Tetrahedron Vol 47, No 10/11, pp 1877-1886, 1991
Printed in Great Britain

0040-4020/91 $3 00+00

CONDENSED HETEROAROMATIC RING SYSTEMS. XVIII.[1] PALLADIUM-CATALYZED CROSS-COUPLING REACTION OF ARYL BROMIDES WITH (*Z*)-1-ETHOXY-2-TRIBUTYLSTANNYLETHENE AND ITS UTILIZATION FOR CONSTRUCTION OF CONDENSED HETEROAROMATICS

Takao Sakamoto, Yoshinori Kondo, Akito Yasuhara, and Hiroshi Yamanaka*

Pharmaceutical Institute, Tohoku University, Aobayama, Aoba-ku, Sendai 980, Japan

(*Received in Japan 24 November* 1990)

The palladium-catalyzed cross-coupling reaction of bromobenzenes or bromoheteroarenes such as pyridine, thiophene, indole with (*Z*)-1-ethoxy-2-tributylstannylethene gives good yields of the corresponding (*Z*)-1-ethoxy-2-(aryl and heteroaryl)ethenes This method is effective for introducing an ethoxyethenyl group into an aromatic and heteroaromatic ring and is proved to have versatile utility for the construction of benzo[*b*]furan, indole, isocoumarin rings from 2-bromophenol, 2-bromoaniline, and 2-bromobenzoate derivatives

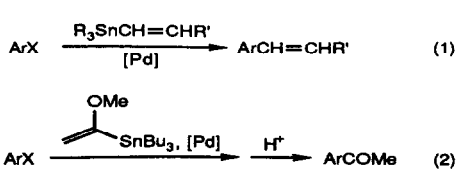
Although the palladium-catalyzed cross-coupling reaction of aryl or heteroaryl halides with olefins is one of the useful methods for introduction of olefinic side-chains to aromatic or heteroaromatic rings[3], the method has limitations for the synthesis of β–alkoxyethenylarenes from aryl halides and alkoxyethenes For example, Andersson *et al* [4] have reported that the cross-coupling reaction of iodobenzene with butoxyethene in the presence of palladium-charcoal or palladium acetate gives a mixture of 1-butoxy-2-phenylethene and 1-butoxy-1-phenylethene

On the other hand, the palladium-catalyzed reaction of bromo- and iodobenzenes with (*E*)-tris(2-ethoxyethenyl)borane to give (*E*)-1-ethoxy-2-phenylethenes in good yields has been reported by Miyaura *et al* [5]

Here we report the palladium-catalyzed cross-coupling reaction of aryl and heteroaryl bromides including π-deficient heteroaryl bromides with (*Z*)-1-ethoxy-2-tributylstannylethenes (**2**), together with construction of some condensed heteroaromatic ring systems using the 1-ethoxy-2-(2-substituted aryl)ethenes thus obtained

Results and Discussion

The palladium-catalyzed cross-coupling reaction of aryl halides with trialkyl(aryl)stannylolefins has been explored recently[6,7](eqs 1 and 2)



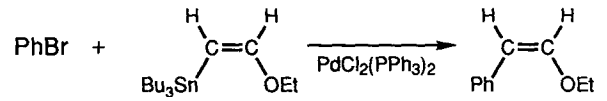
Scheme I

While 1-methoxy-1-tributylstannylethene has been utilized to synthesize aryl methyl ketones from aryl halides as shown in eq 2, (*Z*)-1-ethoxy-2-tributylstannylethene (**2**), which is easily synthesized as a stable liquid by addition of tributylstannane to ethoxyacetylene and is known to be a precursor of the lithium reagent,[8] has not been used in the palladium-catalyzed cross-coupling reaction prior to our preliminary report [2]

Cross-Coupling Reaction of Aryl Bromides

Reaction conditions for the palladium-catalyzed cross-coupling reaction of bromobenzene (**1a**) with **2** were examined. As shown in Table I, **1a** reacts smoothly with **2** in dimethylformamide (DMF) in the presence of dichlorobis-(triphenylphosphine)palladium [$PdCl_2(PPh_3)_2$] and tetraethylammonium chloride to produce (*Z*)-(2-ethoxyethenyl)-benzene (**3a**) in 78% yield (Table I, entry 4).

Table I



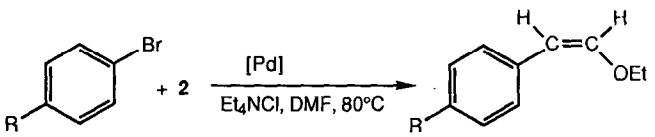
1a **2** **3a**

Entry	Solvent	Additive	Temp. (°C)	Time (h)	Yield (%)
1	THF	—	65	3	52
2	DMF	—	80	2	52
3	THF	Et_4NCl	65	3	59
4	DMF	Et_4NCl	80	2	78

Under these same reaction conditions, the substituent effect for the cross-coupling reaction was investigated using 4-substituted bromobenzenes (**1b-j**). As shown in Table II, electron-withdrawing groups such as nitro and ethoxycarbonyl group tend to facilitate the cross-coupling reaction. In the case of 1,4-dibromobenzene (**1d**), monoethoxyethenylation is achieved by using an equimolecular amount of **2**.

It should be noted that the presence of primary amino and hydroxyl groups retards the reaction completely (Table II, entries 4 and 6), while protection of these groups by alkylation or acylation relieves the retardation (Table II, entries 5, 7-9).

