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Catalytic amounts of triarylaminium salt initiated aerobic oxidative coupling of *N*-aryl tetrahydroisoquinolines†

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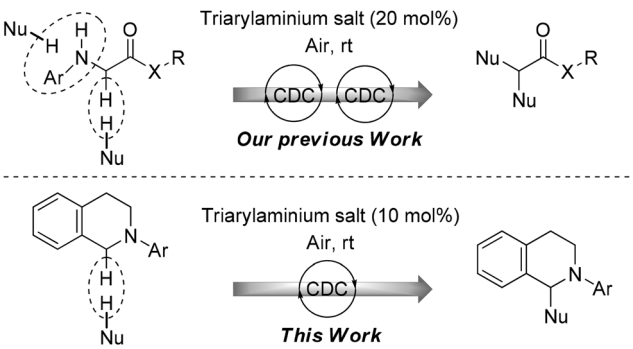
A novel stable radical cation triarylaminium salt able to induce aerobic oxidative α-C–H functionalization of tertiary amines in catalytic amounts has been developed. The reaction is performed in the absence of any other additives under mild conditions and only requires atmosphere air as a sustainable co-oxidant.

Introduction

Carbon–hydrogen (C–H) bonds are ubiquitous in organic molecules, which are traditionally considered unreactive. The activation of C–H bonds has become an significant area in research on modern organic chemistry.[1] The direct functionalizations of C–H bonds in the α-position to a nitrogen atom are of special interest for both industry and academia.[2–4] Among these reactions, the oxidative coupling of secondary amines such as glycine derivatives[2] and tertiary amines such as *N*-aryl tetrahydroisoquinolines[3,4] with nucleophiles has gained a lot of attention. Recently, various transition metal catalyzed oxidative dehydrogenative coupling reactions of amines have been reported.[3] In addition, metal-free methods using a stoichiometric amount of an oxidant, such as DDQ, $PhI(OAc)_2$, H_2O_2, tropylium ion, or the TEMPO Oxoammonium Salt, have also been reported.[4] However, the catalytic metal-free aerobic oxidative dehydrogenative coupling of amines is still very rare.[5] Our group has a long-standing interest in the stable triarylaminium salt initiated radical cation mediated transformations and their synthetic potential.[6] Very recently, we discovered that triarylaminium salt could catalyze the reaction of glycine derivatives with indoles in the absence of any other additives and only required atmosphere air as a co-oxidant.[7] An aerobic double oxidative dehydrogenative Friedel–Crafts alkylation cascade reaction occurred to deliver a series of bisindolylmethane (BIM) derivatives (Scheme 1). Jia *et al.* also reported that triarylaminium salt/$InCl_3$/O_2 system could catalyze the reaction of glycine esters with alkenes or alkynes in a one-pot dehydrogenative Povarov/oxidation tandem process to construct substituted quinolines.[8] These previous studies indicated that the triarylaminium salt induced aerobic oxidative coupling reaction is an interesting subject, whereas the application of this catalytic system for oxidative coupling of tertiary amines with various nucleophiles has not yet been developed. Herein we describe a highly efficient oxidative C–C, C–P coupling reaction of *N*-aryl tetrahydroisoquinolines initiated by commercially available and bench-stable tris(4-bromophenyl)-aminium hexachloro-antimonate ($TBPA^{+\bullet}SbCl_6^-$, **1**).



Scheme 1 Triarylaminium salt induced aerobic oxidative coupling of amines.

Results and discussion

For the optimization studies, we chose *N*-phenyl tetrahydroisoquinoline (**2a**) and indole (**3a**) as model substrates.[9] As shown in Table 1, the best yield (89%) was achieved with 10 mol% $TBPA^{+\bullet}SbCl_6^-$ in THF at room temperature in 6 h. No appreciable differences of the transformation were observed when the reaction time was prolonged from 6 h to 12 h or oxygen was used instead of air. Under the optimized conditions (Table 1,

