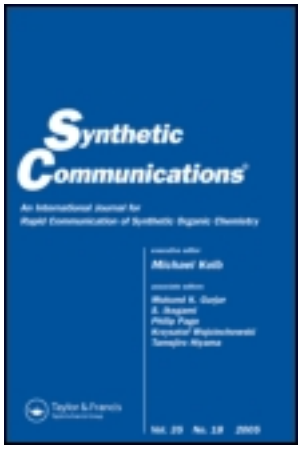

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TRACELESS SULFONE LINKER FOR THE SOLID-PHASE ORGANIC SYNTHESIS OF 1-(*E*)-STYRYL-4-SUBSTITUTED-1,2,3-TRIAZOLES

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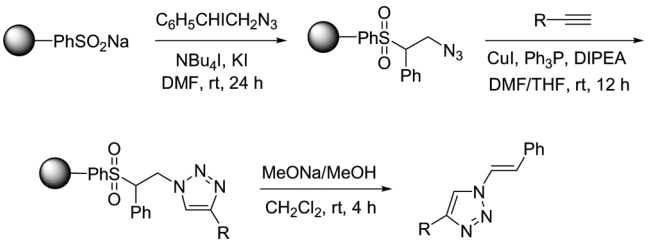
GRAPHICAL ABSTRACT



Abstract *A novel, facile, solid-phase, organic synthesis of 1-(*E*)-styryl-4-substituted-1,2,3-triazoles in good yields and purities via traceless sulfone linker has been developed. Key steps involved in this synthetic procedure include (i) sulfone alkylation of sulfinate resin with (2-azido-1-iodoethyl)benzene, (ii) [3 + 2] cycloaddition with terminal alkynes in the presence of CuI, and (iii) traceless product release by base-mediated elimination process.*

Keywords Click chemistry; 1,4-disubstituted-1,2,3-triazole; elimination reaction; 1-(*E*)-styryl substituent; solid-phase organic synthesis; sulfone linker

INTRODUCTION

Combinatorial chemistry, together with the solid-phase organic synthesis (SPOS) technique, has been employed as an efficient methodology for the high-speed synthesis of structurally diverse compounds for the drug discovery community.[1] The SPOS approach provides many advantages in terms of separation and purification of materials and unique opportunities in controlling organic reactions.[2] 1,2,3-Triazoles are some of the most useful heterocycles[3] and have been widely used in many research fields such as materials, chemical, and biological sciences.[4] Because of their

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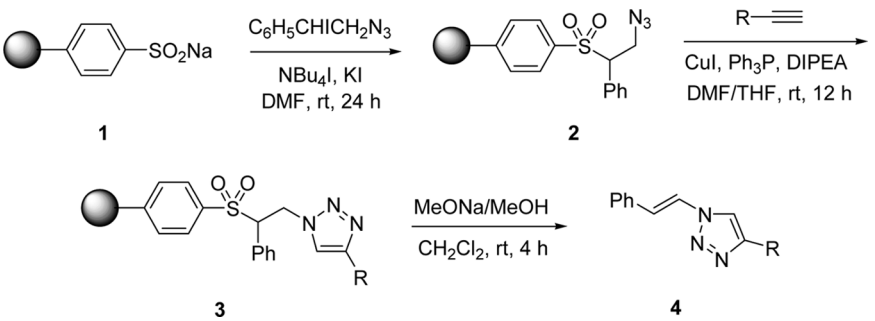
importance, the synthesis of 1,2,3-triazoles from various azides and alkynes has been widely studied in solution phase.[5,6] Nevertheless, among them, little attention has been paid to the preparation of styryl-substituted 1,2,3-triazoles.[7] To our knowledge, only a few papers have reported the solid-phase synthesis of 1,2,3-triazoles up to now.[8] Moreover, there are no reported examples involving the SPOS of styryl-substituted 1,2,3-triazoles. Therefore, the development of a versatile SPOS procedure toward functionalized 1,2,3-triazoles containing the styryl moiety is still in demand. It is well known that the sulfonyl group is an important activating moiety introduced in an intermediate molecule for the construction of carbon–carbon bonds and other transformations.[9] The sulfonyl group is readily converted to a leaving group, making a carbon–carbon double bond via a base-promoted β-elimination route.[10] Furthermore, sulfinate-functionalized resins have been developed efficiently and utilized in SPOS, and the resulting sulfone linker has been found to be both a robust and a versatile linker.[11–13] Recently, several research groups, [8h,14–16] including ours, [17] have been interested in the development of sulfone-linking strategies for SPOS methods to explore sulfone-based chemical transformations. As a part of our ongoing research program focused on the use of a versatile traceless sulfone linker in SPOS, we herein present an efficient solid-phase synthetic approach for the preparation of 1-(*E*)-styryl-4-substituted-1,2,3-triazoles, as shown in Scheme 1.

