

Novel stereoselective synthesis of (*E*)-cinnamonitriles via Heck arylation of acrylonitrile catalysed by a silica-supported bidentate arsine palladium(0) complex

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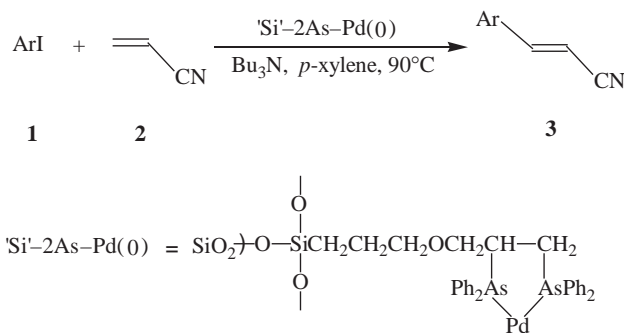
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(*E*)-Cinnamonitriles have been synthesised stereoselectively in high yields via Heck arylation of acrylonitrile with aryl iodides catalysed by a silica-supported bidentate arsine palladium(0) complex. This polymeric palladium(0) complex can be recovered and reused without noticeable loss of activity.

Keywords: (*E*)-cinnamonitrile, Heck arylation, supported palladium catalyst, bidentate palladium(0) complex, stereoselective synthesis

Cinnamonitriles are important synthetic intermediates and many methods can be used for the synthesis of cinnamonitriles, such as the reaction of cinnamaldehydes with dimethylsulfur diimides,¹ Wittig–Horner reaction of (EtO)₂POCH₂CN with aldehydes² and the treatment of acid chlorides with sulfonamides.³ In recent years, more attention has been given to the stereoselective synthesis of (*E*) and (*Z*)-cinnamonitriles. Huang *et al.*⁴ reported that (*Z*)-cinnamonitriles were prepared in 78–98% yields by the desulfonylation of α -phenylsulfonyl-cinnamonitriles in the presence of NaHTe. Guo and Zhang⁵ found that (*E*)-cinnamonitriles could be obtained in 68–85% yields by a procedure of reduction of α -phenylsulfonyl-cinnamonitriles with SmI₂ in THF–MeOH solution. Although these methods have provided useful routes for stereoselective synthesis of (*E*) and (*Z*)-cinnamonitriles, sometimes the α -phenylsulfonylcinnamonitriles are not readily available. A convenient alternative technical synthesis of (*E*)-cinnamonitriles is the Heck arylation of aryl iodides with acrylonitrile, the homogeneous palladium complexes such as [Pd(OAc)₂] or [PdCl₂(PPh₃)₂] are usually used as the catalysts in the arylation reaction.^{6,7} The amount of catalyst used is about 1 mol% of reactant; however, use of homogeneous palladium catalysts is still uneconomic for large-scale preparation in the laboratory and for industrial production. As Heck⁸ has noted, practical application of the reaction under such conditions is not feasible due to its expense. Polymer-bound organotransition metal complexes having high activity and selectivity offer several significant advantages in synthetic and industrial chemistry; among these, the ease of separation of the catalyst from the desired reaction products and the ease of recovery and reuse of the catalyst are most important. Recently, we have found that the silica-supported bidentate arsine palladium(0) complex [*Si*'–2As–Pd(0)] is a highly active catalyst for Heck arylation of styrene and acrylic acid with aryl iodides.⁹ Herein we wish to report that (*E*)-cinnamonitriles can be synthesised stereoselectively via Heck arylation of acrylonitrile with aryl iodides catalysed by a silica-supported bidentate arsine palladium(0) complex (Scheme 1).

Treatment of iodobenzene (2 mmol) with acrylonitrile (4 mmol) in *p*-xylene (0.3 ml) at 90°C for 6 h in the presence of [*Si*'–2As–Pd(0)] (0.01 mmol), and Bu₃N (2.2 mmol) afforded (*E*)-cinnamonitrile in 89% yield. When [Pd(OAc)₂] (0.01 mmol) was used as the catalyst, (*E*)-cinnamonitrile was obtained in 78% yield under same conditions. We applied the reaction to various substituted iodobenzenes, typical results are summarised in Table 1. As seen from the Table 1, the arylation reactions of acrylonitrile with substituted iodobenzenes also proceeded smoothly and a variety of substituted (*E*)-cinnamonitriles were obtained in high yields. The arylation reaction can tolerate a variety of functional



Scheme 1

Table 1 Synthesis of (*E*)-cinnamonitriles **3a–g** according to Scheme 1

Entry	Arl	Product	Yield ^a /%
1	C ₆ H ₅ I	3a	89
2	4-CH ₃ C ₆ H ₄ I	3b	87
3	4-CH ₃ OC ₆ H ₄ I	3c	92
4	4-ClC ₆ H ₄ I	3d	94
5	4-O ₂ NC ₆ H ₄ I	3e	90
6	3-O ₂ NC ₆ H ₄ I	3f	92
7	4-CH ₃ OCOC ₆ H ₄ I	3g	91

^aIsolated yield based on the aryl iodide **1** used.

groups on the aryl iodides, both strongly electron donating and withdrawing substituents can be present. This polymeric catalyst can be easily recovered by simple filtration. When [*Si*'–2As–Pd(0)] was used in four consecutive runs for the arylation reaction of acrylonitrile with 4-chloriodobenzene, (*E*)-4-chlorocinnamonitrile was formed in 94, 92, 93 and 92% yield, respectively. Although the cost of this polymeric catalyst is slightly higher than that of [Pd(OAc)₂], the [*Si*'–2As–Pd(0)] has higher activity than [Pd(OAc)₂] in arylation reactions of acrylonitrile with aryl iodides and can be recovered and reused without noticeable loss of activity.