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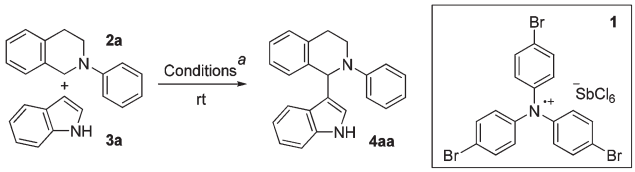
Table 1 Screening of reaction conditions[a]



Entry	Conditions	Yield[b] (%)
1	20 mol% **1**, CH_2Cl_2, air, rt, 6 h	50
2	20 mol% **1**, $CHCl_3$, air, rt, 6 h	—
3	20 mol% **1**, $(CH_2Cl)_2$, air, rt, 6 h	45
4	20 mol% **1**, MeCN, air, rt, 6 h	65
5	20 mol% **1**, THF, air, rt, 6 h	86
6	20 mol% **1**, EtOAc, air, rt, 6 h	—
7	20 mol% **1**, Acetone, air, rt, 6 h	—
8	10 mol% **1**, THF, air, rt, 6 h	89
9	5 mol% **1**, THF, air, rt, 6 h	78
10	10 mol% **1**, THF, air, rt, 12 h	89
11	10 mol% **1**, THF, O_2, rt, 6 h	88

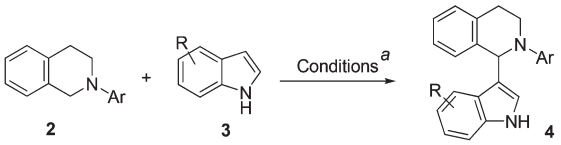
[a] Reaction conditions: **2a** (0.1 mmol), **3a** (0.1 mmol), **1** (0.01 mmol), solvent (1 mL), air (1 atm), rt, 6 h. [b] Yields were determined by NMR spectroscopy.

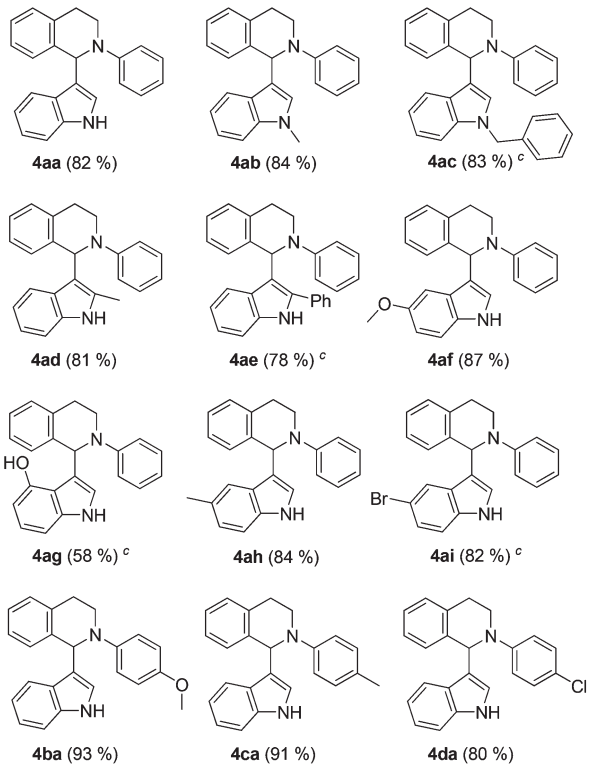
entry 8), we probed the scope and generality of both indoles and tetrahydroisoquinolines for the TBPA radical cation induced aerobic α-arylation (Table 2). Initially, we investigated different substituted indoles. *N*-Me and *N*-Bn protected indoles gave the corresponding products in high yields (Table 2, **4ab**, **4ac**). Indoles with electron-donating groups or electron-withdrawing groups on C2, C4 and C5 all worked well with *N*-phenyl tetrahydroisoquinoline under the present reaction conditions (Table 2, **4aa–4ai**). The steric hindrance did not affect the yield of the reaction significantly (Table 2, **4ae**). An unprotected hydroxyl group was tolerated in this reaction (Table 2, **4ag**). The introduction of a halogen atom into this system made this method more useful for further transformation (Table 2, **4ai**). Furthermore, we explored the variety of tetrahydroisoquinolines. For both electron-donating and electron-withdrawing groups, the desired products were achieved in high yields (Table 2, **4ba–4da**). The success of C–C bond formation of tertiary amines by using triarylaminium salt **1** encouraged us to investigate C–P bond coupling reactions. α-Amino phosphoric derivatives are valuable precursors of a number of biologically active molecules and have aroused a lot of synthetic interest.[10] In this work, a variety of phosphites and phosphine oxides could react with tertiary amines in the presence of **1** to give the desired products in high yields (Table 3).

