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TRIPHENYL PHOSPHINE DITRIFLATE: A GENERAL OXYGEN ACTIVATOR

James B. Hendrickson and Steven M. Schwartzman
Department of Chemistry, Brandeis University
Waltham, Massachusetts 02154

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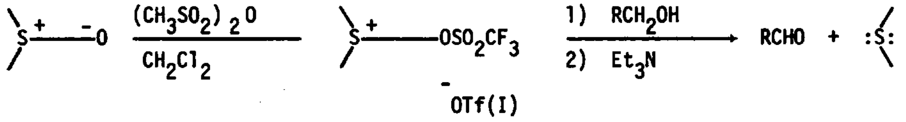
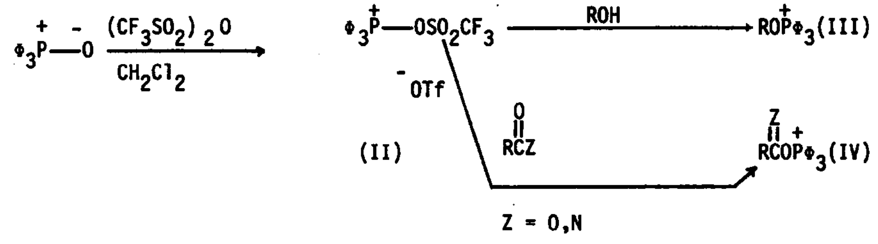
The trifluoromethane sulfonyl ("trifyl") group has been shown to be an effective activator for sulfoxonium oxidations[1] (dimethylsulfide ditriflate (I), Equation 1), by virtue of the exceptionally strong electron withdrawing capabilities of the trifyl group.[2,3] Recent interest in the phosphonium complexes of alcohols[4,5] and acyl derivatives[6] has prompted us to investigate the electrophilic properties of triphenylphosphine ditriflate.

Triphenylphosphine oxide was found to react at 0° C with trifluoromethane sulfonic anhydride producing the complex II, which could be precipitated as a white solid from methylene chloride-ethyl ether (m.p. 74-75° C) (Equation 2). Exposure of this compound to air or water caused rapid decomposition. However, the complex is stable for several months when stored in a nitrogen atmosphere. The NMR ($CDCl_3$) displays a broad doublet centered at 7.75 δ and a small multiplet at 7.22 δ.



(1)



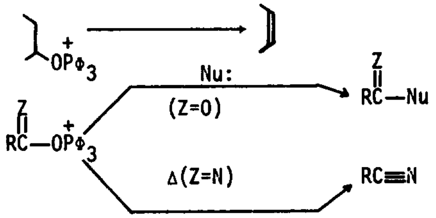
(2)

Complexation of alcohols with II was found to be an immediate reaction at room temperature. Inspection of the α methylene absorptions (NMR) supports the presence of complex III (Table I).

Table I. ROH $\xrightarrow{\Phi_3P(OTf)_2}$ $RO\overset{+}{P}\Phi_3$

Alcohol	α Methylene Absorption (δ)	α Methylene Absorption after Complexation (δ)
Menthol	3.40 (m)	4.20 (m)
$+CH_2OH$	3.21 (s)	3.53 (s)
Cyclohexanol	3.49 (m)	4.35 (m)
Cyclohexylmethanol	3.50 (d, J=5)	3.80 (d, J=6)
ΦCH_2CH_2OH	2.83 (t, J=6.5)	3.05 (bt, J=6.5)
	β CH_2 - 3.80 (t, J=6.5)	β CH_2 - 4.37 (dt, J=6.5, 12)

The further reaction of III and IV (following complexation with II) was envisioned as follows:



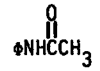
(3)

Quenching the solutions with deuterium oxide provided the alcohol and triphenylphosphine oxide quantitatively (by NMR).

