# Facile Synthesis of Phosphonium Salts from Alcohols

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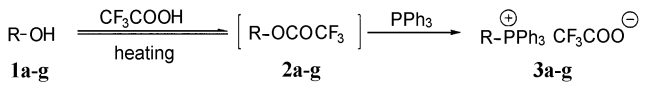
Since its development the Wittig reaction has remained one of the best routes for the construction of carbon-carbon double bonds.[1] The Wittig reagent necessary for the reaction is produced by deprotonation of the corresponding phosphonium salt generated by the quaternization of a phosphine with an organic halide.[2] Synthesis of phosphonium salt often requires forcing conditions. Frequently, the phosphine and organic halide must be heated to reflux for several hours, and in some cases days, to obtain the desired phosphonium salt.[2] In these respects, development of a new methodology for the preparation of phosphonium salt is necessary from alkyl halide[3a] or from other easily available precursors.[3b-c]

Thus, we have investigated the reaction of alcohols and triphenylphosphine in a one pot reaction to generate the phosphonium salt. Hydroxy functionality in alcohol can be activated as its protonated form, halide, sulfonate, or ester. The concept utilizing the protonated hydroxy group as a leaving group in the reaction with phosphine by the use of triphenylphosphine hydrobromide has been published.[3b-c] However, severe drawbacks in this reaction occurred by the fact that the use of sealed tube and/or high temperature (160-180 °C) was necessary.

In this paper, we report facile synthesis of phosphonium salt by the use of in situ generated trifluoroacetates of alcohols.[4] As shown in Scheme 1 the reaction of various alcohols **1a-g** in the presence of triphenylphosphine (1.1 equiv) in trifluoroacetic acid (50 °C-reflux) gave the phosphonium salts **3a-g** in reasonable yields (48-95%) including methyl alcohol, 1-hexanol, benzylic and allylic alcohols.

Some representative results are summarized in Table 1, and the following procedure is typical: The reaction mixture of **1d** (1.1 g, 10 mmol) and $Ph_3P$ (2.9 g, 11 mmol) in trifluoroacetic acid (5 mL) was heated to 50-60 °C for 12 h. After cooling to room temperature, the reaction mixture was poured into cold water, extracted with methylene chloride, dried with magnesium sulfate, and evaporated to dryness. Passing through a short silica gel column (EtOAc/EtOH, 9 : 1) afforded analytically pure phosphonium salt **3d** (4.34 g, 93%).[5]

The reaction might proceed via the corresponding trifluoroacetate derivatives **2a-g**,[4] which are good alkylating reagents toward $Ph_3P$ either in the present form or in their protonated form (Scheme 1). The same reaction of **1d** in formic acid (reflux, 12 h) gave 49% isolated yield of the corresponding phosphonium salt, while in acetic acid (reflux, 12 h)

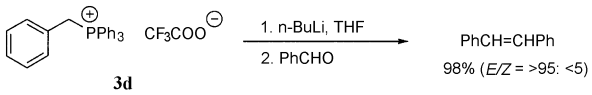



**Scheme 1**

**Table 1**. Synthesis of phosphonium salts

| Entry | Alcohols (**1**) | Conditions | Products (**3**, % yield) |
|---|---|---|---|
| a | $CH_3OH$[a] | reflux, 20 h | $CH_3$–$PPh_3$ $CF_3COO$ (48%) |
| b | OH | reflux, 20 h | $PPh_3$ $CF_3COO$ (78%) |
| c | OH | reflux, 20 h | $PPh_3$ $CF_3COO$ (95%) |
| d | OH | 50–60 °C, 12 h | $PPh_3$ $CF_3COO$ (93%) |
| e | $CH_3$ OH | 50–60 °C, 12 h | $CH_3$ $PPh_3$ $CF_3COO$ (90%) |
| f | OH | reflux, 20 h | $PPh_3$ $CF_3COO$ (91%) |
| g | OH COOEt | 50–60 °C, 12 h | COOEt $PPh_3$ $CF_3COO$ (90%, *Z*/*E* = 83:17)[b] |

[a]Excess used of MeOH. [b]Ratio determined from $^1H$ NMR spectrum.




**Scheme 2**

no reaction was observed. Moreover the counter anion part, trifluoroacetate, did not show any deteriorative effect in the next Wittig reaction as exemplified by using **3d** for the formation of stilbene in Scheme 2.

## References

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5. Representative spectroscopic data of **3d**: mp 171-173 °C; $^{1}$H NMR (DMSO-$d_6$) $\delta$ 5.15 (d, $J$ = 15.6 Hz, 2H), 6.98-7.93 (m, 20H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 28.30 (d, $J$ = 46.7 Hz), 117.51 (q, $J$ = 297.8 Hz, $CF_3COO$-), 118.03 (d, $J$ = 84.9 Hz), 128.14 (d, $J$ = 8.5 Hz), 128.58 (d, $J$ = 4.2 Hz), 129.02 (d, $J$ = 3.0 Hz), 130.32 (d, $J$ = 12.8 Hz), 131.05 (d, $J$ = 5.5 Hz), 134.23 (d, $J$ = 9.8 Hz), 135.32 (d, $J$ = 2.4 Hz), 158.05 (q, $J$ = 30.3 Hz, $CF_3COO$-); IR (KBr) 3388, 2924, 2882, 2808, 1686, 1439 (C-P), 1200, 1112 cm$^{-1}$.