (**6l**) was studied. Dicyclopentadiene **6g** was oxidized to the corresponding enone<sup>12</sup> **7g** with high conversion and in moderate yield (entry 6). The oxidation of limonene (**6h**) gave a mixture of carvone<sup>13a</sup> (**7h**) and isopiperitenone<sup>13b</sup> (**7i**, entry 7). This oxidative system led exclusively to verbenone<sup>14</sup> (**7k**) when applied to  $\alpha$ -pinene (**6i**, entry 8). It is interesting to note that oxidation of  $\Delta$ -3-carene (**6l**) gave only enedione<sup>15</sup> **7l** as an isolable product instead of the expected mono C–H bond-oxidation product.

The prominent trend displayed in Table 1 is that the conversion of the allylic substrates is higher than that of benzylic substrates, except for the substrate **6b**. The data reveal that the reactivity of the PIFA/TBHP system decreases with the structure of the substrates. Clearly, the benzylic substrates **6c,e,f**, the most sterically hindered substrates, show a lower reactivity, while the more accessible benzylic and allylic  $\text{CH}_2$  group is more readily oxidized. Presumably, steric repulsion of the substituent attached to the benzylic and allylic  $\text{CH}_2$  group hinders the proton abstraction by *tert*-butyloxidanyl.

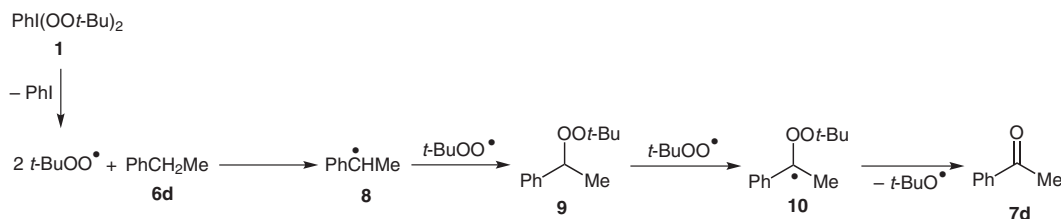
**Table 1** Oxidations of Substrates **6b–l** with the PIFA/TBHP System<sup>a</sup>

Entry	Substrate	Product	Conv. (%) <sup>b</sup>	Yield (%) <sup>c</sup>
1			>99	80
2			40	65
3			75	60
4			15	85
5			20	80
6			75	45
7			>99	51
8			70	50
9			90	35

<sup>a</sup> Reaction conditions: substrate (2 mmol), PIFA (5 mmol), TBHP (40 mmol),  $\text{NaHCO}_3$  (20 mmol),  $\text{CH}_2\text{Cl}_2$  (20 mL),  $-30^\circ\text{C}$  to r.t., 6 h.

<sup>b</sup> Conversion based on substrate consumption; after complete PIFA consumption, a sample of the crude reaction mixture was taken and the conversions determined by  $^1\text{H}$  NMR analysis with diphenylmethane (except for entry 2) as internal standard; error ca.  $\pm 5\%$  of the stated values.

<sup>c</sup> Isolated yield based on the converted starting material.



**Scheme 2** Proposed mechanism for the generation of *tert*-butyloxidanyl and oxidation of ethylbenzene (**6d**) to acetophenone (**7d**)

A plausible mechanism for the generation of *tert*-butyloxidanyl and oxidation of ethylbenzene (**6d**) to acetophenone (**7d**) is depicted in Scheme 2. Initially, nucleophilic attack of TBHP on PIFA leads to the formation of the reactive intermediate peroxyiodane **1** by exchanging two trifluoromethyl acetate groups for two *tert*-butylperoxy groups.<sup>16</sup> Homolytic cleavage of the hypervalent iodine(III)–peroxy bond in **1** gives *tert*-butyloxidanyl and iodobenzene. Then hydrogen abstraction from the benzylic position of ethylbenzene by the *tert*-butyloxidanyl forms the carbon-centered benzylic radical **8** and *tert*-butyl alcohol. Coupling of this radical with *tert*-butyloxidanyl<sup>17</sup> may generate **9**, which undergoes decomposition via a radical pathway, resulting in the formation of acetophenone (**7d**).

