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Synthesis of some 2-alkyl-5-(4-vinylphenyl)-2*H*-tetrazole compounds via the Wittig reaction and investigation by X-ray crystallography

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Abstract: Tetrazoles are frequently used in industry and medicine. However, molecules that have both tetrazole and alkenyl groups are rare. For this purpose, new 2-alkyl-5-(4-vinylphenyl)-2*H*-tetrazole (BF5a-i, 63-99%) derivative compounds containing both styrene and tetrazole were synthesized with a high yield under mild conditions by the Wittig reaction. Their structures were verified by spectroscopic methods (FT-IR, ^{1}H NMR, ^{13}C-APT NMR, HRMS, and X-Ray crystallography (for BF5a).

Keywords: Tetrazole; styrene; X-ray crystallography; Wittig reaction; dehydration.

1. Introduction

Tetrazole, a nitrogen-containing heteroaromatic compound, is used biologically as a bioisostere of carboxylic acid (1*H*-tetrazole, pKa: 4.90[1]; formic acid, pKa: 3.75; acetic acid, pKa:4,75 [2]). Therefore, carboxyl groups are changed with tetrazole groups for derivatization in bioactivity studies[3-5]. Tetrazoles can be deprotonated and derivatized with alkyl groups in alkaline conditions. Various compounds that are used for the treatment of some diseases include substituted tetrazole [6-8]. For instance, losartan (trade name: Cozaar), which is available on the market, is used as a blood pressure medicine containing 5-alkyl-1*H*-tetrazole, and cefamandole (trade name: Mandol) is used as a broad-spectrum antibiotic containing alkylthiotetrazole. In the studies carried out, it has been determined that this effect of drugs with toxic effects decreases with the addition of tetrazole to the structure [9,10]. Besides the fields of medicine, chemistry, and biology, tetrazoles are frequently used in explosives, recording systems, and photography [11-13].

Molecules containing both a tetrazole ring and an alkenyl group in their structure can be converted into many different molecules containing a tetrazole ring via the alkenyl group. Therefore, in this study, it was aimed to synthesize some new molecules with alkyl tetrazole at one end and styrene at the other. As a result, twenty-three new intermediate-step products and nine final products, which could be used as monomers or drug-active ingredients, were synthesized.

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2. Experimental

All compounds were used by purchasing from Sigma-Aldrich, Merck, ABCR Reagent, and Acros Organics companies without any purification process. FT-IR (Thermo Scientific IS5/ID5), NMR (Bruker 300MHz Ultrashield and Avance III 500 MHz), HRMS (Agilent LC/MS-High Resolution Quadrupole Mass Time-of-Flight (Q-TOF)), and X-Ray Crystallography (Bruker Smart Apex II Quazar) were used to confirm the structure of compounds. $CDCl_3$ containing TMS is used as an NMR solvent. Silica gel (60 F_{254}, 230-400 mesh) is used in flash chromatography.

2.1. Chemistry

2.1.1 Synthesis of 1-(4-(1H-tetrazole-5-yl)phenyl)ethan-1-one ***(BF2)*** *and 4-(1H-tetrazole-5-yl)benzaldehyde (****BF7****)*

Sodium azide (0.33 g, 6 mmol) was added to gradually the solution of triethylamine hydrochloride (0.83 g, 6 mmol) in 40 mL toluene. The reaction mixture was stirred for ten minutes at room temperature. Appropriate derivatives of benzonitrile (BF1 or BF6, 5 mmol) dissolved in 10 mL of toluene were added dropwise to this mixture, over 5 minutes. It was heated under a condenser at 100°C for 16 hours. The reaction was monitored by TLC (methanol-ethyl acetate (1:3)). The mixture was extracted with water (3x10mL). The water phase was acidified with 3M HCl to pH=2-3. The white solid precipitated was filtered and crystallized from the hexane-ethyl acetate solvent.

*1-(4-(1H-tetrazole-5-yl)phenyl)ethan-1-one (****BF2****)*: White solid, 92%, mp: 190-192°C, lit. 191.7–192.3°C [14].

*4-(1H-tetrazole-5-yl)benzaldehyde (****BF7****)*: White solid, 90%, mp: 184-186˚C, lit. 182–184˚C [15].

*2.1.2. General synthesis of 1-(4-(2-Alkyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (****BF31a-i****) and 4-(2-Alkyl-2H-tetrazole-5-yl)benzaldehyde (****BF81a-i****)*

Appropriate derivatives of 1*H*-tetrazole (BF2 or BF7, 5 mmol, 1 eq.) were dissolved in 50 mL of DMF. Dry potassium carbonate (0.82 g, 6 mmol, 1.2 eq.) was added to room temperature and stirred for 1 hour. At the end of this period, the appropriate alkyl halide (6 mmol, 1.2 eq.) was added dropwise and heated under a condenser at 110°C. The reaction was ended when no differentiation was observed in TLC. Ice-water mixture was added to the reaction mixture and extracted with ethyl acetate (5x15 mL). The organic phase (ethyl acetate phase) was dried with Na_2SO_4 and the compounds were separated from each other by flash chromatography ($60F_{254}$ Silica gel, 230-400 Mesh) using the appropriate solvent pair of hexane-ethyl acetate [16].

*1-(4-(2-Methyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (****BF31a****)*:White solid, 77%, mp: 149-152˚C; IR (neat, ATR): 3044 (=C-H), 2963 (C-H), 1672 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.26 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 8.10 (d, 2H, H_c, J_{bc}:8.3 Hz) –CH; 4.45 (s, 3H, H_d) –CH_3; 2.67 (s, 3H, H_a) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.4 (2); 164.2 (7); 138.1 (3); 131.4 (6); 128.8 (4); 126.8 (5); 39.6 (8); 26.6 (1). HRMS (ESI): $[M-H]^-$ $C_{10}H_9N_4O$ found *m/z*: 201.0807; calcd. 201.0782.

*1-(4-(2-Ethyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (****BF31b****)*: White solid, 79%, mp: 77-79˚C; IR (neat, ATR): 2999 (=C-H), 2922 (C-H), 1672 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.27 (d, 2H, H_b, J_{bc}:8,4 Hz) –CH; 8.08 (d, 2H, H_c, J_{bc}:8.5 Hz) –CH; 4.74 (q, 2H, H_d, J_{de}:7.3 Hz) -CH_2; 2.66 (s, 3H, H_a) –CH_3; 1.71 (t, 3H, H_e, J_{de}:7.3 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.4 (2); 164.0 (7); 138.1 (3); 131.6 (6); 128.8 (4); 126.8 (5); 48.5 (8);26.6 (1); 14.5 (9). HRMS (ESI): $[M+H]^+$ $C_{11}H_{13}N_4O$ found *m/z*: 217,1138; calcd. 217.1084.

