# A NOVEL AND EFFICIENT METHOD FOR THE SYNTHESIS OF β-TRIAZOLYL-ALKENES VIA THE PHASE TRANSFER CATALYZED WITTIG REACTION

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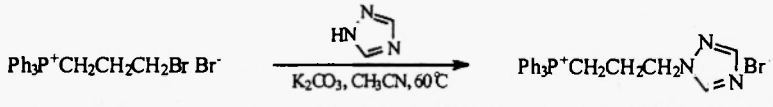
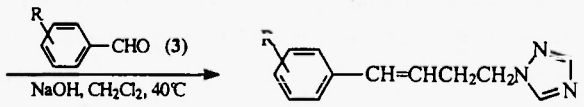
**Abstract** : N-Alkylation of phosphonium salt **1** with 1H-1,2,4-triazole gave γ-triazolylpropyltriphenylphosphonium bromide **2**, which reacted with aromatic aldehydes **3** under the phase transfer conditions to afford β-triazolylalkenes **4**.

The synthesis and biological activity of azole compounds have received continuing attention in the last three decades.[1] Many N-vinyl azoles were found to be effective fungicides and plant growth regulators, such as diniconazole (S-3308) and uniconazole (S-3307). As part of an ongoing programme and interest in the ylide chemistry and biologically active compounds,[2] here we wish to report a novel and efficient method for the synthesis of β-triazolylalkenes via the phase transfer catalyzed Wittig reaction.




**1** **2**




**4**

A solid-liquid N-alkylation of γ-bromopropyltriphenylphosphonium bromide (**1**) with 1H-1,2,4-triazole in acetonitrile at 60 °C for 6 hrs gave γ-triazolylpropyltriphenylphosphonium bromide (**2**) in good yield. In this reaction, the reaction temperature and time were two key factors. With a higher reaction temperature and/or a longer reaction time, side-reactions occurred and the yield of phosphonium salt **2** was reduced significantly.

The phosphonium salt **2** reacted with aromatic aldehyde **3** to afford the desired β-triazolylalkenes **4** in satisfactory yield. We investigated the phase transfer catalyzed Wittig reaction under several conditions. As a result, it was found the base of choice was critical, with the use of potassium carbonate instead of sodium hydroxide as the base, the Wittig reaction could not take place, even under refluxing conditions overnight, and this may be attributed to the relatively weak basicity of potassium carbonate. In addition, the effects of solvent were studies, the polar solvents such as dichloromethane, tetrahydrofuran and dioxane were advantageous to this reaction. Further, we also examined the effects of reaction time, temperature and the molar ratio of the substrates on the Wittig reaction. The best result was obtained when phosphonium salt **2** reacted with 1.2 equiv of aromatic aldehyde **3** in the presence of sodium hydroxide in dichloromethane at 40 °C for 5 hrs.

The stereochemistry of this reaction showed a moderate (*Z*)-selectivity under the above reaction conditions, in accordance with the known stereochemical course of the phase transfer catalyzed Wittig reaction of unstable ylide.[3] The yield of β-triazolylalkene **4** was dependent on the electronic effect and position of substituent on the benzene ring of the aromatic aldehyde. An electron-withdrawing substituent resulted in a better yield. On the other hand, for the same substituent, the yield decreased in the order of *para*, *meta*, and *ortho* (see Table).

Table Compounds **4** prepared

| No | **4a** | **4b** | **4c** | **4d** | **4e** | **4f** | **4g** | **4h** |
|---|---|---|---|---|---|---|---|---|
| R | H | 4-F | 3-F | 4-Cl | 3-Cl | 2-Cl | 3-Br | 2-Br |
| Yield (%)[a] | 64 | 78 | 75 | 72 | 70 | 65 | 67 | 62 |
| *Z* : *E*[b] | 77 : 23 | 69 : 31 | 67 : 33 | 72 : 28 | 74 : 26 | 69 : 31 | 68 : 32 | 67 : 33 |
| No | **4i** | **4j** | **4k** | **4l** | **4m** | **4n** | **4o** | **4p** |
| R | 4-$NO_2$ | 3-$NO_2$ | 2-$NO_2$ | 4-Me | 4-MeO | 4-$Me_2N$ | 2,4-$Cl_2$ | 3,4-$Cl_2$ |
| Yield (%)[a] | 80 | 78 | 75 | 57 | 51 | 46 | 68 | 69 |
| *Z* : *E*[b] | 66 : 34 | 69 : 31 | 71 : 29 | 73 : 27 | 70 : 30 | 68 : 32 | 53 : 47 | 59 : 41 |

[a]Isolated yields were based on phosphonium salt **2**. [b]*Z*/*E* ratios were determinated by GC and $^1$H NMR.