Table II



1b-k **3b-k**

Entry	Compd No.	R	Time (h)	Yield of **3**
1	**1b**	NO_2	2	86
2	**1c**	COOEt	1	73
3	**1d**	Br	1.5	56
4	**1e**	OH	12	0 (42)[a]
5	**1f**	OMe	18	67
6	**1g**	NH_2	18	0 (52)[a]
7	**1h**	NMe_2	18	22 (44)[a]
8	**1i**	NHAc	18	71
9	**1j**	NHCOOEt	18	65

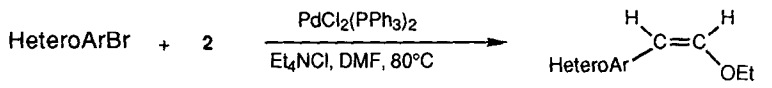
a) The figures in parentheses show the recoveries of the bromobenzenes.

The findings described above suggest that the cross-coupling reactions would also be realized in π-deficient heteroaromatic ring systems. In fact, 2-bromo- (**4a**), 3-bromo- (**4b**), and 4-bromo-2,6-dimethylpyridine (**4c**) react smoothly under identical conditions to give the corresponding ethoxyethenylpyridines (**7a-c**) in satisfactory yields.

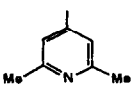
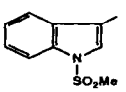
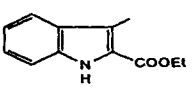
Furthermore, 2-bromothiophene (**5**), 3-bromo-1-methylsulfonylindole (**6a**), and ethyl 3-bromoindole-2-carboxylate (**6b**) react with **2** to give 2-(2-ethoxyethenyl)thiophene (**8**), 3-(2-ethoxyethenyl)-1-methylsulfonylindole (**9a**), and ethyl 3-(2-ethoxyethenyl)indole-2-caboxylate (**9b'**), respectively (Table III, entries 4 and 5).

Except for entry 6 of Table III, all the products have a *Z*-configuration in the side-chain double bond. From the reaction of **6b**, however, the geometrical isomer (**9b'**) with *E*-configuration is isolated after 18 h reaction time as the sole product. The reaction for a shorter time (*e.g.* 8 h) affords a mixture of *E*-(**9b'**) and *Z*-isomer (**9b**) which ratio is determined by ^{1}H NMR spectra to be 8 : 3. The results explain that the *Z*-isomer (**9b**) firstly formed may be transformed into the thermally stable *E*-isomer (**9b'**) by heating with the palladium-catalyst for a long time.

Table III



4a-c, 5, 6a,b **7a-c, 8, 9a,b**

Entry	Compd No.	Het-Ar	Time (h)	Yield (%)	Product No.
1	**4a**		3.5	62	**7a**
2	**4b**		5	72	**7b**
3	**4c**		12	70	**7c**
4	**5**		2.5	68	**8**
5	**6a**		9	83	**9a**
6	**6b**		18	65	**9b**[a]

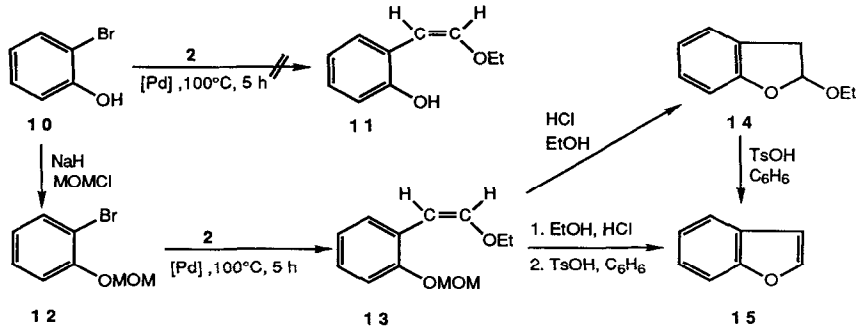
a) The configuration of the product is *E*-configuration.

Synthesis of Condensed Heteraromatics

To shown the utility of these cross-coupling reactions, we applied them to the facile synthesis of such bicyclic heteroaromatics as benzo[*b*]furan, indole, isocoumarin, and pyranopyridinones.

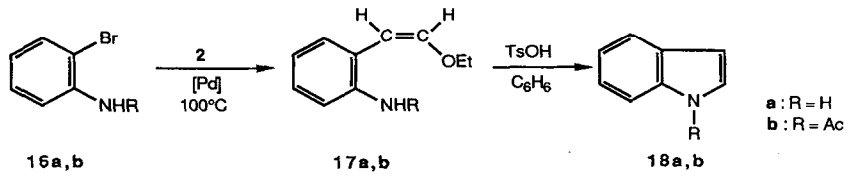
As expected from the result shown in Table II, the reaction of 2-bromophenol (**10**) with **2** does not give (*Z*)-2-(2-ethoxyethenyl)phenol (**11**); however, 2-(methoxymethoxy)bromobenzene (**12**) does react with **2** to give the desired 2-ethoxyethenyl derivative (**13**). Treatment of **13** with hydrochloric acid in ethanol gives 2-ethoxy-2,3-dihydrobenzo[*b*]furan (**14**) which is easily aromatized to benzo[*b*]furan (**15**) by *p*-toluenesulfonic acid (TsOH) in boiling benzene. Additionally, it is possible to convert **13** into **15** without isolation of **14**. In the latter case, a better yield (73%) of **15** is

observed than that obtained by the two-step procedure (76% x 58%).