*1-(4-(2-Propyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31c**)* :White solid, 82%, mp: 51-52°C; IR (neat, ATR): 3011 (=C-H), 2966 (C-H), 1676 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.7 (d, 2H, H_b, J_{bc}:8.2 Hz) –CH; 8.08 (d, 2H, H_c, J_{bc}:8.2 Hz) –CH; 4.65 (t, 2H, H_d, J_{de}:7.1 Hz) -CH_2; 2.66 (s, 3H, H_a) –CH_3, 2.20-2.05 (m, 2H, H_e) -CH_2; 1.02 (t, 3H, H_f, J_{ef}:7.4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.2 (2); 163.8 (7); 138.0 (3); 131.5 (6); 128.7 (4); 126.7 (5); 54.7 (8); 26.5 (1); 22.7 (9); 10.8 (10). HRMS (ESI): $[M-H]^-$ $C_{12}H_{13}N_4O$ found *m/z*: 229.1094; calcd. 229.1095.

*1-(4-(2-Butyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31d**)*: Yellow solid, 81%, mp: 38-40°C; IR (neat, ATR): 3011 (=C-H), 2956 (C-H), 1677 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.26 (d, 2H, H_b, J_{bc}:8.2 Hz) –CH; 8.08 (d, 2H, H_c, J_{bc}:8.5 Hz) –CH; 4.68 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.65 (s, 3H, H_a) –CH_3, 2.20-1.90 (m, 2H, H_e) -CH_2; 1.50-1.30 (m, 2H, H_f) -CH_2; 0.93 (t, 3H, H_g, J_{fg}:7.3 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.2 (2); 163.9 (7); 138.0 (3); 131.6 (6); 128.7 (4); 126.9 (5); 52.9 (8); 31.1 (9); 26.6 (1); 19.5 (10); 13.1 (11). HRMS (ESI): $[M+Na]^+$ $C_{13}H_{16}N_4NaO$ found *m/z*: 267.1211; calcd. 267.1216.

*1-(4-(2-Pentyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31e**)*: Yellow solid, 83%, mp: 66-68°C; IR (neat, ATR): 3067 (=C-H), 2952 (C-H), 1677 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.26 (d, 2H, H_b, J_{bc}:8.4 Hz) –CH; 8.08 (d, 2H, H_c, J_{bc}:8.4 Hz) –CH; 4.67 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.66 (s, 3H, H_a) –CH_3, 2.20-2.00 (m, 2H, H_e) -CH_2; 1.50-1.25 (m, 4H, H_f, H_g) -CH_2; 0.92 (t, 3H, H_h, J_{gh}:6.7 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.5 (2); 164.0 (7); 138.1 (3); 131.7 (6); 128.8 (4); 126.9 (5); 53.3 (8); 29.0 (9); 28.4 (10); 26.7 (1); 22.0 (11); 13.8 (12). HRMS (ESI): $[M+H]^+$ $C_{14}H_{19}N_4O$ found *m/z*: 259.1584; calcd. 259.1559.

*1-(4-(2-Hexyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31f**)*: Yellow solid, 95%, mp: 51-54°C; IR (neat, ATR): 2957 (C-H), 1677 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.27 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 8.09 (d, 2H, H_c, J_{bc}:8.4 Hz) –CH; 4.68 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.64 (s, 3H, H_a) –CH_3, 2.16-2.02 (m, 2H, H_e) -CH_2; 1.30-1.15 (m, 6H, H_f, H_g, H_h) -CH_2; 0.90 (t, 3H, H_j, J_{ij}:6.8 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.5 (2); 164.1 (7); 138.2 (3); 131.7 (6); 128.9 (4); 126.9 (5); 53.4 (8); 31.0 (9); 29.3 (10); 26.7 (1); 26.0 (11); 22.4 (12); 13.9 (13). HRMS (ESI): $[M+H]^+$ $C_{15}H_{20}N_4O$ found *m/z*: 273.1715; calcd. 273.1715.

*1-(4-(2-Heptyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31g**)*:Yellow solid, 89%, mp: 72-75°C; IR (neat, ATR): 2953 (C-H), 1677 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.29 (d, 2H, H_b, J_{bc}:6.7 Hz) –CH; 8.09 (d, 2H, H_c, J_{bc}:6.8 Hz) –CH; 4.68 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.63 (s, 3H, H_a) –CH_3, 2.15-2.03 (m, 2H, H_e) -CH_2; 1.40-1.26 (m, 8H, H_f, H_g, H_h, $H_ı$) -CH_2; 0.90 (t, 3H, $H_ı$, J_{hi}:6.7 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.4 (2); 164.1 (7); 138.2 (3); 131.7 (6); 128.9 (4); 126.9 (5); 53.4 (8); 31.5 (9); 29.4 (10); 28.5 (11); 26.7 (12); 26.3 (1); 22.5 (13); 14.0 (14). HRMS (ESI): $[M+H]^+$ $C_{16}H_{22}N_4O$ found *m/z*: 287.1865; calcd. 287.1871.

*1-(4-(2-Octyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31h**)* :Yellow solid, 81%, mp: 58-60°C; IR (neat, ATR): 2987 (=C-H), 2955 (C-H), 1655 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.28 (d, 2H, H_b, J_{bc}:6.7 Hz) –CH; 8.10 (d, 2H, H_c, J_{bc}:6.8 Hz) –CH; 4.69 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.63 (s, 3H, H_a) –CH_3, 2.18-2.04 (m, 2H, H_e) -CH_2; 1.45-1.25 (m, 10H, H_f, H_g, H_h, $H_ı$, H_i) -CH_2; 0.89 (t, 3H, H_j, J_{ij}:6.9 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.5 (2); 164.1 (7); 138.2 (3); 131.7 (6); 128.9 (4); 126.9 (5); 53.4 (8); 31.7 (9); 29.4 (10); 28.9 (11); 28.8 (12); 26.7 (1); 26.3 (13); 22.6 (14); 14.0 (15). HRMS (ESI): $[M+H]^+$ $C_{17}H_{24}N_4O$ found. *m/z*: 301.2031; calcd. 301.2028.

*1-(4-(2-Benzyl-2H-tetrazole-5-yl)phenyl)ethan-1-one (**BF31i**)*:White solid, 85%, mp: 114-120°C; IR (neat, ATR): 3067 (=C-H), 2963 (C-H), 1681 (C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ= 8.25 (d, 2H, H_b, J_{bc}:8.20 Hz) –CH; 8.06 (d, 2H, H_c, J_{bc}:8.2 Hz) –CH; 7.50-7.30 (m, 5H, H_e) –CH; 5.83 (s, 2H, H_d) -CH_2; 2.65 (s, 3H, H_a) –CH_3. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 197.4 (2); 164.4 (7); 138.2 (3); 133.1 (9); 131.4 (6); 129.0 (4); 128.8 (5); 128.4 (10); 126.9 (11); 56.9 (8); 26.7 (1).

1-(4-(1-Methyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32a**)*:Yellow solid, 12%, mp: 59-61˚C; IR (neat, ATR): 2960 (C-H), 1679 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.16 (d, 2H, H_b, J_{bc}:8.4 Hz) –CH; 7.89 (d, 2H, H_c, J_{bc}:8.5 Hz) –CH; 4.23 (s, 3H, H_d) -CH_2; 2.69 (s, 3H, H_a) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.8 (2); 154.4 (7); 139.8 (3); 129.8 (4);129.7 (5); 128.6 (6); 36.0 (8); 27.6 (1). HRMS (ESI): $[M-H]^-$ $C_{10}H_9N_4O$ found *m/z*: 201.0785; calcd. 201.0782.