In summary, the present study provides the first example of direct oxyfunctionalization of benzylic and allylic substrates to the corresponding  $\alpha,\beta$ -unsaturated carbonyl compounds using a PIFA/TBHP system. The combination of PIFA and TBHP is a source for the production of the *tert*-butyloxidanyl, which is an electrophilic oxidant for the conversion of allylic and benzylic substrates into the corresponding enones.

### Acknowledgment

Financial support from Ataturk University is gratefully acknowledged. In addition, M.C. would like to thank the Scientific and Technological Research Council of Turkey (TUBITAK) for a scholarship.

### References and Notes

- (1) (a) *Hypervalent Iodine Chemistry: Modern Developments in Organic Synthesis*; Wirth, T., Ed.; Topics in Current Chemistry Series 224, Springer: Berlin/Tokyo, **2003**. (b) Varvoglis, A. *The Organic Chemistry of Polycoordinated Iodine*; VCH Publishers: New York, **1992**. (c) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: London, **1997**. (d) Moriarty, R. M.; Prakash, O. *Hypervalent Iodine in Organic Chemistry: Chemical Transformations*; Wiley-Interscience: Chichester, **2008**. (e) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, *96*, 1123. (f) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, *102*, 2523. (g) Wirth, T.; Hirt, U. H. *Synthesis* **1999**, 1271. (h) Stang, P. J. *J. Org. Chem.* **2003**, *68*, 2997. (i) Moriarty, R. M. *J. Org. Chem.* **2005**, *70*, 2893. (j) Wirth, T. *Angew. Chem. Int. Ed.* **2005**, *44*, 3656. (k) Varvoglis, A. *Tetrahedron* **1997**, *53*, 1179. (l) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299.
- (2) Milas, N. A.; Plesnicar, B. *J. Am. Chem. Soc.* **1968**, *90*, 4450.
- (3) (a) Plesnicar, B.; Russell, G. A. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 797. (b) Plesnicar, B. *J. Org. Chem.* **1975**, *40*, 3267.
- (4) (a) Ochiai, M.; Ito, T.; Masaki, Y.; Shiro, M. *J. Am. Chem. Soc.* **1992**, *114*, 6269. (b) Ochiai, M.; Ito, T.; Takahashi, H.; Nakanishi, A.; Toyonari, M.; Sueda, T.; Goto, S.; Shiro, M. *J. Am. Chem. Soc.* **1996**, *118*, 7716.
- (5) (a) Traylor, T. G.; Xu, F. *J. Am. Chem. Soc.* **1987**, *109*, 6201. (b) Traylor, T. G.; Fann, W.-P.; Bandyopadhyay, D. *J. Am. Chem. Soc.* **1989**, *110*, 8009. (c) Ochiai, M.; Nakanishi, A.; Ito, T. *J. Org. Chem.* **1997**, *62*, 4253. (d) Ochiai, M.; Kajishima, D.; Sueda, T. *Heterocycles* **1997**, *46*, 71. (e) Ochiai, M.; Kajishima, D.; Sueda, T. *Tetrahedron Lett.* **1999**, *40*, 5541. (f) Ochiai, M.; Nakanishi, A.; Yamada, A. *Tetrahedron Lett.* **1997**, *38*, 3927. (g) *Hypervalent Iodine Chemistry: Reactivities, Properties, Structures*, Topics in Current Chemistry Series 224; Ochiai, M., Ed.; Springer: Berlin / Heidelberg, **2003**. (h) Sueda, T.; Takeuchi, Y.; Suefuji, T.; Ochiai, M. *Molecules* **2005**, *10*, 195. (i) Catino, A. J.; Nichols, J. M.; Forslund, R. E.; Doyle, M. P. *Org. Lett.* **2005**, *7*, 263. (j) Catino, A. J.; Nichols, J. M.; Forslund, R. E.; Doyle, M. P. *Org. Lett.* **2005**, *7*, 2787. (k) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2001**, *123*, 3183. (l) Dohi, T.; Takenaga, N.; Goto, A.; Fujioka, H.; Kita, Y. *J. Org. Chem.* **2008**, *73*, 7365.
- (6) (a) Catir, M.; Kilic, H. *Synlett* **2003**, 1180. (b) Catir, M.; Kilic, H. *Synlett* **2004**, 2151.
- (7) (a) Bonvin, Y.; Callens, E.; Larrosa, I.; Henderson, D. A.; Oldham, J.; Burton, A. J.; Barrett, A. G. M. *Org. Lett.* **2005**, *7*, 4549. (b) Shaabani, A.; Soleimani, K.; Bazgir, A. *Synth. Commun.* **2004**, *34*, 3303.
- (8) **General Procedure for Oxidation of Benzylic and Allylic Substrates with PIFA/TBHP System**  
(Caution! Although we have never experienced an explosion, the oxidation of substrates with PIFA/TBHP system should be carried out behind shields.) To a solution of substrate (2 mmol) and anhyd TBHP (40 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at -30 °C was added NaHCO<sub>3</sub> (20 mmol). Then a freshly prepared solution of PIFA (5.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was added over 2 h. The temperature was slowly increased to r.t. over 4 h. On completion of reaction, the excess TBHP was reduced by adding DMS<sup>18</sup> (40 mmol) and Ti(Oi-Pr)<sub>4</sub> (0.15 mmol) at r.t. while the reaction proceeding was monitored by peroxide testing (KI, AcOH). The suspension was filtered, and the solution was washed with sat. NaHCO<sub>3</sub> solution and H<sub>2</sub>O. The organic layer was dried over MgSO<sub>4</sub>, and the solvent was removed at reduced pressure (20 °C/50 mbar). The products were purified on a silica gel column (40 g) by eluting with hexane–EtOAc (95:5). The first fractions gave iodobenzene. Further elution afforded analytically pure ketone. The ketones **7a–l** are known, and analytical data were found to be identical with those reported.  
**9H-Fluoren-9-one (7b)**  
Yellow solid, mp 81–82 °C (CH<sub>2</sub>Cl<sub>2</sub>–hexane). <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 7.63 (dd, *J* = 7.3, 1.0 Hz, 2H), 7.30–7.20 (m, 2H), 7.48–7.45 (m, 4H). <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):