As outlined in Scheme 1, polystyrene/1% divinylbenzene sodium sulfinate resin **(1)** was allowed to react with (2-azido-1-iodoethyl)benzene[18] in dimethylfor mamide (DMF) in the presence of tetrabutylammonium iodide (NBu_4I) and potassium iodide to afford polymer-supported (2-azido-1-phenyl)ethyl sulfone **(2)** in excellent yield (>95%, determined by elementary analysis of the nitrogen–azide loading = 1.55 mmol/g), which was amenable to Fourier transform infrared (FTIR) monitoring for the complete disappearance of the sulfinate stretch at 960 cm^{-1} and appearance of a characteristic azido band at 2098 cm^{-1}, as well as the two typical sulfone stretches ($\nu_{asym} = 1305\ cm^{-1}$ and $\nu_{sym} = 1145\ cm^{-1}$).

With resin **2** in hand, [3 + 2] cycloaddition reaction of **2** with various terminal alkynes, the key for the success of this protocol was then investigated. It has been reported that the copper-catalyzed alkyne–azide cycloaddition (CuAAC) is a reliable means for the synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles exclusively.[5,6] Based on these results, phenylacetylene was chosen for the template reaction with **2**. To



Scheme 1. Solid-phase synthetic route to 1-(E)-styryl-4-substituted-1,2,3-triazoles.

optimize reaction conditions, several solvents such as tetrallydrofuran (THF), MeCN, demethylformamide (DMF), chimethylsulfoxide (DMSO), *t*-BuOH, CH_2Cl_2, and their cosolvents were tested in the same standard reaction in the presence of catalyst ($CuSO_4$/sodium ascorbate or CuI). After a considerable number of experiments, the 1,3-dipolar cycloaddition of **2** with phenylacetylene was conducted smoothly in DMF/THF (1/2) in the presence of diisopropylethylamine (DIPEA), triphenyl phosphine (Ph_3P), and 10 mol% of CuI at room temperature for 12 h, leading to the polymer-supported (1-phenyl-2-triazolyl)ethyl sulfone **(3a)**. It should be point out that the FTIR spectrum of **3a** also showed the sulfone stretches at 1308 and 1147 cm^{-1}, which were quite similar to the values of resin **2** (sulfone absorption bond at 1305 and 1145 cm^{-1}). Obviously, this transformation (conversion of **2** to **3a**) could not be reliably monitored only by FTIR spectroscopy for the appearance of sulfonyl stretch bands. However, interestingly, this transformation seemed to be quantitative, because no characteristic azido absorption at 2098 cm^{-1} could be detected in the FTIR spectrum of **3a** after completing this cycloaddition reaction. In the progress of this transformation, it was found that the signal of the azido group (2098 cm^{-1}) has distinctly shrunk after 8 h of reaction time, and another 4 h of reaction time leading to a complete disappearance of the characteristic azido absorption.

Subsequently, base-mediated β-elimination cleavage conditions of resin **3a** for liberating the target molecule 1-styryl-4-phenyl-1*H*-1,2,3-triazole **(4a)** was examined. After various reaction conditions were evaluated by varying reaction time, temperature, base, and solvent, such as Et_3N/CH_2Cl_2, DBU/CH_2Cl_2, CH_3ONa/CH_2Cl_2, and *t*-BuOK/THF, the best results were obtained by treating resin **3a** with CH_3ONa/CH_3OH in CH_2Cl_2 at room temperature for 4 h. In the FTIR spectrum of the residue resin, no sulfone absorption peaks were observed, indicating this cleavage step was complete. Fortunately, without further purification, the crude product **4a** was obtained in high purity (96%, indicating by high-performance liquid chromotography [HPLC] analysis) after removal of excess cleavage reagent and evaporation of residual solvent. Then passing the crude product through a flash silica-gel column chromatography eluted with ethyl acetate/hexane afforded pure target compound **4a** in 90% yield based on the loading of starting resin **1** (Table 1, entry 1).

Table 1. The yields and purities of 1-(*E*)-styryl-4-substituted-1*H*-1,2,3-triazoles (**4a**–**4i**)

Entry	R	Product	Yield[a] (%)	Purity[b] (%)
1	C_6H_5	**4a**	90	96
2	4-$CH_3CH_2C_6H_4$	**4b**	90	96
3	2-$CH_3C_6H_4OCH_2$	**4c**	88	95
4	2-$CH_3OC_6H_4OCH_2$	**4d**	87	98
5	2-$NO_2C_6H_4OCH_2$	**4e**	85	95
6	4-$NO_2C_6H_4OCH_2$	**4f**	84	97
7	2-$ClC_6H_4OCH_2$	**4g**	86	96
8	2-Naphthoxymethyl	**4h**	84	97
9	n-C_4H_9	**4i**	85	98

[a]Overall isolated yields based on polystyrene-supported sodium sulfinate **1** (2. 0 mmol /g).
[b]Determined by HPLC of crude cleavage product ($\lambda = 254$ nm).