1-(4-(1-Propyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32c**)*:Yellow solid, 14%, mp: 65-68˚C; IR (neat, ATR): 3050 (=C-H), 2969 (C-H), 1684 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.16 (d 2H, H_b, J_{bc}:7.9 Hz) –CH; 7.82 (d, 2H, H_c, J_{bc}:7.9 Hz) –CH; 4.42 (t, 2H, H_d, J_{de}:7.1 Hz) -CH_2; 2.69 (s, 3H, H_a) –CH_3; 2.10-1.90 (m, 2H, H_e) –CH_2; 1.10-0.80 (3H, H_f)–CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.0 (2); 153.4 (7); 138.9 (3); 129.0 (4); 129.0 (5); 128.3 (6); 49.8 (8); 26.7 (1); 23.2 (9); 10.9 (10). HRMS (ESI): $[M+H]^+$ $C_{12}H_{15}N_4O$ found *m/z*: 231.1246; calcd. 231.1279.

1-(4-(1-Pentyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32e**)*:Yellow solid, 13%, mp: 67-69˚C; IR (neat, ATR): 3090 (=C-H), 2953 (C-H), 1670 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.15 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 7,81 (d, 2H, H_c, J_{bc}:8.3 Hz) –CH; 4.44 (t, 3H, H_d, J_{de}:7.3 Hz) -CH_2; 2.69 (s, 3H, H_a) –CH_3; 2.00-1.80 (m, 2H, H_e) –CH_2; 1.40-1.25 (m, 4H, H_f, H_g) –CH_2; 0.87 (t, 3H, H_h, J_{gh}:6.8 Hz)–CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.0 (2); 153.4 (7); 138.9 (3); 129.0 (4); 129.0 (5); 128.3 (6); 48.3 (8); 29.4 (9); 28.3 (10); 26.7 (1); 21.9 (11); 13.7 (12). HRMS (ESI): $[M-H]^-$ $C_{14}H_{17}N_4O$ found *m/z*: 257.1406; calcd. 257.1408.

1-(4-(1-Hexyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32f**)*:Yellow solid, 10%; IR (neat, ATR): 3006 (=C-H), 2955 (C-H), 1670 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.16 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 7.81 (d, 2H, H_c, J_{bc}:8.3 Hz) –CH; 4.45 (t, 3H, H_d, J_{de}:7.4 Hz)-CH_2; 2.69 (s, 3H, H_a) –CH_3; 2.00-1.80 (m, 2H, H_e) –CH_2; 1.40-1.25 (m, 6H, H_f, H_g, H_h) –CH_2; 0.85 (t, 3H, H_h, J_{gh}:6,.6 Hz)–CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 201.0 (2); 158.1 (7); 143.6 (3); 133.7 (4); 133.7 (5); 133.1 (6); 53.0 (8); 35.6 (9); 34.4 (10); 31.4 (1); 30.6 (11); 27.0(12); 18.5 (13). HRMS (ESI): $[M-H]^-$ $C_{15}H_{19}N_4O$ found *m/z*: 271.1559; calcd. 271.1564.

1-(4-(1-Octyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32h**)*:Yellow solid, 9%, mp: 64-65˚C; IR (neat, ATR): 2954 (C-H), 1681 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.01 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 7.81 (d, 2H, H_c, J_{bc}:8.1 Hz) –CH; 4.45 (t, 2H, H_d, J_{de}:7.3 Hz) -CH_2; 2.69 (s, 3H, H_a) –CH_3, 2.00-1.90 (m, 2H, H_e) -CH_2; 1.40-1.20 (m, 10H, H_f, H_g, H_h, H_i, H_i) -CH_2; 0.86 (t, 3H, H_j, J_{ij}:6.9 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 196.9 (2); 153.4 (7); 138.9 (3); 129.0 (4); 129.0 (5); 128.0 (6); 48.3 (8); 31.6 (9); 29.7 (10); 28.9 (11); 28.7 (12); 26.7 (1); 26.2 (13); 22.5 (14); 14.0 (15).

1-(4-(1-Benzyl-1*H-tetrazole-5-yl)phenyl)ethan-1-one (**BF32i**)*: Yellow solid, 11%, mp: 105-107˚C; IR (neat, ATR): 3066 (=C-H), 2958 (C-H), 1698 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.08 (d, 2H, H_b, J_{bc}:8.4 Hz) –CH; 7.72 (d, 2H, H_c, J_{bc}:8.4 Hz) –CH; 7.40-7.00 (m, 5H, H_e) –CH; 5.66 (s, 2H, H_d) -CH_2; 2.66 (s, 3H, H_a) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 197.0 (2); 153.8 (7); 138.9 (3); 133.6 (9); 129.2 (4); 129.1 (5); 128.9 (6); 127.9 (10); 127.1 (11); 51.6 (8); 26.7 (1).

4-(2-Methyl-2*H-tetrazole-5-yl)benzaldehyde (**BF81a**)*:White solid, 82%, mp: 130-133˚C, lit. E.N.:138-140˚C; IR (neat, ATR): 3038 (=C-H), 2923 (C-H), 1691 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.09 (s, 1H) CH; 8.33 (d, 2H, H_b, J_{bc}:8.3 Hz) –CH; 8.02 (d, 2H, H_c, J_{bc}:8.2 Hz) –CH; 4,44 (s, 3H, H_d) –CH_3[17].

4-(2-Ethyl-2*H-tetrazole-5-yl)benzaldehyde (**BF81b**)*:White solid, 79%, mp: 93-96˚C; IR (neat, ATR): 2985 (C-H), 2849-2739(O=C-H), 1692 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.09 (s, 1H) CH; 8.34 (d, 2H, H_c, J_{bc}:8.2 Hz) –CH; 8.01 (d, 2H, H_b, J_{bc}:8.1 Hz) –CH; 4,74 (q, 2H, H_d, J_{de}:7.3 Hz) -CH_2; 1,71 (t, 3H, H_e, J_{de}:7.3 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 192.8 (1); 165.0 (6); 138.2 (2); 133.8 (5); 131.0 (3); 128.1 (4); 48.9 (7); 14.7 (8).

*4-(2-Propyl-2H-tetrazole-5-yl)benzaldehyde (**BF81c**)*[18]:White solid, 81%, mp: 41-43°C; IR (neat, ATR): 2969 (C-H), 2838-2743(O=C-H), 1699 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.06 (s, 1H) CH; 8,31 (d, 2H, H_c, J_{bc}:7.0 Hz) –CH; 7.98 (d, 2H, H_b, J_{bc}:7.0 Hz) –CH; 4.63 (t, 2H, H_d, J_{de}:6.7 Hz) -CH_2; 2.20-2.00 (m, 2H, H_e)-CH_2; 0.99 (t, 3H, H_f, J_{ef}:6.8 Hz) -CH_3. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 191.6 (1); 163.9 (6); 137.3 (2); 132.9 (5); 130.1 (3); 127.3 (4); 54.9 (7); 22.8 (8); 10.9 (9). HRMS (ESI): $[M+H]^+$ $C_{11}H_{13}N_4O$ found *m/z*: 217.1064; calcd. 217.1011.

