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A generalised route for the synthesis of β-furyl-α,β-unsaturated aldehydes through Suzuki reactions

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Abstract

A general method for the synthesis of β-(2-furyl)-α,β-unsaturated aldehydes is described using the Suzuki coupling reaction of furan-2-boronic acids and β-bromo-α,β-unsaturated aldehyde derivatives.

Keywords: Suzuki reaction; β-(2-Furyl)-α,β-unsaturated aldehyde; Furan-2-boronic acid; β-Bromo-α,β-unsaturated aldehyde

A large number of substituted phenanthrenes, phenanthropyrans and their 9,10-dihydro derivatives (e.g., gymnopusin, erianthridin and coeloginin)[1–9] have been isolated from Himalayan orchids. Some of these compounds have been reported to exhibit significant biological activities (Fig. 1).

In our ongoing work towards the synthesis of such phenanthrene derivatives we required β-furylacrolein derivatives. These compounds are precursors for the synthesis of substituted phenanthrenes via intramolecular Diels–Alder reactions (Scheme 1).

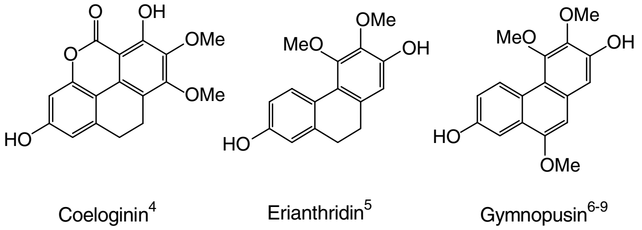

Fig. 1.

In this connection, we have studied the Suzuki coupling reaction[8–10] of several β-bromoacroleins with furan-boronic acids and we report here a high yielding general method for the synthesis of β-(2-furyl)-α,β-unsaturated aldehydes **6**–**10** (Scheme 2).

The required bromoaldehydes[11] **1**–**5** were prepared via modified Vilsmeier–Haack reactions from the corresponding ketones and PBr_3/DMF–$CHCl_3$ following a standard procedure.[11] 1-Bromo-6-methoxy-3,4-dihydronaphthalene-2-aldehyde (**3c**) (1 mmol) on treatment with furan-2-boronic acid **A** (1.15 mmol) and Et_3N (3 mmol) in DMF (3–4 mL) in the presence of $Pd(PPh_3)_4$ (1 mol %) as catalyst under an argon atmosphere furnished **8e** in 86% yield as a yellow solid (entry 17). IR, ^{1}H NMR and ^{13}C spectra[12] of **8e** were in good agreement with the assigned structure. Following similar reactions, other furoacrolein derivatives were prepared in 50–92% yields. The compounds were characterized by spectroscopic (IR/NMR/MS) analysis. The results are summarized in Table 1.

It is interesting to note that in the case of **3b**, of the two bromo substituents, the 1-bromo rather than the 7-bromo took part in the Suzuki coupling reaction almost exclusively (entries 15 and 16).The Suzuki coupling reaction of **4** with furan-2-boronic acid and 5-formylfuran-2-boronic acid led to the formation of the fully aromatic compounds **9a** and **9b**, respectively (entries 19 and 20). At present we are unable to explain this observation.

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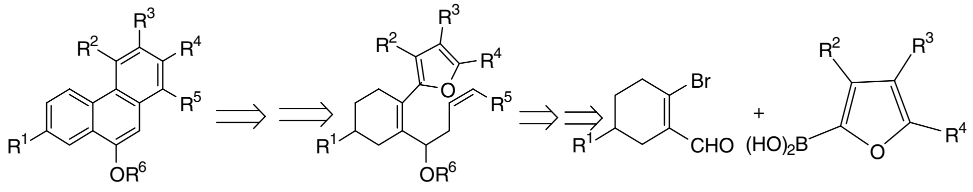
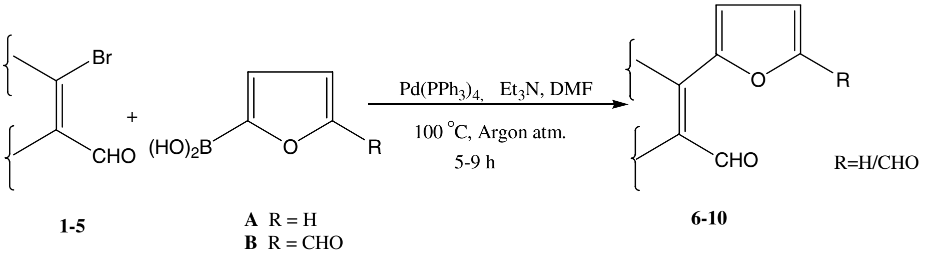


Scheme 1.