To test the scope of the protocol, a variety of 1-styryl-4-substituted-1*H*-1,2,3-triazoles (**4a**–**4i**) were prepared from different terminal alkynes with resin **2** under the optimized conditions. As seen from Table 1, both aromatic and aliphatic alkynes underwent the reaction smoothly to afford the corresponding products **4a**–**4i** in good to excellent yields (84–90%) with excellent purities (95–98%). It is noteworthy that all target compounds were formed with complete (*E*) stereoselectivities, which were confirmed by the coupling constants of the olefinic protons in their NMR spectra. For instance, in the ^{1}H NMR spectrum of 1-(*E*)-styryl-4-(4-nitrophenoxymethyl)-1*H*-1,2,3-triazole **(4f)**, the coupling constants ($J = 14.8$ Hz) between the two olefinic protons at $\delta = 7.77$ and 7.22 ppm were observed, which indicated exclusive production of *E*-isomer. Additionally, the ^{1}H NMR spectrum of **4f** exhibited a distinct singlet at $\delta = 7.99$ ppm for the triazolyl C_5–H proton, and its IR spectrum displayed C=C olefin absorption at 1655 cm^{-1} and characteristic band at 1509 cm^{-1}, indicating the presence of a nitro group. It should be pointed out that the analogous 1-styryl-1,2,3-triazoles with substituents in the benzene ring can also be prepared using the present method. For example, when using 1-(2-azido-1-iodoethyl)-4-methylbenzene in place of (2-azido-1-iodoethyl)benzene, together with phenylacetylene as a reaction substrate, the corresponding target molecule, 1-*(E)*-(4-methylstyryl)-4-phenyl-1*H*-1,2,3-triazole **(4a′)** was obtained in 88% yield.

In summary, a facile protocol for the solid-phase synthesis of 1-(*E*)-styryl-4-substituted-1*H*-1,2,3-triazoles has been developed based on traceless sulfone linker. Simple workup, mild reaction conditions, and good to excellent yields make this methodology attractive and suitable for combinatorial library production.

EXPERIMENTAL

Melting points were determined on an X_4 melting-point apparatus and are uncorrected.^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance (400-MHz) spectrometer, using $CDCl_3$ as the solvent and TMS as an internal standard. FTIR spectra were taken on a Perkin-Elmer SP One FTIR spectrophotometer. Microanalyses were performed with a Carlo Erba 1106 elemental analyzer. High-performance liquid chromatography (HPLC) analysis was performed on Agilent 1100 automated system having a photodiode array (PDA) detector ($\lambda_{max} = 254$ nm used for this study). Polystyrene/1% divinylbenzene sodium sulfinate (2.0 mmol $-SO_2Na$/g) was purchased from Tianjin Nankai Hecheng Science and Technology Co. (100–200 mesh). (2-Azido-1-iodoethyl)-benzene [18] was prepared according to the procedure in the literature. Terminal alkynes (**3c–3h**) were prepared by alkylation of the corresponding phenols with propargyl bromide in the presence of K_2CO_3 in acetone under refluxing conditions using a method similar to that described in the literature.[19] The terminal alkynes (**3a, 3b**, and **3i**) and other chemicals were obtained from commercial suppliers (Aldrich, USA, and Shanghai Chemical Company, China) and used without purification prior to use. All organic solvents were dried by standard methods.

Preparation of Polymer-Supported (2-Azido-1-phenyl)ethyl Sulfone (2)

Resin **1** (2.0 g, 3.6 mmol) was swollen in a mixture of DMF (20 mL) by gently shaking the resin–DMF mixture at room temperature for 30 min. Then

(2-azido-1-iodoethyl)benzene (5.0 mmol), tetrabutylammonium iodide (1.0 mmol), and potassium iodide (5.0 mmol) were added to this mixture, and the resulting reaction mixture was shaken at room temperature under a nitrogen atmosphere for 24 h. After filtration, the resin was washed successively with DMF, H_2O, CH_3OH, and Et_2O (2×10 mL of each) and then dried under reduce pressure over phosphorous pentoxide at 50–60 °C to afford resin **2** as yellow beads (azide loading = 1.55 mmol/g). IR (KBr): $\nu = 3061, 3030, 2934, 2098, 1583, 1498, 1448, 1304, 1292, 1145, 1082, 915, 811, 762\ cm^{-1}$.

General Procedure for the Synthesis of 1-(*E*)-Styryl-4-substituted-1*H*-1,2,3-triazoles (4a–4i)

Alkyne (3.0 mmol), CuI (191 mg, 10 mol%), DIPEA (0.4 mL, 500 mol%), and Ph_3P (262 mg, 10 mol%) were added to the suspension of the resin **2** (645 mg, 1.0 mmol) preswollen in DMF /THF (1:2, 15 mL) and then shaken at room temperature for 12 h. The resin was collected by filtration; washed with pyridine, CH_2Cl_2, THF, and Et_2O (2×10 mL of each); and dried under vacuum overnight to yield resin **3a–3i**. Subsequently, after resin **3a–3i** was swollen in a mixture of THF (10 mL) and CH_3OH (5 mL) for 1 h, sodium methoxide (0.16 g, 3.0 mmol) was added to the suspension and then shaken at room temperature for 4 h. The resin was filtered and washed with THF/H_2O (1/1), THF, and Et_2O (2×10 mL of each). Evaporation of the solvent from the filtrate afforded crude product **4a**–**4i** with more than 95% purity determined by HPLC, which was further purified by flash silica-gel column chromatography and eluted with ethyl acetate/hexane to provide pure product **4a–4i** for structures analysis.