Scheme II

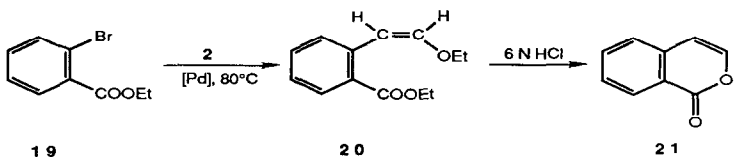
Similarly, the reaction of 2-bromoacetanilide (**16b**) with **2** gives (*Z*)-2-(2-ethoxyethenyl)acetanilide (**17b**) as a single product which cyclizes to 1-acetylindole (**18b**) by treatment with TsOH in benzene. Although the reason is not clear at present, 2-bromoaniline (**16a**), unlike 4-bromoaniline (**1d**), reacts with **2**; the expected 2-(2-ethoxyethenyl)aniline (**17a**) is isolated as an unstable oil. Evidence for the structure of **17a** was obtained by treatment of the crude product with TsOH, which afforded indole (**18a**) in 29% overall yield.



Scheme III

Previously, we have reported the synthesis of isocoumarin derivatives using the palladium-catalyzed cross-coupling reaction of 2-bromobenzonitrile with terminal acetylenes as a key reaction, but according to this manner, the synthesis of isocoumarin (**21**) by this method results in poor yield.[9] Thus, a modified synthesis of **21** and related pyranopyridinones was examined.

When ethyl 2-bromobenzoate (**19**) is allowed to react with **2** at 80°C for 1 h, ethyl (*Z*)-2-(2-ethoxyethenyl)benzoate (**20**) is isolated in good yield. The cyclization of **20** into **21** is easily accomplished under acidic conditions.

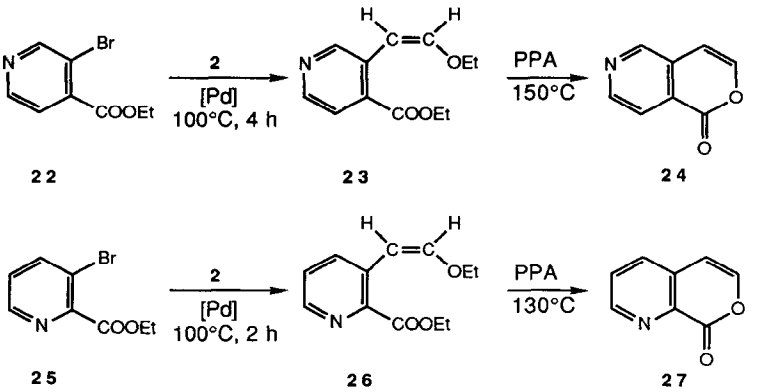


Scheme IV

Similarly, as illustrated in Scheme IV, 1*H*-pyrano[3,4-*c*]pyridin-1-one (**24**) and 1*H*-pyrano[3,4-*b*]pyridin-1-one (**27**) are synthesized from ethyl 3-bromopyridine-4-carboxylate (**22**) and ethyl 3-bromopyridine-2-carboxylate (**25**) *via* the

corresponding (2-ethoxyethenyl)pyridines (**2 3** and **2 6**), respectively.

On the basis of these results, the palladium-catalyzed cross-coupling reaction of **2** with ethyl bromopyridinecarboxylates (**2 2** and **2 5**) may provide a general method for the syntheses of pyranopyridinones without substituent on the α-pyrone moiety.



Scheme V

Acknowledgement.

This work was supported by a Grant-in-Aid for Scientific Research from The Ministry of Education, Science and Culture, Japan.

Experimental Section

^{1}H NMR spectra were recorded at 60 MHz with JEOL JNM-PMX 60 spectrometer. Chemical shifts are quoted as δ (ppm) relative to tetramethylsilane (TMS). IR spectra were measured with a JASCO IR 810 spectrometer. Mass spectra (MS) were taken with a JMS-DX303.

General Procedure for the Palladium-Catalyzed Cross-Coupling Reaction of Aryl or Heteroaryl Halides with (*Z*)-1-Ethoxy-2-tributylstannylethene (2).

A mixture of aryl or heteroaryl bromide (1 mmol), (*Z*)-1-ethoxy-2-tributylstannylethene (**2**) (1 mmol), Et_4NCl (1 mmol), $PdCl_2(PPh_3)_2$ (0.03 mmol), and DMF (5 ml) was stirred at 80°C for 2 h. After cooling, a solution of KF (1.1 mmol) in water was added to the mixture which was stirred for 30 min. The mixture was filtered over Celite and partitioned between water and ether. The ethereal layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography followed by distillation or recrystallization.

(*Z*)-(2-Ethoxyethenyl)benzene (3a) (Table I, entry 4).

According to the general procedure, bromobenzene (**1 a**) (0.94 g, 6 mmol) was treated with **2** (2.16 g, 6 mmol), Et_4NCl (1.03 g, 6 mmol), and $PdCl_2(PPh_3)_2$ (80 mg) to give (*Z*)-(2-ethoxyethenyl)benzene (**3**) (0.69 g, 78%) as a colorless liquid; bp 80°C / 3 mmHg. ^{1}H NMR ($CDCl_3$) δ : 1.30 (t, *J* = 7.0 Hz, 3H), 3.92 (q, *J* = 7.0 Hz, 2H), 5.20 (d, *J* = 7.0 Hz, 1H), 7.1 - 7.7 (m, 5H). Oxime: mp 98 - 98.5°C (lit.[10] mp 96.5 - 98°C). ^{1}H NMR ($CDCl_3$) δ : 3.70 (s, 1H), 3.80 (s, 2H), 7.28 (s, 5H), 9.3 - 9.5 (br, 1H).

