Oxidative Coupling of 1-(2,6-Dichlorobenzoyl)pyrroles and -pyrazoles and Alkyl Acrylates by Palladium(II) Acetate

Toshio ITAHARA,* Kazukuni KAWASAKI, and Fumio OUSETO
Institute of Chemistry, College of Liberal Arts, Kagoshima University, Korimoto, Kagoshima 890
(Received April 21, 1984)

Treatments of 1-(2,6-dichlorobenzoyl)-, 3-acetyl-1-(2,6-dichlorobenzoyl)-, 1-(2,6-dichlorobenzoyl)-2-formyl-, and 1-(phenylsulfonyl)pyrroles with palladium acetate and alkyl acrylates gave the corresponding α-alkenyl-substituted pyrroles in good yields, while the reaction of 1-(2,6-dichlorobenzoyl)-2,5-dimethylpyrrole gave small amounts of β-alkenyl-substituted pyrroles. Under similar conditions, 1-(2,6-dichlorobenzoyl)pyrazole and 1-(2,6-dichlorobenzoyl)-3,5-dimethylpyrazole reacted with palladium acetate and alkyl acrylates to give the corresponding 4-alkenyl-substituted pyrazoles. The reaction of 1-(2,6-dichlorobenzoyl)-4-methylpyrazole gave 5-alkenyl-substituted pyrazole.

Palladium(II) salts-assisted alkenylation of arenes is a useful method for the direct synthesis of aromatic-substitued olefins.[1] Fujiwara *et al.* reported the alkenylation of heteroarenes with palladium acetate and olefins.[2,3] We reported that 2,6-dichlorobenzoyl group was an effective protecting substituent for the alkenylation of 1-acylindoles[4] and the arylation of 1-acylpyrroles with arenes.[5] Pyrrolyl-, pyrazolyl-, and imidazolyl-acrylic acids and their esters are important precursors for the synthesis of physiologically active compounds. These observations led us to examine reactions of 1-(2,6-dichlorobenzoyl)pyrroles, -pyrazoles, and -imidazoles with palladium acetate and alkyl acrylates. The treatment of 1-(2,6-dichlorobenzoyl)pyrroles with palladium acetate and alkyl acrylates gave alkyl 3-(2-pyrrolyl)acrylates in high yields. The reaction of 1-(phenylsulfonyl)pyrrole (**10**) also gave alkenyl-substituted pyrroles. Furthermore, 1-(2,6-dichlorobenzoyl)pyrazoles reacted with palladium acetate and alkyl acrylates to give alkyl 3-(4-pyrazolyl)acrylates, while an attempted oxidative coupling of 1-(2,6-dichlorobenzoyl)imidazoles and methyl acrylate failed under our experimental conditions.

Results and Discussion

Although it was reported that the treatment of 1-methylpyrrole with styrene in the presence of palladium acetate gave small amounts of 2- and 3-styryl-1-methylpyrroles,[2] the reaction of 1-methyl- and 1-benzoylpyrroles with palladium acetate and methyl acrylate in acetic acid at reflux temperature gave complex

	R^1	R^2	R^3
13	H	H	H
14a	H	MeOCOCH=CH	H
14b	H	EtOCOCH=CH	H
15	Me	H	Me
16a	Me	MeOCOCH=CH	Me
16b	Me	EtOCOCH=CH	Me
17	H	Me	H
18a	H	Me	MeOCOCH=CH