1-(*E*)-Styryl-4-phenyl-1*H*-1,2,3-triazole (4a). Pale yellow viscous oil; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.79–7.77$ (m, 2 H), 7.72 (s, 1 H), 7.42–7.32 (m, 8 H), 5.80 (s, 1 H), 5.48 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 146.6$, 142.0, 133.7, 129.2, 128.9, 128.0, 127.8, 127.4, 126.4, 124.8, 118.8, 108.4; IR (film): $\nu = 3061$, 2925, 2854, 1644, 1577, 1456, 1429, 1267, 1233, 1074, 1021, 898, 808, 763, 692 cm^{-1}. Anal. calcd. for $C_{16}H_{13}N_3$: C, 77.71; H, 5.30; N, 17.00. Found: C, 77.66; H, 5.36; N 17.05.

1-(*E*)-Styryl-4-(4-ethylphenyl)-1*H*-1,2,3-triazole (4b). Pale yellow viscous oil; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.90$ (s, 1 H), 7.71–7.68 (m, 2 H), 7.41–7.29 (m, 5 H), 7.19–7.12 (m, 2 H), 5.78 (s, 1 H), 5.47 (s, 1 H), 2.60 (q, $J = 7.2$ Hz, 2 H), 1.20 (t, $J = 7.2$ Hz, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 147.7$, 144.6, 143.1, 134.7, 129.9, 128.9, 128.4, 127.7, 127.4, 125.8, 119.5, 109.3, 28.7, 15.5; IR (film): $\nu = 3028$, 2964, 2928, 1642, 1496, 1445, 1265, 1230, 1017, 896, 839, 800, 772, 693 cm^{-1}. Anal. calcd. for $C_{18}H_{17}N_3$: C, 78.52; H, 6.22; N, 15.26. Found: C, 78.47; H, 6.27; N, 15.32.

1-(*E*)-Styryl-4-(2-methylphenoxymethyl)-1*H*-1,2,3-triazole (4c). Pale yellow solid, mp 129–130 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.90$ (s, 1 H), 7.77 (d, $J = 14.4$ Hz, 1 H), 7.48 (d, $J = 7.2$ Hz, 2 H), 7.41–7.32 (m, 3 H), 7.19–7.13 (m, 3 H), 6.97 (d, $J = 8.4$ Hz, 1 H), 6.92 (d, $J = 14.4$ Hz, 1 H), 5.28 (s, 2 H), 2.04 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 156.4$, 145.2, 133.5, 130.8, 129.0, 128.9, 127.0, 126.9, 126.8, 123.0, 122.1, 121.1, 120.0, 111.5, 62.2, 16.3; IR (KBr): $\nu = 3136$, 3096, 2927, 1655, 1493, 1454, 1383, 1350, 1239, 1050, 1021, 950, 752 cm^{-1}.

Anal. calcd. for $C_{18}H_{17}ON_3$: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.16; H, 5.93; N, 14.38.

1-(*E*)-Styryl-4-(2-methoxyphenoxymethyl)-1*H*-1,2,3-triazole (4d). White solid, mp 123–124 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1 H), 7.75 (d, *J* = 14.8 Hz, 1 H), 7.47 (d, *J* = 7.6 Hz, 2 H), 7.41–7.31 (m, 3 H), 7.15 (d, *J* = 14.8 Hz, Hz, 1 H), 7.07 (d, *J* = 7.6 Hz, 1 H), 6.97–6.88 (m, 3 H), 5.35 (s, 2 H), 3.88 (s, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 149.6, 147.5, 144.8, 133.5, 129.0, 128.8, 126.8, 122.9, 122.0, 121.9, 120.9, 120.3, 114.3, 111.9, 63.1, 55.9; IR (KBr): ν = 3153, 3115, 2953, 1654, 1590, 1570, 1503, 1465, 1456, 1439, 1393, 1359, 1325, 1288, 1251, 1177, 1123, 1054, 1026, 1010, 956, 875, 750 cm^{-1}. Anal. calcd. for $C_{18}H_{17}O_2N_3$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.27; H, 5.52; N, 13.72.

1-(*E*)-Styryl-4-(2-nitrophenoxymethyl)-1*H*-1,2,3-triazole (4e). Pale yellow solid, mp 134–135 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04 (s, 1 H), 7.87 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.76 (d, *J* = 14.8 Hz, 1 H), 7.58–7.54 (m, 1 H), 7.48 (d, *J* = 7.2 Hz, 2 H), 7.41–7.30 (m, 4 H), 7.22 (d, *J* = 14.8 Hz, 1 H), 7.10–7.06 (m, 1 H), 5.42 (s, 2 H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 151.4, 143.6, 140.2, 134.3, 133.4, 129.0, 128.8, 126.8, 125.7, 122.8, 122.4, 121.2, 120.7, 115.4, 63.7; IR (KBr): ν = 3071, 2957, 1658, 1606, 1517, 1347, 1275, 1251, 1168, 1044, 993, 957, 862, 775, 750, 693 cm^{-1}. Anal. calcd. for $C_{17}H_{14}O_3N_4$: C, 63.35; H, 4.38; N, 17.38. Found: C, 63.40; H, 4.44; N, 17.43.

