Synthesis of Ethoxyethynylarenes by the Palladium-Catalyzed Reaction of Aryl Iodides with Ethoxy(trialkylstannyl)acetylenes[1)]

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Palladium-catalyzed reaction of aryl and heteroaryl iodides with ethoxy(trialkylstannyl)acetylenes gave the ethoxyethynylarenes and -heteroarenes, which were easily transformed by hydration reaction into ethyl areneacetates and heteroareneacetates.

Keywords palladium-catalyzed reaction; aryl iodide; ethoxy(trialkylstannyl)acetylene; ethoxyethynylarene; ethyl areneacetate

Palladium-catalyzed reaction of aryl halides or triflates with terminal acetylenes has been developed as a useful synthetic method of arylacetylenes,[2)] since the first reports appeared in 1975.[3-5)] Although terminal acetylenes substituted with alkyl, aryl, hydroxymethyl, alkoxymethyl, and trimethylsilyl groups are generally used in this palladium-catalyzed reaction, acetylenes having electron-attracting or -donating groups are resistant to this reaction. The problem can be overcome by using metalloacetylenes instead of terminal acetylenes. For example, the reaction of iodobenzenes with acetylenes having electron-attracting groups such as a perfluoroalkyl[6)] or an ethoxycarbonyl group[7)] failed to give the expected products, but zinc derivatives of the acetylenes smoothly reacted with iodobenzenes to give the corresponding perfluoroalkylethynylbenzenes or ethyl phenylpropiolates.[6,7)] Aryl- and heteroarylpropiolates were also obtained by the palladium-catalyzed reaction using ethyl tributylstannylpropiolate.[7)]

Here we report the palladium-catalyzed reaction of aryl and heteroaryl iodides with trialkylstannylacetylenes having an electron-donating ethoxyl group, ethoxy(trialkylstannyl)acetylenes, to give ethoxyethynylarenes and -heteroarenes which were easily transformed into ethyl arylacetates and heteroarylacetates.[8)]

The reaction of iodobenzene (**1a**) with ethoxyacetylene in the presence of dichlorobis(triphenylphosphine)palladium [$PdCl_2(PPh_3)_2$] and cuprous iodide in triethylamine at room temperature gave resinous products. On the other hand, ethoxyethynylbenzene (**3a**) was obtained in 60% yield, when **1a** and ethoxy(tributylstannyl)acetylene (**2a**) were allowed to react in the presence of $PdCl_2(PPh_3)_2$ and tetraethylammonium chloride in dimethylformamide (DMF) at room temperature for 1 h. As shown in Table I, when tetrahydrofuran (THF) was used as a solvent, a somewhat lower yield of **3a** was observed. A comparable yield was obtained using acetonitrile as a solvent, but the reaction afforded by-products which made the chromatographic separation difficult. The reaction of bromobenzene under similar conditions failed to give the expected product.

In order to examine the scope of the reaction, 4-substituted iodobenzenes (**1b**—**i**) and some heteroaryl iodides (**1j**—**n**) were allowed to react under the conditions shown in Table II. The iodobenzenes except for 4-acetylamino- (**1g**) and 4-(*N*,*N*-dimethylamino)iodobenzene (**1i**) gave the expected ethoxyethynylbenzenes in 45—66% yields.

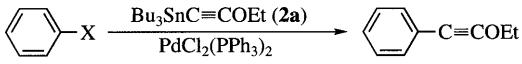
In the case of the heteroaryl iodides, the products obtained from the reaction of 2- and 4-iodopyridine were unstable, and were converted by hydration reaction into the corresponding pyridineacetates.

When the reaction of iodobenzenes and heteroaryl iodides with ethoxy(trimethylstannyl)acetylene (**2b**) instead of **2a** was carried out to examine the effect of the stannyl group, the same products were obtained, as expected, in slightly different yields (Table II).

It is well known that acetylenes are easily hydrated in the presence of mercury sulfate in acidic media to yield ketones. The hydration of ethoxyethynylarenes (**3**) proceeded smoothly in the presence of sulfuric acid in aqueous acetone without mercury sulfate, except for the reaction of **3h**, to give ethyl areneacetates in the yields shown in Table III.

