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FIRST EXAMPLES OF METAL-CATALYZED CROSS-COUPLING OF VINYL- AND ETHYNYLTETRAZOLES WITH ARYL HALIDES

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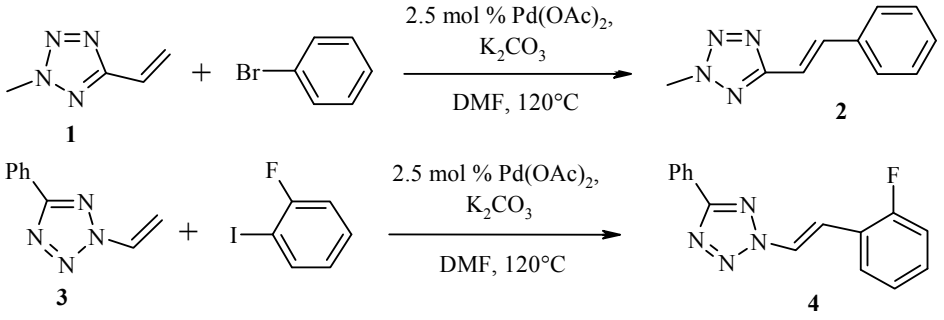
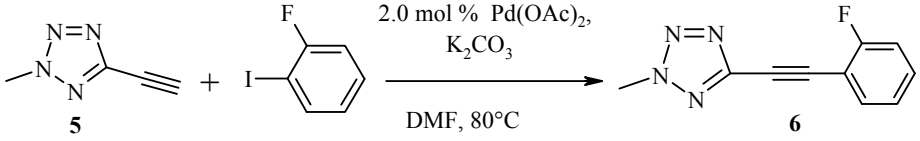
Individual chemical reactions of C,N-vinyltetrazoles and ethynyltetrazoles occurring principally with opening of the CH_2=CH and CH≡C bonds have currently been reported [1, 2]. For the first time we have carried out a palladium-catalyzed arylation of the 2-methyl-5-vinyl- (**1**) and 5-phenyl-2-vinyltetrazoles (**3**) *via* Heck reaction [3] to prepare the (*E*)-styryltetrazoles **2**, **4**.



Sonogashira cross-coupling [3] of 5-ethynyl-2-methyltetrazole (**5)** and 1-fluoro-2-iodobenzene gave the 5-[(2-fluorophenyl)ethynyl]-2-methyltetrazole (**6)**.



^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-300 instrument (300 and 75 MHz respectively) using $CDCl_3$ and chemical shifts were measured relative to the solvent signals (^{1}H at 7.26 ppm and ^{13}C at 77.16 ppm). Mass spectra were obtained on a Waters LCT Premier LC MS instrument (ESI, TOF).

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Tetrazoles **1, 3, 5** were prepared by methods [1, 2, 4].

Synthesis of Compounds 2 and 4 (General Method). K_2CO_3 (5.44 mmol), $Pd(OAc)_2$ (0.0092 mmol), and the corresponding aryl halide (4.08 mmol) were added to a solution of the tetrazole **1** or **3** (2.72 mmol) in DMF (4 ml). The reaction mixture was stirred at 120ºC, poured into water (25 ml), extracted with ethyl acetate (2×10 ml), and the combined extract was dried over anhydrous sodium sulfate. Solvent was evaporated and the product was purified by column chromatography on SiO_2.

(*E*)-2-Methyl-5-styryltetrazole (2). Yield 80%; mp 87-88ºC. R_f 0.40 (hexane–ethyl acetate, 9:1). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 4.35 (3H, s, CH_3); 7.14, 7.73 (1H, two d, *J* = 16.7, CH=CH); 7.38 (3H, m, Ph); 7.56 (2H, d, Ph). ^{13}C NMR spectrum, δ, ppm: 39.45 (CH_3); 113.51 (CH=CH–Ph); 127.23, 128.93, 129.12; 135.80 (CH=CH–Ph); 136.40 (Ph); 164.48 (CN_4). Mass spectrum, *m/z*: 187 $[M+H]^+$. Found, %: C 64.45; H 5.30; N 30.25. $C_{10}H_{10}N_4$. Calculated, %: C 64.50; H 5.41; N 30.09.

(*E*)-2-(2-Fluorostyryl)-5-phenyltetrazole (4). Yield 60%; mp 139-140ºC, R_f 0.30 (hexane–ethyl acetate, 9:1). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.17 (2H, m, Ar); 7.33 (1H, m, Ar); 7.50 (4H, m, Ar); 7.72, 8.14 (1H, two d, *J* = 14.0, CH=CH); 8.21 (2H, d, Ar). ^{13}C NMR spectrum, δ, ppm: 116.23, 116.52; 118.46 (CH=CH–Ph); 121.20, 124.75, 124.93, 127.00, 127.22, 129.08, 129.40, 130.72; 130.80 (CH=CH–Ph); 159.34, 162.28; 164.98 (CN_4). Mass spectrum, *m/z*: 287 $[M+H]^+$. Found, %: C 67.60; H 4.10; N 21.00. $C_{15}H_{11}FN_4$. Calculated, %: C 67.66; H 4.16; N 21.04.

5-((2-Fluorophenyl)ethynyl)-2-methyltetrazole (6). K_2CO_3 (5.00 mmol), $Pd(OAc)_2$ (0.008 mmol), and the aryl halide (3.00 mmol) were added to a solution of the tetrazole (2.50 mmol) in DMF (4 ml). The reaction mixture was stirred at 80ºC and then treated as in the method for the synthesis of tetrazoles **2, 4**. Yield 84%; mp 110-111ºC. R_f 0.25 (hexane–dichloromethane, 7:3). ^{1}H NMR spectrum, δ, ppm: 4.38 (3H, s, CH_3); 7.20 (2H, m, Ar); 7.39 (1H, s, Ar); 7.58 (1H, s, Ar). ^{13}C NMR spectrum, δ, ppm: 39.93 (CH_3); 81.84 (C≡C–Ar); 87.02 (C≡C–Ar); 109.00, 116.6, 125.69, 133.38; 151.03 (CN_4); 161.22, 166.23 (Ar). Mass spectrum, *m/z*: 203 $[M+H]^+$. Found, %: C 59.70; H 3.30; N 27.60. $C_{10}H_7FN_4$. Calculated, %: C 59.40; H 3.49; N 27.71.

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REFERENCES

1. V. N. Kizhnyaev and L. I. Vereshchagin, *Usp. Khim.*, **72**, 159 (2003).
2. S. R. Buzilova, V. M. Shul'gina, G. A. Gareev, and L. I. Vereshchagin, *Khim. Geterotsikl. Soedin.*, 842 (1980). [*Chem. Heterocycl. Comp.*, **16**, 658 (1980)].
3. E. Negishi (editor), *Handbook of Organopalladium Chemistry for Organic Synthesis*, John Wiley and Sons, New York (2002), p. 3279
4. Yu. R. Pavlyukova, R. E. Trifonov, E. V. Yugai, P. A. Aleshunin, I. V. Tselinskii, and V. A. Ostrovskii, *Zh. Org. Khim.*, **44**, 1732 (2008).