1-(*E*)-Styryl-4-(4-nitrophenoxymethyl)-1*H*-1,2,3-triazole (4f). Pale yellow solid, mp 149–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.22–8.19 (m, 2 H), 7.99 (s, 1 H), 7.77 (d, *J* = 14.8 Hz, 1 H), 7.48 (d, *J* = 7.6 Hz, 2 H), 7.42–7.33 (m, 3 H), 7.22 (d, *J* = 14.8 Hz, 1 H), 7.11–7.07 (m, 2 H), 5.36 (s, 2 H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 163.0, 143.1, 141.9, 133.3, 129.0, 128.8, 126.8, 126.0, 122.7, 122.6, 120.6, 114.9, 62.3; IR (KBr): ν = 3080, 2930, 2875, 1655, 1607, 1591, 1509, 1495, 1459, 1348, 1297, 1249, 1176, 1153, 1113, 1048, 1018, 1006, 951, 868, 846, 751, 696 cm^{-1}. Anal. calcd. for $C_{17}H_{14}O_3N_4$: C, 63.35; H, 4.38; N, 17.38. Found: C, 63.31; H, 4.43; N, 17.44.

1-(*E*)-Styryl-4-(2-chlorophenoxymethyl)-1*H*-1,2,3-triazole (4g). Pale yellow solid, mp 106–108 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.76 (d, *J* = 14.8 Hz, 1 H), 7.47 (d, *J* = 7.2 Hz, 2 H), 7.41–7.32 (m, 4 H), 7.26–7.19 (m, 2 H), 7.15 (d, *J* = 15.6 Hz, 1 H), 6.92–6.89 (m, 1 H), 5.34 (s, 2 H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 153.7, 144.4, 133.5, 130.4, 129.0, 128.9, 127.9, 126.8, 123.2, 122.9, 122.2, 120.3, 116.2, 114.3, 63.4; IR (KBr): ν = 3104, 3086, 2931, 1654, 1587, 1485, 1388, 1350, 1242, 1161, 1133, 1049, 1018, 969, 856, 750 cm^{-1}. Anal. calcd. for $C_{17}H_{14}ClON_3$: C, 65.49; H, 4.53; N, 13.48. Found: C, 65.42; H, 4.58; N, 13.52.

1-(*E*)-Styryl-4-(2-naphthoxymethyl)-1*H*-1,2,3-triazole (4h). White solid, mp 158–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (s, 1 H), 7.97–7.74 (m, 4 H), 7.48–7.44 (m, 3 H), 7.40–7.34 (m, 5 H), 7.23–7.20 (m, 1 H), 7.19 (d, *J* = 14.8 Hz, Hz, 1 H), 5.40 (s, 2 H); ^{13}C NMR (400 MHz, $CDCl_3$): δ = 156.1, 144.6, 134.4, 133.5, 129.7, 129.2, 129.1, 128.9, 127.7, 126.9, 126.8, 126.6, 124.0, 122.9, 122.1, 120.1, 118.7, 107.3, 62.0; IR (KBr): ν = 3055, 2917, 1658, 1627, 1599, 1511, 1461, 1390, 1260, 1218,

1183, 1119, 1043, 951, 837, 818, 749, 694 cm^{-1}. Anal. calcd. for $C_{21}H_{17}ON_3$: C, 77.04; H, 5.23; N, 12.84. Found: C, 77.00; H, 5.28; N, 12.90.

1-(*E*)-Styryl-4-(N-Butyl)-1*H*-1,2,3-triazole (4i). Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.98$ (s, 1 H), 7.75 (d, $J = 14.8$ Hz, 1 H), 7.42–7.38 (m, 2 H), 7.34–7.27 (m, 3 H), 7.15 (d, $J = 14.8$ Hz, 1 H), 2.70 (t, $J = 7.2$ Hz, 2 H), 1.68–1.60 (m, 2 H), 1.41–1.39 (m, 2 H), 0.98 (t, $J = 7.6$ Hz, 3 H); ^{13}C NMR (400 MHz, $CDCl_3$): $\delta = 147.2$, 135.9, 133.9, 128.7, 128.1, 126.9, 125.7, 118.8, 32.3, 26.0, 22.6, 14.1; IR (neat): $\nu = 3050$, 2923, 1655, 1625, 1600, 1464, 1390, 1263, 1222, 1180, 1119, 1040, 950, 835, 750, 695 cm^{-1}. Anal. calcd. for $C_{14}H_{17}N_3$: C, 73.98; H, 7.54; N, 18.49. Found: C, 73.92; H, 7.61; N, 18.53.