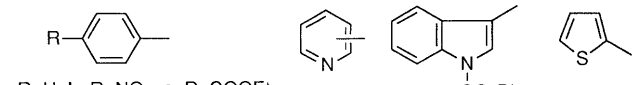
In conclusion, the introduction of an ethoxyethynyl group on the aromatic ring was accomplished in one step

TABLE I. Palladium-Catalyzed Reaction of Halobenzenes with **2a**



1 (X=I, Br) **3a**

X	Solvent	Reaction temp. (°C)	Additive	Reaction time (h)	Yield (%)
I	DMF	50	—	1	10
I	DMF	Room temp.	—	3	42
I	DMF	Room temp.	Et_4NCl	1	60
I	THF	Room temp.	Et_4NCl	2	45
I	MeCN	Room temp.	Et_4NCl	1	57
I	MeCN	Reflux	Et_4NCl	1	0
Br	DMF	Room temp.	Et_4NCl	18	0
Br	DMF	Reflux	Et_4NCl	18	0



a: R=H; **b**: R=NO_2; **c**: R=COOEt
d: R=CN; **e**: R=Me; **f**: R=OMe
g: R=NHAc; **h**: R=NCH_2OMe (SO_2Ph)
i: R=NMe_2

j: 2-
k: 3-
l: 4-

m

n

Chart 1

TABLE II. Palladium-Catalyzed Reaction of Aryl Iodides with **2a, b**

$$\underset{\textbf{1a—n}}{ArI} \xrightarrow[PdCl_2(PPh_3)_2,\ Bu_4NCl,\ DMF]{R_3SnC\equiv COEt\ (\textbf{2a, b})} \underset{\textbf{3a—n}}{ArC\equiv COEt}$$

Product	R=Bu			R=Me		
	Reaction temp. (°C)	Reaction time (h)	Yield (%)	Reaction temp. (°C)	Reaction time (h)	Yield (%)
3a	Room temp.	1	60	Room temp.	6	53
3b	Room temp.	1	52	Room temp.	2	80
3c	Room temp.	5	59	Room temp.	4	75
3d	Room temp.	1.5	59	Room temp.	3	60
3e	Room temp.	15	45	Room temp.	3	75
3f	Room temp.	1.5	66	Room temp.	6	54
3g	50	2	0	50	2	0
3h	50	3	62	50	2	61
3i	50	12	0	*b)*	—	—
3j	50	1.5	*a)*	*b)*	—	—
3k	50	2	61	50	5	64
3l	Room temp.	0.5	*a)*	*b)*	—	—
3m	50	2	60	50	5	60
3n	Room temp.	5	45	Room temp.	3	60

a) The crude products were hydrated without isolation to the pyridineacetate. *b*) Not tried.

TABLE III. Hydration Reaction of **3a—n** to Ethyl Areneacetates (**4a—n**)

$$\underset{\textbf{3a—n}}{ArC\equiv COEt} \xrightarrow[acetone]{H_2O,\ H_2SO_4} \underset{\textbf{4a—n}}{ArCH_2COOEt}$$

Product	Reaction temp. (°C)	Reaction time (h)	Yield (%)
4a	Room temp.	0.5	40 [75]*a)*
4b	Reflux	2.5	62
4c	Reflux	2	59
4d	Room temp.	12	81
4e	Room temp.	0.5	51
4f	Room temp.	6	60
4h′	Reflux.	1.5	62*b)*
4j	Reflux.	2	16
4k	Reflux.	8	88
4l	Reflux.	2	22
4m	Reflux.	2	70
4n	Room temp.	12	32

a) The value in the brackets refers to gas-chromatographic yield. *b*) The product was ethyl 4-(*N*-methylsulfonylamino)phenylacetate (**4h′**).

by using palladium-catalyzed reaction of aryl iodides with ethoxy(trialkylstannyl)acetylenes. The subsequent hydration reaction of the ethoxyethynylarenes provides a synthetic approach to areneacetates, along with other methods such as the palladium-catalyzed reactions of aryl halides with ethyl tributylstannylacetate[10] and with ethoxycarbonylmethylzinc bromide.[11]

