

# A unique site-selective reaction of ketones with new recyclable hypervalent iodine(III) reagents based on a tetraphenylmethane structure†

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We have synthesized new recyclable reagents having a tetraphenylmethane backbone and used them in the site-selective  $\alpha$ -tosyloxylation of ketones.

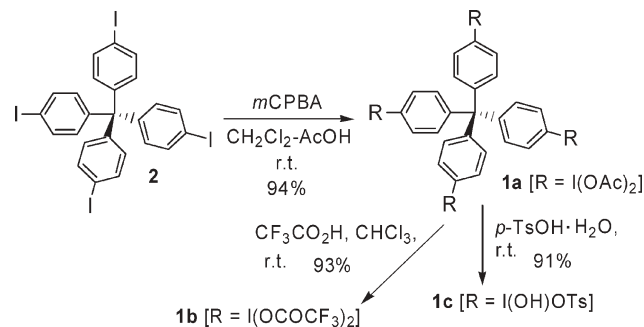
Over the past two decades, hypervalent iodine(III) reagents have received much attention due to their low toxicity, ready availability, easy handling, and reactivities similar to those of heavy metal reagents<sup>1</sup> and in particular, recyclable reagents such as polymer-supported<sup>2–4</sup> and perfluoroalkyl-substituted<sup>5</sup> reagents have been recognized as a useful tool to meet the recent demand for environmentally benign, ecologically conscious chemical processes. From these circumstances, we have currently developed novel, highly recyclable hypervalent iodine(III) reagents having an adamantane core, in which their high reactivities are obviously derived from their well-defined tetrahedral structures so as not to interfere with each iodine(III) site.<sup>6</sup> This hypothesis prompted us to seek other new hypervalent iodine(III) alternatives. In this communication, we report the concise synthesis of new recyclable iodine(III) reagents **1a–c** having a more small tetraphenylmethane backbone and utilize them to a unique site-selective  $\alpha$ -tosyloxylation of ketones.

We have synthesized new reagents **1a–c** according to Scheme 1.‡ Thus, tetrakis(4-iodophenyl)methane **2** is readily accessible from tetraphenylmethane in a single step.<sup>7</sup> Attempts to oxidize **2** to tetrakis[4-(diacetoxyiodo)phenyl]methane **1a** under standard oxidation conditions, peracetic acid (30% H<sub>2</sub>O<sub>2</sub> and acetic anhydride),

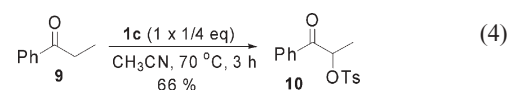
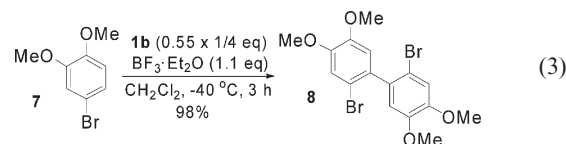
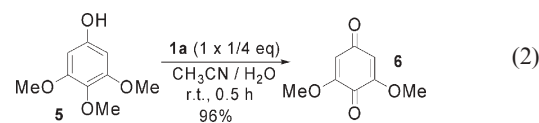
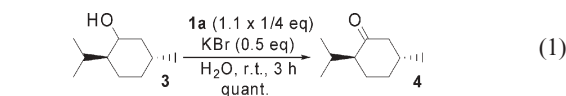
sodium perborate (NaBO<sub>3</sub>) in acetic acid, or sodium periodate (NaIO<sub>4</sub>) and so on, unexpectedly gave disappointing results. Further investigations finally led us to succeed in synthesizing **1a** in 94% yield using *m*-chloroperbenzoic acid (*m*CPBA) in CH<sub>2</sub>Cl<sub>2</sub>–acetic acid (AcOH) (1 : 1). Several iodine(III) derivatives such as **1b** and **1c** could be also synthesized from **1a** by typical synthetic procedures as reported for phenyliodine bis(trifluoroacetate) (PIFA),<sup>8</sup> hydroxy(tosyloxy)iodobenzene (HTIB)<sup>9a</sup> in satisfactory yields. These compounds **1a–c** are quite stable and can be stored at room temperature for long periods without any decomposition.