Investigations of the crude products **3** by ¹H NMR spectroscopy (300 MHz) showed their isomeric purities of more than 98%, the *trans*-selectivity was near quantitative. The stereochemistry of products **3** was easily established, since the spectra of products **3** give rise to a doublet at δ 5.43–6.24 with coupling constant of *J* = 16.0–16.7 Hz, typical of *trans* positioned protons.

In conclusion, we have developed a novel approach to the stereoselective synthesis of (*E*)-cinnamonitriles via Heck arylation of acrylonitrile with aryl iodides catalysed by a silica-supported bidentate arsine palladium(0) complex. The present method has some attractive advantages such as readily available starting materials, straightforward and simple procedure, the ease of recovery and reuse of the palladium catalyst.

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Experimental

^1H NMR spectra were recorded on a JEOL FX-90Q (90 MHz) and an AZ-300 MHz spectrometer with TMS as an internal standard in CDCl_3 as solvent. IR spectra were obtained on a Perkin-Elmer 683 instrument. Melting points were taken with a Yanaco micro melting point apparatus and are uncorrected. The silica-supported bidentate arsine palladium(0) complex ('Si'-2As-Pd(0)) was prepared according to a literature procedure,⁹ the arsenic and palladium content was 1.39 mmol/g and 0.42 mmol/g, respectively. Bu_3N and *p*-xylene were distilled before use.

General procedure for the synthesis of (E)-cinnamonitriles 3a–g: A mixture of acrylonitrile (4 mmol), aryl iodide (2.0 mmol), Bu_3N (2.2 mmol), *p*-xylene (0.3 ml) and the 'Si'-2As-Pd(0) catalyst (0.01 mmol) was stirred under N_2 in an oil bath at 90°C for 6 h. The mixture was cooled and dissolved in Et_2O (30 ml). The 'Si'-2As-Pd(0) catalyst was separated from the mixture by filtration, washed with distilled water (2×10 ml), EtOH (3×10 ml) and Et_2O (3×10 ml) and reused in the next run. The ethereal solution was washed with 5 N HCl (2×10 ml), brine (4×10 ml) and dried (MgSO_4) and filtered. After evaporation of the filtrate, the residue was purified by column chromatography on a silica gel, eluting with light petroleum–ethyl acetate (9:1).

Compound 3a: ν_{max} (film)/ cm^{-1} 2212, 1630, 1596, 1489, 1330, 965; δ_{H} 7.30 (s, 5H), 7.26 (d, $J = 16.5$ Hz, 1H), 5.60 (d, $J = 16.5$ Hz, 1H).

Compound 3b: m.p. $69\text{--}70^\circ\text{C}$ (lit.¹⁰ m.p. $70\text{--}71^\circ\text{C}$); ν_{max} (KBr)/ cm^{-1} 2215, 1633, 1594, 1488, 1380, 1300, 969; δ_{H} 7.32–6.89 (m, 5H), 5.43 (d, $J = 16.7$ Hz, 1H), 2.26 (s, 3H).

Compound 3c: m.p. $62\text{--}63^\circ\text{C}$ (lit.¹⁰ m.p. 64°C); ν_{max} (KBr)/ cm^{-1} 2210, 1618, 1594, 1490, 1380, 1310, 1189, 967; δ_{H} 7.43–6.82 (m, 5H), 5.50 (d, $J = 16.5$ Hz, 1H), 3.76 (s, 3H).

Compound 3d: m.p. $82\text{--}83^\circ\text{C}$ (lit.¹⁰ m.p. $84\text{--}85^\circ\text{C}$); ν_{max} (KBr)/ cm^{-1} 2217, 1635, 1593, 1489, 1315, 965, 800; δ_{H} 7.30 (s, 4H), 7.27 (d, $J = 16.7$ Hz, 1H), 5.43 (d, $J = 16.7$ Hz, 1H).

Compound 3e: m.p. $198\text{--}199^\circ\text{C}$ (lit.¹⁰ m.p. 200°C); ν_{max} (KBr)/ cm^{-1} 2217, 1620, 1596, 1519, 1490, 1343, 969, 857, 774; δ_{H} 8.43–8.11 (m, 2H), 7.91–7.55 (m, 3H), 6.24 (d, $J = 16.0$ Hz, 1H).

Compound 3f: m.p. $157\text{--}158^\circ\text{C}$ (lit.¹⁰ m.p. 159°C); ν_{max} (KBr)/ cm^{-1} 2210, 1625, 1599, 1521, 1472, 1357, 966, 868, 733; δ_{H} 8.35–7.45 (m, 5H), 6.20 (d, $J = 16.0$ Hz, 1H).

Compound 3g: m.p. $144\text{--}145^\circ\text{C}$ (lit.¹¹ m.p. $143\text{--}145^\circ\text{C}$); ν_{max} (KBr)/ cm^{-1} 2215, 1715, 1622, 1607, 1287, 1104, 972, 959; δ_{H} 8.08 (d, $J = 9.0$ Hz, 2H), 7.52 (d, $J = 9.0$ Hz, 2H), 7.43 (d, $J = 16.0$ Hz, 1H), 6.00 (d, $J = 16.0$ Hz, 1H), 3.94 (s, 3H).

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