In summary, we provide a novel and efficient method for the synthesis β-triazolylalkenes via the phase transfer catalyzed Wittig reaction under mild conditions.

## Experimental

The melting points were uncorrected. Elemental analyses were measured by a Perkin-Elmer 2400 apparatus. IR spectra were recorded on a Shimadzu IR-408 spectrometer. $^1$H NMR spectra were taken on a Varian XL-200 spectrometer with TMS as the internal standard. Mass spectra were obtained on a HP 5988A spectrometer. Gas chromatographic analyses were performed on a HP 5988A GC-MS instrument using a 25 m × 0.2 mm × 0.3 μm capillary column and HP-5 as liquid phase. Reagents and solvents were purified in the usual way. 3-Bromopropyltriphenylphosphonium bromide (**1**) was prepared according to literature procedure.[4]

### 3-(1H-1, 2, 4-triazol-1-yl)propyltriphenylphosphonium bromide (2)

A mixture of phosphonium salt **1** (4.64 g, 10 mmol), 1H-1,2,4-triazole (0.83 g, 12 mmol) and potassium carbonate (3.1 g, 24 mmol) in acetonitrile (25 mL) was stirred at 60 °C for 6 hrs. At the end of the reaction, the mixture was filtrated and washed with acetonitrile (2 × 10 mL), the filtrate was concentrated in vacuo. After ether (30 mL) was added, the precipitate was collected by filtration and recrystallized from dichloromethane-diethyl ether, a white solid was obtained as product **2** (3.84g, 85 %), m. p. 215-216 °C. IR (KBr), ν: 3370, 2947, 2850, 1660, 1450, 1230, 765, 713 $cm^{-1}$. $^1$H NMR ($CDCl_3$), δ: 2.22-2.46 (m, 2H, $CH_2$), 3.88-4.10 (m, 2H, $CH_2P$), 4.98 (t, 2H, $CH_2N$, J = 6.8 Hz), 7.25-7.89 (m, 15H, 3 × $C_6H_5$), 8.05, 8.37 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 372 ($M^+$–Br, 2), 303 (4), 289 (100), 215 (39), 183 (42), 108 (13). Anal. Calcd for $C_{23}H_{23}BrN_3P$: C, 61.06; H, 5.09; N, 9.29. Found: C, 61.22; H, 5.03; N, 9.24.

### General procedure for the synthesis of 1-aryl-4-(1, 2, 4-triazol-1-yl)-1-butenes (4)

A mixture of phosphonium salt **2** (6.78 g, 15 mmol), aromatic aldehyde **3** (18 mmol) and sodium hydroxide powder (0.6 g, 15 mmol) in dichloromethane (40 mL) was stirred at 40 °C for 5 hrs. The inorganic salt was removed by filtration, the filtrate was concentrated under reduced pressure to give a residue. This was purified by short column chromatography on silica gel with acetone-ether (1:2) to give the product **4**. Its *Z*/*E* ratio was determined by GC and $^1$H NMR.

**4a** : IR (film), ν: 3050, 2870, 1660, 1450, 1270, 1150, 975, 745 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.91-2.48 (m, 2H, $CH_2$), 4.10-4.36 (m, 2H, $CH_2N$), 5.62-6.34 (m, 2H, CH = CH), 7.21-7.53 (m, 5H, $C_6H_5$), 8.01, 8.34 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 199 ($M^+$, 0.27), 129 (100), 115 (64), 102 (14), 91 (19). Anal. Calcd for $C_{12}H_{13}N_3$: C, 72.36; H, 6.53; N, 21.11. Found: C, 72.35; H, 6.61; N, 21.04.

**4b** : IR (film), ν: 3032, 2875, 1650, 1450, 1275, 1143, 965, 744 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.03-2.51 (m, 2H, $CH_2$), 4.12-4.36 (m, 2H, $CH_2N$), 5.52-6.46 (m, 2H, CH = CH), 7.35-7.73 (m, 4H, $C_6H_4$), 8.04, 8.37 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 217 ($M^+$, 0.24), 148 (100), 147 (58), 129 (2), 115 (23), 102 (3). Anal. Calcd for $C_{12}H_{12}FN_3$: C, 66.36; H, 5.53; N, 19.35. Found: C, 66.18; H, 5.59; N, 19.21.

**4c** : IR (film), ν: 3040, 2850, 1665, 1450, 1260, 1157, 980, 734 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.89-2.52 (m, 2H, $CH_2$), 4.31-4.53 (m, 2H, $CH_2N$), 5.77-6.64 (m, 2H, CH = CH), 7.24-7.48 (m, 4H, $C_6H_4$), 8.03, 8.31 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 217 ($M^+$, 0.35), 148 (100), 147 (65), 129 (2), 115 (21), 102 (1). Anal. Calcd for $C_{12}H_{12}FN_3$: C, 66.36; H, 5.53; N, 19.35. Found: C, 66.21; H, 5.60; N, 19.26.