1-(*E*)-(4-Methylstyryl)-4-phenyl-1*H*-1,2,3-triazole (4a'). White solid, mp 88–89 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.92$ (s, 1 H), 7.70–7.65 (m, 2 H), 7.42–7.30 (m, 5 H), 7.12 (d, $J = 7.8$ Hz, 2 H), 5.81 (s, 1 H), 5.50 (s, 1 H), 2.31 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 147.4$, 138.2, 133.5, 132.2, 130.3, 129.3, 128.7, 128.0, 126.8, 126.5, 125.6, 117.7, 21.2; IR (film): $\nu = 3058$, 2927, 2856, 1640, 1450, 1430, 1377, 1265, 1231, 1075, 1020, 895, 821, 765, 690 cm^{-1}. Anal. calcd. for $C_{17}H_{15}N_3$: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.03; H; 5.86; N, 16.14.

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REFERENCES

1. (a) Guillier, F.; Orain, D.; Bradley, M. Linkers and cleavage strategies in solid-phase organic synthesis and combinatorial chemistry. *Chem. Rev.* **2000**, *100*, 2091–2158; (b) Krchňák, V.; Holladay, M. W. Solid-phase heterocyclic chemistry. *Chem. Rev.* **2002**, *102*, 61–92; (c) Lu, J.; Toy, P. H. Organic polymer supports for synthesis and for reagent and catalyst immobilization. *Chem. Rev.* **2009**, *109*, 815–838.
2. (a) Döwald, F. Z. *Organic Synthesis on Solid Phase: Supports, Linkers, Reactions*, 2nd ed.; Wiley-VCH: Weinehim, 2002; (b) Scott, P. *Linker Strategies in Solid-Phase Organic Synthesis*; Wiley-VHC: Weinheim, 2009.
3. Fan, W. Q.; Katritzky, A. R. In *Comprehensive Heterocyclic Chemistry II*; A. R. Katritzky, C. W. Rees, C. W. V. Scriven (Eds.); Elsevier: Oxford, 1996; Vol. 4, pp. 1–126.
4. Krasiski, A.; Radi, Z.; Manetsch, R.; Raushel, J.; Taylor, P.; Sharpless, K. B.; Kolb, H. C. In situ selection of lead compounds by click chemistry: Target-guided optimization of acetylcholinesterase inhibitors. *J. Am. Chem. Soc.* **2005**, *127*, 6686–6692; (b) Binder, W. H.; Kluger, C. Azide/alkyne-"Click" reactions: Application in material science and organic synthesis. *Curr. Org. Chem.* **2006**, *10*, 1791–1815; (c) Suijkerbuijk, B. M. J. M.; Aerts, B. N. H.; Dijkstra, H. P.; Lutz, M.; Spek, A. L.; Koten, G. V.; Gebbink, R. J. M. K. "Click" 1,2,3-triazoles as tunable ligands for late transition metal complexes. *Dalton Trans. Dalton Trans.* **2007**, 1273–1276.
5. For recent reviews, see: (a) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. CuI-catalyzed alkyne–azide "click" cycloadditions from a mechanistic and synthetic perspective. *Eur. J. Org. Chem.* **2006**, 51–68; (b) Gil, M. V.; Arevalo, M. G.; Lopez, O. Click

chemistry-What's in a name? Triazole synthesis and beyond. *Synthesis.* **2007**, 1589–1620; (c) Moses, J. E.; Moorhouse, A. D. The growing applications of click chemistry. *Chem. Soc. Rev.* **2007**, *36*, 1249–1262; (d) Meldal, M.; Tornøe, C. W. Cu-catalyzed azide-alkyne cycloaddition. *Chem. Rev.* **2008**, *108*, 2952–3015; (e) Amblard, F.; Cho, J. H.; Schinazi, R. F. Cu(I)-catalyzed Huisgen azide−alkyne 1,3-dipolar cycloaddition reaction in nucleoside, nucleotide, and oligonucleotide chemistry. *Chem. Rev.* **2009**, *109*, 4207–4220; (f) Kappe, C. O.; Van der Eycken, E. Click chemistry under non-classical reaction conditions. *Chem. Soc. Rev.* **2010**, *39*, 1280–1290; (g) Hein, J. E.; Fokin, V. V. Copper-catalyzed azide–alkyne cycloaddition (CuAAC) and beyond: new reactivity of copper (I) acetylides. *Chem. Soc. Rev.* **2010**, *39*, 1302–1315.

