Hypervalent iodine in synthesis 87: The synthesis of 2,5-diaryl-2H-tetrazoles

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In the presence of cuprous iodide and potassium carbonate, N-arylation of 5-aryl-2H-tetrazole with a diaryliodonium salt proceeds smoothly in DMF at room temperature to give 2, 5-diaryl-2H-tetrazoles in moderate to good yield.

Keywords: hypervalent iodine, N-arylation, 2, 5-diaryl-2H-tetrazole

2, 5-Diaryl-2H-tetrazoles are valuable synthons in organic chemistry. For example, they are key precursors for the formation of the short-lived 1, 3-dipolar systems, the 1, 3-diarylnitrile imines which add to reactive multiple bonds giving 5-membered heterocyclic adducts.[1-6] There are several synthetic routes for 2, 5-diaryl-2H-tetrazoles reported in the literature. They may be obtained from the reaction of benzaldehyde *p*-chlorophenylhydrazone with phenyl azide,[7] from the reaction of phenylsulfonylbenzhydrazidoyl chlorides with arylhydrazines,[8] and from the reaction of the phenylsulfonylhydrazones of aromatic aldehydes with arenediazonium salts.[9] However, these methods have some disadvantages, such as harsh reaction conditions, unavailable starting materials and unsatisfactory yields. Hence, the development of an efficient synthetic method for 2, 5-diaryl-2H-terazoles is still required.

Our recent research on the transition metal-catalysed arylation reactions with diaryliodonium salts showed that diaryliodonium salts are efficient electrophilic arylation agents.[10] We considered that the N-arylation of the easily obtained 5-aryl-2H-tetrazoles[11] would be a convenient method for the synthesis of 2, 5-diaryl-2H-tetrazoles. Here we report the first example of the synthesis of 2, 5-diaryl-2H-tetrazoles via the N-arylation of 5-aryl-2H-tetrazoles. We found that in the presence of CuI and K_2CO_3, N-arylation of 5-aryl-2H-tetrazole with diaryliodonium salt proceeded smoothly in DMF at room temperature and was complete within 4–5h to give 2, 5-diaryl-2H-tetrazole in moderate to good yield (Scheme1). Diaryliodonium salts with various substituents (such as methyl, chloro, bromo and nitro) and several 5-aryl-2H-tetrazoles were tested. It was found that the reaction was general for these substrates. The results are summarised in Table 1.

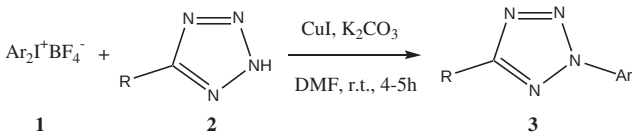
In conclusion, we have provided a convenient synthetic method for 2, 5-diaryl-2H-tetrazoles by the copper-catalysed reaction of diaryliodonium salts with 5-aryl-2H-tetrazoles. It has some advantages over previous methods, such as the availability of starting materials, simple procedure, mild reaction conditions and higher yields.

Experimental

Melting points were uncorrected. ^{1}H NMR data were recorded on an Avance 400 spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. IR spectra were determined on Vector 22 infrared spectrometer with KBr pallet. MS spectra were recorded on HP5859B mass spectrometer. Elemental analyses were performed on EA1110.

Diaryliodonium salts[12] and 5-aryl-2H-tetrazoles[11] were prepared as described in the literature.

General procedure for preparation of 2,5-diaryl tetrazoles: A mixture of the diaryliodonium salt **1** (1mmol), 5-substituted tetrazole **2** (1.2mmol), K_2CO_3 (2mmol), CuI (10mol%) and DMF (5ml) was stirred under a nitrogen atmosphere at room temperature for 4–5h. The reaction mixture was diluted with saturated NH_4Cl aqueous (20ml), and extracted with diethyl ether (3×15ml). The combined organic layers were washed with brine, and dried over anhydrous sodium sulfate. After removal of the solvent under vacuum, the residue was chromatographed on silica gel plate using c-hexane/ethyl acetate (6:1) as a developer to give pure product **3**.



1 **2** **3**

Scheme 1

Physical and spectroscopic data

2, 5-Diphenyl-2H-tetrazole **3a**: m.p. 102–103°C (lit.[13] 101.5–102°C). ^{1}H NMR δ_H ($CDCl_3$) 7.51–7.60 (6H, m), 8.20–8.28 (4H, m). IR ν_{max}/cm^{-1} 1278, 1075, 1018, 994.