**4d** : IR (film), ν: 3045, 2850, 1667, 1455, 1270, 1153, 974, 723 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.99-2.48 (m, 2H, $CH_2$), 4.12-4.38 (m, 2H, $CH_2N$), 5.59-6.31 (m, 2H, CH = CH), 7.25-7.63 (m, 4H, $C_6H_4$), 8.05, 8.35 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 235 ($M^+$+2, 0.06), 233 ($M^+$, 0.18), 166 (7), 164 (21), 129 (100), 115 (35), 102 (3). Anal. Calcd for $C_{12}H_{12}ClN_3$: C, 61.68; H, 5.14; N, 17.99. Found: C, 61.55; H, 5.20; N, 17.88.

**4e** : IR (film), ν: 3033, 2926, 1670, 1450, 1265, 1155, 980, 743 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.96-2.51 (m, 2H, $CH_2$), 4.13-4.32 (m, 2H, $CH_2N$), 5.61-6.42 (m, 2H, CH = CH), 7.23-7.81 (m, 4H, $C_6H_4$), 8.01, 8.34 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 235 ($M^+$+2, 0.11), 233 ($M^+$, 0.32), 166 (5), 164 (16), 129 (100), 115 (27), 102 (2). Anal. Calcd for $C_{12}H_{12}ClN_3$: C, 61.68; H, 5.14; N, 17.99. Found: C, 61.60; H, 5.24; N, 17.82.

**4f** : IR (film), ν: 3030, 2895, 1677, 1450, 1271, 1145, 975, 738 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.91-2.59 (m, 2H, $CH_2$), 4.12-4.56 (m, 2H, $CH_2N$), 5.82-6.51 (m, 2H, CH = CH), 7.39-7.92 (m, 4H, $C_6H_4$), 8.05, 8.35 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 235 ($M^+$+2, 0.06), 233 ($M^+$, 0.18), 166 (5), 164 (16), 129 (100), 115 (27), 102 (2). Anal. Calcd for $C_{12}H_{12}ClN_3$: C, 61.68; H, 5.14; N, 17.99. Found: C, 61.57; H, 5.19; N, 17.88.

**4g** : IR (film), ν: 3050, 2870, 1675, 1450, 1275, 1150, 965, 740 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.83-2.31 (m, 2H, $CH_2$), 4.10-4.37 (m, 2H, $CH_2N$), 5.59-6.31 (m, 2H, CH = CH), 7.23-7.48 (m, 4H, $C_6H_4$), 8.01, 8.38 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 279 ($M^+$+2, 0.22), 277 ($M^+$, 0.23), 210 (12), 208 (13), 129 (100), 115 (34), 102 (3). Anal. Calcd for $C_{12}H_{12}BrN_3$: C, 51.80; H, 4.32; N, 15.11. Found: C, 51.71; H, 4.40; N, 15.06.

**4h** : IR (film), ν: 3035, 2930, 1665, 1475, 1268, 1155, 965, 735 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.92-2.45 (m, 2H, $CH_2$), 4.01-4.43 (m, 2H, $CH_2N$), 5.56-6.48 (m, 2H, CH = CH), 7.24-7.73 (m, 4H, $C_6H_4$), 8.05, 8.31 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 279 ($M^+$+2, 0.27), 277 ($M^+$, 0.28), 210 (12), 208 (13), 129 (100), 115 (35), 102 (3). Anal. Calcd for $C_{12}H_{12}BrN_3$: C, 51.80; H, 4.32; N, 15.11. Found: C, 51.69; H, 4.41; N, 15.02.

**4i** : IR (film), ν: 3040, 2875, 1680, 1450, 1275, 1250, 980, 743 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.01-2.49 (m, 2H, $CH_2$), 4.11-4.32 (m, 2H, $CH_2N$), 5.78-6.85 (m, 2H, CH = CH), 7.42-8.01 (m, 4H, $C_6H_4$), 8.07, 8.35 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 244 ($M^+$, 0.23), 207 (13), 175 (44), 158 (33), 129 (100), 115 (61), 102 (6). Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.02; H, 4.92; N, 22.95. Found: C, 58.91; H, 4.98; N, 22.85.

**4j** : IR (film), ν: 3032, 2875, 1680, 1450, 1270, 1150, 975, 743 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.05-2.41 (m, 2H, $CH_2$), 4.17-4.41 (m, 2H, $CH_2N$), 5.73-6.68 (m, 2H, CH = CH), 7.48-8.05 (m, 4H, $C_6H_4$), 8.07, 8.36 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 244 ($M^+$, 2), 207 (3), 175 (50), 158 (35), 129 (100), 115 (79), 102 (6). Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.02; H, 4.92; N, 22.95. Found: C, 58.95; H, 5.00; N, 22.79.