*4-(2-Butyl-2H-tetrazole-5-yl)benzaldehyde (**BF81d**)*:White solid, 85%, mp: 68-70°C; IR (neat, ATR): 2962 (C-H), 2839-2741(O=C-H), 1692 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.09 (s, 1H) CH; 8.34 (d, 2H, H_c, J_{bc}:8.1 Hz) –CH; 8.00 (d, 2H, H_b, J_{bc}:8.1 Hz) –CH; 4.69 (t, 2H, H_d, J_{de}:7.1 Hz) -CH_2; 2.20-2.00 (m, 2H, H_e)-CH_2; 1.50-1.25 (m, 2H, H_f) – CH_2; 0.99 (t, 3H, H_g, J_{fg}:7.4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 191.6 (1); 163.9 (6); 137.3 (2); 132.9 (5); 130.2 (3); 127.3 (4); 53.1 (7); 31.2 (8); 19.6 (9); 13.3 (10). HRMS (ESI): $[M+H]^+$ $C_{12}H_{15}N_4O$ found *m/z*: 231.1230; calcd. 231.1246.

*4-(2-Pentyl-2H-tetrazole-5-yl)benzaldehyde (**BF81e**)*:Yellow liquid, 63%; IR (neat, ATR): 2953 (C-H), 2812-2724(O=C-H), 1695 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 10.09 (s, 1H) CHO; 8,33 (d, 2H, H_c, J_{bc}:8.2 Hz) –CH; 8.01 (d, 2H, H_b, J_{bc}:8.2 Hz) –CH; 4.69 (t, 2H, H_d, J_{de}:7.2 Hz) -CH_2; 2.15-2.00 (m, 2H, H_e)-CH_2; 1.50-1.30 (m, 4H, H_f, H_g) – CH_2; 1.00-0.90 (t, 3H, H_h) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ=191.5 (1); 163.7 (6); 137.2 (2); 132.8 (5); 130.0 (3); 127.2 (4); 53.3 (7); 28.9 (8); 28.3 (9); 21.8 (10); 13.6 (11).

*4-(2-Hexyl-2H-tetrazole-5-yl)benzaldehyde (**BF81f**)*:Yellow liquid, 62%; IR (neat, ATR): 3049 (=C-H), 2955 (C-H), 2859-2741(O=C-H), 1696 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 10.08 (s, 1H) CHO; 8.35 (d, 2H, H_c, J_{bc}:8.0 Hz) –CH; 8.01 (d, 2H, H_b, J_{bc}:8.0 Hz) –CH; 4.68 (t, 2H, H_d, J_{de}:7.1 Hz) -CH_2; 2.20-2.00 (m, 2H, H_e)-CH_2; 1.40-1.20 (m, 8H, H_f, H_g, H_h, H_i) – CH_2; 0.88 (t, 3H, H_i, J_{ii}:6.8 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 191.4 (1); 163.7 (6); 137.2 (2); 132.8 (5); 130.1 (3); 127.2 (4); 53.4 (7); 30.9 (8); 29.2 (9); 25.9 (10); 22.3 (11); 13.8 (12).

*4-(2-Heptyl-2H-tetrazole-5-yl)benzaldehyde (**BF81g**)*:Yellow liquid, 83%; IR (neat, ATR): 3085 (=C-H), 2949 (C-H), 2853-2731(O=C-H), 1696 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 10.08 (s, 1H) CHO; 8.32 (d, 2H, H_c, J_{bc}:8.0 Hz) –CH; 8.00 (d, 2H, H_b, J_{bc}:7.8 Hz) –CH; 4.69 (t, 2H, H_d, J_{de}:7.1 Hz) -CH_2; 2.20-2.00 (m, 2H, H_e)-CH_2; 1.45-1.25 (m, 6H, H_f, H_g, H_h) – CH_2; 0.88 (t, 3H, H_i, J_{hi}:6.7 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 191.6 (1); 163.9 (6); 137.3 (2); 133.0 (5); 130.2 (3); 127.3 (4); 53.4 (7); 31.5 (8); 29.4 (9); 28.5 (10); 26.3 (11); 22.5 (12); 14.0 (13).

*4-(2-Octyl-2H-tetrazole-5-yl)benzaldehyde (**BF81h**)*:White liquid, 81%, mp: 134-138°C; IR (neat, ATR): 2924 (C-H), 2855-2730(O=C-H), 1701 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 10.09 (s, 1H) CH; 8.34 (d, 2H, H_c, J_{bc}:8.1 Hz) –CH; 8.01 (d, 2H, H_b, J_{bc}:8.1 Hz) –CH; 4.68 (t, 2H, H_d, J_{de}:7.0 Hz) -CH_2; 2.20-2.00 (m, 2H, H_e) -CH_2; 1.50-1.25 (m, 10H, H_f, H_g, H_h, H_i, H_i) – CH_2; 0.87 (t, 3H, H_j, J_{ij}:7,4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 191.6 (1); 163.9 (6); 137.3 (2); 132.9 (5); 130.2 (3); 127.3 (4); 53.4 (7); 31.6 (8); 29.3 (9); 28.9 (10); 28.8 (11); 26.3 (12); 22.5 (13); 14.0 (14).

*4-(2-Benzyl-2H-tetrazole-5-yl)benzaldehyde (**BF81i**)*[19]**:**White solid, 65%, mp:115-116°C, lit.mp:117-118°C. IR (neat, ATR): 3032 (=C-H), 2971 (C-H), 1694 (C=O) cm^{-1}

*4-(1-Methyl-1H-tetrazole-5-yl)benzaldehyde (**BF82a**)*:White solid, mp: 142-144°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.12 (s, 1H) CH; 8.11 (d, 2H, H_b, J_{bc}:8.4 Hz) –CH; 7.97 (d, 2H, H_c, J_{bc}:8.1 Hz) –CH; 4,24 (s, 3H, H_d) –CH_3[17].

*4-(1-Ethyl-1H-tetrazole-5-yl)benzaldehyde (**BF82b**)*:White solid, 12%, mp: 45-47°C; IR (neat, ATR): 3087 (=C-H), 2997 (C-H), 2856-2755(O=C-H), 1694 (C=O) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 10.14 (s, 1H) CH; 8.10 (d, 2H, H_c, J_{bc}:8.4 Hz) –CH; 7.90 (d, 2H, H_b, J_{bc}:8.2 Hz) –CH; 4.53 (q, 2H, H_d, J_{de}:7.3 Hz) -CH_2; 1,62 (t, 3H, H_e, J_{de}:7.3 Hz) -CH_3.

2.1.3. General synthesis of 1-(4-(2-Alkyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (BF4a-i)

Sodium borohydride (0.95 g, 25 mmol, 5 eq.) and (1-(4-(1-alkyl-2*H*-tetrazole-5-yl)phenyl)ethane-1-one) (BF31a-i, 5 mmol, 1 eq) dissolved in 30 mL of THF were refluxed for 30 minutes. After this period, 8 mL of MeOH was added to the reaction mixture at room temperature and refluxed for an hour. The progress of the reaction was monitored by TLC and completed. Then, saturated NH_4Cl (10 mL) solution was added to the reaction mixture at room temperature to quench and stirred for 1.5 hours. The organic phase was separated from the mixture. The aqueous phase was extracted with ethyl acetate (4x15mL) and all organic phases were combined. The organic phase was dried with Na_2SO_4; the solvent was removed under reduced pressure [20].