The iodine(III) reagent **1a** was easily purified by recrystallization from acetic acid and separated from the partially oxidized byproducts. A single-crystal X-ray analysis of the reagent **1a** is shown in Fig. 1.§ It reveals that it has four symmetrical equivalent iodine(III) sites and a pentagonal–planar arrangement of three strong and two weak secondary bonds around each iodine(III) center, which are similar to those in previously reported adamantane reagents.

The reactivities of these new reagents **1a–c** have been examined in several oxidative transformations. As expected, the oxidation of alcohol [eqn. (1)]<sup>4a,d,e</sup> and phenol [eqn. (2)],<sup>4c</sup> an oxidative biarylcoupling reaction<sup>4b</sup> [eqn. (3)], and the  $\alpha$ -tosyloxylation of a ketone [eqn. (4)]<sup>9</sup> smoothly proceeded with excellent yields.

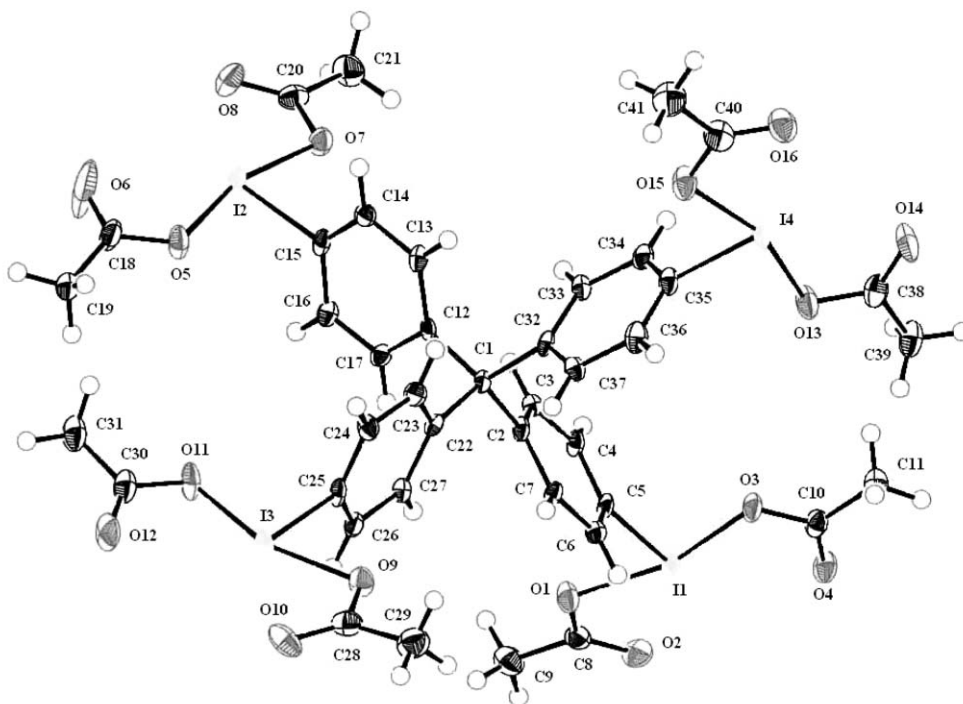


**Scheme 1** Preparation of tetrakis[4-(diacetoxyiodo)phenyl]methane (**1a**) and transformation of **1a** to **1b** and **1c**.



† Electronic supplementary information (ESI) available: details of experimental procedures and analytical data for new compounds. See <http://www.rsc.org/suppdata/cc/b5/b501475a/>  
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In all cases, tetraiodide **2**, formed after the reactions were completed, hardly soluble in MeOH, could be recovered as a pure form after a simple work-up. Since tetraphenylmethane-based molecule **2** is about four times less soluble than an analogous



**Fig. 1** ORTEP drawing of **1a**. Selected bond lengths [Å] and angles [°]: I1–C5 2.092(5), I1–O1 2.130(4), I1–O2 2.817(4), I1–O3 2.171(4), I1–O4 2.886(4), O1–I1–C5 81.3(2), O3–I1–C5 80.1(2), O1–I1–O3 161.3(1).

adamantane-based molecule in MeOH,<sup>10</sup> **2** was usually obtained with nearly quantitative yield. These results showed that the new reagents **1a–c** are versatile reagents with respect to reactivity as well as recyclability, compared to other iodine(III) reagents.