It is worth noting that when diaryl phosphines were used instead of diaryl phosphine oxides, the same products were obtained in excellent yield (Scheme 2).

To evaluate the practicability of our method, the reactions of *N*-phenyl tetrahydroisoquinoline (**2a**) with indole (**3a**) or diethyl phosphite (**5a**) have been performed on a 20 mmol scale in a single batch. To our delight, no obvious loss of yields were observed (isolated yield: 78% and 91% respectively). It indicated that this protocol not only is atom-efficient and environmentally benign but also could be conveniently scaled up in industry.

Table 2 Scope of $TBPA^{+\bullet}SbCl_6^-$ induced aerobic indolation of sp^3 C–H bonds[b]



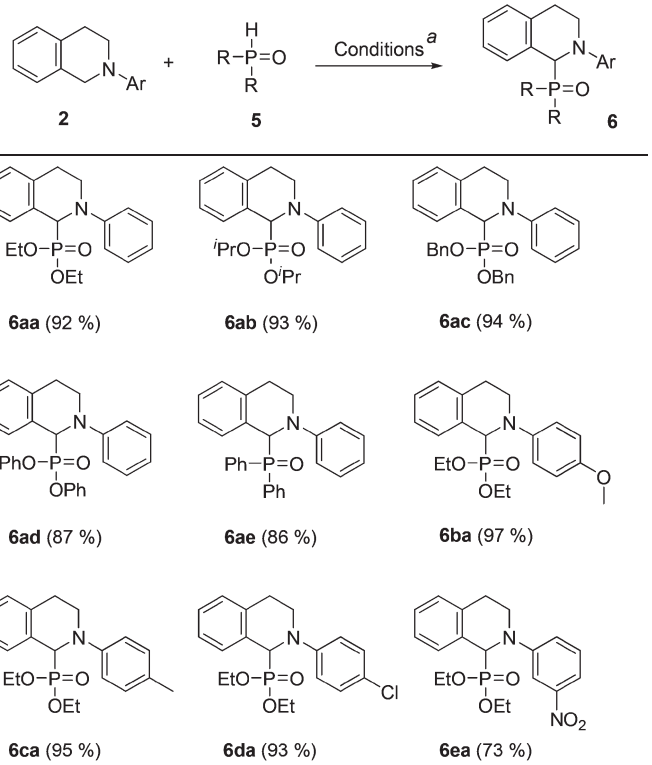


[a] Standard reaction conditions: tetrahydroisoquinolines **2** (1.0 mmol), indoles **3** (1.0 mmol), **1** (0.1 mmol), THF (10 mL), ambient air, rt, 6–12 h. [b] Isolated yields of the isolated products. [c] 40 °C.

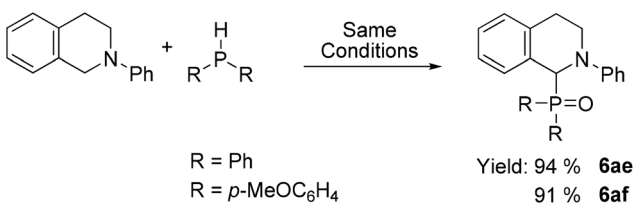
Extending the nucleophile scope further turned out to be rather difficult. In contrast to our expectations, the more nucleophilic nitromethane and malonic acid esters hardly reacted under these conditions. It seems the reaction performance was not related to nucleophilicity. This may be due to the oxidation step being the limiting factor and that it depends on the nucleophile present. The exact reason for this phenomenon is not yet clear, and more detailed investigation of the reaction conditions are currently ongoing in our laboratory.