*1-(4-(2-Methyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4a**)*:White solid, 96%, mp: 77-79°C; IR (neat, ATR): 3297 (O-H), 3035 (=C-H), 2965 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.03 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.45 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.79 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.35 (s, 3H, H_e) –CH_3; 2.04 (s, 1H) –OH; 1.49 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.8 (7); 148.1 (3); 126.7 (4); 125.9 (6); 125.8 (5); 69.7 (2); 39.3 (8); 24.9 (1). HRMS (ESI): $[M+Na]^+$ $C_{10}H_{12}N_4NaO$ found *m/z*: 227.0903; calcd. 227.0899.

*1-(4-(2-Ethyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4b**)*:White solid, 92%, mp: 44-45°C; IR (neat, ATR): 3376 (O-H), 2971 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.02 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.45 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.91 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.65 (q, 2H, H_e, J_{ef}:7.3 Hz) -CH_2; 4.50-4.00 (s, 1H) –OH; 1.63 (t, 3H, H_f, J_{ef}:6.4 Hz) –CH_3; 1.48 (d, 3H, H_a, J_{ab}:6.5 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.3 (7); 148.1 (3); 126.3 (4); 125.6 (6); 125.5 (5); 69.1 (2); 48.0 (8); 24.8 (1); 14.0 (9).

*1-(4-(2-Propyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4c**)*:Yellow liquid, 98%; IR (neat, ATR): 3377 (O-H), 2969 (C-H) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$): δ= 8,03 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.45 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.91 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.56 (t, 2H, H_e, J_{ef}:7.0 Hz) -CH_2; 4.00-3.80 (s, 1H) –OH; 2.20-2.00 (m, 2H, H_f) -CH_2; 1.48 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3; 0.95 (t, 3H, H_g, J_{fg}:7.4 Hz) -CH_3. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 164.4 (7); 148.2 (3); 126.5 (4); 125.8 (6); 125.6 (5); 69.3 (2); 54.4 (8); 24.9 (1); 22.5 (9); 10.6 (10).

*1-(4-(2-Butyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4d**)*:Yellow liquid, 97%; IR (neat, ATR): 3391 (O-H), 3029 (=C-H), 2962 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.03 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.45 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.91 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.61 (t, 2H, H_e, J_{ef}:7.1 Hz) -CH_2; 4.00-3.50 (s, 1H) –OH, 2.15-1.95 (m, 2H, H_f) -CH_2; 1.50 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3; 1.45-1.30 (m, 2H, H_g) -CH_2; 0.95 (t, 3H, H_h, J_{gh}:7.4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.4 (7); 148.2 (3); 126.5 (4); 125.8 (6); 125.6 (5); 69.3 (2); 52.6 (8); 30.9 (9); 24.9 (1); 19.2 (10); 13.0 (11). HRMS (ESI): $[M+H]^+$ $C_{13}H_{19}N_4O$ found m/z: 247.1604; calcd. 247.1559.

*1-(4-(2-Pentyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4e**)*:White solid, 94%, mp: 39-40°C; IR (neat, ATR): 3399 (O-H), 3029 (=C-H), 2956 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.88 (d, 2H, H_d, J_{dc}:6.8 Hz) –CH; 7.30 (d, 2H, H_c, J_{dc}:7.0 Hz) –CH; 4.79 (q, 1H, H_b, J_{ab}:6.2 Hz)-CH; 4.43 (t, 2H, H_e, J_{ef}:6.8 Hz) -CH_2; 4.40-4.00 (s, 1H) –OH; 2.00-1.80 (m, 2H, H_f) -CH_2; 1.33 (d, 3H, H_a, J_{ab}:6.2 Hz) –CH_3; 1.30-1.10 (m, 4H, H_g, H_h) -CH_2; 0.76 (t, 3H, H_i, J_{hi}:6.7 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.6 (7); 148.5 (3); 126.6 (4); 125.9 (6); 125.8 (5); 69.4 (2); 53.0 (8); 28.8 (9); 28.3 (10); 25.1 (1); 21.8 (11); 13.6(12). HRMS (ESI): $[M+H]^+$ $C_{14}H_{21}N_4O$ found *m/z*: 261.1735; calcd. 261.1715.

*1-(4-(2-Hexyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4f**)*:White solid, 97%, mp: 37-38°C; IR (neat, ATR): 3205 (O-H), 3035 (=C-H), 2956 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.95 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.36 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.82 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.49 (t, 2H, H_e, J_{ef}:7.1 Hz) -CH_2; 4.00-3.60 (s, 1H) –OH; 2.00-1.80 (m, 2H, H_f) -CH_2; 1.39 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3; 1.35-1.10 (m, 6H, H_g, H_h, H_i) -CH_2; 0.78 (t, 3H, H_i, J_{ii}:6.9 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$):

δ= 164.6 (7); 148.4 (3); 126.7 (4); 126.0 (6); 125.8 (5); 69.5 (2); 53.0 (8); 30.9 (9); 29.1 (10); 25.9 (11); 25.1 (1); 22.2 (12); 13.8 (13).

*1-(4-(2-Heptyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4g**)*:White solid, 95%, mp: 47-50˚C; IR (neat, ATR): 3315 (O-H), 3026 (=C-H), 2952 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.12 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.49 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 4.67 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.64 (t, 2H, H_e, J_{ef}:7.1 Hz) -CH_2; 2.27 (s, 1H) –OH, 2.20-2.05 (m, 2H, H_f) -CH_2; 1.53 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3; 1.40-1.20 (m, 8H, H_g, H_h, $H_ı$, H_i) -CH_2; 0.88 (t, 3H, H_j, J_{ij}:6.7 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.8 (7); 148.0 (3); 126.9 (4); 126.6 (6); 125.8 (5); 70.1 (2); 53.2 (8); 31.5 (9); 29.3 (10); 28.5 (11); 26.3 (12); 25.2 (1); 22.4 (13); 14.0 (14). HRMS (ESI): $[M+H]^+$ $C_{16}H_{25}N_4O$ found *m/z*: 289.2037; calcd. 289.2028.

*1-(4-(2-Octyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4h**)*:White solid, 98%, mp: 49-52˚C; IR (neat, ATR): 3321 (O-H), 3041 (=C-H), 2954 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.93 (d, 2H, H_d, J_{dc}:8.2 Hz) –CH; 7.33 (d, 2H, H_c, J_{dc}:8.1 Hz) –CH; 4.80 (q, 1H, H_b, J_{ab}:6.4 Hz)-CH; 4.49 (t, 2H, H_e, J_{ef}:7.1 Hz) -CH_2; 3.70-3.50 (s, 1H) –OH; 2.00-1.80 (m, 2H, H_f) -CH_2; 1.37 (d, 3H, H_a, J_{ab}:6.4 Hz) –CH_3; 1.25-1.10 (m, 10H, H_g, H_h, $H_ı$, H_i, H_j) -CH_2; 0.75 (t, 3H, H_k, J_{jk}:6.9 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.7 (7); 148.4 (3); 126.7 (4); 126.1 (6); 125.8 (5); 69.6 (2); 53.1 (8); 31.6 (9); 29.2 (10); 28.9 (11); 28.8 (12); 26.2 (13); 25.2 (1); 22.5 (14); 14.0 (15). HRMS (ESI): $[M+H]^+$ $C_{17}H_{27}N_4O$ found *m/z*: 303.2194; calcd. 303.2185.