(*Z*)-1-(2-Ethoxyethenyl)-4-nitorobenzene (3b)

Compound **3b** was a colorless liquid, bp 140-150°C / 3 mmHg ^{1}H NMR ($CDCl_3$) δ 1 40 (t, *J* = 8 0 Hz, 3H), 4 07 (q, *J* = 8 0 Hz, 2H), 5 30 (d, *J* = 7 0 Hz, 1H), 6 40 (d, *J* = 7 0 Hz, 1H), 7 66 (d, *J* = 9 0 Hz, 2H), 8 13 (d, *J* = 9 0 Hz, 2H) IR ($CHCl_3$) 1510,1345 cm^{-1} MS *m/z* (relative intensity) 193 (M^+, 100), 165 (73) High-resolution MS calcd for $C_{10}H_{11}N_3O$ 193 0738 Found 193 0724

Ethyl (*Z*)-4-(2-Ethoxyethenyl)benzoate (3c)

Compound **3c** was a colorless liquid, bp 150°C / 3 mmHg ^{1}H NMR ($CDCl_3$) δ 1 33 (t, *J* = 7 0 Hz, 3H), 1 36 (t, *J* = 7 0 Hz, 3H), 4 00 (q, *J* = 7 0 Hz, 2H), 4 36 (q, *J* = 7 0 Hz, 2H), 5 26 (d, *J* = 6 0 Hz, 1H), 6 26 (d, *J* = 6 0 Hz, 1H), 7 66 (d, *J* = 10 0 Hz, 2H), 8 00 (d, *J* = 10 0 Hz, 2H) IR ($CHCl_3$) 1715,1280, 1105 cm^{-1} MS *m/z* (relative intensity) 220 (M^+, 40), 192 (17), 133 (100), 118 (7), 103 (14), 175 (12), 147 (39) High-resolution MS calcd for $C_{13}H_{16}O_3$ 220 1099 Found 220 1114

(*Z*)-4-Bromo-1-(2-ethoxyethenyl)benzene (3d).

Compound **3d** was a colorless liquid, bp 60-80°C / 3 mmHg ^{1}H NMR ($CDCl_3$) δ 1 33 (t, *J* = 6 0 Hz, 3H), 3 97 (q, *J* = 6 0 Hz, 2H), 5 16 (d, *J* = 7 0 Hz, 1H), 6 23 (d, *J* = 7 0 Hz, 1H), 7 46 (s, 4H) MS *m/z* (relative intensity) 228 (M^++2, 85), 226 M^+, 88), 200 (63), 198 (66), 171 (46), 169 (48), 118 (96), 91 (100) High-resolution MS calcd for $C_{10}H_{11}BrO$ 225 9993, 227 9973 Found 225 9998, 227 9983

(*Z*)-4-(2-Ethoxyethenyl)anisole (3f)

Compound **3f** was a colorless liquid, bp 120°C / 3 mmHg ^{1}H NMR ($CDCl_3$) δ 1 30 (t, *J* = 8 0 Hz, 3H), 3 69 (s, 3H), 3 89 (q, *J* = 8 0 Hz, 2H), 5 13 (d, *J* = 7 0 Hz, 1H), 6 07 (d, *J* = 7 0 Hz, 1H), 6 79 (d, *J* = 8 0 Hz, 2H), 7 53 (d, *J* = 8 0 Hz, 2H) MS *m/z* (relative intensity) 178 (M^+, 100), 149 (65), 135 (13), 121 (74), 107 (3) High-resolution MS calcd for $C_{11}H_{14}O_2$ 178 0993 Found 178 0988

(*Z*)-4-(2-Ethoxyethenyl)-*N*,*N*-dimethylaniline (3h)

Compound **3h** was a viscous liquid ^{1}H NMR ($CDCl_3$) δ 1 33 (t, *J* = 7 0 Hz, 3H), 2 93 (s, 6H), 3 92 (q, *J* = 7 0 Hz, 2H), 5 13 (d, *J* = 6 0 Hz, 1H), 6 03 (d, *J* = 6 0 Hz, 1H), 6 67 (d, *J* = 9 0 Hz, 2H), 7 47 (d, *J* = 9 0 Hz, 2H) MS *m/z* (relative intensity) 191 (M^+, 77), 177 (9), 163 (11), 162 (97), 134 (100), 118 (16) High-resolution MS calcd for $C_{12}H_{17}NO$ 191 1309 Found 191 1318

(*Z*)-4-(2-Ethoxyethenyl)acetanilide (3i).

Compound **3h** was a viscous liquid ^{1}H NMR ($CDCl_3$) δ 1 30 (t, *J* = 7 0 Hz, 3H), 2 07 (s, 3H), 3 92 (q, *J* = 7 0 Hz, 2H), 5 13 (d, *J* = 7 0 Hz, 1H), 6 13 (d, *J* = 7 0 Hz, 1H), 7 46 (s, 4H), 8 2 - 8 5 (br, 1H) IR ($CHCl_3$) 3020, 1685, 1520 cm^{-1} MS *m/z* (relative intensity) 205 (M^+, 100), 177 (6), 163 (22), 134 (90), 117 (3), 106 (84) High-resolution MS calcd for $C_{12}H_{15}NO_2$ 205 1102 Found 205 1096

Ethyl (*Z*)-4-(2-Ethoxyethenyl)phenyl carbanilate (3j)

Compound **3h** was a viscous liquid ^{1}H NMR ($CDCl_3$) δ 1 26 (t, *J* = 7 0 Hz, 3H), 1 33 (t, *J* = 8 0 Hz, 3H), 3 94 (q, *J* = 7 0

Hz, 2H), 4 21 (q, J = 8 0 Hz, 2H), 5 17 (d, J = 7 0 Hz, 1H), 6 15 (d, J = 7 0 Hz, 1H), 6 8 -7 0 (br, 1H), 7 30 (d, J = 10 0 Hz, 2H), 7 56 (d, J = 10 0 Hz, 2H) IR ($CHCl_3$) 1730,1658 cm^{-1} MS m/z (relative intensity) 235 (M^+, 100), 207 (10), 190 (4), 160 (43), 178 (44), 134 (23), 132 (43) High-resolution MS calcd for $C_{13}H_{17}NO_3$ 235 1207 Found 235 1190

(*Z*)-2-(2-Ethoxyethenyl)pyridine (7a).