Experimental

General Comments Melting points are uncorrected. Boiling points are bath temperatures of the Kugelrohr apparatus. IR spectra were measured on a JASCO IR-A1 spectrophotometer. ^{1}H-NMR spectra were recorded on a JEOL PMX-60 (60 MHz) spectrometer using tetramethylsilane as an internal standard. Chemical shifts are expressed in δ (ppm) values, and coupling constants are expressed in hertz (Hz). The following abbreviations are used: s=singlet, d=doublet, dd=double doublet, ddd=double double doublet, t=triplet, q=quartet, m=multiplet, br=broad. MS were recorded on a JEOL JMS-PX303 spectrometer.

Ethoxy(tributylstannyl)- (**2a**) and ethoxy(trimethylstannyl)acetylene (**2b**) were synthesized according to the literature.[12] Since **2a** was difficult to purify by distillation or silica gel column chromatography, 1.3 eq of crude **2a** to aryl halides was used.

General Procedure for the Palladium-Catalyzed Reaction of Aryl Iodides (1) with Ethoxy(trialkylstannyl)acetylenes (2) A mixture of an aryl iodide (**2a** or **2b**), Et_4NCl, and $PdCl_2(PPh_3)_2$ in DMF was allowed to react under the conditions shown in Table II. The reaction mixture was diluted with H_2O and extracted with Et_2O. The Et_2O extract was washed with H_2O and dried over $MgSO_4$. The residue obtained from the Et_2O extract was purified by silica gel column chromatography.

Ethoxyethynylbenzene (3a) 1) The residue obtained from the reaction mixture of iodobenzene (**1a**) (0.60 g, 3 mmol), ethoxy(tributylstannyl)-acetylene (**2a**) (1.44 g, 4 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (15 ml) was chromatographed using hexane as an eluent. Yield 0.26 g.

2) The residue obtained from the reaction mixture of **1a** (0.60 g, 3 mmol), ethoxy(trimethylstannyl)acetylene (**2b**) (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (15 ml) was chromatographed using the same solvent. Yield 0.23 g. Colorless liquid, bp 80 °C/3 mmHg (lit.[13] bp 53—55 °C/0.01 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.43 (3H, t, J=6 Hz), 4.22 (2H, q, J=6 Hz), 7.1—7.5 (5H, m). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250. MS *m/z*: 146.0739 (Calcd for $C_{10}H_{10}O$: 146.0732).

4-Nitro-1-(ethoxyethynyl)benzene (3b) 1) The residue obtained from the reaction mixture of 4-nitroiodobenzene (**1b**) (0.50 g, 2 mmol), **2a** (0.93 g, 2.6 mmol), Et_4NCl (0.33 g, 2 mmol), and $PdCl_2(PPh_3)_2$ (70 mg, 0.1 mmol) in DMF (10 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.20 g.

2) The residue obtained from the reaction mixture of **1b** (0.75 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (60 mg, 0.09 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.46 g. Yellow viscous liquid. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.42 (3H, t, J=7 Hz), 4.32 (2H, q, J=7 Hz), 7.50 (2H, d, J=9 Hz), 8.17 (2H, d, J=9 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250, 1520, 1345. MS *m/z*: 191.0589 (Calcd for $C_{10}H_9NO_3$: 191.0582).

Ethyl 4-(Ethoxyethynyl)benzoate (3c) 1) The residue obtained from the reaction mixture of ethyl 4-iodobenzoate (**1c**) (1.10 g, 4 mmol), **2a** (1.87 g, 5.2 mmol), Et_4NCl (0.66 g, 4 mmol), and $PdCl_2(PPh_3)_2$ (0.14 g, 0.2 mmol) in DMF (20 ml) was chromatographed using hexane as an eluent. Yield 0.51 g.

2) The residue obtained from the reaction mixture of **1c** (0.83 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (60 mg, 0.09 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.52 g. Colorless viscous liquid. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.42 (3H, t, J=7 Hz), 1.48 (3H, t, J=7 Hz), 4.35 (2H, q, J=7 Hz), 4.45 (2H, q, J=7 Hz), 7.52 (2H, d, J=8 Hz), 8.08 (2H, d, J=8 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2288, 1722. MS *m/z*: 218.0961 (Calcd for $C_{13}H_{14}O_3$: 218.0943).

