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A Convenient Synthesis of 3,5-Diaryl-1,2,4-selenadiazoles

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ABSTRACT

3,5-Diaryl-1,2,4-selenadiazoles were prepared in high yields from primary selenoamides using poly[styrene(iodosodiacetate)] as oxidant. The polymer reagent could be regenerated and reused.

Key Words: Primary selenoamide; 3,5-Diaryl-1,2,4-selenadiazole; Poly[styrene(iodosodiacetate)].

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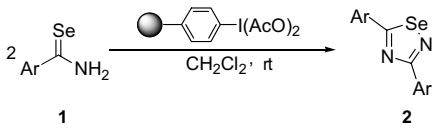
1,2,4-Selenadiazole derivatives have potential biological activities and are important intermediates in medicinal chemistry.[1] 1,2,4-Selenadiazoles were firstly synthesized by treatment of selenocarboxamides with iodine in 1904.[2] Up to now, several methods have been developed for the preparation of 1,2,4-selenadiazole derivatives.[3–6] Geordeler[3] described a method for the synthesis of 5-amino-3-alkyl- and 5-amino-3-aryl-1,2,4-selenadiazoles from *N*-haloamidies and potassium selenocyanate. Shafiee[4] reported the reaction of α-bromoketones with selenobenzamide to form the title compounds. The title compounds can also be obtained from the reaction of primary selenoamides with I_2,[5] NBS[6] or other oxidants.[6] However, most of these methods seem to have some limitations such as laborious manipulation or low yields. In this article, we report a convenient method for the synthesis of 3,5-diaryl-1,2,4-selenadiazoles.

We firstly prepared the 3,5-diaryl-1,2,4-selenadiazoles from primary selenoamides with (diacetoxyiodo)benzene which was extensively used in organic synthesis as an efficient oxidant.[7–9] Primary selenoamide **1a** was treated with (diacetoxyiodo)benzene in CH_2Cl_2 at room temperature for 10 min to afford **2a** in high yield (Table 1, Entry 1). This result encouraged us to examine oxidation of other primary selenoamides with (diacetoxyiodo)benzene. As we can see from **Table 1** (Entries 1–3), this method is applicable to oxidizing primary selenoamides to 3,5-diaryl-1,2,4-selenadiazoles in high yields. But the desired oxidation products

Table 1. Synthesis of 3,5-diaryl-1,2,4-selenadiazoles.

Entry	Substrate, Ar	Product	Yield[a] (%)	Purity[b]
1	**1a**, C_6H_5	**2a**	95[c]	—
2	**1b**, *p*-ClC_6H_4	**2b**	92[c]	—
3	**1e**, *p*-$CH_3C_6H_4$	**2e**	93[c]	—
4	**1a**, C_6H_5	**2a**	93[d]	>90
5	**1b**, *p*-ClC_6H_4	**2b**	90[d]	>90
6	**1c**, *p*-BrC_6H_4	**2c**	88[d]	>90
7	**1d**, *p*-FC_6H_4	**2d**	83[d]	>90
8	**1e**, *p*-$CH_3C_6H_4$	**2e**	87[d]	>90
9	**1f**, *p*-$CH_3OC_6H_4$	**2f**	85[d]	>90
10	**1g**, *p*-$(CH_3)_2NC_6H_4$	**2g**	80[d]	>90
11	**1a**, C_6H_5	**2a**	92[e]	>90

[a]Yields based on **1**.
[b]Determined by ^{1}H NMR (400 MHz) of crude product.
[c]Reaction with (diacetoxyiodo)benzene.
[d]Reaction with poly[styrene(iodosodiacetate)].
[e]Use regenerated poly[styrene(iodosodiacetate)].



Scheme 1.

are contaminated by the by-product iodobenzene after reaction. Sometimes, chromatographic techniques should be used to purify the products. Therefore, we chose poly[styrene(iodosodiacetate)][10] which was prepared from linear polystyrene and had the similar reactivity to (diacetoxyiodo)benzene to replace (diacetoxyiodo)benzene to carry out the corresponding reaction (Sch. 1).

Compared with (diacetoxyiodo)benzene, the use of poly[styrene(iodosodiacetate)] offers a simple and convenient work-up and the by-product poly(iodostyrene) can be regenerated and reused with no loss of activity. The results of this reaction are summarized in Table 1 (Entries 4–11).

In conclusion, we have developed a convenient method to prepare 3,5-diaryl-1,2,4-selenadiazoles from primary selenoamides using poly[-styrene(iodosodiacetate)] as oxidant with the advantages of ease of manipulation, short reaction times, high yields and regeneration, and recycling of the polymer reagent with no loss of reactivity.

EXPERIMENTAL

Poly[styrene(iodosodiacetate)] was prepared as Lit.[10] described and its functional group is 2.80 mmol/g by iodometry. Melting points were uncorrected. ^{1}H NMR spectra were recorded at 400 MHz on a Brucker AC-400 spectrometer in $CDCl_3$ with TMS as internal standard. ^{13}C NMR spectra were recorded on a Bruker AC-400 (100 MHz) spectrometer in $CDCl_3$. Infrared spectra were determined on a Bruker Vector 22 instrument using KBr pellets. Mass spectra were recorded on a HP 5989B MS spectrometer. Elemental analyses were performed on an EA-1110 instrument.