**4k** : IR (film), ν: 3050, 2900, 1665, 1450, 1270, 1155, 965, 743 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.00-2.45 (m, 2H, $CH_2$), 4.10-4.45 (m, 2H, $CH_2N$), 5.70-6.75 (m, 2H, CH = CH), 7.42-8.02 (m, 4H, $C_6H_4$), 8.06, 8.34 (2s, 2H, 2 × CH = N). MS

(EI), m/z (%): 244 ($M^+$, 3), 207 (8), 175 (45), 158 (30), 129 (100), 115 (60), 102 (7). Anal. Calcd for $C_{12}H_{12}N_4O_2$: C, 59.02; H, 4.92; N, 22.95. Found: C, 58.90; H, 4.95; N, 22.89.

**4l** : IR (film), ν: 3035, 2930, 1664, 1475, 1265, 1156, 965, 734 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.98-2.52 (m, 2H, $CH_2$), 2.64 (s, 3H, $CH_3$), 4.11-4.52 (m, 2H, $CH_2N$), 5.52-6.52 (m, 2H, CH = CH), 7.24-7.69 (m, 4H, $C_6H_4$), 8.05, 8.35 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 213 ($M^+$, 0.29), 144 (50), 129 (100), 115 (27), 102 (2), 91 (21). Anal. Calcd for $C_{13}H_{15}N_3$: C, 73.24; H, 7.04; N, 19.72. Found: C, 73.27; H, 7.10; N, 19.63.

**4m** : IR (film), ν: 3050, 2920, 1680, 1485, 1270, 1125, 980, 738 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.90-2.57 (m, 2H, $CH_2$), 3.67 (s, 3H, $CH_3O$), 4.07-4.39 (m, 2H, $CH_2N$), 5.55-6.34 (m, 2H, CH = CH), 7.20-7.51 (m, 4H, $C_6H_4$), 8.01, 8.34 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 229 ($M^+$, 0.96), 160 (100), 129 (33), 115 (42), 102 (6), 91 (37). Anal. Calcd for $C_{13}H_{15}N_3O$: C, 68.12; H, 6.55; N, 18.34. Found: C, 68.01; H, 6.63; N, 18.28.

**4n** : IR (film), ν: 3034, 2870, 1675, 1440, 1278, 1160, 975, 743 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.01-2.48 (m, 2H, $CH_2$), 2.67 (s, 6H, 2 × $CH_3$), 4.15-4.43 (m, 2H, $CH_2N$), 5.63-6.41 (m, 2H, CH = CH), 7.17-7.51 (m, 4H, $C_6H_4$), 8.01, 8.37 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 242 ($M^+$, 46), 173 (100), 172 (84), 160 (95), 129 (17), 115 (39), 102 (4), 91 (13). Anal. Calcd for $C_{14}H_{18}N_4$: C, 69.42; H, 7.44; N, 23.14. Found: C, 69.40; H, 7.52; N, 23.08.

**4o** : IR (film), ν: 3045, 2910, 1670, 1440, 1275, 1165, 968, 740 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 1.98-2.48 (m, 2H, $CH_2$), 4.01-4.32 (m, 2H, $CH_2N$), 5.71-6.32 (m, 2H, CH = CH), 7.21-7.51 (m, 3H, $C_6H_3$), 8.03, 8.31 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 271 ($M^+$+4, 0.11), 269 ($M^+$+2, 0.65), 267 ($M^+$, 0.98), 165 (33), 163 (100), 129 (45), 115 (39), 102 (2). Anal. Calcd for $C_{12}H_{11}Cl_2N_3$: C, 53.75; H, 4.11; N, 15.68. Found: C, 53.66; H, 4.18; N, 15.65.

**4p** : IR (film), ν: 3032, 2870, 1675, 1450, 1270, 1160, 970, 734 $cm^{-1}$. $^1H$ NMR ($CDCl_3$), δ: 2.05-2.47 (m, 2H, $CH_2$), 4.15-4.47 (m, 2H, $CH_2N$), 5.64-6.49 (m, 2H, CH = CH), 7.15-7.49 (m, 3H, $C_6H_3$), 8.07, 8.35 (2s, 2H, 2 × CH = N). MS (EI), m/z (%): 271 ($M^+$+4, 0.06), 269 ($M^+$+2, 0.37), 267 ($M^+$, 0.55), 165 (33), 163 (100), 129 (53), 115 (44), 102 (3). Anal. Calcd for $C_{12}H_{11}Cl_2N_3$: C, 53.75; H, 4.11; N, 15.68. Found: C, 53.68; H, 4.19; N, 15.61.

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