

PhI-Catalyzed α -Tosyloxylation of Ketones with *m*-Chloroperbenzoic Acid and *p*-Toluenesulfonic Acid

Yukiharu Yamamoto,^a Hideo Togo^{*a,b}

^a Graduate School of Science and Technology, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan

^b Department of Chemistry, Faculty of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan
E-mail: togo@faculty.chiba-u.jp

Received 12 January 2006

Abstract: Various α -tosyloxyketones were efficiently prepared in high yields from the reaction of ketones with *m*-chloroperbenzoic acid and *p*-toluenesulfonic acid in the presence of a catalytic amount of iodobenzene at warming temperature.

Key words: iodobenzene, α -tosyloxyketones, ketones, *m*-chloroperbenzoic acid, *p*-toluenesulfonic acid, catalysts

Synthetic use of hypervalent iodines for organic synthesis has been studied widely.¹ Especially, (diacetoxyiodo)benzene, iodosylbenzene, and [hydroxy(tosyloxy)iodo]benzene (Koser's reagent) are the most popular and useful trivalent iodine reagents for organic synthesis as alternatives to toxic heavy-metal reagents.² Among them, [hydroxy(tosyloxy)iodo]benzene is an efficient sole reagent for the direct α -tosyloxylation of ketones.³ α -Tosyloxyketones are very important strategic precursors for the construction of various heteroaromatics such as thiazoles, oxazoles, selenazoles, imidazoles, pyrazoles, benzofurans and lactones.³ We have also studied synthetic uses of [hydroxy(tosyloxy)iodo]arenes, 1-(arenesulfonyloxy)benziodoxolones, and poly[4-hydroxy(tosyloxy)iodo]styrene for the construction of thiazoles, imidazoles, imidazo[1,2-*a*]pyridines, and 2,1-benzothiazines.⁴

Recently, we reported an efficient one-pot preparation of various [hydroxy(sulfonyloxy)iodo]arenes from iodoarenes with *m*-chloroperbenzoic acid (MCPBA) and sulfonic acids at room temperature.⁵ Here, as a part of our study for synthetic use of [hydroxy(sulfonyloxy)iodo]arenes for organic synthesis,⁴ we would like to report PhI-catalyzed α -tosyloxylation of various ketones with MCPBA and *p*-toluenesulfonic acid (PTSA).

Table 1 shows the effect of the amount of ArI to provide α -tosyloxyacetophenone from acetophenone with MCPBA and PTSA in acetonitrile at warming temperature, and indicates that α -tosyloxyacetophenone is obtained in good yields using PhI in the range of 0.1–1.0 equivalents (entries 1–6).⁶ The present reaction does not proceed at all in the absence of PhI and therefore PhI acts as a catalyst (entry 7). Among PhI, *p*-CH₃C₆H₄I, *p*-CH₃OC₆H₄I, and *p*-ClC₆H₄I, PhI is the most effective for the α -tosyloxylation of ketones (entries 8–11). Under the present conditions,

Table 1 ArI-Catalyzed α -Tosyloxylation of Acetophenone with MCPBA and PTSA⁶

Entry	ArI (equiv)	Temp (°C)	Yield (%) ^a
1	PhI (1.0)	80	89
2	PhI (0.5)	80	83
3	PhI (0.2)	80	80
4	PhI (0.1)	80	76
5	PhI (0.05)	80	66
6	PhI (0.01)	80	19
7	PhI (0)	80	0 ^b
8	PhI (0.1)	50	85
9	<i>p</i> -CH ₃ C ₆ H ₄ I (0.1)	50	80
10	<i>p</i> -CH ₃ OC ₆ H ₄ I (0.1)	50	51
11	<i>p</i> -ClC ₆ H ₄ I (0.1)	50	63
12		50	52

^a Isolated yield.

^b Acetophenone was recovered in 67% yield.

the formation of Baeyer–Villiger oxidation products is not observed.

Poly(4-iodostyrene)⁷ was not so very effective as catalyst under the present conditions, probably due to its insolubility (entry 12), though poly[4-hydroxy(tosyloxy)iodo]styrene is an efficient polymer-supported reagent for α -tosyloxylation of ketones and aldehydes.^{4e,f} Based on these results, various ketones, alkyl aryl ketones, dialkyl ketones, cyclic ketone, were treated with MCPBA and PTSA in the presence of 0.1 equivalent of PhI to provide the corresponding α -tosyloxyketones in good yields as shown in Table 2. A plausible reaction pathway for the present reaction is shown in Scheme 1. Thus, PhI is oxidized by MCPBA in the presence of PTSA to generate [hydroxy(tosyloxy)iodo]benzene in situ, which then