Compound **7a** was a colorless liquid, bp 80°C / 3 mmHg ^1H NMR ($CDCl_3$) δ 1 32 (t, J = 7 0 Hz, 3H), 3 97 (q, J = 7 0 Hz, 2H), 5 55 (d, J = 7 0 Hz, 1H), 6 40 (d, J = 7 0 Hz, 1H), 7 33 (dd, J = 4 0, 1 0 Hz, 1H), 7 5 - 8 1 (m, 2H), 8 48 (dd, J = 3 0, 1 0 Hz, 1H) MS m/z (relative intensity) 149 (M^+, 100), 120 (55), 106 (47), 92 (70), 72 (26) High-resolution MS calcd for $C_9H_{11}NO$ 149 0840 Found 149 0841

(*Z*)-3-(2-Ethoxyethenyl)pyridine (7b)

Compound **7b** was a colorless liquid, bp 80°C / 3 mmHg ^1H NMR ($CDCl_3$) δ 1 32 (t, J = 7 0 Hz, 3 H), 3 98 (q, J = 7 0 Hz, 2H), 5 12 (d, J = 7 0 Hz, 1H), 6 28 (d, J = 7 0 Hz, 1H), 7 18 (dd, J = 8 0, 5 0 Hz, 1H), 7 98 (dd, J = 8 0, 2 0 Hz, 1H), 8 33 (dd, J = 5 0, 2 0 Hz, 1H), 8 90 (d, J = 2 0 Hz, 1H) MS m/z (relative intensity) 149 (M^+, 100), 121 (94), 106 (15), 92 (88), 83 (75), 78 (13) High-resolution MS calcd for $C_9H_{11}NO$ 149 0840 Found 149 0848

(*Z*)-2-(4-Ethoxyethenyl)-2,6-dimethylpyridine (7c)

Compound **7c** was a colorless liquid, bp 120-130°C / 14 mmHg ^1H NMR ($CDCl_3$) δ 1 36 (t, J = 7 0 Hz, 3H), 2 47 (s, 6H), 4 03 (q, J = 7 0 Hz, 2H), 5 10 (d, J = 6 0 Hz, 1H), 6 30 (d, J = 6 0 Hz, 1H), 7 15 (s, 2H) MS m/z (relative intensity) 177 (M^+, 100), 149 (50), 121 (46), 106 (21) High-resolution MS calcd for $C_{11}H_{15}NO$ 177 1153 Found 177 1161

(*Z*)-2-(2-Ethoxyethenyl)thiophene (8)

Compound **8** was a colorless liquid, bp 50°C / 3 mmHg ^1H NMR ($CDCl_3$) δ 1 33 (t, J = 8 0 Hz, 3H), 3 97 (q, J = 8 0 Hz, 2H), 5 59 (d, J = 6 0 Hz, 1H), 6 13 (d, J = 6 0 Hz, 1H), 6 8 - 7 2 (m, 3H) MS m/z (relative intensity) 154 (M^+, 28), 126 (39), 125 (25), 113 (100) High-resolution MS calcd for $C_8H_{10}OS$ 154 0452 Found 154 0455

(*Z*)-3-(2-Etoxyethenyl)-1-methylsulfonylindole (9a)

Compound **9a** was a viscous liquid ^1H NMR ($CDCl_3$) δ 1 37 (t, J=7 0 Hz, 3H), 3 03 (s, 3H), 4 06 (q, J=7 0 Hz, 2H), 5 50 (d, J=7 0 Hz, 1H), 6 36 (d, J=7 0 Hz, 1H), 7 2 - 8 0 (m, 5H) IR($CHCl_3$) 1370, 1170 cm^{-1} MS m/z (relative intensity) 265 (M^+, 52), 186 (82), 158 (100), 130 (99) High-resolution MS calcd for $C_{13}H_{15}O_3NS$ 265 0773 Found 265 0758

Ethyl (*E*)-3-(2-Ethoxyethenyl)indole-2-carboxylate (9b') (Table III, entry 6)

According to the general procedure, ethyl 3-bromoindole-2-carboxylate (**6b**) (1 2 g, 3 80 mmol) was treated with **2** (1 40 g, 3 80 mmol), Et_4NCl (0 62 g, 3 80 mmol), and $PdCl_2(PPh_3)_2$ (130 mg) in DMF (10 ml) for 18 h to give ethyl (*E*)-3-(2-ethoxyethenyl)indole-2-carboxylate (**9b'**) (0 64 g, 65%) as pale yellow prisms (*n*-C_6H_{14} - Et_2O), mp 114 - 115°C ^1H NMR ($CDCl_3$) δ 1 38 (t, J= 7 0 Hz, 3H), 1 41 (t, J= 7 0 Hz, 3H), 4 02 (q, J= 7 0 Hz, 2H), 4 43 (q, J= 7 0 Hz, 2H), 6 67 (d, J = 13 0 Hz, 1H), 7 40 (d, J= 13 0 Hz, 1H), 7 0-8 1 (m, 4H), 8 7 - 9 0 (br, 1H) IR ($CHCl_3$) 3460, 1690 cm^{-1} *Anal* Calcd for $C_{15}H_{17}NO_3$ C, 69 48, H, 6 61, N, 5 40 Found C, 69 26, H, 6 78, N, 5 30