6. For recent selected examples on the preparation of 1,4-disubstituted 1,2,3 triazoles: (a) Dabiri, M.; Salehi, P.; Bahramnejad, M.; Sherafat, F. Synthesis of diheterocyclic compounds based on triazolyl methoxy phenylquinazolines via a one-pot four-component-click reaction. *J. Comb. Chem.* **2010**, *12*, 638–642; (b) Fletcher, J. T.; Reilly, J. E. Fast dye salts provide fast access to azidoarene synthons in multi-step one-pot tandem click transformations. *Tetrahedron Lett.* **2011**, *52*, 5512–5515; (c) Zhang, W.; Su, C.; Kuang, C.; Yang, Q. Stereoselective synthesis of phenyl-1,2,3-triazoles containing (*E*)-vinyl halide group via a one-pot, three-component reaction. *Synth. Commun.* **2011**, *41*, 1267–1275; (d) McIntosh, M. L.; Johnston, R. C.; Pattawong, O.; Ashburn, B. O.; Naffziger, M. R.; Cheong, P. H.-Y.; Carter, R. G. Synthesis and computational analysis of densely functionalized triazoles using o-nitrophenylalkynes. *J. Org. Chem.* **2012**, *77*, 1101–1112; (e) Rajesh, R.; Raghunathan, R. Regioselective synthesis of C_2-symmetric triazolophanes via copper (I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction. *Synth. Commun.* **2012**, *42*, 2256–2266; (f) Ponpandian, T.; Muthusubramanian, S. Tandem Knoevenagel-[3 + 2] cycloaddition-elimination reactions: one-pot synthesis of 4,5-disubstituted 1,2,3-(NH)-triazoles. *Tetrahedron Lett.* **2012**, *53*, 59–63; (g) Kaïm, L. E.; Grimaud, L.; Purumandla, S. R. Four-component synthesis of indazole through Ugi-azide coupling. *Synlett.* **2012**, *23*, 295–297.
7. (a) Jiang, H.; Feng, Z.; Wang, A.; Liu, X.; Chen, Z. Palladium-catalyzed alkenylation of 1,2,3-trizoles with terminal conjugated alkenes by direct C–H bond functionalization. *Eur. J. Org. Chem.* **2010**, 1227–1230; (b) Kavitha, M.; Mahipal, B.; Mainkar, P. S.; Chandrasekhar, S. Click reaction on in situ generated β-azidostyrenes from cinnamic acid using CAN–NaN_3: synthesis of *N*-styryl triazoles. *Tetrahedron Lett.* **2011**, *52*, 1658–1662.
8. (a) Zaragoza, F.; Petersen, S. V. Solid-phase synthesis of substituted 1,2,3-triazoles. *Tetrahedron.* **1996**, *52*, 10823–10826; (b) Tornøe, C. W.; Christensen, C.; Meldal, M. Peptidotriazoles on solid phase: [1,2,3]-Triazoles by regiospecific copper (I)-catalyzed 1,3-dipolar cycloadditions of terminal alkynes to azides. *J. Org. Chem.* **2002**, *67*, 3057–3064; (c) Blass, B. E.; Coburn, K. R.; Faulkner, A. L.; Hunn, C. L.; Natchus, M. G.; Parker, M. S.; Portlock, D. E.; Tullis, J. S.; Wood, R. Solid-phase synthesis of functionalized 1,2,3-triazoles. *Tetrahedron Lett.* **2002**, *43*, 4059–4061; (d) Harju, K.; Vahermo, M.; Mutikainen, I.; Yli-Kauhaluoma, J. Solid-phase synthesis of 1,2,3-triazoles via 1,3-dipolar cycloaddition. *J. Comb. Chem.* **2003**, *5*, 826–833; (e) Gao, Y.-N.; Lam, Y.-L. *Org. Lett.* **2006**, *8*, 3283–3285; (f) Wang, Y.-G.; Xu, W-M.; Huang, X. An efficient solid-phase synthesis of substituted isoxazole, triazole, and cycloalkadiene derivatives using supported selenium resin. *Synthesis* **2007**, 28–32; (g) Cao, J.; Huang, X. *J. Comb. Chem.* **2008**, *10*, 526–533; (h) Gao, D.; Zhai, H.; Parvez, M.; Back, T. G. 1,3-dipolar cycloadditions of acetylenic sulfones in solution and on solid supports. *J. Org. Chem.* **2008**, *73*, 8057–8068; (i) Cohrt, A. E. Jensen, J. F.; Nielsen, T. E. Traceless azido linker for the solid-phase synthesis of *N*H-1,2,3-triazoles via cu-catalyzed azide−alkyne cycloaddition reactions. *Org. Lett.* **2010**, *12*, 5414–5417.
9. Simpkins, N. S. *Sulphones in Organic Synthesis*; Pergamon Press: Oxford, 1993.