Some control experiments were carried out in order to reveal the mechanism of this transformation. Firstly, the reaction of **2a** with **3a** or **5a** in argon atmosphere (in the absence of molecular oxygen) furnished no product [Scheme 3, eqn (1) and (3)], indicating that molecular oxygen is definitely crucial for the reaction. Secondly, a stoichiometric amount of TEMPO was employed in the standard reaction as radical scavenger;

Table 3 Scope of $TBPA^{+\bullet}SbCl_6^-$ induced aerobic phosphonation of sp^3 C–H bonds[b]

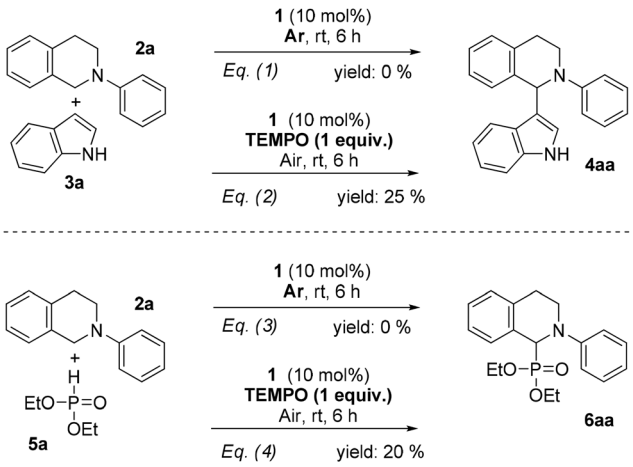


[a] Standard reaction conditions: tetrahydroisoquinolines **2** (1.0 mmol), phosphorus reagents **5** (1.0 mmol), **1** (0.1 mmol), THF (15 mL), ambient air, rt, 5–8 h. [b] Isolated yields of the isolated products.

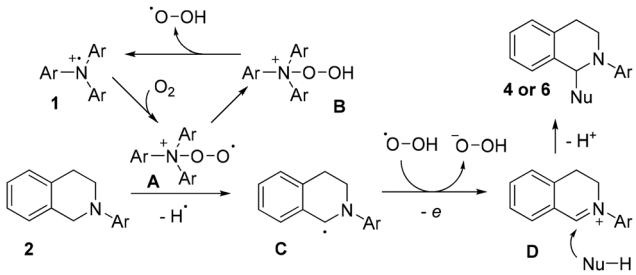


Scheme 2

a significant drop in yield was observed [Scheme 3, eqn (2) and (4)]. This result suggested that the present reaction includes a radical process. Consequently, based on experimental observations, a plausible mechanism for this triarylaminium salt catalyzed aerobic transformation is illustrated in Scheme 4. TBPA radical cation **1** couples with oxygen to generate a distonic[11] peroxy radical cation **A**, which abstracts a hydrogen atom from **2** to afford a free radical **C**. On the other hand, after homolytic cleavage of the peroxide intermediate **B**, a TBPA radical cation is regenerated and a peroxy radical (˙O–OH) is formed. Subsequent one-electron oxidation of **C** offers an intermediate **D**, followed by nucleophilic addition leading to the product **4** or **6**. We also tried the reaction in the presence of a catalytic or even stoichiometric amount of H_2O_2 or TBHP, but the starting materials remained unchanged after



Scheme 3 Control experiments.



Scheme 4 Proposed reaction mechanism.

stirring for 24 h, which implied that peroxides could not be the terminal oxidant. More details of the mechanism are currently under investigation.

Experimental

General information

The starting materials, reagents and solvents, purchased from commercial suppliers, were used without further purification. Literature procedures were used for the preparation of *N*-aryl tetrahydroisoquinoline. Analytical TLC was performed with silica gel GF254 plates, and the products were visualized by UV detection. Flash chromatography was carried out using silica gel 200–300. ^{1}HNMR (400 MHz) and ^{13}CNMR (100 MHz) spectra were measured with $CDCl_3$ or acetone-d_6 as solvent. High-resolution electrospray ionization (HRESI) mass spectra were recorded by a QTOF-2 Micromass spectrometer.