4-(Ethoxyethynyl)benzonitrile (3d) 1) The residue obtained from the reaction mixture of 4-iodobenzonitrile (**1d**) (0.69 g, 3 mmol), **2a** (1.44 g, 4 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (15 ml) was chromatographed using hexane–CH_2Cl_2 (2 : 1) as an eluent. Yield 0.30 g.

2) The residue obtained from the reaction mixture of **1d** (0.69 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (60 mg, 0.09 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.31 g. Colorless viscous liquid. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.45 (3H, t, J=7 Hz), 4.27 (2H, q, J=7 Hz), 7.40 (2H, d, J=8 Hz), 7.52 (2H, d, J=8 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2250, 2225. MS *m/z*: 171.0696 (Calcd for $C_{11}H_9NO$: 171.0684).

4-(Ethoxyethynyl)toluene (3e) 1) The residue obtained from the reaction mixture of 4-iodotoluene (**1e**) (0.55 g, 2.5 mmol), **2a** (1.17 g, 3.25 mmol), Et_4NCl (0.41 g, 2.5 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (10 ml) was chromatographed using hexane as an eluent. Yield 0.36 g.

2) The residue obtained from the reaction mixture of **1e** (0.65 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.36 g. Colorless liquid, bp 120 °C/3 mmHg (lit.[14] bp 77—79 °C/0.01 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.40 (3H, t, J=7 Hz), 2.30 (3H, s), 4.20 (2H, q, J=7 Hz), 7.07 (2H, d, J=8 Hz), 7.23 (2H, d, J=8 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2260. MS *m/z*: 160.0909 (Calcd for $C_{11}H_{12}O$: 160.0888).

4-(Ethoxyethynyl)anisole (3f) 1) The residue obtained from the

reaction mixture of 4-iodoanisole (**1f**) (0.70 g, 3 mmol), **2a** (1.44 g, 4 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (15 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.35 g.

2) The residue obtained from the reaction mixture of **1f** (0.70 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.28 g. Colorless viscous liquid. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.40 (3H, t, J=7 Hz), 3.37 (3H, s), 4.15 (2H, q, J=7 Hz), 6.75 (2H, d, J=8 Hz), 7.27 (2H, d, J=8 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2260. MS m/z: 176.0846 (Calcd for $C_{11}H_{12}O_2$: 176.0837).

4-Ethoxyethynyl-*N*-methylsulfonyl-*N*-(methoxymethyl)aniline (3h) 1) The residue obtained from the reaction mixture of *N*-methylsulfonyl-*N*-methoxymethyl-4-iodoaniline (**1h**) (1.02 g, 3 mmol), **2a** (1.44 g, 4 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (15 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.53 g.

2) The residue obtained from the reaction mixture of **1h** (1.02 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (60 mg, 0.09 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.46 g. Colorless needles (hexane–acetone), mp 97—98 °C. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.42 (3H, t, J=7 Hz), 2.95 (3H, s), 3.38 (3H, s), 4.83 (2H, q, J=7 Hz), 4.88 (2H, s), 7.32 (4H, s). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2266. *Anal.* Calcd for $C_{13}H_{17}NO_4S$: C, 55.11; H, 6.25; N, 4.94; S, 11.31. Found: C, 55.04; H, 6.24; N, 4.73; S, 11.40.

3-(Ethoxyethynyl)pyridine (3k) 1) The residue obtained from the reaction mixture of 3-iodopyridine (**1k**) (0.41 g, 2 mmol), **2a** (0.93 g, 2.6 mmol), Et_4NCl (0.33 g, 2 mmol), and $PdCl_2(PPh_3)_2$ (70 mg, 0.1 mmol) in DMF (10 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.18 g.

