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A Mild and Catalytic Decarboxylation of α-Iminoacids by Tributyl Phosphine.

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Dedicated to the memory of Sir Derek BARTON.

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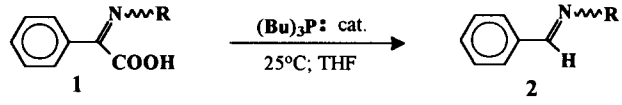
Abstract : α-Iminoacids, prepared from α-keto acids and primary amines, undergo decarboxylation to the corresponding imines by reaction with a catalytic amount of tributylphosphine. No reaction has been observed with α-keto acids or their phenyl-hydrazone, tosyl-hydrazone or oxime derivatives under the same conditions. However, carboxy-azines react rapidly with tributylphosphine and give the corresponding aldazines quantitatively. The mechanism of this reaction is also discussed.

Schiff bases from α-keto acids are essential intermediates in biological transamination processes carried out by pyridoxal enzymes.[1, 2] These compounds are also known for their thermal instability. In boiling benzene, α-iminoacids formed from the reaction of benzoylformic acid with aliphatic amines, are smoothly decarboxylated. This reaction has already been described and used for thioamide synthesis.[3,4] However, aromatic *Schiff* bases from benzoylformic acid seem to be thermally more stable and need prolonged heating in order to be decarboxylated in good yields. Recent research has shown the utility of $(Bu)_3P$ as catalyst in organic chemistry.[5,6,7] For example, Leahy and coworkers have proven that $(Bu)_3P$ can replace the tertiary amine in the Baylis-Hillman reaction.[8] We report, in this article, an easy and very mild decarboxylation of aromatic α-imino acids by tributylphosphine which acts as an efficient catalyst (Scheme 1).



1 2

Scheme 1.

65-100%

Table 1 summarizes the results of various substituted α-iminoacids which underwent decarboxylation with tributylphosphine to form imines at room temperature.

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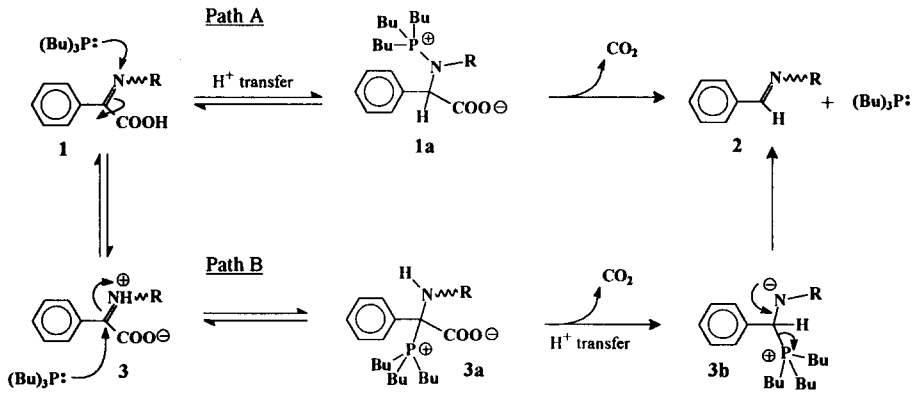
Table 1. Decarboxylation of Iminoacids 1 by Tributylphosphine.

Entry	R	$(Bu)_3P$	Solvent	Time	Yields of 2 [a]
1.	C_6H_5	2%	THF	50 min	99%
2.	*p*-$tBuC_6H_4$	2%	THF	80 min	99%
3.	*p*-$CH_3OC_6H_4$	2%	THF	10 h	95%
4.	*p*-$(Me)_2NC_6H_4$	2%	Pyr.	1 h	99%
5.	*p*-HOC_6H_4	2%	THF/Pyr.	2 h	99%
6.	*p*-ClC_6H_4	2%	THF	48 h	65%
7.	$C_6H_5CH_2$	2%	THF/Pyr.	19 h	80%
8.	C_4H_9	2%	THF	72 h	77%
		50%	THF	24 h	97%

[a] Gas Chromatographic yields. For all these reactions, the authentic samples were prepared from the reaction of benzaldehyde and the corresponding amine, retention time and other physicochemical properties (IR, NMR, mp) were then compared with the product.

This catalyzed decarboxylation can be achieved without isolation of the iminoacid. Thus, benzoylformic acid and aniline react in the presence of 5% of $(Bu)_3P$ (25°C; CH_2Cl_2; 3h.) to give the corresponding imine in 90% yield.

In order to explain the catalytic function of $(Bu)_3P$, two mechanisms can be proposed (Scheme 2).



Scheme 2.