*1-(4-(2-Benzyl-2H-tetrazole-5-yl)phenyl)ethan-1-ol (**BF4i**)*:White solid, 98%, mp: 97-99˚C; IR (neat, ATR): 3296 (O-H), 3035 (=C-H), 2965 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.92 (d, 2H, H_c, J_{dc}:8.2 Hz) –CH; 7.40-7.10 (m, 7H, H_c, H_g) –CH; 5.62 (s, 2H, H_e) -CH_2; 4.76 (q, 1H, H_b, J_{ba}:6.4 Hz)-CH; 2.94 (s, 1 H) -OH; 1.34 (d, 3H, H_a, J_{ab}:6.4) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 165.0 (7); 148.2 (3); 133.1 (9); 128.8 (4); 128.7 (5); 128.2 (10); 126.8 (11); 125.9 (6); 125.7(11); 69.6 (2); 56.6 (8); 25.0 (1). HRMS (ESI): $[M+H]^+$ $C_{16}H_{17}N_4O$ found *m/z*: 281.1413; calcd. 281.1402.

*2.1.4. General Synthesis of 2-Alkyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5a-i**)*

Appropriate derivatives of aldehyde (BF81, 2 mmol, 1 eq.), potassium carbonate (0.55 g, 4 mmol, 2 eq.), and triphenyl methylphosphonium bromide (0.86 g, 2.4 mmol, 1 eq.) were dissolved in dry 1,4-dioxane (30 mL) and refluxed for 30 hours. The reaction mixture was filtrated to get rid of precipitates. The reaction solvent was removed under reduced pressure. Then, the compounds were separated by flash chromatography ($60F_{254}$ Silica gel, 230-400 Mesh) using the appropriate solvent pair of hexane-ethyl acetate [21].

*2-Methyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5a**)*:White solid, 98%, mp: 83-86˚C; IR (neat, ATR): 3084 (=C-H), 2957 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.97 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.39 (d, 2H, H_d, J_{de}:8.3 Hz) –CH; 6.62 (dd, 1H, H_c, J_{cb}:10,9Hz, J_{ca}:17,6Hz) -CH; 5.71 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.20 (d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.22 (b, 3H, H_f) –CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.9 (7); 139.3 (3); 136.1 (2); 126.9 (4); 126.6 (5); 126.6 (6); 115.1 (1); 39.4 (8).

*2-Ethyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5b**)*:White solid, 90%, mp: 136-142˚C; IR (neat, ATR): 3058 (=C-H), 2988 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.13 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.54 (d, 2H, H_d, J_{de}:8.3 Hz) –CH; 6.77 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.85 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.34 (d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.71 (q, 2H, H_f, J_{fg}:7.4 Hz) -CH_2; 1.69 (t, 3H, H_e, J_{fg}:7.4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.8 (7); 139.3 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.1 (1); 48.3 (8); 14.6 (9). HRMS (ESI): $[M+H]^+$ $C_{11}H_{13}N_4$ found *m/z*: 201.1125; calcd. 201.1140.

*2-Propyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5c**)*:Yellow liquid, 95%; IR (neat, ATR): 3026 (=C-H), 2967 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.12 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.51 (d, 2H, H_d, J_{de}:8.2 Hz) –CH; 6.74 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.82 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.31

(d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.58 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.10-2.00 (m, 2H, H_g)- CH_2; 0.98 (t, 3H, $H_ı$, $J_{ıg}$= 7.4 Hz) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.7 (7); 139.3 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.0 (1); 54.7 (8); 22.8 (9); 10.9 (10).

*2-Butyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5d**)*:Yellow liquid, 94%; IR (neat, ATR): 3085 (=C-H), 2954 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.10 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.53 (d, 2H, H_d, J_{de}:8.4 Hz) –CH; 6.80 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.85 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.34 (d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.66 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.15-2.00 (m, 2H, H_g) -CH_2, 1.55-1.30 (m, 2H, H_h)- CH_2; 0.99 (t, 3H, $H_ı$, $J_{hı}$:7.3 Hz) -CH_3. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 164.7 (7); 139.3 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.0 (1); 52.8 (8); 31.3 (9); 19.6 (10); 13.3 (11). HRMS (ESI): $[M+Na]^+$ $C_{13}H_{16}N_4Na$ found *m/z*: 251.1265; calcd. 251.1273.

*2-Pentyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5e**)*:White solid, 92%, mp: 35-37°C; IR (neat, ATR): 3090 (=C-H), 2949 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.12 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.53 (d, 2H, H_d, J_{de}:8.4 Hz) –CH; 6.77 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.85 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.34 (d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.65 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.15-2.00 (m, 2H, H_g)- CH_2; 1.45-1.30 (m, 4H, H_h, $H_ı$)- CH_2; 0.95-0.85 (t, 3H, H_i) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ=163.7 (7); 138.3 (3); 135.2 (2); 125.9 (4); 125.9 (6); 125.6 (5); 114.0 (1); 52.1 (8); 28.0 (9); 27.5 (10); 21.0 (11); 13.8 (12). HRMS (ESI): $[M+Na]^+$ $C_{14}H_{18}N_4$ found *m/z*: 265.1422; calcd. 265.1429.

*2-Hexyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5f**)*:Yellow liquid, 91%; IR (neat, ATR): 3084 (=C-H), 2959 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.12 (d, 2H, H_e, J_{de}:8.1 Hz) –CH; 7.52 (d, 2H, H_d, J_{de}:8.3 Hz) –CH; 6.75 (dd, 1H, H_c, J_{cb}:10.5Hz, J_{ca}:17.4Hz) -CH; 5.83 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.31 (d, 1H, H_b, J_{cb}:11.0Hz) -CH; 4.62 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.10-1.95 (m, 2H, H_g)- CH_2; 1.45-1.20 (m, 6H, H_h, $H_ı$, H_i)- CH_2; 0.87 (t, 3H, H_i) -CH_3. ^{13}C-APT NMR (75 MHz, $CDCl_3$): δ= 164.7 (7); 139.3 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.0 (1); 53.1 (8); 31.0 (9); 29.3 (10); 26.0 (11); 22.3 (12); 13.9 (13). HRMS (ESI): $[M+H]^+$ $C_{15}H_{21}N_4$ found *m/z*: 257.1761; calcd. 257.1766.

*2-Heptyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5g**)*:White solid, 89%, mp: 35-38°C; IR (neat, ATR): 3084 (=C-H), 2942 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.10 (d, 2H, H_e, J_{de}:7.9 Hz) –CH; 7.49 (d, 2H, H_d, J_{de}:8.3 Hz) –CH; 6.72 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.80 (d, 1H, H_a, J_{ac}:17.6Hz) -CH; 5.28 (d, 1H, H_b, J_{cb}:10.9Hz) -CH; 4.58 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.10-1.95 (m, 2H, H_g)- CH_2; 1.40-1.15 (m, 8H, H_h, $H_ı$, H_i, H_j)- CH_2; 0.95-0.80 (t, 3H, H_k) -CH_3. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 164.7 (7); 139.3 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.0 (1); 53.1 (8); 31.5 (9); 29.3 (10); 28.5 (11); 26.3 (12); 22.4 (13); 13.9 (14). HRMS (ESI): $[M+H]^+$ $C_{15}H_{21}N_4$ found *m/z*: 271.1917; calcd. 271.1923.