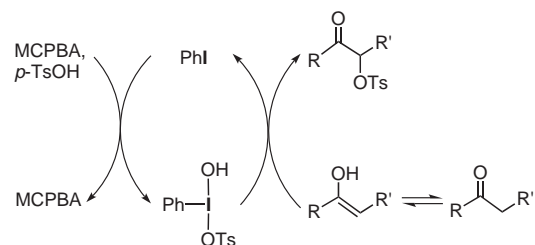
Table 2 PhI-Catalyzed α -Tosyloxylation of Ketones with MCPBA and PTSA

$\text{R}-\text{C}(=\text{O})-\text{CH}_2-\text{R}' \xrightarrow[\text{MeCN, 50 }^\circ\text{C, 5 h}]{\text{PhI (0.1 equiv), MCPBA (1.1 equiv), } p\text{-TsOH}\cdot\text{H}_2\text{O (1.1 equiv)}} \text{R}-\text{C}(=\text{O})-\text{CH}(\text{OTs})-\text{R}'$			
Entry	R	R'	Yield (%) ^a
1	C ₆ H ₅	H	85
2	<i>p</i> -CH ₃ C ₆ H ₄	H	75
3	<i>p</i> -ClC ₆ H ₄	H	88
4	<i>p</i> -NO ₂ C ₆ H ₄	H	88
5	C ₆ H ₅	CH ₃	74
6	C ₆ H ₅	C ₇ H ₁₅	63
7	C ₂ H ₅	CH ₃	76 (88) ^b
8	C ₅ H ₁₁	C ₄ H ₉	67
9	-(CH ₂) ₅ -		69 ^c

^a Isolated yield.^b CF₃CO₂H (2.0 equiv) was added.^c Reaction was carried out at 30 °C.

reacts with the enol form of ketone to provide α -tosyloxyketone. As related reactions, very recently, PhI-catalyzed efficient α -acetoxylation of ketones with MCPBA in AcOH in the presence of BF₃·OEt₂ and water was reported to provide the corresponding α -acetoxyketones in moderate isolated yields.⁸ In these reactions, addition of water is crucial and BF₃·OEt₂ is also essential for the α -acetoxylation of ketones. However, our present α -tosyloxylation of ketones with MCPBA proceeds in acetonitrile without any additive or using of acidic solvent. Hypervalent iodine(III)-catalyzed oxidation of β -(4-hydroxyaryl)propanoic acids with MCPBA was also reported to give the corresponding spirolactones.⁹ The present reaction is close to these studies. However, in view of the synthetic utility of α -tosyloxyketones for various types of heterocyclic compounds, we believe that the present α -tosyloxylation method is very useful.

Further synthetic study for PhI-catalyzed organic synthesis with MCPBA is underway in this laboratory.

**Scheme 1** Plausible Reaction Pathway for PhI-Catalyzed α -Tosyloxylation of Ketones.

Acknowledgment

Financial support of a Grant-in-Aid for Scientific Research (No. 16655012) from the Ministry of Education, Science, Sports and Culture of Japan is gratefully acknowledged.