Cross-Coupling Reaction of 6b with 2 for 8 h

According to the general procedure, **6b** (0 5 g, 1 9 mmol) was treated with **2** (0 67 g, 1 9 mmol), Et_4NCl (0 31 g, 1 9 mmol), and $PdCl_2(PPh_3)_2$ (50 mg) in DMF (5 ml) for 8 h to give an *E*/*Z*-mixture of ethyl 3-(2-ethoxyethenyl)indole-2-carboxylate (0 22 g, 45%) as a yellow viscous liquid ^1H NMR ($CDCl_3$) δ 1 38 (t, *J* = 7 0 Hz, 3H), 1 41 (t, *J* = 7 0 Hz, 3H), 4 02 (q, *J* = 7 0 Hz, 2H), 4 43 (q, *J* = 7 0 Hz, 2H), 6 10 (d, *J* = 7 0 Hz, 0 27H), 6 25 (d, *J* = 7 0 Hz, 0 27H), 6 67 (d, *J* = 13 0 Hz, 0 73H), 7 40 (d, *J* = 13 0 Hz, 0 73H), 7 0-8 1 (m, 4H), 9 1 - 9 4 (br, 1H)

(*Z*)-1-(2-Ethoxyethenyl)-2-(methoxymethoxy)benzene (13)

Compound **13** was a colorless liquid, bp 120-130°C / 3 mmHg Yield 79% ^1H NMR ($CDCl_3$) δ 1 33 (t, *J* = 7 0 Hz, 3H), 3 38 (s, 3H), 3 87 (q, *J* = 7 0 Hz, 2H), 5 08 (s, 2H), 5 55 (d, *J* = 7 0 Hz, 1H), 6 15 (d, *J* = 7 0 Hz, 1H), 7 9 - 8 1 (m, 3H), 7 9-8 0 (m, 1H) MS *m*/*z* (relative intensity) 208 (M^+, 26), 180 (21), 165 (100), 135 (71), 121 (47) High-resolution MS calcd for $C_{12}H_6O_3$ 208 1099 Found 208 1106

2-(2-Ethoxyethenyl)acetanilide (17b).

Compound **17b** was a viscous liquid Yield 72% ^1H NMR ($CDCl_3$) δ 1 32 (t, *J* = 6 0 Hz, 3H), 3 90 (q, *J* = 6 0 Hz, 2H), 5 27 (d, *J* = 7 0 Hz, 1H), 6 20 (d, *J* = 7 0 Hz, 1H), 7 00-7 83 (m, 4H), 7 9 -8 2 (br, 1H) IR ($CHCl_3$) 3020,1685 cm^{-1} MS *m*/*z* (relative intensity) 205 (M^+, 69), 176 (9), 162 (9), 134 (86), 117 (100), 106 (67 84) High-resolution MS calcd for $C_{12}H_{15}NO_2$ 205 1102 Found 205 1123

Ethyl (*Z*)-2-(2-Ethoxyethenyl)benzoate (20)

Compound **20** was a colorless liquid, bp 170°C / 3 mmHg Yield 80% ^1H NMR ($CDCl_3$) δ 1 33 (t, *J* = 8 0 Hz, 3H), 1 38 (t, *J* = 8 0 Hz, 3H), 3 98 (q, *J* = 8 0 Hz, 2H), 4 35 (q, *J* = 8 0 Hz, 2H), 6 00 (d, *J* = 8 0 Hz, 1H), 6 22 (d, *J* = 8 0 Hz, 1H), 7 1 - 7 3 (m, 2H), 7 6 - 8 0 (m, 2H) IR ($CHCl_3$) 1710 cm^{-1} MS *m*/*z* (relative intensity) 220 (M^+, 96), 191 (10), 175 (44), 147 (60), 118 (100) High-resolution MS calcd for $C_{13}H_{16}O_3$ 220 1099 Found 220 1086

Ethyl (*Z*)-3-(2-Ethoxyethenyl)pyridine-4-carboxylate (23)

Compound **23** was a colorless viscous liquid Yield 66% ^1H NMR ($CDCl_3$) δ 1 33 (t, *J* = 7 0 Hz, 3H), 1 36 (t, *J* = 7 0 Hz, 3H), 4 00 (q, *J* = 7 0 Hz, 2H), 4 38 (q, *J* = 7 0 Hz, 2H), 5 95 (d, *J* = 7 0 Hz, 1H), 6 37 (d, *J* = 7 0 Hz, 3H), 7 58 (d, *J* = 5 0 Hz 1H), 8 40 (d, *J* = 5 0 Hz, 2H), 9 38 (s, 1H) IR ($CHCl_3$) 1725 cm^{-1} MS *m*/*z* (relative intensity) 221 (M^+, 100), 192 (2), 176 (10), 147 (66) High-resolution MS calcd for $C_{12}H_{15}NO_3$ 221 1038 Found 221 1051

Ethyl 3-(2-Ethoxyethenyl)pyridine-2-carboxylate (26)