The complex III is stable at room temperature (24 hours) even in the presence of potassium carbonate. However, when heated to 100° C for ~ one hour, III cleanly eliminates [menthol → menthenes (100% by NMR)]. Alternately the reaction can be carried out in the absence of base by simply distilling the product [menthol → menthenes (70%) cyclohexanol → cyclohexene (90%)]. Primary alcohols appeared unreactive, whereas tertiary alcohols formed a wide array of products at room temperature.

A general, one step activation of acids is a desirable transformation, which is currently being investigated by several groups.[7-9] It was found that when II (in CH_2Cl_2) reacted with acetic acid followed by the addition of 3 equivalents of aniline, acetanilide was isolated in 80% yield, after stirring overnight at room temperature. Other acyl derivatives have been formed cleanly under similar conditions (Table II).

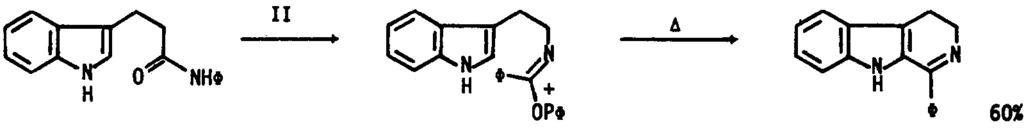
Table II. $RCOOH \xrightarrow{\Phi_3P(OTf)_2} \xrightarrow{Nu:} RCONu$

Acid	Nucleophile	Product	Yield
CH_3COOH	ΦNH_2	 $\Phi NH\overset{O}{\overset{\Vert}{C}}CH_3$	80%
$\Phi COOH$	ΦNH_2	 $\Phi\overset{O}{\overset{\Vert}{C}}NH\Phi$	53%
Veratric	$+NH_2$	t-butyl veratric acid amide	87%
m-$NO_2\Phi COOH$	EtOH	m-$NO_2\Phi COOEt$	74%
2,4,6-Trimethoxy-benzoic	EtOH	Ethyl-(2,4,6-Tri-methoxy)-benzoate	78%
ΦCH_2COOH	ΦNH_2	$\Phi CH_2CONH\Phi$	67%

Amide dehydrations can be carried out by stirring the complex IV (Z=N) at room temperature overnight in methylene chloride. Purification of the resultant cyanides produced the following isolated yields:

Amide	Nitrile	
$\Phi CONH_2$	$\Phi C{\equiv}N$	70%
Anthranilamide	Anthranilonitrile	84%
3,5 Dimethoxy-benzamide	3,5 Dimethoxybenzo-nitrile	54%

An NMR study of the complexation of II with benzanilide (V) displayed a pronounced down-field shift of the main aromatic absorptions of V (7.51 δ, 7.61 δ, 7.67 δ → 7.68 δ, 7.79 δ, 7.82 δ, no N-H absorption) with aqueous workup returning V in over 90% yield. This evidence pointed to the possibility of conducting a Bishler-Naparalski cyclodehydration utilizing the complex (VII) of II with compound VI:



VI VII VIII

After refluxing VII in 1,2-dichloroethane for two hours, the dihydro β-carboline VIII could be isolated in 60% yield after chromatographic purification [NMR (CDCl$_3$) m/8.35 δ (1H) m/7.43 δ (9H), t/4.00 δ (J=8, 2H), t/2.92 δ (J=8, 2H).

Triphenylphosphine ditriflate has thus been shown to be an efficient, mild electrophile capable of activating a wide variety of oxygenated species, i.e., effecting dehydrations of alcohols and amides and activating acids towards attack by nucleophiles.

An illustrative procedure is as follows: 1.57 ml (10 mM) of triflic anhydride in 20 ml methylene chloride was added dropwise to 2.78 g (10 mM) of triphenylphosphine oxide in 20 ml methylene chloride at 0° C. After 15 minutes, 1.21 g benzamide (10 mM) in 5 ml methylene chloride was added dropwise. The reaction was warmed to room temperature, stirred for 24 hours, then the product distilled, the fraction boiling at 185-195° C being collected, yielding 720 mg clear liquid, identical on comparison with authentic sample of benzonitrile.

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