Scheme 2.

Table 1

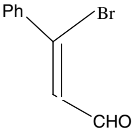
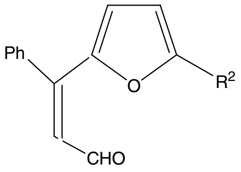
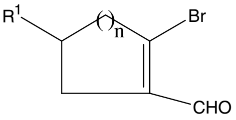
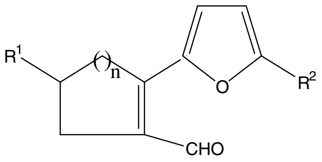
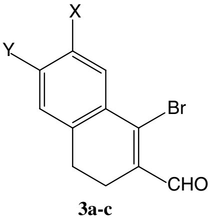
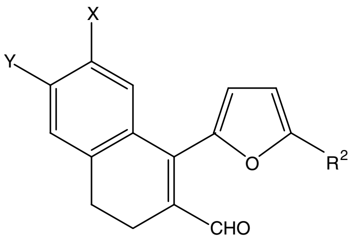
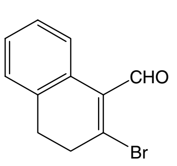
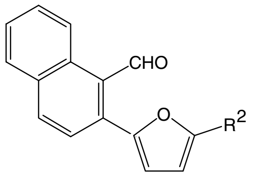
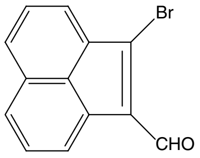
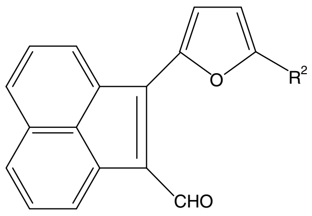
Entry	Bromoaldehyde	Boronic acid $\mathbf{A}^{a}$ or $\mathbf{B}^{a}$	Product	Time (h)	Conversion (%)	Isolated yield (%)	Melting point (°C)
	 **1**		 **6a-b**				
1	**1**	**A**	**6a** $R^2 = H$	6	100	53	Viscous liquid
2	**1**	**B**	**6b** $R^2 = CHO$	6	100	50	Viscous liquid
	 **2a-e**		 **7a-j**				
3	**2a** $n = 1$, $R^1 = H$	**A**	**7a** $n = 1$, $R^1 = H$, $R^2 = H$	5	100	75	55–57
4	**2a**	**B**	**7b** $n = 1$, $R^1 = H$, $R^2 = CHO$	6	100	70	101–102
5	**2b** $n = 2$, $R^1 = H$	**A**	**7c** $n = 2$, $R^1 = H$, $R^2 = H$	7	95	71	42–43
6	**2b**	**B**	**7d** $n = 2$, $R^1 = H$, $R^2 = CHO$	6.5	100	62	58–60
7	**2c** $n = 2$, $R^1 = Me$	**A**	**7e** $n = 2$, $R^1 = Me$, $R^2 = H$	6	100	54	Oil
8	**2c**	**B**	**7f** $n = 2$, $R^1 = Me$, $R^2 = CHO$	7	100	50	Viscous liquid
9	**2d** $n = 2$, $R^1 = {}^tBu$	**A**	**7g** $n = 2$, $R^1 = {}^tBu$, $R^2 = H$	6.5	90	67	50–52
10	**2d**	**B**	**7h** $n = 2$, $R^1 = {}^tBu$, $R^2 = CHO$	7	90	60	Viscous liquid
11	**2e** $n = 4$, $R^1 = H$	**A**	**7i** $n = 4$, $R^1 = H$, $R^2 = H$	6	100	78	Oil
12	**2e**	**B**	**7j** $n = 4$, $R^1 = H$, $R^2 = CHO$	6	100	70	Oil
	 **3a-c**		 **8a-f**				

Table 1 (*continued*)

Entry	Bromoaldehyde	Boronic acid **A**[a] or **B**[a]	Product	Time (h)	Conversion (%)	Isolated yield (%)	Melting point (°C)
13	**3a** X = H, Y = H	**A**	**8a** X = H, Y = H, R^2 = H	5.75	95	77	58–60
14	**3a**	**B**	**8b** X = H, Y = H, R^2 = CHO	6	100	69	106–108
15	**3b** X = Br, Y = H	**A**	**8c** X = Br, Y = H, R^2 = H	8	85	57	88–90
16	**3b**	**B**	**8d** X = Br, Y = H, R^2 = CHO	9	85	72	138–140
17	**3c** X = H, Y = OMe	**A**	**8e** X = H, Y = OMe, R^2 = H	5.5	90	86	106–108
18	**3c**	**B**	**8f** X = H, Y = OMe, R^2 = CHO	5.5	96	92	130
	 **4**		 **9a-b**				
19	**4**	**A**	**9a** R^2 = H	6	100	53	Semi-solid
20	**4**	**B**	**9b** R^2 = CHO	6	100	53	115–117
	 **5**		 **10a-b**				
21	**5**	**A**	**10a** R^2 = H	5.5	98	84	100
22	**5**	**B**	**10b** R^2 = CHO	5.5	100	73	140

[a] A = Furan-2-boronic acid, B = 5-formylfuran-2-boronic acid.