Compound **26** was a pale yellow viscous liquid Yield 76% ^1H NMR ($CDCl_3$) δ 1 32 (t, *J* = 7 0 Hz, 3H), 1 36 (t, *J* = 7 0 Hz, 3H), 4 02 (q, *J* = 7 0 Hz, 2H), 4 52 (q, *J* = 7 0 Hz, 2H), 6 10 (d, *J* = 8 0 Hz, 1H), 6 42 (d, *J* = 8 0 Hz, 3H), 7 10 (dd, *J* = 7 0, 4 0 Hz, 1H), 8 05 (dd, *J* = 7 0, 2 0 Hz, 1H), 8 70 (dd, *J* = 4 0, 2 0 Hz, 1H) IR ($CHCl_3$) 1725 cm^{-1} MS *m*/*z* (relative intensity) 221 (M^+, 58), 192 (52), 176 (100), 147(14) High-resolution MS calcd for $C_{12}H_{15}NO_3$ 221 1052 Found 221 1051

2,3-Dihydro-2-ethoxybenzo[*b*]furan (14)

A mixture of **1 3** (1 04 g, 5 mmol), 3 N HCl (0 1 ml), and EtOH (10 ml) was stirred at room temperature for 24 h The EtOH was removed under reduced pressure to give the residue which was neutralized with 3 N K_2CO_3 and extracted with ether The ethereal layer was dried over $MgSO_4$ and concentrated under reduced pressure The residue was purified by silica gel column chromatography using *n*-C_6H_{14}-CH_2Cl_2 (3 1) as an eluent The product obtained from the *n*-C_6H_{14}-CH_2Cl_2 (3 1) eluate was distilled under reduced pressure to give 2,3-dihydro-2-ethoxybenzo[*b*]furan (**1 4**) (0 48 g, 58%) as a colorless liquid, bp 120°C / 3 mmHg ^{1}H NMR ($CDCl_3$) δ 1 20 (t, *J* = 7 0 Hz, 3H), 3 0 - 3 3 (m, 2H), 3 68 (q, *J* = 7 0 Hz, 1H), 3 86(q, *J* = 7 0 Hz, 1H), 5 72 (dd, *J* = 7 0, 4 0 Hz, 1H), 6 7 - 7 3 (m, 4H) *Anal* Calcd for $C_{10}H_{12}O_2$ C, 73 15, H, 7 37 Found C, 73 18, H, 7 53

Benzo[*b*]furan (15)

(a) A mixture of **1 4** (0 5 g, 3 04 mmol), TsOH•H_2O (50 mg), and benzene (10 ml) was refluxed for 30 min After cooling, the mixture was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography using *n*-C_6H_{14} as an eluent The product obtained from the *n*-C_6H_{14} eluate was distilled under reduced pressure to give benzo[*b*]furan (**1 5**) as a colorless liquid (0 28 g, 76%), bp 70-80°C / 30 mmHg (lit [11] bp 173-174°C) ^{1}H NMR ($CDCl_3$) δ 2 45 (s, 3H), 6 53 (d, *J* = 4 0 Hz, 1H), 7 2 - 7 6 (m, 4H), 8 3 - 8 5 (m, 1H)

(b) A mixture of **1 3** (1 04 g, 5 mmol), 3 N HCl (0 1 ml), and EtOH (10 ml) was stirred at room temperature for 24 h The EtOH was removed under reduced pressure to give the residue which was neutralized with 3 N K_2CO_3 and extracted with ether The ethereal layer was dried over $MgSO_4$ and concentrated under reduced pressure The residue was dissolved in benzene (10 ml), and TsOH•H_2O (50 mg) was added The mixture was refluxed for 30 min After cooling, the mixture was concentrated under reduced pressure, and the residue was purified by silica gel column chromatography using *n*-C_6H_{14} as an eluent The product obtained from the *n*-C_6H_{14} eluate was distilled under reduced pressure to give a colorless liquid (0 43 g, 73%)

Indole (18a)

According to the general procedure, 2-bromoaniline (**16a**) (0 86 g, 5 mmol) was treated with **2** (1 81 g, 5 mmol), Et_4NCl (0 83 g, 5 mmol), and $PdCl_2(PPh_3)_2$ (160 mg) in DMF (10 ml) for 1 5 h to give a yellow viscous liquid (**17a**) The liquid was dissolved in benzene (10 ml), and TsOH•H_2O (100 mg) was added The mixture was stirred at room temperature for 26 h The benzene was removed under reduced pressure, and the residue was purified by silica gel column chromatography using CH_2Cl_2 as an eluent The product obtained from the CH_2Cl_2 eluate was recrystallized from EtOH to give indole (**18a**) as colorless scales (0 20 g, 29%), mp 54-54 5°C (lit [12] mp 53°C) ^{1}H NMR ($CDCl_3$) δ 2 45 (s, 3H), 6 53 (d, *J* = 4 0 Hz, 1H), 7 2 - 7 6 (m, 4H), 8 3 - 8 5 (m, 1H) IR ($CHCl_3$) 3030, 1700 cm^{-1}

1-Acetylindole (18b)

A mixture of **17b** (0 51 g, 2 mmol), TsOH•H_2O (50 mg), and benzene (10 ml) was refluxed for 2 h The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using CH_2Cl_2 as an eluent The product obtained from the CH_2Cl_2 eluate was distilled under reduced pressure to give acetylindol (**18b**) as a colorless liquid (0 32 g, 70%), bp 100°C / 3 mmHg (lit [13] bp 140 - 150°C / 12 mmHg) ^{1}H NMR ($CDCl_3$) δ 2 45 (s, 3H), 6 53 (d, *J* = 4 0 Hz, 1H), 7 1 - 7 6 (m, 4H), 8 3 - 8 5(m, 1H) IR ($CHCl_3$) 3030, 1700 cm^{-1}

