

## Synthesis of Chiral Diaryliodonium Salts, 1,1'-Binaphthyl-2-yl(phenyl)iodonium Tetrafluoroborates: Asymmetric $\alpha$ -Phenylation of $\beta$ -Keto Ester Enolates

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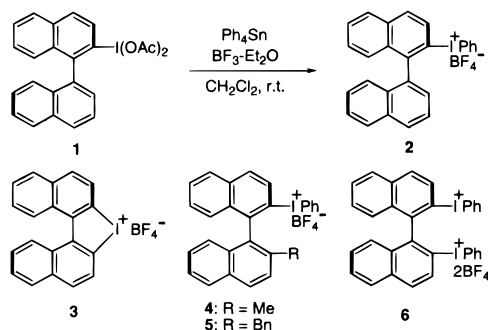
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Diaryliodonium salts are versatile reagents in organic synthesis and serve as highly activated species of aryl halides in nucleophilic aromatic substitutions at the ipso positions.<sup>1</sup> Their high reactivity is probably due to the excellent nucleofugality of the aryl iodonium group, which shows a leaving group ability about 10<sup>6</sup> times greater than that of triflate.<sup>2</sup> Simple unactivated aromatic halides tend to be nonreactive in bimolecular displacement reactions and, consequently, fail to react with metal enolates under standard experimental conditions;<sup>3,4</sup> however, it has been well established that diaryliodonium salts undergo transfer of one of the aryl groups to enolate anions under mild conditions to give the  $\alpha$ -arylated carbonyl compounds.<sup>5</sup>

Although some chiral onium reagents such as sulfonium, ammonium, phosphonium, and arsonium salts are employed in asymmetric synthesis,<sup>6</sup> to date there have been no reports of the synthesis of optically active diaryliodonium salts or of their use in asymmetric synthesis.<sup>7,8</sup> We report herein, for the first time, the synthesis and characterization of the chiral diaryliodonium salts, 1,1'-binaphthyl-2-yl(phenyl)iodonium tetrafluoroborates and

their derivatives. These chiral diaryliodonium salts allow asymmetric  $\alpha$ -phenylation of cyclic  $\beta$ -keto esters.<sup>9</sup>

Among the most general methods for the regioselective synthesis of organoiodonium salts is Lewis acid-catalyzed group 14 metal–iodine(III) exchange.<sup>10</sup> Attempts at Si–I(III) exchange of racemic 2-(diacetoxyiodo)-1,1'-binaphthyl (**1**)<sup>8a</sup> with phenyltrimethylsilane in the presence of BF<sub>3</sub>–Et<sub>2</sub>O, however, did not result in formation of the desired 1,1'-binaphthyl-2-yl(phenyl)iodonium tetrafluoroborate (**2**) but, instead, gave a cyclic five-membered iodonium salt **3**, presumably produced via the more facile intramolecular cyclization at the C-2' position.<sup>11</sup> Tetraphenylgermane also afforded **3**; however, use of the more reactive organostannane dramatically changed the reaction course and resulted in Sn–I(III) exchange under mild conditions. Treatment of (*S*)-(+)-**1** with tetraphenylstannane (1 equiv) in the presence of BF<sub>3</sub>–Et<sub>2</sub>O (2 equiv) in dichloromethane at room temperature for 18 h in nitrogen afforded the chiral diaryliodonium salt (*S*)-(–)-**2** as colorless prisms (mp 236 °C; [ $\alpha$ ]<sub>D</sub><sup>24</sup> –47.3° (c 0.91, acetone);  $\geq$ 98% ee)<sup>12</sup> in 76% yield. Tin- $\lambda^3$ -iodane exchange of (*S*)-2-(diacetoxyiodo)-2'-methyl-1,1'-binaphthyl, prepared from (*S*)-2-bromo-2'-methyl-1,1'-binaphthyl<sup>14</sup> via bromine–iodine exchange, followed by sodium perborate oxidation in acetic acid, afforded the (*S*)-2'-methylbinaphthylidoniolium salt **4** (82%). Similarly, (*S*)-2'-benzyl- $\lambda^3$ -iodane **5** was prepared from the known (*S*)-2'-benzyl-2-bromo-1,1'-binaphthyl.<sup>15</sup> Reaction of C<sub>2</sub> chiral (*R*)-2,2'-bis(diacetoxyiodo)-1,1'-binaphthyl<sup>8a</sup> with tetraphenylstannane (2 equiv) gave the bisiodonium salt (*R*)-(–)-**6** (hygroscopic colorless powder; mp 222 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> –234.6° (c 0.55, acetone)) as a 1:1 inclusion complex with diethyl ether in 90% yield.