*2-Octyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5h**)*:White solid, 99%, mp: 35-38°C; IR (neat, ATR): 3089 (=C-H), 2920 (C-H) cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ= 8.13 (d, 2H, H_e, J_{de}:8.3 Hz) –CH; 7.54 (d, 2H, H_d, J_{de}:8.4 Hz) –CH; 6.77 (dd, 1H, H_c, J_{cb}:10.8Hz, J_{ca}:18 Hz) -CH; 5.85 (d, 1H, H_a, J_{ac}:18.3 Hz) -CH; 5.34 (d, 1H, H_b, J_{cb}:11 Hz) -CH; 4.64 (t, 2H, H_f, J_{fg}:7.1 Hz) -CH_2; 2.20-1.95 (m, 2H, H_g)- CH_2; 1.40-1.15 (m, 10H, H_h, $H_ı$, H_i, H_j, H_k)- CH_2; 0.89 (t, 3H, H_l, J_{kl}:6.9) -CH_3. ^{13}C-APT NMR (125 MHz, $CDCl_3$): δ= 164.7 (7); 136.2 (3); 136.2 (2); 126.9 (4); 126.8 (6); 126.6 (5); 115.0 (1); 53.2 (8); 31.0 (9); 29.3 (10); 26.0 (11); 22.3 (12); 13.9 (15).

*2-Benzyl-5-(4-vinylphenyl)-2H-tetrazole (**BF5i**):*White solid, 63%, mp: 75-77°C; IR (neat, ATR): 3032 (=C-H), 2983 (C-H) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.00 (d, 2H, H_e, J_{de}:8.2 Hz) –CH; 7.41 (d, 2H, H_d, J_{de}:8.2 Hz) –CH; 7.30-7.20 (m, 5H, H_g) -Ar; 6.65 (dd, 1H, H_c, J_{cb}:10.9Hz, J_{ca}:17.6Hz) -CH; 5.80-5.60 (m, 3H, H_a, H_f) –CH, CH_2; 5.22 (d, 1H, H_b, J_{cb}:10.9Hz) –CH. ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 165.1 (7); 139.3 (3); 136.1 (2); 133.3 (9/6); 128.9, 128.8, 128.3, 126.9, 126.5 (4,5,10,11,12); 115.1 (1); 56.7 (8). HRMS (ESI): $[M+H]^+$ $C_{16}H_{15}N_4$ found *m/z*: 263.1308; calcd. 263.1297.

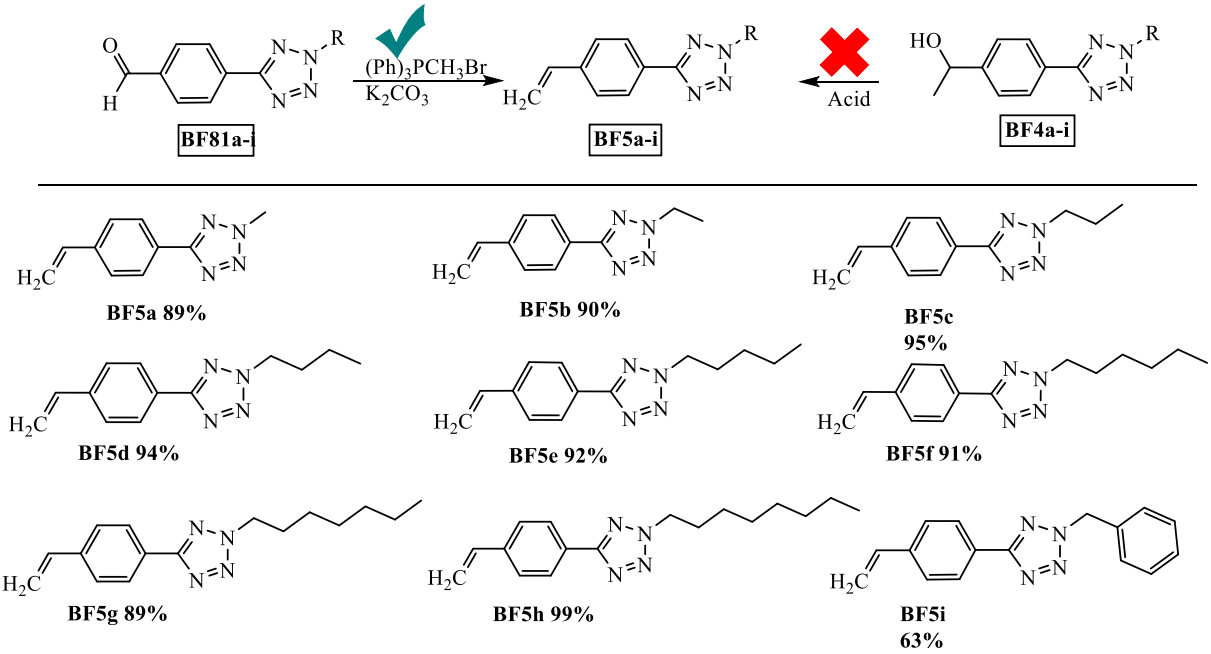
3. Results and Discussion

In this study, derivatives of 2-alkyl-5-(4-vinylphenyl)-2*H*-tetrazole compounds were synthesized. In the first synthesis step, 4-acetylbenzonitrile, sodium azide, and triethyl ammonium chloride were reacted to obtain 1-(4-(1*H*-tetrazole-5-yl)phenyl)ethan-1-one (**BF2**). Then, in the presence of potassium carbonate in DMF, the proton has been removed from tetrazole, and appropriate alkyl bromide was added to the reaction mixture. The reaction was continued for 16 hours, after which time, alkyl tetrazoles formed [1-(4-(2-alkyl-2*H*-tetrazole-5-yl)phenyl)ethan-1-one (**BF31**, 77-95%) and 1-(4-(1-alkyl-1*H*-tetrazole-5-yl)phenyl)ethan-1-one (**BF32**, 9-14%)] were separated by flash chromatography. The corresponding 1-(4-(2-alkyl-2*H*-tetrazole-5-yl)phenyl)ethan-1-one compounds (**BF31a-i**) in THF were reduced to 1-(4-(2-alkyl-2*H*-tetrazole-5-yl)phenyl)ethan-1-ol compounds (**BF4a-i**) by the MeOH-$NaBH_4$ system with high efficiency. Then, the reduced products were converted to 2-alkyl-5-(4-vinylphenyl)-2*H*-tetrazole compounds (**BF5a-i**).