2) The residue obtained from the reaction mixture of **1k** (0.31 g, 1.5 mmol), **2b** (0.38 g, 1.65 mmol), Et_4NCl (0.25 g, 1.5 mmol), and $PdCl_2(PPh_3)_2$ (30 mg, 0.04 mmol) in DMF (3 ml) was chromatographed using the same solvent. Yield 0.14 g. Colorless liquid, bp 120 °C/3 mmHg. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.40 (3H, t, J=6 Hz), 4.23 (2H, q, J=6 Hz), 7.15 (1H, dd, J=8, 6 Hz), 7.60 (1H, ddd, J=8, 2, 2 Hz), 8.43 (1H, d, J=2 Hz), 8.53 (1H, d, J=2 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2267. MS m/z: 147.0683 (Calcd for C_9H_9NO: 147.0684).

3-Ethoxyethynyl-1-(phenylsulfonyl)indole (3m) 1) The residue obtained from the reaction mixture of 3-iodo-1-(phenylsulfonyl)indole (**1m**) (0.96 g, 2.5 mmol), **2a** (1.17 g, 3.25 mmol), Et_4NCl (0.41 g, 2.5 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (10 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 2) as an eluent. Yield 0.59 g.

2) The residue obtained from the reaction mixture of **1m** (1.15 g, 3 mmol), **2b** (0.77 g, 3.3 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (60 mg, 0.09 mmol) in DMF (5 ml) was chromatographed using the same solvent. Yield 0.72 g. Colorless viscous liquid. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.47 (3H, t, J=7 Hz), 4.25 (2H, q, J=7 Hz), 7.1—8.0 (10H, m). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2260. MS m/z: 325.0757 (Calcd for $C_{18}H_{15}NO_3$: 325.0773).

2-Ethoxyethynylthiophene (3n) 1) The residue obtained from the reaction mixture of 2-iodothiophene (**1n**) (0.55 g, 2.5 mmol), **2a** (1.17 g, 3.25 mmol), Et_4NCl (0.41 g, 2.5 mmol), and $PdCl_2(PPh_3)_2$ (70 mg, 0.1 mmol) in DMF (10 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.36 g.

2) The residue obtained from the reaction mixture of **1n** (1.05 g, 5 mmol), **2b** (1.28 g, 5.5 mmol), Et_4NCl (0.83 g, 5 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (10 ml) was chromatographed using the same solvent. Yield 0.46 g. Colorless liquid, bp 80 °C/3 mmHg. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.40 (3H, t, J=7 Hz), 4.22 (2H, q, J=7 Hz), 6.8—7.2 (3H, m). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2225. MS m/z: 152.0295 (Calcd for C_8H_8OS: 152.0296).

General Procedure for the Hydration Reaction of Ethoxyethynylarenes (3) A mixture of an ethoxyethynylarene (**3**), H_2SO_4, H_2O, and acetone was allowed to react under the conditions shown in Table III. The reaction mixture was diluted with H_2O, made alkaline with solid K_2CO_3, and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over $MgSO_4$. The residue obtained from the $CHCl_3$ extract was purified by recrystallization or silica gel column chromatography.

Ethyl Phenylacetate (4a) The residue obtained from the reaction mixture of **2a** (90 mg, 0.62 mmol), H_2O (1 ml), H_2SO_4 (0.10 g, 1 mmol), and acetone (4 ml) was chromatographed using hexane as an eluent. Yield 40 mg. Colorless liquid, bp 100 °C/4 mmHg (lit.[15] bp 67—69 °C/0.1 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.26 (3H, t, J=7 Hz), 3.63 (2H, s), 4.18 (2H, q, J=7 Hz), 7.33 (5H, s). IR ν_{max}^{neat} cm^{-1}: 1730.

Ethyl 4-Nitrophenylacetate (4b) The residue obtained from the reaction mixture of **2b** (0.19 g, 1 mmol), H_2O (2 ml), H_2SO_4 (0.20 g, 2 mmol), and acetone (8 ml) was chromatographed using hexane–CH_2Cl_2 (2 : 1) as an eluent. Yield 0.13 g. Pale yellow scales (hexane), mp 63—64 °C. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.35 (3H, t, J=7 Hz), 3.85 (2H, s), 4.30 (2H, q, J=7 Hz), 7.60 (2H, d, J=9 Hz), 8.27 (2H, d, J=9 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1520, 1350. *Anal.* Calcd for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70. Found: C, 57.17; H, 5.25; N, 6.58.