References and Notes

- (1) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, **1997**.
- (2) Reviews: (a) Ochiai, M. *Rev. Heteroat. Chem.* **1989**, 2, 92. (b) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (c) Stang, P. J. *Angew. Chem., Int. Ed. Engl.* **1992**, 31, 274. (d) Prakash, O.; Saini, N.; Sharma, P. K. *Synlett* **1994**, 221. (e) Kitamura, T. *Yuki Gosei Kagaku Kyokashii* **1995**, 53, 893. (f) Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, 96, 1123. (g) Umemoto, T. *Chem. Rev.* **1996**, 96, 1757. (h) Kita, Y.; Takada, T.; Tohma, H. *Pure Appl. Chem.* **1996**, 68, 627. (i) Togo, H.; Hoshina, Y.; Nogami, G.; Yokoyama, M. *Yuki Gosei Kagaku Kyokashii* **1997**, 55, 90. (j) Varvoglis, A. *Tetrahedron* **1997**, 53, 1179. (k) Zhdankin, V. V. *Rev. Heteroat. Chem.* **1997**, 17, 133. (l) Muraki, T.; Togo, H.; Yokoyama, M. *Rev. Heteroat. Chem.* **1997**, 17, 213. (m) Kitamura, T.; Fujiwara, Y. *Org. Prep. Proced. Int.* **1997**, 29, 409. (n) Varvoglis, A.; Spyroudis, S. *Synlett* **1998**, 221. (o) Zhdankin, V. V.; Stang, P. J. *Tetrahedron* **1998**, 54, 10927. (p) Moriarty, R. M.; Prakash, O. *Adv. Heterocycl. Chem.* **1998**, 69, 1. (q) Togo, H.; Katohgi, M. *Synlett* **2001**, 565. (r) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2002**, 102, 2523.
- (3) Reviews: (a) Moriarty, R. M.; Vaid, R. K.; Koser, G. F. *Synlett* **1990**, 365. (b) Koser, G. F. *Aldrichimica Acta* **2001**, 34, 89. (c) Prakash, O.; Saini, N.; Sharma, P. K. *Heterocycles* **1994**, 38, 409. Papers: (d) Neilands, O.; Karele, B. J. *Org. Chem. USSR* **1970**, 6, 885. (e) Koser, G. F.; Wettach, R. H.; Troup, J. M.; Bertram, A. F. *J. Org. Chem.* **1976**, 41, 3609. (f) Koser, G. F.; Wettach, R. H. *J. Org. Chem.* **1977**, 42, 1476. (g) Koser, G. F.; Wettach, R. H.; Smith, C. S. *J. Org. Chem.* **1980**, 45, 1543. (h) Koser, G. F.; Relenyi, A. G.; Kalos, A. N.; Rebrovic, L.; Wettach, R. H. *J. Org. Chem.* **1982**, 47, 2487. (i) Moriarty, R. M.; Penmasta, R.; Awasthi, A. K.; Epa, W. R.; Prakash, I. J. *Org. Chem.* **1989**, 54, 1101. (j) Moriarty, R. M.; Vaid, R. K.; Hopkins, T. E.; Vaid, B. K.; Prakash, O. *Tetrahedron Lett.* **1990**, 31, 201. (k) Tuncay, A.; Dustman, J. A.; Fisher, G.; Tuncay, C. I. *Tetrahedron Lett.* **1992**, 33, 7647. (l) Moriarty, R. M.; Vaid, B. K.; Duncan, M. P.; Levy, S. G.; Prakash, O.; Goyal, S. *Synthesis* **1992**, 845. (m) Prakash, O.; Goyal, S. *Synthesis* **1992**, 629. (n) Prakash, O.; Rani, N.; Goyal, S. *J. Chem. Soc., Perkin Trans. 1* **1992**, 707. (o) Prakash, O.; Saini, N.; Sharma, P. K. *Synlett* **1994**, 221. (p) Vrama, R. S.; Kumar, D.; Liesen, P. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4093. (q) Lee, J. C.; Choi, J.-H. *Synlett* **2001**, 234.
- (4) Monomer reagents: (a) Muraki, T.; Togo, H.; Yokoyama, M. *J. Org. Chem.* **1999**, 64, 2883. (b) Nabana, T.; Togo, H. *J. Org. Chem.* **2002**, 67, 4362. (c) Misu, Y.; Togo, H. *Org. Biomol. Chem.* **2003**, 1, 1342. (d) Ueno, M.; Nabana, T.; Togo, H. *J. Org. Chem.* **2003**, 68, 6424. Polymer reagents: (e) Abe, S.; Sakuratani, K.; Togo, H. *Synlett* **2001**, 22. (f) Abe, S.; Sakuratani, K.; Togo, H. *J. Org. Chem.* **2001**, 66, 6174. (g) Sakuratani, K.; Togo, H. *ARKIVOC* **2003**, (vi), 11. (h) Ueno, M.; Togo, H. *Synthesis* **2004**, 2673.
- (5) Yamamoto, Y.; Togo, H. *Synlett* **2005**, 2486.

(6) **Typical Procedure for PhI-Catalyzed α -Tosyloxylation of Ketones with MCPBA and PTSA**

To a solution of acetophenone (120 mg, 1 mmol) in MeCN (5 mL) were added iodobenzene (20 mg, 0.1 mmol), PTSA monohydrate (209 mg, 1.1 mmol) and MCPBA (65% purity, 292 mg, 1.1 mmol). The mixture was stirred for 5 h at 50 °C under an Ar atmosphere. After the reaction, the reaction mixture was poured into sat. aq NaHCO₃ solution and extracted with CHCl₃ (3 × 30 mL). The organic layer was dried over Na₂SO₄. After removal of the solvent under reduced pressure, α -tosyloxyacetophenone was obtained in an almost pure state. If necessary, the residue was purified by short column chromatography (eluent: hexane–EtOAc,

3:1) to give pure α -tosyloxyacetophenone in 85% (247 mg) yield.

α -Tosyloxyacetophenone

Mp 90 °C (lit.¹⁰ mp 90–91 °C). IR (KBr): 1715, 1360, 1180 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ = 2.45 (s, 3 H), 5.27 (s, 2 H), 7.35 (d, J = 8.5 Hz, 2 H), 7.47 (t, J = 8.2 Hz, 2 H), 7.61 (t, J = 8.2 Hz, 1 H), 7.85 (m, 4 H).

Other α -tosyloxyketones were also identified by comparison with previously prepared authentic compounds.^{4d}

- (7) Togo, H.; Sakuratani, K. *Synlett* **2002**, 1966.
- (8) Ochiai, M.; Takeuchi, Y.; Katayama, T.; Sueda, T.; Miyamoto, K. *J. Am. Chem. Soc.* **2005**, *127*, 12244.
- (9) Dohi, T.; Maruyama, A.; Yoshimura, M.; Morimoto, K.; Tohma, H.; Kita, Y. *Angew. Chem. Int. Ed.* **2005**, *44*, 6193.