Thus in conclusion, we have developed a general method for the preparation of β-(2-furyl)-α,β-unsaturated aldehydes. We are utilising these compounds for the preparation of phenanthrene derivatives.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.01.010.

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12. *Selected analytical data*: Compound **7c**: IR (KBr) 1645 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 1.56–1.62 (2H, m), 1.64–1.70 (2H, m), 2.31 (2H, t, $J = 6$), 2.51–2.54 (2H, m), 6.40 (1H, dd, $J = 1.8$, 3.2 Hz), 6.43 (1H, d, $J = 3.2$ Hz), 7.45 (1H, br s), 10.04 (1H, s) ppm. MS (ESI-MS positive ion) m/z 177.09 $[M+H]^+$,199.05 $[M+Na]^+$.

    Compound **8c**: IR (KBr) 1669 cm^{-1}, ^1H NMR (400 MHz, $CDCl_3$) δ 2.64–2.68 (2H, m), 2.28 (2H, m), 6.60 (1H, t, $J = 3.2$ Hz), 6.63 (1H, d, $J = 3.2$ Hz), 7.13 (1H, d, $J = 8$ Hz), 7.26 (1H, br s), 7.43 (1H, dd, $J = 1.6$, 8 Hz), 7.65 (1H, d, $J = 1.2$ Hz), 9.87 (1H, s) ppm; HRMS (ESI, 70 eV): $m/z = 302.9966$ $[M^+{+}H]$ (calculated mass for $C_{15}H_{12}O_2Br$: 303.0022 $[M^+{+}H]$).

Compound **8d**: IR (KBr) 1656, 1677 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.68–2.71 (2H, m), 2.83 (2H, m), 6.79 (1H, d, $J = 3.6$ Hz), 7.13–7.16 (2H, m), 7.41–7.47 (2H, m), 9.75 (1H, s), 9.81 (1H, s) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.6, 26.5, 116.8, 120.5, 121.0, 129.6, 130.1, 133.4, 134.3, 137.0, 139.7, 139.9, 152.4, 153.5, 177.7, 191.1 ppm; HRMS (ESI, 70 eV): $m/z = 330.9926$ [M$^+$+H] (calculated mass for $C_{16}H_{12}O_3Br$: 330.9972 [M$^+$+H]).

Compound **8e**: IR (KBr) 1646 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.63–2.67 (2H, m), 2.82 (2H, m), 3.83 (3H, s), 6.55–6.56 (1H, dd, $J = 1.9$, 3.3 Hz), 6.59 (1H, d, $J = 3.3$ Hz), 6.71 (1H, dd, $J = 2.6$, 8.6 Hz), 6.77 (1H, br d, $J = 2.5$ Hz), 7.06 (1H, d, $J = 8.6$ Hz), 7.60 (1H, br d, $J = 1.1$ Hz), 9.82 (1H, s) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ 20.7, 27.9, 55.3, 111.1, 111.8, 113.7, 115.1, 126.1, 129.9, 134.7, 141.1, 142.7, 143.9, 147.9, 161.2, 192.5 ppm; HRMS (ESI, 70 eV): $m/z = 255.0893$ [M$^+$+H] (calculated mass for $C_{16}H_{15}O_3$: 255.1023 [M$^+$+H]).

Compound **8f**: IR (KBr) 1656, 1678 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.66–2.70 (2H, m), 2.84 (2H, m), 3.83 (3H, s), 6.71 (1H, dd, $J = 2.6$, 8.6 Hz), 6.76 (1H, d, $J = 3.5$ Hz), 6.79 (1H, d, $J = 2.6$ Hz), 6.95 (1H, d, $J = 8.6$ Hz), 7.39 (1H, d, $J = 3.5$ Hz), 9.72 (1H, s), 9.76 (1H, s) ppm; MS (ESI-MS, positive ion) m/z: 283.12 [M+H]$^+$, 305.08 [M+Na]$^+$. HRMS (ESI, 70 eV): $m/z = 305.0791$ [M+Na]$^+$ (calculated mass for $C_{17}H_{14}O_4Na$: 305.0790 [M+Na]$^+$).