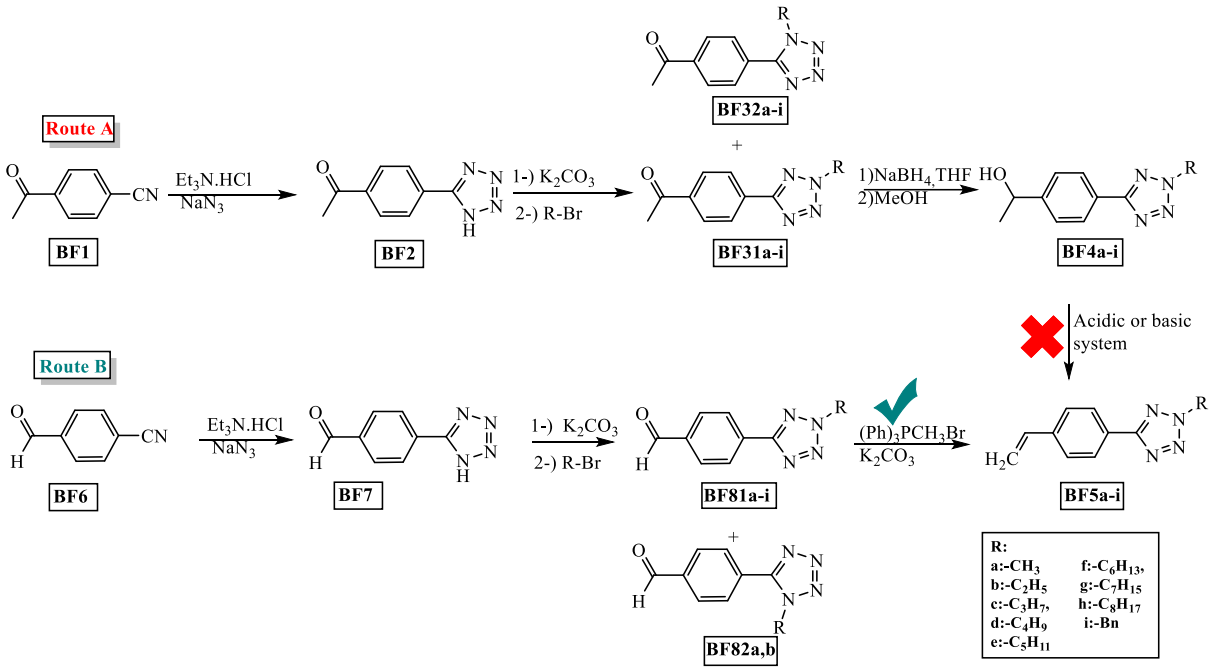
When the acid or acid/base systems, which are generally used to obtain alkenes from alcohols, were tried it was observed that different products were formed beside the desired alkene, no matter how much the conditions were changed. When checking with TLC in these reactions was observed at least three products were formed. It is thought that the products obtained may be ethers, and the targeted/untargeted alkenes [22,23]. Experimental results are given in Table 1. Therefore, as a result of the experiments performed, synthesis steps were optimized for obtaining the alkene desired (Scheme 2).

In the first step of the revised synthesis, 4-cyanobenzaldehyde, sodium azide, and triethyl ammonium chloride were reacted to obtain 4-(1*H*-tetrazole-5-yl)benzaldehyde (**BF7**). Then, in the presence of potassium carbonate in DMF, corresponding alkyl bromide was added to the reaction mixture and heated. The products formed in the reaction [4-(2-alkyl-2*H*-tetrazole-5-yl)benzaldehyde (**BF81a-i**) and 4-(1-alkyl-1*H*-tetrazole-5-yl)benzaldehyde (BF82a-b)] were separated by flash chromatography. For the synthesis of the final products (**BF5a-i**) the Wittig reaction was carried out. The structures of a product obtained were verified by spectroscopic methods (FT-IR, ^{1}H NMR, ^{13}C-APT NMR, HRMS, and X-Ray crystallography (for **BF5a**)).

1-Alkyl-1*H*-tetrazole and 2-alkyl-2*H*-tetrazole compounds are formed when the attachment of the alkyl group to the tetrazole compounds. ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy are used to recognize these two products according to each other. In previously a study, ^{1}H NMR spectroscopy was used and reported that the protons of the first alkyl group of 1-alkyl-1*H*-tetrazole have more chemical shift value than the other [24,25]. In another study, the opposite was explained [26,27].



Scheme 1. The final compounds (BF5a-i) and their yields



Scheme 2. Synthetic pathways are proposed for the synthesis of BF5 thoroughly.
a) Synthesis of BF5 via acid-catalyzed. **b**) Synthesis of BF5 via the Witting reaction

For example, Still *et al*. In their study in 1972, they reported that the chemical shift values of the protons of the methyl group in the N2 position of the compound they synthesized were observed at 4.42 ppm and that the structure of this compound was 2-alkyl-2*H*-tetrazole[28]. To eliminate these different approaches, the structure of the BF5a compound we obtained in our study was confirmed by X-ray crystallography (Figure 1). When the ^{1}H NMR spectrum of this structure was examined, it was observed that these protons were at 4.22 ppm (Figure 1).

Table 1. Reagents for the synthesis of styrene tetrazole derivatives

Entry	Reagent	Temperature (°C)	Time (hours)	Products[b]
1	$POCl_3$/Py	rt	16	3
2	96%H_2SO_4/HOAc	rt	1	4
3	85% H_3PO_4	rt	2	4
4	85% H_3PO_4	80	2	4
5	96% H_2SO_4	50	2	4
6	20% H_2SO_4	50	2	4
7	1) 47% HI 2) EtONa	50	0.5[a]	3
8	1) MsCl 2) EtONa	reflux	16[a]	4

[a)] after the addition EtONa, [b)] the observed product number when checked with TLC

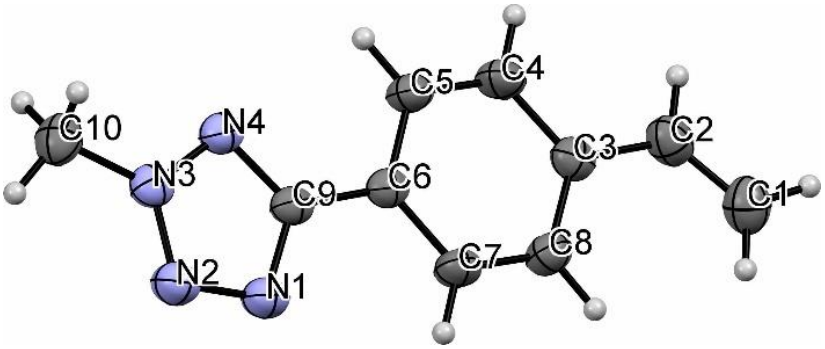


Figure 1. ORTEP image of compound BF5a

4. Conclusion

In this study, new compounds containing 2-alkyl-2*H*-tetrazole and styrene groups were synthesized. The corresponding alkene syntheses from alcohols with dehydration applied in the last step of the designed synthesis route failed. For this reason, the Wittig method was applied in this step. As a result, nine novel 2-alkyl-5-(4-vinylphenyl)-2*H*-tetrazole compounds, BF5a-i, were synthesized in high yield and under mild conditions. The structure of one of these compounds was elucidated by X-ray crystallography and eliminated the confusion as to whether 1-alkyl or 2-alkyl was the main product in the alkylation of tetrazole compounds.

Conflicts of Interest

No conflict of interest was declared by the authors.

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Supporting Information

Supporting information accompanies this paper on http://www.acgpubs.org/journal/organic-communications

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