Both the structure and the absolute configuration of (*S*)-(–)-**2** were unambiguously established by single-crystal X-ray analysis. The PLUTO representation of Figure 1, which includes the counteranion (BF<sub>4</sub><sup>–</sup>) of another molecule, exhibits an essentially square-planar arrangement with four bonds to iodine [I–C(1), I–C(21), I–F(1), and I–F(2')].<sup>16</sup> Notably, the phenyl ring and one of the naphthyl rings are almost parallel, with a dihedral

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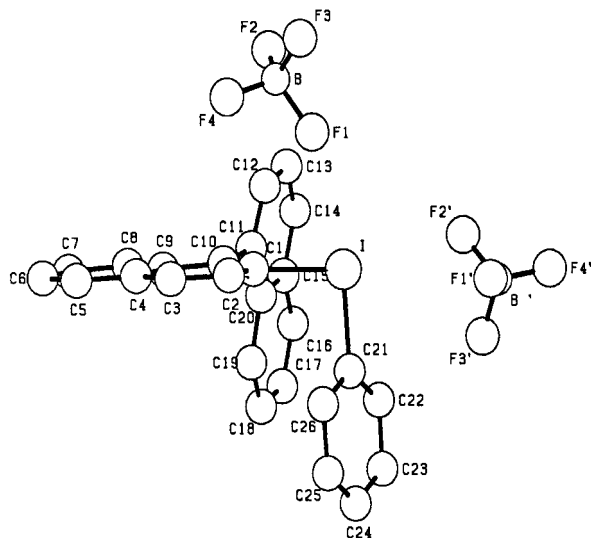
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**Figure 1.** PLUTO representation of the iodonium salts (*S*)-(-)-**2** with an extra  $\text{BF}_4^-$  anion from the second molecule.

angle of  $16.0^\circ$ , similar to the shifted, stacked structure of a benzene dimer.<sup>17</sup>

Exposure of the potassium enolate of 2-(methoxycarbonyl)-1-indanone (**7a**) (generated by the reaction with *t*-BuOK) to the chiral diaryliodonium salt (*S*)-**2** (*t*-BuOH at room temperature, 20 h) gave selectively the  $\alpha$ -phenylated indanone **8a** in 65% yield. No formation of *O*-phenyl derivative was observed. This reaction is highly regioselective in the sense that there is no evidence for transfer of the binaphthyl group of **2** to the cyclic  $\beta$ -keto ester **7a**. This selectivity is in marked contrast to the reported ortho steric effects that the unsymmetrical diaryliodonium salts experience: nucleophilic ipso substitutions occur preferentially at the aryl groups with sterically demanding ortho substituents, so as to provide maximum relief of the steric strain.<sup>18</sup> The chiral (*S*)-2-iodo-1,1'-binaphthyl was easily recovered in higher than 80% yields, without loss of optical purity, and reused.

The degree of asymmetric induction of **8a** (37% ee), determined by  $^1\text{H}$  NMR (400 MHz) analysis in the presence of the chiral shift reagent  $\text{Eu}(\text{hfc})_3$ , is only moderate, but it is the first

(12) The optical purity of (*S*)-(-)-**2** was determined from the  $^1\text{H}$  NMR spectra of the corresponding  $\alpha$ -methoxy- $\alpha$ -(trifluoromethyl)phenylacetic acid (MTPA) derivative, prepared by the following ligand exchange sequence: (i) ligand exchange with KI in MeOH–H<sub>2</sub>O yielding the diaryliodonium iodide; (ii) formation of the acetoxyiodane by reaction with silver acetate; and (iii) ligand exchange with (*R*)-MTPA in chlorobenzene under reduced pressure, leading to the formation of 2-((2-methoxy-(2-trifluoromethyl)phenylacetoxy)-phenyliodo)-1,1'-binaphthyl.<sup>13</sup>

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(16) The X-ray structure of **2** revealed a fluorine-bridged polymeric structure of  $(\text{F}-\text{B}-\text{F}-\text{I})_n$ . The bond angles  $\text{C}(1)-\text{I}-\text{C}(21)$ ,  $\text{C}(1)-\text{I}-\text{F}(1)$ ,  $\text{C}(21)-\text{I}-\text{F}(2')$ , and  $\text{F}(1)-\text{I}-\text{F}(2')$  are  $93.8(2)$ ,  $76.4(2)$ ,  $100.0(2)$ , and  $85.7(2)^\circ$ , respectively.