Path A involves a nucleophilic attack of the phosphine on the nitrogen atom of the iminoacid **1** (neutral form) giving intermediate **1a** which should decarboxylate very rapidly (phosphonium leaving group in β-position to the carboxylic group). On the other hand, the zwiterionic form **3** of an iminoacid possess a

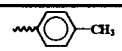
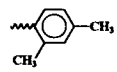
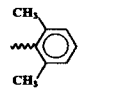
strong electrophilic center able to react with a nucleophilic agent such as a phosphine. However, this process involves the formation of very reactive anion coming from the decarboxylation of intermediate **3a**.

The reaction of trialkyl phosphites with α-iminoacids has been previously studied.[9] The reaction products, in this case, are a dialkyl(α-amino) phophonate and methyl (*N*-phenylbenzimidoyl)-formate coming from a nucleophilic attack by the phosphite on the azomethine group (mechanism similar to path B), following by an Arbuzov type reaction.

We found, during our study, that tributylphosphine seems to act differently giving an intermediate with P-N bond according to path A.

First, the rate and yield of this catalyzed reaction are strongly related to the steric hindrance close to the nitrogen atom (table 2).

Table 2. Decarboxylation of Iminoacids **1** by Tributylphosphine.

Entry	R	$(Bu)_3P$	Solvent	Time	Yields of **2** [a]
1.		2%	THF	75 min	100%
2.		2% 100%	THF	48 h 20 h	45% 52%
3.		100%	THF	40h	11%

[a] Gas Chromatographic yields. For all these reactions, the authentic samples were prepared from the reaction of benzaldehyde and the corresponding amine, retention time and other physicochemical properties (IR, NMR, mp) were then compared with the product.

Attempts to trap ylide coming from the decarboxylation of **3a** with electrophilic agents such as benzaldehyde or benzylbromide, were all unsuccessful. Furthermore, the influence of acids and bases is in agreement with our mechanism proposal (Table 3).

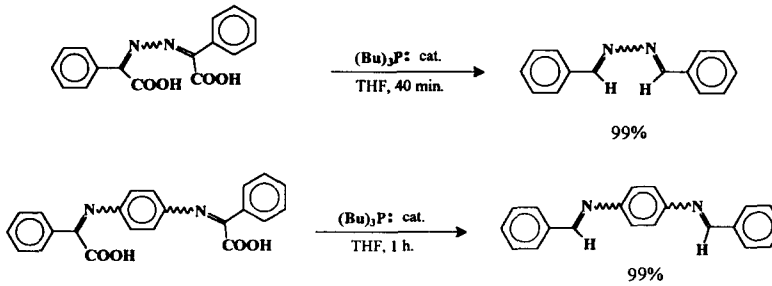
Table 3. Influence of acids and bases[a].

Entry	Acid or Base	Time	Yields of **2**	$T^{1/2}$
1.	No	50 min	100%	15 min
2.	CF_3COOH (10 eq.)	48 h	80%	20 h
3.	CH_3COOH (10 eq.)	15 min	100%	3 min
4.	$(Et)_2NH$ (1 eq.)	5 days	73%	40 h
5.	$(ipr)_2NH$ (1 eq.)	5 days	46%	120 h
6.	Pyridine (10 eq.)	40 min	100%	12 min
7.	$(Et)_3N$ (1 eq.)	4 days	80%	24 h
8.	DABCO (1 eq.)	37 h	81%	12 h
9.	BTMG[b] (10 eq.)	8 h	94%	2 h 30min

[a] Reaction conditions : (*N*-phenylbenzimidoyl) formic acid (R = C_6H_5) (1 mmol); $(Bu)_3P$ (0.02 mmol); THF; 25°C.
[b] BTMG : *N-tert*-Butyl, *N'-N', N''-N''*-tetramethylguanidine.

Although acetic acid (acting as a proton donor) increases the rate of the decarboxylation, strong acids like TFA, able to protonate the N-atom of the iminoacid, are powerful inhibitors of this reaction. The influence of amines are related to their nucleophilic properties rather than basicity. The nucleophilicity of amines probably acts on the azomethine group and gives an intermediate (similar to **3a**) which does not undergo decarboxylation but inhibits the attack of the phosphine.

This decarboxylation can be extended to other compounds like azine or bis-iminoacids prepared as previously described.[10,11] These substrates underwent quantitative double decarboxylation in less than one hour in presence of 2% of tributylphosphine (Scheme 3).



Scheme 3.

In conclusion, we have reported a new catalytic property of $(Bu)_3P$ in a decarboxylation reaction involving intermediates with a P-N bound. This reaction allows a facile preparation of aromatic imines in high yields.

Typical experimental procedure. To a stirred mixture of iminoacid (1 mmol) in dry THF or pyridine (20 mL) was added Bu_3P (5 µL; 0.02 mmol) under argon at room temperature. The solvent was removed under reduced pressure to afford the imine in essentially quantitative yield. All the imines are known compounds. The quantification of CO_2 was determined by absorption in $Ba(OH)_2$ aq., followed by weighing $BaCO_3$ formed (after filtration and drying).

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