2-(4-Methylphenyl)-5-phenyl-2H-tetrazole **3b**: m.p. 104–105°C (lit.[14] 103°C). ^{1}H NMR δ_H ($CDCl_3$) 2.46 (3H, s), 7.37 (2H, m), 7.50–7.53 (3H, m), 8.08 (2H, m), 8.24–8.27 (2H, m). IR ν_{max}/cm^{-1} 1281, 1074, 1013, 999.

2-(4-Chlorophenyl)-5-phenyl-2H-tetrazole **3c**: m.p. 121–122°C (lit.[8] 120.5–121.5°C). ^{1}H NMR δ_H ($CDCl_3$) 7.52–7.57 (5H, m), 8.16 (2H, m), 8.23–8.26 (2H, m). IR ν_{max}/cm^{-1} 1279, 1090, 1074, 1011, 996.

2-(4-Bromophenyl)-5-phenyl-2H-tetrazole **3d**: m.p. 123–124°C (lit.[8] 121–122°C). ^{1}H NMR δ_H ($CDCl_3$) 7.50–7.55 (3H, m), 7.72 (2H, d, *J*=9.0Hz), 8.10 (2H, d, *J*=9.0Hz), 8.25 (2H, m). IR ν_{max}/cm^{-1} 1279, 1064, 1008, 995.

2-(3-Nitrophenyl)-5-phenyl-2H-tetrazole **3e**: m.p. 132–133°C ^{1}H NMR δ_H ($CDCl_3$) 7.56 (3H, m), 7.79–7.83 (1H, m), 8.27–8.30 (2H, m), 8.37 (1H, m), 8.60 (1H, m),9.09 (1H, m). IR ν_{max}/cm^{-1} 1540, 1351, 1060, 1018, 992. Anal. Calcd. for $C_{13}H_9N_5O_2$: C 58.43, H 3.39, N 26.21. Found: C 58.27, H 3.46, N 26.08%. MS *m/z* 239 (M^+-N_2, 29.97), 193 (13.19), 105(33.27), 90 (100).

Table 1 Copper-catalysed *N*-arylation of 5-aryl-2H-tetrazole

Entry	Ar	*R*	Product	Yield/%[a]
1	Ph	Ph	**3a**	77
2	4-$CH_3C_6H_4$	Ph	**3b**	72
3	4-ClC_6H_4	Ph	**3c**	70
4	4-BrC_6H_4	Ph	**3d**	63
5	3-$NO_2C_6H_4$	Ph	**3e**	75
6	Ph	4-$CH_3OC_6H_4$	**3f**	67
7	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	**3g**	60
8	4-ClC_6H_4	4-$CH_3OC_6H_4$	**3h**	63
9	Ph	4-ClC_6H_4	**3i**	66
10	4-$CH_3C_6H_4$	4-ClC_6H_4	**3j**	63
11	4-ClC_6H_4	4-ClC_6H_4	**3k**	62
12	4-BrC_6H_4	4-ClC_6H_4	**3l**	60
13	Ph	$PhCH_2$	**3m**	59
14	4-$CH_3C_6H_4$	$PhCH_2$	**3n**	57
15	4-ClC_6H_4	$PhCH_2$	**3o**	54
16	4-BrC_6H_4	$PhCH_2$	**3p**	53

[a]Isolated yield based on diaryliodonium salt.

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5-(4-Methoxyphenyl)-2-phenyl-2H-tetrazole **3f**: m.p. 107–108°C (lit.[8] 107–108°C). ^{1}H NMR δ_H ($CDCl_3$) 3.89 (3H, s), 7.04 (2H, m), 7.49 (1H, m), 7.56 (2H, m), 8.19 (4H, m). IR ν_{max}/cm^{-1} 1289, 1070, 1008, 992.

5-(4-Methoxyphenyl)-2-(4-methylphenyl)-2H-tetrazole **3g**: m.p. 109–111°C (lit.[8] 111–112°C). ^{1}H NMR δ_H ($CDCl_3$) 2.45 (3H, s), 3.89 (3H, s), 7.04 (2H, d, *J*=8.6Hz), 7.36 (2H, d, *J*=8.6Hz), 8.06 (2H, d, *J*=8.5Hz), 8.18 (2H, d, *J*=8.5Hz). IR ν_{max}/cm^{-1} 1286, 1078, 1007, 993.

2-(4-Chlorophenyl)-5-(4-methoxyphenyl)-2H-tetrazole **3h**: m.p. 138–140°C (lit.[8] 140–141°C). ^{1}H NMR δ_H ($CDCl_3$) 3.89 (3H, s), 7.04 (2H, d, *J*=8.9Hz), 7.55 (2H, d, *J*=8.9Hz), 8.14-8.19 (4H, m). IR ν_{max}/cm^{-1} 1287, 1097, 1071, 1008, 991.

