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Tetraarylphosphonium Inner-Salts (TAPIS) as Both Lewis Base Catalyst and Phase Tag

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ARTICLE INFO

ABSTRACT

Article history: Received Received in revised form Accepted Available online Tetraarylphosphonium inner-salts (TAPIS) have been designed, synthesized and verified as recyclable and reusable Lewis base catalysts. The resulted TAPIS catalyst has been successfully applied in Michael addition, cyanation and trifluoromethylation reactions.

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Phosphonium salts are versatile compounds that have been used as phase transfer catalysts,¹ organic reagents,² ionic liquids³ and other applications.⁴ Tetraarylphosphonium salts (TAPS) with the formular $[Ar^{1}(Ar^{2})_{3}P^{+}]X^{-}$ can be readily prepared by coupling reactions of an aryl halide (Ar¹-X) and a triarylphosphine ((Ar²)₃P.⁵ Unlike its alkyl derivatives as well as ammonium counterparts, tetrarylphosphoniums (TAPs) are rather stable salts that can be readily modified and functionalized. In addition, the ionic nature also makes possible tunable solubility and hence facile phase separation with TAPs.⁶ Capitalized on these intriguing properties, we aim to explore tetrarylphosphonium (TAP) moiety as functional building block for the design of new organocatalysts, meanwhile as phase tags to facilitate catalyst recovery and reuse.⁷ Previously, the use of teraarylphosphoniums has been reported for supported organic synthesis and phase transfer catalysis.8 Herein, we reported a structurally simple and distinctive tetraarylphosphonium inner-salt (TAPIS) as a recoverable and reusable Lewis base catalyst (Figure 1).

The TAPIS catalyst could be readily prepared by Ni-catalyzed phosphonium formation from triphenylphosphine and phenols, following by a simple treatment with NaOH (Figure 1).⁹ The zwitter ionic TAPIS were obtained as viscous syrup or powder solid. The x-ray structure of TAPIS **C6** verified the zwitter ionic structure feature. These TAPIS compounds are generally well soluble in polar solvents, but less soluble in non-polar solvents such as ether or hexane, which can meet the requirements of biphasic application.

The Michael addition reaction is one of the fundamental bondforming process in organic chemistry and is an extremely

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powerful tool for synthesis of functionalized organic molecules.¹⁰ Within this process, the addition of 1,3-dicarbonyl compounds to nitroalkenes has attracted particular interest due to the reactivity of the resulting nitrocarbonyl adducts.¹¹ Therefore, explorative research of catalytic activity and recyclability of TAPIS is carried out on this type of catalytic Michael transformation.



Figure 1. The TAP catalytic strategy and the synthesis of TAPIS catalyst.

Tetrahedron



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Figure 2. Catalytic evaluation of TAPISs in the Michael addition.

The obtained TAPIS was then tested in the reaction of acetoacetate and nitrostyrene (Figure 2). The reaction proceeded smoothly in the presence of 10 mol% TAPIS to give the desired adduct at room temperature. In comparison, the parent phenols C1-C3 showed no activity in the reactions, verifying the Lewis base properties of the inner salts. Among the isomeric zwitterions examined, the para-isomer C6 showed much better activity than its ortho-isomer C4 and meta-isomer C5. With C6, the reaction gave 87% isolated yield in 1 h. The loading of C6 could be reduced to 1 mol%, maintaining reasonable yield (24 h, 65% vield). The spacing of the charge moiety seems to be critical and the use of naphthalene bridged TAPIS C8 led to poor activity (24 h, 72% yield). The TAPIS catalysis could be further applied in the cyanation reaction with TMSCN.¹² In the presence of 10 mol% C6, the cyanation reaction with chalcone 4 occurred selectivity to form the conjugate addition product 6 in 87% yield. In the trifluoromethylation reaction with TMSCF₃, the reaction afforded selectively 1,2-adduct 8 in 53% yield. The cyanation reaction with nitrostyrene has also been examined, and the reaction afforded a dicyantion adduct 9 in 53% yield with one equivalent of TAPIS C6. In this case, C6 also served as a base to promote the elimination of nitro group.¹³



Figure 3. Lewis base catalysis of TAPIS C6 in other reactions.

The applicability of the TAPIS catalysis was further tested in the Michael addition to nitrostyrenes using 10 mol% of **C6** (Table 1). Nitrostyrenes bearing either electron-donating substituents or electron-withdrawing substituents at the *ortho*, *meta* or *para* position were tolerated with excellent yields, although diastereoselectivities of these reactions were generally moderate (**3b-3s**). The reactions proceeded very well with Michael acceptors bearing other aromatic rings, such as thiophene (**3l**) and naphthalene (**3r**). Alkyl nitroalkenes have also been examined, showing unfortunately much lower activity. The reaction also worked well with 1,3-diketone (**3t**), cyclic ketoester (**3u**) and malononitrile (**3v**). The biphasic properties TAPIS catalysis was then examined in a model Michael addition reaction (Table 2). TAPIS **C6** could be readily recycled by precipitation with diethyl ether. Recycled TAPIS **C6** was directly used in the next run and demonstrated comparable activities (Table 2, entries 1-3). Loss of activity was observed since the fourth use of **C6**, but good activities could still be achieved (Table 2, entries 4-6).

Table 1. Scope of nitroalkenes.^a



^a All reactions were carried out in a 0.2 mmol scale using C6 as catalyst at room temperature for 1 h.

Mechanistically, the TAPIS catalysis in the conjugate additions reactions follows a typical Lewis base pathway, wherein the TAPIS-stabilized enolate as the key intermediate. The lower activity of *ortho*-TAPIS **C4** over its meta- and para isomers (**C5** and **C6**) could be explained by its reduced basicity as a result of a combined steric and close ion-pair effect.



In conclusion, we have developed a novel type of tetraarylphosphonium inner-salts Lewis base catalyst. Tetraarylphosphonium inner salt backbone can not only act as a

Lewis base catalytic moiety, but also as phase tag to facilitate recycling and reuse of the catalyst. The explorations of chiral tetraarylphosphonium salts in asymmetric catalysis are currently underway in our laboratory.



Table 2. Recycling studies for the Micheal reaction of 1s and ethyl acetoacetate.^a

Number of Cycles	Yield (%)	
1	97	
2	94	
3	91	
4	85	
5	84	
6	77	

^aReaction conditions: **1s** (1.0 mmol), **2** (1.2 mmol), catalyst (0.10 mmol), solvent (3.0 mL), room temperature, 1 h.

Acknowledgments

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Tetrahedron Synthesis of structurally distinctive tetraarylphosphonium inner-salts (TAPIS)

- TAPIS backbone could act as a Lewis base catalytic moiety
- TAPIS could act as phase tag to facilitate recycling Accepted and reuse of the catalyst

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