

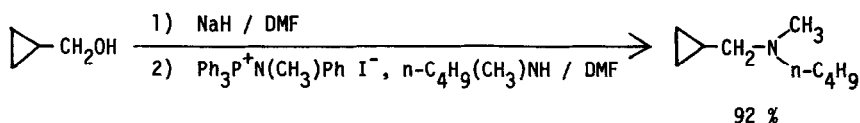
A NOVEL METHOD FOR SYNTHESIS OF UNSYMMETRICAL SECONDARY AND TERTIARY AMINES
FROM REACTIONS OF ALCOHOLS WITH AMINES BY UTILIZING AMINOPHOSPHONIUM SALTS

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Recently, an efficient method for synthesis of unsymmetrical amines from primary or secondary amines by palladium catalyst was explored (1). We now wish to report a novel method for synthesis of these amines from alcohols by utilizing versatile aminophosphonium reagent $\text{Ph}_3\text{P}^+\text{NR}^1\text{R}^2 \text{X}^-$ (1) (2). This method has certain advantages over the previous methods for conversion of alcohols to amines (3-5), since the reaction can be accomplished under mild conditions with high versatility and efficiency.

In a typical procedure, to a solution of the sodium cyclopropylcarbonylalkoxide (5 mM) prepared on treatment with sodium hydride in dimethylformamide (5 ml) was added a solution of N,N-methylphenyltriphenylphosphonium iodide 2 (5 mM) and N-methyl-n-butylamine (10 mM) in DMF (5 ml) in one portion, and the mixture was stirred at 80° for 2 hr. After usual work-up, distillation gave N,N-methyl-n-butylcyclopropylcarbonylamine* in 92 % yield.



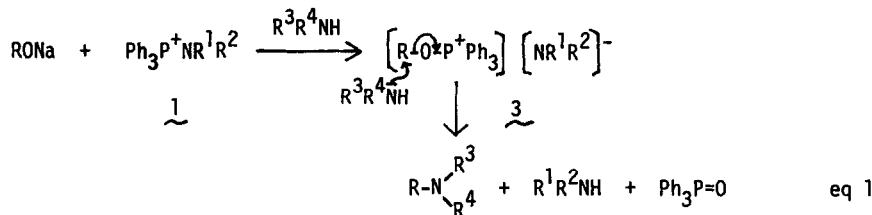
Typical synthetic examples of unsymmetrical amines are summarized in the Table.

For synthesis of secondary amines, benzene is recommended instead of DMF.

Allyl alcohols can also be converted into the corresponding amines stereoselectively. Thus, treatment of trans- and cis-cinnamyl alcohols with a mixture of 2 and N-methylaniline at 25° for 2 hr afforded trans- and cis-N,N-methylphenylcinnamylamines* in 60 % (trans/cis=93/7) and 56 % (trans/cis=7/93) yields, respectively

These reactions can be envisioned as shown in eq 1 Displacement of 1 with RONA via

pentavalent phosphorus intermediacy would give phosphonium salt 3. Subsequent nucleophilic attack of added amines R^3R^4NH at the carbon of the alkoxy group of 3 would form the tertiary amines RNR^3R^4 along with phosphine oxide and amines (R^1R^2NH).



Analogously, azide ion can attack 3 to give azide compounds. Thus, treatment of a mixture of PhCH_2ONa and 2 with sodiumazide gave benzylazide in 90 % yield.

We are exploring other valuable applications of this reaction.

TABLE Synthesis of Unsymmetrical Amines (RNR^3R^4) from Reactions of Alcohols (ROH) with Amines ($\text{R}^3\text{R}^4\text{NH}$) by Utilizing 2^a

Alcohols (ROH)	Amines ($\text{R}^3\text{R}^4\text{NH}$)		Solvent	Yields of RNR^3R^4 ^b
R	R^3	R^4		(%)
PhCH_2	CH_3	$n\text{-C}_4\text{H}_9$	DMF	95
PhCH_2	C_2H_5	C_2H_5	DMF	99
$n\text{-C}_3\text{H}_7$	CH_3	CH_2Ph	DMF	90
$\text{CH}_2=\text{CH}-\text{CH}_2$	CH_3	Ph	DMF	86
$n\text{-C}_3\text{H}_7$	H	$n\text{-C}_6\text{H}_{13}$	C_6H_6	90
$n\text{-C}_4\text{H}_9$	H	CH_2Ph	C_6H_6	97

a) The reaction was carried out at 80° for 1 hr b) Yields based on alcohols

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* Satisfactory analytical and spectral data have been obtained