5-(4-Chlorophenyl)-2-phenyl-2H-tetrazole **3i**: m.p. 109–110°C (lit.[8] 108–108.5°C). ^{1}H NMR δ_H ($CDCl_3$) 7.50–7.61 (5H, m), 8.18–8.21 (4H, m). IR ν_{max}/cm^{-1} 1273, 1090, 1068, 1011, 995.

5-(4-Chlorophenyl)-2-(4-methylphenyl)-2H-tetrazole **3j**: m.p. 139–141°C (lit.[8] 141–142°C). ^{1}H NMR δ_H ($CDCl_3$) 2.43 (3H, s), 7.37 (2H, d, *J*=8.5Hz), 7.50 (2H, d, *J*=8.5Hz), 8.06 (2H, d, *J*=8.6Hz), 8.19 (2H, d, *J*=8.6Hz). IR ν_{max}/cm^{-1} 1273, 1089, 1070, 1011, 995.

2, 5-Bis(4-chlorophenyl)-2H-tetrazole **3k**: m.p. 176–177°C (lit.[8] 177–178°C). ^{1}H NMR δ_H ($CDCl_3$) 7.50–7.57 (4H, m), 8.14–8.20 (4H, m). IR ν_{max}/cm^{-1} 1273, 1099, 1067, 1010, 992.

2-(4-Bromophenyl)-5-(4-chlorophenyl)-2H-tetrazole **3l**: m.p. 173–175°C (dec.) (lit.[8] 176–177°C dec.). ^{1}H NMR δ_H ($CDCl_3$) 7.51 (2H, d, *J*=8.6Hz), 7.72 (2H, d, *J*=8.6Hz), 8.09 (2H, d, *J*=8.6Hz), 8.19 (2H, d, *J*=8.6Hz). IR ν_{max}/cm^{-1} 1272, 1090, 1065, 1008, 991.

5-Benzyl-2-phenyl-2H-tetrazole **3m**: m.p. 54–55°C ^{1}H NMR δ_H ($CDCl_3$) 4.34 (2H, s), 7.26 (1H, m), 7.33 (2H, m), 7.39(2H, m), 7.47(1H, m), 7.53(2H, m), 8.1(2H,m). IR ν_{max}/cm^{-1} 1295, 1096, 1071, 1001. Anal. Calcd. for $C_{14}H_{12}N_4$: C 71.17, H 5.12, N 23.71. Found: C 70.92, H 5.10, N 23.82. MS *m/z* 237(M+H, 29.51), 208 (M-N_2, 57.48), 91(100), 90(11.28).

5-Benzyl-2-(4-methylphenyl)-2H-tetrazole **3n**: m.p.54–55°C ^{1}H NMR δ_H ($CDCl_3$) 2.41(3H, s), 4.33(2H, s), 7.25(1H, m), 7.29–7.33 (4H, m), 7.38(2H, m), 7.95(2H, m). IR ν_{max}/cm^{-1} 1292, 1096, 1002. Anal. Calcd. for $C_{15}H_{14}N_4$: C 71.98, H 5.63, N 22.38. Found: C 71.69, H 5.65, N 21.92. MS *m/z* 251(M+H, 3.06), 222(M-N_2, 20.32), 105(100), 91(9.84), 90(6.84).

5-Benzyl-2-(4-chlorophenyl)-2H-tetrazole **3o**: m.p. 50–51°C ^{1}H NMR δ_H ($CDCl_3$) 4.33 (2H, s), 7.27 (1H, m), 7.31–7.39 (4H, m), 7.50(2H, m), 8.0(2H, m). IR ν_{max}/cm^{-1} 1280, 1091, 999. Anal. Calcd. for $C_{14}H_{11}ClN_4$: C 62.11, H 4.10, N 20.69. Found: C 61.89, H 4.15, N 20.48. MS *m/z* 271(M+H, 0.87), 244(M+2-N_2, 6.53), 242(M-N_2, 20.57), 125(100), 127(33), 91(13.76), 90(37.69).

5-Benzyl-2-(4-bromophenyl)-2H-tetrazole **3p**: m.p. 66–67°C ^{1}H NMR δ_H ($CDCl_3$) 4.33(2H, s), 7.26(1H, m), 7.31–7.38(4H, m), 7.66(2H, m), 7.99(2H, m). IR ν_{max}/cm^{-1} 1279, 1095, 1071, 998. Anal. Calcd. for $C_{14}H_{11}BrN_4$: C 53.34, H 3.52, N 17.78. Found: C 53.35, H 3.49, N 17.84. MS *m/z* 288(M+2-N_2, 18.52), 286(M-N_2, 19.01), 171(75.95), 169(75.48), 91(25.93), 90(100).

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