$\delta$  = 195.8, 146.4, 136.6, 136.1, 131.0, 126.2, 122.2.

**3,7,7-Trimethylbicyclo[4.1.0]hept-3-ene-2,5-dione (71)**

Pale yellow solid; mp 94–96 °C (CH<sub>2</sub>Cl<sub>2</sub>–hexane). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 6.50–6.48 (m, 1 H), 2.33–2.29 (m, 2 H), 1.96 (d, *J* = 1.8 Hz, 3 H), 1.31 (s, 3 H) 1.30 (s, 3 H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 195.2, 194.6, 150.2, 137.8, 40.0, 39.1, 33.9, 29.3, 16.4, 15.6.

- (9) (a) Silvestre, S. M.; Salvador, J. A. R. *Tetrahedron* **2007**, *63*, 2439. (b) Fang, X.-Q.; Xu, H.-J.; Jiang, H.; Liu, Y.-C.; Fu, Y.; Wu, Y.-D. *Tetrahedron Lett.* **2009**, *50*, 312.
- (10) Bellale, E. V.; Bhalerao, D. S.; Akamanchi, K. G. *J. Org. Chem.* **2008**, *73*, 9473.
- (11) Suman, L. J.; Vishal, B. S.; Bir, S. *Tetrahedron* **2006**, *62*, 6841.
- (12) Dilling, W. L.; Plepys, R. A. *J. Org. Chem.* **1970**, *35*, 2971.
- (13) (a) Rothman, E. S.; Day, A. R. *J. Am. Chem. Soc.* **1954**, *76*, 111. (b) Anglea, T. A.; Pinder, A. R. *Tetrahedron* **1987**, *43*, 5537.
- (14) Kosugi, H.; Ku, J.; Kato, M. *J. Org. Chem.* **1998**, *63*, 6939.
- (15) Corey, E. J.; Burke, H. J. *J. Am. Chem. Soc.* **1956**, *78*, 174.
- (16) Catir, M.; Kilic, H.; Nardello-Rataj, V.; Aubry, J.-M.; Kazaz, C. *J. Org. Chem.* **2009**, *74*, 4560.
- (17) McLaughlin, E. C.; Choi, H.; Wang, K.; Chiou, G.; Doyle, M. P. *J. Org. Chem.* **2009**, *74*, 730.
- (18) Adam, W.; Balci, M.; Kilic, H. *J. Org. Chem.* **2000**, *65*, 5926.

Copyright of Synlett is the property of Georg Thieme Verlag Stuttgart and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.