Ethyl 4-Ethoxycarbonylphenylacetate (4c) The residue obtained from the reaction mixture of **2c** (0.50 g, 2.3 mmol), H_2O (4.5 ml), H_2SO_4 (0.50 g, 5.1 mmol), and acetone (18 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.32 g. Colorless liquid. bp 150 °C/3 mmHg. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.25 (3H, t, J=7 Hz), 1.38 (3H, t, J=7 Hz), 3.68 (2H, s), 4.17 (2H, q, J=7 Hz), 4.40 (2H, q, J=7 Hz), 7.40 (2H, d, J=10 Hz), 8.00 (2H, d, J=10 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1712. MS m/z: 236.1052 (Calcd for $C_{13}H_{16}O_4$: 236.1049).

Ethyl 4-Cyanophenylacetate (4d) The residue obtained from the reaction mixture of **2d** (0.17 g, 1 mmol), H_2O (2 ml), H_2SO_4 (0.20 g, 2 mmol), and acetone (8 ml) was recrystallized from EtOH. Yield 0.15 g. Colorless needles. mp 86.5—88 °C (lit.[16] mp 97 °C). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.28 (3H, t, J=7 Hz), 3.88 (2H, s), 4.37 (2H, q, J=7 Hz), 7.35 (2H, d, J=8 Hz), 7.65 (2H, d, J=8 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 2230, 1730. *Anal.* Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.92; H, 5.94; N, 7.36.

Ethyl 4-Methylphenylacetate (4e) The residue obtained from the reaction mixture of **2e** (0.21 g, 1.3 mmol), H_2O (2.6 ml), H_2SO_4 (0.26 g, 2.65 mmol), and acetone (10 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 0.12 g. Colorless liquid, bp 130 °C/20 mmHg. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.22 (3H, t, J=7 Hz), 2.30 (3H, s), 3.55 (2H, s), 4.13 (2H, q, J=7 Hz), 7.23 (4H, s). IR ν_{max}^{neat} cm^{-1}: 1739. MS m/z: 178.0976 (Calcd for $C_{11}H_{14}O_2$: 178.0994).

Ethyl 4-Methoxyphenylacetate (4f) The residue obtained from the reaction mixture of **2f** (0.60 g, 0.5 mmol), H_2O (1 ml), H_2SO_4 (0.98 g, 1 mmol), and acetone (4 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 1) as an eluent. Yield 40 mg. Colorless liquid, bp 100 °C/3 mmHg (lit.[17] bp 138—140 °C/30 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.27 (3H, t, J=7 Hz), 3.57 (2H, s), 3.80 (3H, s), 4.18 (2H, q, J=7 Hz), 6.90 (2H, d, J=9 Hz), 7.22 (2H, d, J=9 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. MS m/z: 194.0941 (Calcd for $C_{11}H_{14}O_3$: 194.0943).

Ethyl 4-(*N*-Methylsulfonylamino)phenylacetate (4h') The residue obtained from the reaction mixture of **2h** (0.53 g, 1.8 mmol), H_2O (4 ml), H_2SO_4 (0.37 g, 3.8 mmol), $HgSO_4$ (0.50 g, 1.8 mmol), and acetone (16 ml) was chromatographed using CH_2Cl_2 as an eluent. Yield 0.67 g. Colorless prisms, mp 82—83 °C (hexane–acetone). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.23 (3H, t, J=8 Hz), 2.97 (3H, s), 3.62 (2H, s), 4.15 (2H, q, J=7 Hz), 7.23 (4H, s), 7.5—7.7 (1H, br). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3380, 1730. *Anal.* Calcd for $C_{11}H_{15}NO_4S$: C, 51.35; H, 5.88; N, 5.44; S, 12.46. Found: C, 51.24; H, 5.83; N, 5.32; S, 12.56.

Ethyl 3-Pyridineacetate (4k) The residue obtained from the reaction mixture of **2k** (0.73 g, 5 mmol), H_2O (10 ml), H_2SO_4 (0.98 g, 10 mmol), and acetone (40 ml) was chromatographed using CH_2Cl_2 as an eluent. Yield 0.73 g. Colorless liquid, bp 120 °C/3 mmHg (lit.[11] bp 115—120 °C/3 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.23 (3H, t, J=7 Hz), 3.62 (2H, s), 4.17 (2H, q, J=7 Hz), 7.27 (1H, dd, J=8, 5 Hz), 8.5—8.7 (2H, m). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1732.