General Procedure for the Synthesis of 3,5-Diaryl-1,2,4-selenadiazoles

Poly[styrene(iodosodiacetate)] (0.36 g, 1.0 mmol) was added at room temperature to a stirred solution of primary selenoamide (1.0 mmol)

in CH_2Cl_2 (20 mL) and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was filtrated and the filtrate was washed with saturated $NaHCO_3$ (20 mL), extracted with CH_2Cl_2 (2×10 mL) and dried over $MgSO_4$. After evaporating the solvent, ether (20 mL) was added to cause precipitation, the precipitate was collected by filtration for reusing, and the filtrate was evaporated the solvent to give the product.

Compound 2a. M.p.: 84–85°C (Lit[5]: 85°C). ^{1}H NMR: δ (ppm): 8.40–8.42 (m, 2H), 8.00–8.02 (m, 2H), 7.46–7.67 (m, 6H). IR (KBr): 3050, 2923, 1517, 1485, 1453, 1444, 1322, 1300, 1234, 1104, 967, 756, 703, 680 cm^{-1}.

Compound 2b. M.p.: 166–167°C (Lit[5]: 168°C). ^{1}H NMR: δ (ppm): 7.62 (d, $J = 8.4$ Hz, 4H), 7.47 (d, $J = 8.7$ Hz, 4H); IR (KBr): 2924, 1590, 1507, 1477, 1399, 1090, 1014, 832, 735 cm^{-1}.

Compound 2c. M.p.: 161–162°C (Lit[5]: 162°C). ^{1}H NMR: δ (ppm): 8.24–8.26 (m, 1H), 7.84–7.86 (m, 1H), 7.60–7.65 (m, 4H), 7.51–7.53 (m, 2H); IR (KBr): 2924, 1584, 1507, 1474, 1394, 1311, 1069, 1012, 965, 830, 732 cm^{-1}.

Compound 2d. Colorless needle, m.p.: 171–172°C. ^{1}H NMR: δ (ppm): 8.37–8.40 (m, 2H), 7.99–8.02 (m, 2H), 7.14–7.22 (m, 4H). IR (KBr): 2924, 1604, 1511, 1487, 1409, 1232, 1156, 1114, 1104, 969, 842, 832, 739 cm^{-1}. MS (m/z): 50 (12.9), 75 (14.5), 94 (35.1), 95 (10.9), 121 (100), 122 (8.8), 201 (56.3); 322 (4.9, M + 1). ^{13}C NMR: 130.9, 130.8, 130.4, 130.3, 116.7, 116.5, 115.8, 115.6. Anal. calcd. for $C_{14}H_8F_2N_2Se$: C, 52.34; H, 2.49 ; N, 8.72; Found: C, 52.28 ; H, 2.56; N, 8.83.

Compound 2e. M.p.: 121–122°C (Lit[5]: 122°C). ^{1}H NMR: δ (ppm): 8.27–8.29 (d, $J = 8.0$ Hz, 2H), 7.87–7.89 (d, $J = 8.0$ Hz, 2H), 7.27–7.30 (m, 4H), 2.41 (s, 6H). IR (KBr): 3013, 2917, 1607, 1522, 1485, 1401, 1314, 1292, 1275, 1231, 1201, 1173, 1094, 1036, 1019, 964, 829, 816, 735, 693 cm^{-1}.

Compound 2f. M.p.: 136–137°C (Lit[5]: 137°C). ^{1}H NMR: δ (ppm): 8.32–8.34 (m, 1H), 7.92–7.94 (m, 1H), 7.57–7.59 (m, 4H), 6.93–7.00 (m, 2H), 3.85–3.88 (m, 6H). IR (KBr): 3000, 2938, 2840, 1606, 1509, 1490, 1413, 1303, 1279, 1250, 1176, 1167, 1090, 1025, 963, 831, 742, 682 cm^{-1}.

Compound 2g. Colorless needle, m.p.: 143–144°C. ^{1}H NMR: δ (ppm): 7.45–7.47 (d, $J = 8.0$ Hz, 4H), 6.62–6.64 (d, $J = 8.0$ Hz, 4H), 3.03 (s, 12H); IR (KBr): 2909, 1608, 1527, 1447, 1372, 1226, 1173, 1123, 1066, 942, 818, 656 cm^{-1}. MS (m/z): 42 (10.7), 51 (3.5), 77 (4.0), 91 (2.5), 102 (11.9), 129 (11.8), 145 (67.2), 147 (10.7), 226 (8.10), 372 (12.7, M + 1). ^{13}C NMR: 152.5, 133.4, 120.8, 111.4, 97.4, 39.9. Anal. calcd. for $C_{18}H_{20}N_4Se$: C, 58.22; H, 5.39; N, 15.09. Found: C, 58.31; H, 5.32; N, 15.11.

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