Preparation of $TBPA^{+\bullet}SbCl_6^-$

$TBPA^{+\bullet}SbCl_6^-$ is a commercially available, inexpensive and bench-stable reagent. It can also be synthesized according to literature procedures and used as freshly prepared as follows: Tris-(*p*-bromophenyl)amine (TBPA, 4.8 g) was dissolved in DCM (20 mL) and a solution of $SbCl_5$ (2 mL) in DCM (20 mL) was added slowly. The reaction mixture was then poured into

dry ether (50 mL). The obtained blue precipitate was washed thoroughly with dry ether and dried.

General procedure for $TBPA^{+\bullet}SbCl_6^-$ induced aerobic indolation of *N*-aryl tetrahydroisoquinolines

N-Aryl tetrahydroisoquinolines (**2**, 1 mmol) and indoles (**3**, 1 mmol) were dissolved in THF (10 mL) at ambient temperature; $TBPA^{+\bullet}SbCl_6^-$ (1, 0.1 mmol) was then added in one portion under stirring. The reactions were performed under an air atmosphere (open flask) at room temperature and completed within 6–12 hours as monitored by TLC. The products were isolated by column chromatographic separation.

General procedure for $TBPA^{+\bullet}SbCl_6^-$ induced aerobic phosphonation of *N*-aryl tetrahydroisoquinolines

N-Aryl tetrahydroisoquinolines (2, 1 mmol) and phosphorous reagents (5, 1 mmol) were dissolved in THF (10 mL) at ambient temperature; $TBPA^{+\bullet}SbCl_6^-$ (1, 0.1 mmol) was then added in one portion under stirring. The reactions were performed under an air atmosphere (open flask) at room temperature and completed within 6 hours as monitored by TLC. The products were isolated by column chromatographic separation.

1-(1*H*-Indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4aa)[3b]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.39–7.10 (m, 8H), 7.10–6.96 (m, 3H), 6.77 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 1.3 Hz, 1H), 6.17 (s, 1H), 3.62 (dd, J = 7.6, 4.6 Hz, 2H), 3.07 (m, 1H), 2.80 (m, 1H).

1-(1-Methyl-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4ab)[3b]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 1H), 7.37–7.10 (m, 8H), 7.02 (ddd, J = 7.9, 4.9, 1.8 Hz, 3H), 6.76 (t, J = 7.3 Hz, 1H), 6.50 (s, 1H), 6.17 (s, 1H), 3.77–3.50 (m, 5H), 3.15–2.99 (m, 1H), 2.81 (m, 1H).

1-(1-Benzyl-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4ac)

White oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.1 Hz, 1H), 7.39–6.89 (m, 14H), 6.77 (t, J = 7.1 Hz, 1H), 6.63 (s, 1H), 6.21 (s, 1H), 5.15 (s, 2H), 3.73–3.50 (m, 2H), 3.06 (m, 1H), 2.90–2.70 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.0, 137.6, 137.5, 137.0, 135.6, 129.2, 128.9, 128.7, 128.5, 128.5, 128.1, 127.5, 127.3, 126.7, 126.4, 125.8, 121.9, 120.4, 119.4, 118.3, 118.2, 116.2, 109.8, 56.9, 49.9, 42.5, 26.8. HRMS (EI) for $C_{30}H_{26}N_2$, calcd: 414.2096, found: 414.2091.

1-(2-Methyl-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4ad)

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.24–6.95 (m, 9H), 6.90 (t, J = 7.3 Hz, 1H), 6.84 (t, J = 7.3, 1H), 5.96 (s, 1H), 3.80–3.47 (m, 2H), 3.16–2.90 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.7, 138.2, 137.1, 135.8, 135.3, 133.0, 128.8, 128.5, 128.2, 128.1, 128.0, 126.2, 121.8, 120.9, 120.6, 120.4, 119.8, 114.9, 110.7, 57.1, 47.3, 28.4. HRMS (EI) for $C_{24}H_{22}N_2$, calcd: 338.1783, found: 338.1785.