Isocoumarin (21)

A mixture of **2 0** (0 44 g, 2 mmol) and 6 N HCl (10 ml) was stirred at 100°C for 2 h After cooling, the mixture was

neutralized with K_2CO_3 and extracted with ether The ethereal layer was dried over $MgSO_4$ and evaporated under reduced pressure The residue was purified by silica gel column chromatography using CH_2Cl_2-AcOEt (2 1) as an eluent The product obtained from the CH_2Cl_2-AcOEt (2 1) eluate was distilled under reduced pressure to give isocoumarin (**2 1**) as a colorless solid (0 23 g, 76%), mp 48 0 - 48 5°C (lit [14] 47°C) ^{1}H NMR ($CDCl_3$) δ 6 47 (d, *J* = 6 0 Hz, 1H), 7 23 (d, *J* = 6 0 Hz, 1H), 7 2 - 7 7 (m, 3H), 8 2 -8 3 (m, 1H) IR ($CHCl_3$) 1730 cm^{-1}

1*H*-Pyrano[3,4-*c*]pyridin-1-one (24)

A mixture of **2 3** (0 40 g, 1 8 mmol) and polyphosphoric acid (PPA) (1 0 g) was stirred at 100°C for 7 h After cooling, the mixture was poured into ice-water, neutralized with K_2CO_3, and extracted with $CHCl_3$ The $CHCl_3$ layer was dried over $MgSO_4$ and evaporated under reduced pressure The residue was purified by silica gel column chromatography using AcOEt as an eluent The product obtained from the AcOEt eluate was recrystallized from *n*-C_6H_{14}-acetone to give 1*H*-pyrano[3,4-*c*]pyridin-1-one (**2 4**) (110 mg, 45%) as colorless needles, mp 137-138 5°C ^{1}H NMR ($CDCl_3$) δ 6 63 (d, *J* = 6 0 Hz, 1H), 7 40 (d, *J* = 6 0 Hz, 1H), 8 07 (d, *J* = 5 0 Hz, 1H), 8 85 (d, *J* = 5 0 Hz, 1H), 8 93 (s, 1H) IR ($CHCl_3$) 1740 cm^{-1} *Anal* Calcd for $C_8H_5NO_2$ C, 65 31, H, 3 43, N, 9 52 Found C, 65 42, H, 3 59, N, 9 48

1*H*-Pyrano[3,4-*b*]pyridin-1-one (27)

By the same procedure for the preparation of **2 4**, 1*H*-pyrano[3,4-*b*]pyridin-1-one (**2 7**) (0 40 g, 60%) was obtained from the reaction of **2 6** (1 00 g, 4 5 mmol) and PPA (1 00 g) as colorless needles, mp 76 5-78°C ^{1}H NMR ($CDCl_3$) δ 6 80 (d, *J* = 6 0 Hz, 1H), 7 43 (dd, *J* = 4 0 Hz, 1H), 7 50 (d, *J* = 6 0 Hz, H), 8 57 (dd, *J* = 8 0, 2 0 Hz, 1H), 8 97 (dd, *J* = 4 0, 2 0 Hz, 1H) IR ($CHCl_3$) 1738 cm^{-1} *Anal* Calcd for $C_8H_5NO_2$ C, 65 31, H, 3 43, N, 9 52 Found C, 65 43, H, 3 58, N, 9 44

References and Notes

1 Part XVII Sakamoto, T , Nagano, T , Kondo, Y , Yamanaka, H *Synthesis* **1990**, 215 - 218

2 A part of this work has been published as a communication Sakamoto, T , Kondo, Y , Yasuhara, A , Yamanaka, H *Heterocycles* **1990**, *31*, 219- 221

3 (a) Heck, R F *Org React (New York)*, **1982**, *27*, 345 - 396
(b) Heck, R F *Palladium Reagents in Organic Synthesis*, Academic New York, 1985

4 Andersson, C -M , Hallberg, A , Davis, G D , Jr *J Org Chem* **1987**, *52*, 3529 - 3536

5 (a) Miyaura, N , Maeda, K , Sugiome, H , Suzuki, A *J Org Chem* **1982**, *47*, 2117 - 2120
(b) Satoh, M , Miyaura, N , Suzuki, A *Synthesis* **1987**, 373 -376

6 (a) Solberg, J , Undheim, K *Acta Chem Scand* **1987**, *B41*, 712 -716
(b) McKean, D R , Parrinello, G , Renaldo, A F , Stille, J K *J Org Chem* **1987**, *52*, 422 -424

7 (a) Sonderquist, J A , Leong, W W -H *Tetrahedron Lett* **1983**, *24*, 2361 - 2362
(b) Kosugi, M , Sumiya, T , Obara, Y , Suzuki, M , Sano, H , Migita, T *Bull Chem Soc Jpn* **1987**, *60*, 767 - 768

8 Wollenberg, R H , Albizati, K F , Peries, R *J Am Chem Soc* **1977**, *99*, 7365 - 7367

9 Sakamoto, T , An-naka, M , Kondo, Y , Yamanaka, H *Chem Pharm Bull* **1986**, *34*, 2754 - 2759

10 Smith, H A , McDaniel, E L *J Am Chem Soc* **1955**, *77*, 533 - 535

11 Stoermer, R *Liebigs Ann Chem* **1883**, *219*, 179 - 233

12 Tyson, F T *J Am Chem Soc* **1941**, *63*, 2024 - 2025

13 Plieninger, H , Werst, G *Chem Ber* **1956**, *89*, 2783 - 2789

14 Gabriel, S *Ber* **1903**, *36*, 570 - 579