10. Najera, C.; Yus, M. Desulfonylation reactions: Recent developments. *Tetrahedron.* **1999**, *55*, 10547–10658.
11. Blaney, P.; Grigg, R.; Sridharan, V. Traceless solid-phase organic synthesis. *Chem. Rev.* **2002**, *102*, 2607–2624.
12. McAllister, L. A.; McCormick, R. A.; Procter, D. J. Sulfide- and selenide-based linkers in phase tag-assisted synthesis. *Tetrahedron.* **2005**, *61*, 11527–11576.
13. Kirsteen Gordon, K.; Balasubramanian, S. Solid phase synthesis–designer linkers for combinatorial chemistry: A review. *J. Chem. Technol. Biotechnol.* **1999**, *74*, 835–851.
14. (a) Cheng, W. C.; Lin, C. C.; Kurth, M. J. Dimsyl anion in the monoalkylation of solid-phase alkyl sulfones. *Tetrahedron Lett.* **2002**, *43*, 2967–2970; (b) Hwang, S. H.; Olmstead, M. M.; Kurth, M. J. Solid-phase synthesis of an isoxazolinopyrrole library. *J. Comb. Chem.* **2004**, *6*, 142–148.
15. (a) Li, W. W.; Chen, Y.; Lam, Y. L. A facile solid-phase synthesis of 3,4,6-trisubstituted-2-pyridones using sodium benzenesulfinate as a traceless linker. *Tetrahedron Lett.* **2004**, *45*, 6545–6547; (b) Kong, K.-H.; Tan, C.-K.; Lam, Y. L. Traceless solid-phase synthesis of 6-amino- and 6-hydroxyimino-1,3,5-triazine-2,4-diones and 1,3,5-triazine-2,4,6-triones. *J. Comb. Chem.* **2009**, *11*, 1050–1060.
16. (a) Huang, W.; Cheng, S.; Sun, W. 2-Polystyrylsulfonyl ethanol supports for the solid-phase syntheses of hydantoins and ureas. *Tetrahedron Lett.* **2001**, *42*, 1973–1974; (b) D'herde, J. N. P.; De Clercq, P. J. Carbon – carbon bond formation on solid support. Application of the classical Julia–Lythgoe olefination. *Tetrahedron Lett.* **2003**, *44*, 6657–6659; (c) Hwang, J. Y.; Choi, H.-S.; Lee, D.-H.; Gong, Y.-D. Solid-phase synthesis of 1,3,4-oxadiazole and 1,3,4-thiadiazole derivatives via selective, reagent-based cyclization of acyldithiocarbazate resins. *J. Comb. Chem.* **2005**, *7*, 816–819; (d) McAllister, L. A.; Turner, K. L.; Brand, S.; Stefaniak, M.; Procter, D. J. Solid phase approaches to *N*-heterocycles using a sulfur linker cleaved by SmI_2. *J. Org. Chem.* **2006**, *71*, 6497–6507; (e) Xie, J. W.; Sun, J.; Zhang, G. L.; Houghten, R. A.; Yu, Y. P. Traceless approach for the solid-phase parallel synthesis of trisubstituted oxindoles. *J. Comb. Chem.* **2007**, *9*, 566–568; (f) Chang, Y.-F.; Jiang, Y.-R.; Cheng, W.-C. Traceless sulfone linker cleavage triggered by ozonolysis: Solid-phase synthesis of diverse a-b-unsaturated carbonyl compounds. *Tetrahedron Lett.* **2008**, *49*, 543–547; (g) Lee, T.; Lee, T. D.; Lee, I. Y.; Gong, Y.-D. Solid-**p**hase **s**ynthesis of thiazolo[4,5-b]pyridine derivatives using Friedländer reaction. *J. Comb. Chem.* **2010**, *12*, 95–99.
17. (a) Sheng, S.-R.; Huang, P.-G.; Zhou, W.; Luo, H.-R.; Lin, S.-Y.; Liu, X.-L. A facile solid-phase synthesis of substituted 2(5*H*)-furanones with sulfone traceless linker. *Synlett.* **2004**, 2603–2605; (b) Sheng, S.-R.; Xu, L.; Zhang, X.-L.; Liu, X.-L.; Wei, M.-H. Solid-phase synthesis of substituted butenolides and butyrolactones using a traceless sulfone linker. *J. Comb. Chem.* **2006**, *8*, 805–807; (c) Liu, X.-L.; Sheng, S.-R.; Zhou, W.; Wang, Q.-Y.; Zhang, X.-L.; Gong, B. A facile solid-phase synthesis of cycloalkylphosphonates and 1-cycloalkenylphosphonates using polymer-supported phenylsulfonylmethylphosphonates. *Synth. Commun.* **2007**, *37*, 119–127; (d) Yu, L.-M.; Tang, N.; Sheng, S.-R.; Chen, R.-B.; Liu, X.-L.; Cai, M.-Z. Solid-phase organic synthesis of aryl vinyl ethers using sulfone-linking strategy. *Chin. J. Chem.* **2012**, *30*, 1027–1030.
18. Chouthaiwale, P. V.; Karabal, P. U.; Suryavanshi, G.; Sudalai, A. Regiospecific azidoiodination of alkenes with sodium periodate, potassium iodide, and sodium azide: A high-yield synthesis of β-iodoazides. *Synthesis.* **2010**, 3879–3882.
19. Pérez-Serrano, L.; Blanco-Urgoiti, J.; Casarrubios, L.; Domínguez, G.; Pérez-Castells, J. Synthesis of tricyclic aromatic compounds by the intramolecular Pauson−Khand reaction promoted by molecular sieves. *J. Org. Chem.* **2000**, *65*, 3513–3519.