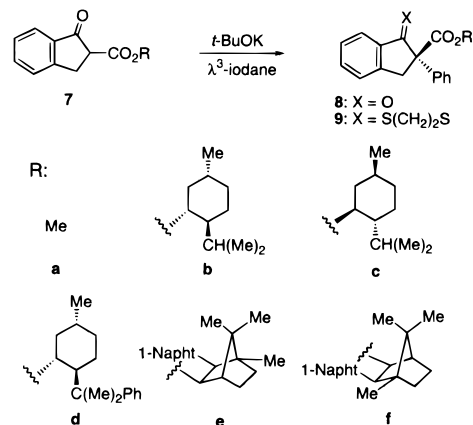
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**Table 1.** Asymmetric Phenylation of the  $\beta$ -Keto Ester **7a** with  $\lambda^3$ -Iodanes

entry	iodane	solvent	$T/^\circ\text{C}$	<b>8a</b> , % yield <sup>a</sup>	% ee
1	<b>2</b>	<i>t</i> -BuOH	25	65	37
2	<b>2</b>	<i>t</i> -BuOH	70	69	38
3	<b>2</b>	<i>t</i> -BuOH–THF	–78	15	40
4	<b>2</b>	<i>t</i> -BuOH	25 <sup>b</sup>	71	37
5	<b>2</b>	<i>t</i> -BuOH	25 <sup>c</sup>	63	40
6	<b>4</b>	<i>t</i> -BuOH	25	68	34
7	<b>5</b>	<i>t</i> -BuOH	25	30	53
8	<b>5</b>	THF	25 <sup>b</sup>	63	44
9	<b>6</b>	<i>t</i> -BuOH	30	51	37

<sup>a</sup> Isolated yields. <sup>b</sup> 2 equiv of  $\text{Ph}_2\text{C}=\text{CH}_2$  was used. <sup>c</sup> 1.1 equiv of 18-crown-6 was used.



demonstration of asymmetric arylation of metal enolates that does not rely on a transition metal catalyst. The results are summarized in Table 1. Changing the reaction temperature from  $-78$  to  $70^\circ\text{C}$  and the solvents from *t*-BuOH to THF, DMF, dichloromethane, or methanol showed negligible effects on the degree of asymmetric induction (33–40% ee). A similar level of ee was obtained in the reaction with 2'-methyl- $\lambda^3$ -iodane (*S*)-**4**; however, the sterically more demanding 2'-benzyl- $\lambda^3$ -iodane (*S*)-**5** resulted in a higher asymmetric induction up to 53% ee (entry 7). Bisiodonium salt (*R*)-**6** gave the  $\alpha$ -phenylated indanone **8a** in 37% ee (entry 9). The absolute configuration of the major enantiomer in these reactions was determined to be *R* by single-crystal X-ray analysis of the dithioacetal derivative **9a**, obtained by repeated fractional recrystallization. The degree of chiral induction achieved by using several chiral  $\beta$ -keto esters **7b–f** and (*S*)-**2** is comparable to that of methyl ester **7a**: 11–47% de.

Thus, in the present study, not only do we demonstrate the first synthesis of chiral diaryliodonium salts, via  $\text{BF}_3$ -catalyzed tin- $\lambda^3$ -iodane exchange, but also, even though asymmetric syntheses using chiral  $\lambda^3$ -organoiodanes were very limited, we were able to achieve direct asymmetric  $\alpha$ -phenylation of enolate anions derived from cyclic  $\beta$ -keto esters by the reaction with binaphthyl(phenyl)iodonium salts.

**Supporting Information Available:** Experimental procedures for the synthesis, characterization, and reaction of diaryliodonium salts; X-ray structural information on (*S*)-**2** and (*S*)-**9a** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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