2-Phenyl-1-(2-phenyl-1*H*-indol-3-yl)-1,2,3,4-tetrahydroisoquinoline (4ae)[3b]

Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.46–6.98 (m, 15H), 6.93 (t, J = 7.4 Hz, 1H), 6.79 (m, 3H), 5.96 (s, 1H), 3.87–3.58 (m, 2H), 3.20–3.00 (m, 2H).

1-(5-Methoxy-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4af)[3b]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.40–7.10 (m, 6H), 7.02 (d, J = 8.7 Hz, 2H), 6.88 (s, 1H), 6.85–6.71 (m, 2H), 6.56 (s, 1H), 6.14 (s, 1H), 3.65 (s, 3H), 3.59 (dd, J = 7.8, 4.4 Hz, 2H), 3.07 (m, 1H), 2.81 (m, 1H).

3-(2-Phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1*H*-indol-4-ol (4ag)

Pale brown solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 7.96 (s, 1H), 7.38–7.01 (m, 11H), 6.83 (d, J = 8.1 Hz, 1H), 6.59 (d, J = 7.6 Hz, 1H), 6.46 (s, 1H), 5.83 (s, 1H), 3.94–3.53 (m, 2H), 3.04–2.67 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.7, 148.1, 139.0, 135.2, 134.0, 129.4, 129.3, 128.3, 127.0, 125.8, 124.3, 123.8, 123.3, 121.5, 118.4, 115.4, 105.2, 102.4, 58.0, 47.1, 25.1. HRMS (EI) for $C_{23}H_{20}N_2O$, calcd: 340.1576, found: 338. 340.1569.

1-(5-Methyl-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4ah)

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.56 (d, J = 8.0 Hz, 1H), 7.39–7.10 (m, 8H), 7.10–6.96 (m, 3H), 6.77 (t, J = 7.3 Hz, 1H), 6.63 (s, 1H), 6.17 (s, 1H), 3.62 (dd, J = 7.6, 4.6 Hz, 2H), 3.07 (m, 1H), 2.80 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9, 137.6, 135.5, 134.9, 129.2, 128.8, 128.8, 128.1, 126.7, 126.6, 125.7, 124.5, 123.7, 119.6, 118.7, 118.2, 116.1, 110.8, 56.7, 42.3, 26.6, 21.6. HRMS (EI) for $C_{24}H_{22}N_2$, calcd: 338.1783, found: 338.1773.

1-(5-Bromo-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (4ai)

White solid. ^{1}H NMR (400 MHz, Acetone) δ 10.27 (s, 1H), 7.67 (d, J = 1.7 Hz, 1H), 7.36 (dd, J = 8.2, 5.6 Hz, 2H), 7.30–7.16 (m, 6H), 7.11 (d, J = 7.9 Hz, 2H), 6.83 (s, 1H), 6.75 (t, J = 7.2 Hz, 1H), 6.27 (s, 1H), 3.77–3.48 (m, 2H), 3.16–2.98 (m, 1H), 2.92–2.77 (m, 2H). ^{13}C NMR (101 MHz, Acetone) δ 149.9, 137.5, 135.7, 135.3, 129.0, 128.7, 128.3, 128.0, 126.6, 126.2, 125.6, 124.0, 122.2, 118.2, 118.1, 115.9, 113.1, 111.8, 56.2, 42.1, 26.4. HRMS (EI) for $C_{23}H_{19}BrN_2$, calcd: 402.0732, found: 402.0739.

1-(1*H*-Indol-3-yl)-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (4ba)[3b]

Pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.40(d, J = 3.0 Hz, 1H), 7.25–7.10(m, 6H), 6.98(t, J = 8.0, 1H), 6.93(d, J = 8.0 Hz, 2H), 6.78(d, J = 8.5 Hz, 2H), 6.50(s, 1H), 5.95 (s, 1H), 3.73(s, 3H), 3.52(m, 1H), 3.45(m, 1H), 3.02(m, 1H), 2.78(m, 1H).