Ethyl 1-Phenylsulfonyl-3-indoleacetate (4m) The residue obtained from the reaction mixture of **2m** (0.50 g, 1.54 mmol), H_2O (3 ml), H_2SO_4 (0.30 g, 3.06 mmol), and acetone (6 ml) was chromatographed using CH_2Cl_2 as an eluent. Yield 0.37 g. Pale yellow prisms, mp 70—70.5 °C (hexane–acetone) ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.22 (3H, t, J=7 Hz), 3.77 (2H, s), 4.23 (2H, q, J=7 Hz), 7.2—7.7 (7H, m), 7.9—8.2. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1730. *Anal.* Calcd for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08; S, 9.34. Found: C, 62.93; H, 5.13; N, 3.99; S, 9.30.

Ethyl 2-Thiopheneacetate (4n) The residue obtained from the reaction mixture of **2n** (0.30 g, 2 mmol), H_2O (4 ml), H_2SO_4 (0.40 g, 4 mmol), and acetone (16 ml) was chromatographed using hexane–CH_2Cl_2 (1 : 2) as an eluent. Yield 0.12 g. Colorless liquid, bp 130 °C/20 mmHg. ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.27 (3H, t, J=7 Hz), 3.82 (2H, s), 4.18 (2H, q, J=7 Hz), 6.9—7.3 (3H, m). IR ν_{max}^{neat} cm^{-1}: 1725. MS m/z: 170.0393 (Calcd for $C_8H_{10}O_2S$: 170.0402).

Ethyl 2-Pyridineacetate (4j) The Et_2O extract obtained from the reaction mixture of 2-iodopyridine (**1j**) (1.20 g, 5 mmol), **2a** (2.20 g, 6 mmol), Et_4NCl (0.82 g, 5 mmol), and $PdCl_2(PPh_3)_2$ (0.16 g, 0.23 mmol)

in DMF (40 ml) was concentrated during addtion of acetone. Water (20 ml) and concentrated H_2SO_4 (0.50 g, 5 mmol) were added to the acetone solution (100 ml), and the mixture was refluxed for 2 h. After evaporation of the solvent, the residue was made alkaline with solid K_2CO_3 and extracted with Et_2O. The Et_2O extract was dried over $MgSO_4$ and evaporated. The residue was column-chromatographed using CH_2Cl_2 as an eluent. The product obtained from the CH_2Cl_2 eluate was distilled under reduced pressure to give a colorless liquid. Yield 0.13 g, bp 120 °C/3 mmHg (lit.[11] bp 110—113 °C/3 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.22 (3H, t, J=7 Hz), 3.82 (2H, s), 4.17 (2H, q, J=7 Hz), 7.0—8.3 (3H, m), 8.3—8.5 (1H, m). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735.

Ethyl 4-Pyridineacetate (4l) The Et_2O extract obtained from the reaction mixture of 4-iodopyridine (**1l**) (0.62 g, 3 mmol), **2a** (1.36 g, 3.6 mmol), Et_4NCl (0.50 g, 3 mmol), and $PdCl_2(PPh_3)_2$ (0.10 g, 0.14 mmol) in DMF (10 ml) was concentrated during addition of acetone. Water (5 ml) and concentrated H_2SO_4 (0.29 g, 3 mmol) were added to the acetone solution (50 ml), and the mixture was refluxed for 2 h. Treatment as described above gave a colorless liquid. Yield 0.11 g, bp 100 °C/3 mmHg (lit.[14] bp 90—91 °C/3.5—4 mmHg). ^{1}H-NMR ($CDCl_3$/TMS) δ: 1.25 (3H, t, J=7 Hz), 3.60 (2H, s), 4.17 (2H, q, J=7 Hz), 7.22 (2H, d, J=5 Hz), 8.53 (2H, d, J=5 Hz). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735.

References and Notes

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