In addition, it is interesting that the reagent **1a** showed a characteristic behavior in selectivity for the  $\alpha$ -tosyloxylation of 2-butanone **11a** (Table 1). Such a regioselectivity is not a general phenomenon.<sup>9</sup> Thus, 2-butanone **11a** gave the 3-tosyloxyated product **12a** as a major product with a 5.1 : 1 selectivity (entry 1). **1c** gave a similar result (entry 2). Phenyliodine diacetate (PIDA) and the polymer-supported reagent poly(diacetoxyiodo)styrene (PDAIS)<sup>2–4</sup> gave **12a** less selectively than did **1a** (entries 3 and 4). Although it has been reported that the reaction occurred preferentially at the less hindered position in the case of

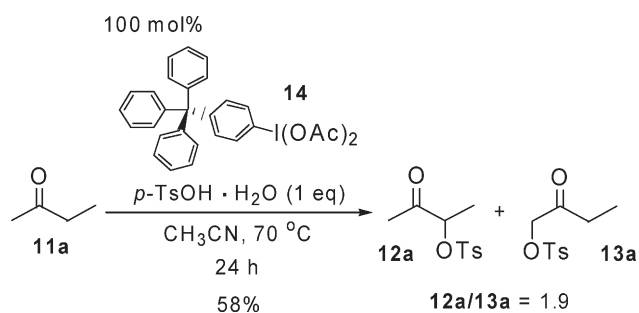
$\alpha$ -sulfonyloxylation of 2-butanone **11a** using PIDA and (+)-10-camphorsulfonic acid,<sup>9b</sup> three times more **12a'** than **13a'** was obtained, (entry 5). Similar to the case for 2-butanone, these site-selective  $\alpha$ -tosyloxylation were observed in other various ketones (entries 6–8).<sup>11</sup>

The following experimental result clearly suggests the structural importance of **1a** to ensure these unique site-selective reactions (Scheme 2). Thus, a compound **14**, which has only one active iodine(III) site, did not show any change in site-selectivity in the reaction of 2-butanone **12a** compared to PIDA and polymer-supported reagent. From this, some kind of beneficial synergistic effects due to the existence of the four active iodine(III) sites in **1a** must be involved in these unique selective reactions.<sup>12</sup>

**Table 1** Comparison of **1a** with other iodine(III) reagents in  $\alpha$ -tosyloxylation of ketones

Entry	I(III)	R <sup>1</sup>	Product	Yield <sup>a</sup> (selectivity of <b>12/13</b> ) <sup>b</sup>
1	<b>1a</b>	Me ( <b>11a</b> )	<b>12a</b> + <b>13a</b> (R <sup>2</sup> = 4-tolyl)	85% (5.1)
2	<b>1c</b> <sup>c</sup>			68% (5.4)
3	PIDA			77% (1.5)
4	PDAIS			36% (1.7)
5 <sup>d</sup>	<b>1a</b>		<b>12a'</b> + <b>13a'</b> (R <sup>2</sup> = (+)-10-camphoryl)	66% (3.0)
6		Pr ( <b>11b</b> )	<b>12b</b> + <b>13b</b> (R <sup>2</sup> = 4-tolyl)	58% (5.2)
7		<i>i</i> Bu ( <b>11c</b> )	<b>12c</b> + <b>13c</b>	56% (9.0)
8		Ph ( <b>11d</b> )	<b>12d</b> + <b>13d</b>	61% (>20)

<sup>a</sup> Isolated yields. <sup>b</sup> Determined by <sup>1</sup>H-NMR after purification. <sup>c</sup> *p*-TsOH·H<sub>2</sub>O was not added. <sup>d</sup> (+)-10-Camphorsulfonic acid and H<sub>2</sub>O were added instead of *p*-TsOH·H<sub>2</sub>O.



Scheme 2  $\alpha$ -Tosyloxylation using **14**.

In conclusion, we have developed new recyclable hypervalent iodine(III) reagents **1a–c**, having a tetraphenylmethane structure. These recyclable reagents are not only useful oxidation tool, but also show a unique selectivity during the  $\alpha$ -sulfonyloxylation reaction of ketones. To our knowledge, this is the first example of the selective  $\alpha$ -functionalization at more hindered position of ketones by hypervalent iodine(III) compounds.<sup>13</sup> Further studies on their reactivities, and applications in these fields are currently underway in our laboratory.