1-(1*H*-Indol-3-yl)-2-*p*-tolyl-1,2,3,4-tetrahydroisoquinoline (4ca)

Pale red solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.40–6.92 (m, 12H), 6.61 (s, 1H), 6.16 (s, 1H), 3.63 (m, 2H), 3.28–3.04 (m, 1H), 2.82 (d, J = 16.3 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 137.5, 136.6, 135.5, 129.7, 128.9, 128.1, 127.7, 126.6, 126.5, 125.6, 124.2, 122.0, 120.2, 119.6, 119.4, 116.6, 111.0, 56.9, 42.7, 26.5, 20.4. HRMS (EI) for $C_{24}H_{22}N_2$, calcd: 338.1783, found: 338.1790.

2-(4-Chlorophenyl)-1-(1*H*-indol-3-yl)-1,2,3,4-tetrahydroisoquinoline (4da)

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.41–7.17 (m, 8H), 7.13 (t, J = 8.0, 1H), 6.97 (d, J = 7.9 Hz, 2H), 6.63 (s, 1H), 6.15 (s, 1H), 3.76–3.48 (m, 2H), 3.09 (m, 1H), 2.87 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 137.1, 136.6, 135.3, 129.0, 128.8, 128.0, 126.8, 126.3, 125.8, 124.1, 122.9, 122.2, 119.9, 119.7, 118.8, 117.0, 111.1, 56.8, 42.6, 26.6. HRMS (EI) for $C_{23}H_{19}ClN_2$, calcd: 358.1237, found: 358.1244.

Diethyl 2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6aa)[10a]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.31 (m, 1H), 7.31–7.07 (m, 5H), 6.98 (d, J = 8.3 Hz, 2H), 6.80 (t, J = 7.6 Hz, 1H), 5.19 (d, J = 20.0 Hz, 1H), 4.24–3.79 (m, 4H), 3.60 (m, 1H), 3.18–2.89 (m, 2H), 1.26 (t, J = 6.8 Hz, 3H), 1.16 (t, J = 6.8 Hz, 3H).

Diisopropyl 2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ab)[10a]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.36 (m, 1H), 7.35–7.07 (m, 5H), 6.98 (d, J = 9.7 Hz, 2H), 6.80 (t, J = 7.6 Hz, 1H), 5.14 (d, J = 19.9 Hz, 1H), 4.76–4.48 (m, 2H), 4.16–3.95 (m, 1H), 3.64 (m, 1H), 3.18–2.82 (m, 2H), 1.30 (m, 6H), 1.17 (d, J = 4.6 Hz, 3H), 0.94 (d, J = 4.6 Hz, 3H).

Dibenzyl 2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ac)[10a]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61–7.09 (m, 16H), 7.00 (d, J = 8.3 Hz, 2H), 6.85 (t, J = 7.6 Hz, 1H), 5.30 (d, J = 19.7 Hz, 1H), 5.13–4.71 (m, 4H), 4.05 (m, 1H), 3.74–3.55 (m, 1H), 3.23–2.88 (m, 2H).

Diphenyl 2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ad)[10b]

White solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 6.7 Hz, 1H), 7.29–6.91 (m, 16H), 6.86–6.77 (m, 2H), 5.53 (d, J = 20.2 Hz, 1H), 4.13–3.97 (m, 1H), 3.68–3.55 (m, 1H), 3.00 (m, 2H).

1-(Diphenylphosphoryl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (6ae)[10d]

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96–7.78 (m, 2H), 7.78–7.66 (m, 2H), 7.55 (m, 1H), 7.51–7.42 (m, 3H), 7.35 (m, 2H), 7.20–7.12 (m, 3H), 7.09 (d, J = 7.5 Hz, 1H), 7.02–6.91 (m, 1H), 6.80 (m, 3H), 6.66 (d, J = 7.8 Hz, 1H), 5.58 (d, J = 10.6 Hz, 1H), 4.05 (m, 1H), 3.59 (m, 1H), 2.99–2.58 (m, 2H).