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## Notes and references

† *Synthesis of 1a*: To a stirred solution of tetrakis-(4-iodophenyl)methane **2** (620 mg, 0.75 mmol) was dissolved in  $\text{CH}_2\text{Cl}_2$  (75 mL)–AcOH (75 mL), then *m*CPBA (1.55 g, 9.0 mmol) was added to the mixture at room temperature. The reaction mixture was stirred for 2 days under the same reaction conditions. The resultant slightly clouded solution was filtered to give clear solution.  $\text{CH}_2\text{Cl}_2$  was removed under reduced pressure and hexanes was added to the residue and stirred for 1 h to precipitate tetrakis[4-(diacetoxyiodo)phenyl]methane **1a**. After filtration, the crude **1a** was washed with hexanes and  $\text{Et}_2\text{O}$  several times, and dried *in vacuo* to give **1a** (910.8 mg, 94%) as a colorless crystal; mp (decomp.) 218–220 °C (from AcOH– $\text{CH}_2\text{Cl}_2$ –hexanes by vapor diffusion method). <sup>1</sup>H NMR ( $\text{CDCl}_3$ , 25 °C):  $\delta$  = 8.02 (d, <sup>3</sup>*J*(H,H) = 9.6 Hz, 8H; ArH), 7.30 (d, <sup>3</sup>*J*(H,H) = 9.6 Hz, 8H; ArH), 2.02 (s, 24H,  $\text{OCOCH}_3$ ). <sup>13</sup>C NMR ( $\text{CDCl}_3$ , 25 °C):  $\delta$  = 176.6, 147.6, 134.8, 133.0, 119.8, 65.69, 20.5. IR (KBr): 1686w, 1637.5w, 1647w, 1560m, 1541w, 1521w, 1508w, 1475w, 1458w, 1396w, 1364w, 1288w, 1003w, 912m, 808w, 743m, 669m  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{41}\text{H}_{40}\text{I}_4\text{O}_{16} \cdot 2\text{H}_2\text{O}$ : C, 36.96; H, 3.33. Found: C, 36.80; H, 3.19%.

§ *Crystal data for 1a*:  $\text{C}_{41}\text{H}_{40}\text{I}_4\text{O}_{16} \cdot 5.19\text{CH}_3\text{CO}_2\text{H} \cdot 0.81\text{CH}_2\text{Cl}_2$ ,  $M = 1676.84$ , triclinic, space group  $\bar{P}1$ ,  $a = 12.520(4)$ ,  $b = 12.608(3)$ ,

$c = 21.064(6)$ ,  $\alpha = 84.26(1)$ ,  $\beta = 79.63(1)$ ,  $\gamma = 72.58(1)$ ,  $V = 3116(1) \text{ \AA}^3$ ,  $Z = 2$ ,  $T = 296(1) \text{ K}$ ,  $\mu = 21.51 \text{ cm}^{-1}$ , 25936 reflections measured, 11753 unique reflections,  $R = 0.036$ ,  $R_w = 0.117$ . CCDC 257522. See <http://www.rsc.org/suppdata/cc/b5/b501475a/> for crystallographic data in CIF or other electronic format.

¶ *Typical procedure for site-selective  $\alpha$ -tosyloxylation reaction of ketones*: A mixture of 2-butanone (14.4 mg, 0.2 mmol), **1a** (64.8 mg, 0.050 mmol), *p*-toluenesulfonic acid monohydrate (38.1 mg, 0.2 mmol),  $\text{CH}_3\text{CN}$  (2 mL) was heated at 70 °C in a sealed tube. After 24 h, the mixture was cooled to ambient temperature. Then, MeOH (2 mL) was added to the reaction mixture and the precipitate was filtered. Recovery of **2** was quantitative. After evaporation, the crude products were purified by column chromatography ( $\text{SiO}_2/\text{hexane-AcOEt} = 10/1$ ) to give pure **12a** and **13a** as a mixture of two isomers (**12a** : **13a** = 5.1 : 1).

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- The solubility of **2** in several solvents at 25 °C is as follows: 12 mg  $\text{L}^{-1}$  (MeOH); 20 mg  $\text{L}^{-1}$  ( $\text{CH}_3\text{CN}$ ); 28 mg  $\text{L}^{-1}$  (*n*-hexane).
- In each cases, an adamantane based reagent gave the products less selectively than that of **1a**: **12/13** 4.3 (for **11a**); 3.1 (for **11b**); 1.9 (for **11c**); 5.3 (for **11d**).
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