Diethyl 2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ba)[10d]

Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, J = 6.6 Hz, 1H), 7.15 (m, 3H), 6.90 (m, 2H), 6.80 (m, 2H), 5.01 (d, J = 21.5 Hz, 1H), 4.25–3.86 (m, 5H), 3.74 (s, 3H), 3.60–3.41 (m, 1H), 2.90 (d, J = 7.8 Hz, 2H), 1.24 (t, J = 6.1 Hz, 3H), 1.15 (t, J = 7.1 Hz, 3H).

Diethyl 2-*p*-tolyl-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ca)[10d]

Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (m, 1H), 7.19–7.08 (m, 3H), 7.02 (d, J = 8.3 Hz, 2H), 6.85 (d, J = 8.7 Hz, 2H), 5.09 (d, J = 20.8 Hz, 1H), 4.20–3.81 (m, 5H), 3.67–3.50 (m, 1H), 2.96 (m, 2H), 2.22 (s, 3H), 1.23 (t, J = 7.1 Hz, 3H), 1.12 (t, J = 7.1 Hz, 3H).

Diethyl 2-(4-chlorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6da)[10d]

Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (m, 1H), 7.30–7.09 (m, 5H), 6.89 (d, J = 9.1 Hz, 2H), 5.10 (d, J = 19.2 Hz, 1H), 4.24–3.76 (m, 5H), 3.65–3.47 (m, 1H), 3.29–2.84 (m, 2H), 1.23 (t, J = 7.1 Hz, 3H), 1.14 (t, J = 7.1 Hz, 3H).

Diethyl 2-(3-nitrophenyl)-1,2,3,4-tetrahydroisoquinolin-1-ylphosphonate (6ea)

Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.62 (m, 1H), 7.39 (m, 2H), 7.32–7.12 (m, 4H), 5.22 (d, J = 17.7 Hz, 1H), 4.13–3.79 (m, 5H), 3.68–3.55 (m, 1H), 3.47–3.31 (m, 1H), 3.12–2.92 (m, 1H), 1.24 (t, J = 7.1 Hz, 3H), 1.16 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 149.6, 149.2, 136.2, 136.1, 130.1, 129.6, 128.5, 128.5, 128.2, 128.1, 128.0, 127.9, 126.2, 126.2, 119.34, 112.4, 108.0, 63.1, 63.0, 62.8, 62.7, 59.3, 57.8, 43.8, 27.3, 16.4, 16.3, 16.3. HRMS (ESI) exact mass for $C_{19}H_{23}N_2O_5P$ $[M + H]^+$ calcd: 391.1423; found: 391.1419.

1-(Dip-tolylphosphoryl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (6af)

White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (m, 2H), 7.59 (m, 2H), 7.42–7.05 (m, 8H), 7.05–6.91 (m, 1H), 6.77 (m, 4H), 5.51 (d, J = 10.5 Hz, 1H), 4.13–3.90 (m, 1H), 3.61 (m, 1H), 2.79 (m, 2H), 2.47 (s, 3H), 2.34 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 150.0, 142.2, 141.9, 136.8, 132.3, 132.2, 131.7, 131.6, 130.2, 129.7, 129.2, 129.0, 128.9, 128.7, 127.9, 127.8, 127.2, 125.4, 119.3, 116.67, 62.4, 61.6, 44.9, 25.5, 21.6, 21.5. HRMS (ESI) exact mass for $C_{29}H_{29}NOP$ $[M + H]^+$ calcd: 438.1987; found: 438.1994.

Conclusions

In summary, we have developed a highly efficient and scalable triarylaminium salt induced aerobic oxidative C–H functionali-

zation of *N*-aryl tetrahydroisoquinolines to form C–C and C–P bonds. Simple organo-SET oxidant induced process and the use of molecular oxygen as the oxidant make this transformation practical and sustainable. $TBPA^{+\bullet}SbCl_6^-$ **1** displays a high activity in oxidative coupling reaction and this highlights the potential of stable radical cation salts in promoting new reactions *via* O_2 involved C–H bond activation. Further exploration of more sustainable and metal-free catalytic systems for aerobic oxidative coupling is ongoing in our laboratory.

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