Bz = 2,6-$Cl_2C_6H_3CO$

Fig. 2

	R	R^1	R^2	R^3	R^4
1	2,6-$Cl_2C_6H_3CO$	H	H	H	H
2a	2,6-$Cl_2C_6H_3CO$	MeOCOCH=CH	H	H	H
2b	2,6-$Cl_2C_6H_3CO$	EtOCOCH=CH	H	H	H
3a	2,6-$Cl_2C_6H_3CO$	MeOCOCH=CH	H	H	MeOCOCH=CH
3b	2,6-$Cl_2C_6H_3CO$	EtOCOCH=CH	H	H	EtOCOCH=CH
4	2,6-$Cl_2C_6H_3CO$	H	Me	MeCO	Me
5a	2,6-$Cl_2C_6H_3CO$	MeOCOCH=CH	Me	MeCO	Me
5b	2,6-$Cl_2C_6H_3CO$	EtOCOCH=CH	Me	MeCO	Me
6	2,6-$Cl_2C_6H_3CO$	H	H	H	OHC
7a	2,6-$Cl_2C_6H_3CO$	MeOCOCH=CH	H	H	OHC
7b	2,6-$Cl_2C_6H_3CO$	EtOCOCH=CH	H	H	OHC
8	2,6-$Cl_2C_6H_3CO$	Me	H	H	Me
9a	2,6-$Cl_2C_6H_3CO$	Me	MeOCOCH=CH	H	Me
9b	2,6-$Cl_2C_6H_3CO$	Me	EtOCOCH=CH	H	Me
10	$C_6H_5SO_2$	H	H	H	H
11b	$C_6H_5SO_2$	EtOCOCH=CH	H	H	H
12b	$C_6H_5SO_2$	EtOCOCH=CH	H	H	EtOCOCH=CH

Fig. 1

Table 1. Alkenylation of 1-(2,6-dichlorobenzoyl)- and 1-(phenylsulfonyl)pyrroles and of 1-(2,6-dichlorobenzoyl)pyrazoles with palladium acetate and alkyl acrylates[a)]

Substrate	CH_2=CHCOOR R	Reaction time h	Conversion %	Products Yield/%[b)]
1	Me	7	75	**2a**: 80; **3a**: 24
1	Et	18	81	**2b**: 76; **3b**: 25
2a	Me	18	67	**3a**: 71
4	Me	7	80	**5a**: 91
4	Et	18	97	**5b**: 85
6	Me	7	34	**7a**: 87
6	Et	14	44	**7b**: 66
8	Me	18	45	**9a**: 30
8	Et	18	45	**9b**: 26
10	Et	7	65	**11b**: 58; **12b**: 30
13	Me	7	29	**14a**: 93
13	Et	7	27	**14b**: 91
15	Me	7	15	**16a**: 61
15	Et	7	14	**16b**: 64
17	Me	7	14	**18a**: 59

a) The reaction was performed by heating an acetic acid solution (40 ml) of substrate (1 mmol), $Pd(OAc)_2$ (1 mmol), and alkyl acrylate (3 mmol) in air at reflux temperature. b) Yield based on the substrate consumed.

reaction mixtures. On the other hand, the treatment of 1-(2,6-dichlorobenzoyl)pyrrole (**1**) with methyl acrylate gave the expected coupling products (**2a**) and (**3a**) in almost quantitative yields based on palladium acetate used. Furthermore, the reaction of **2a** with methyl acrylate and palladium acetate gave **3a**, suggesting that **2a** is the intermediate in the formation of **3a** from **1**. The treatment of **1** with ethyl acrylate also gave the coupling products (**2b**) and (**3b**).

Substituent effects on the oxidative coupling of the pyrroles and alkyl acrylates were further investigated. The treatment of 3-acetyl-1-(2,6-dichlorobenzoyl)-2,4-dimethylpyrrole (**4**) with methyl acrylate and ethyl acrylate gave (**5a**) and (**5b**), respectively. Under similar conditions, 1-(2,6-dichlorobenzoyl)-2-formylpyrrole (**6**) gave (**7a**) and (**7b**), when treated with methyl acrylate and ethyl acrylate, respectively. The fact that the formyl group was transferred intact through the oxidation with palladium acetate was already reported in the case of dimerization[6)] and alkenylation with methyl acrylate[7)] of furfural and of 2-formylthiophenes. When the substrate was 2,5-disubstituted pyrrole such as 1-(2,6-dichlorobenzoyl)-2,5-dimethylpyrrole (**8**) β-alkenyl substituted products were obtained; the treatment of **8** with methyl acrylate and ethyl acrylate in the presence of palladium acetate gave (**9a**) and (**9b**), respectively, although the yields of **9a** and **9b** were not good.

Recently we reported the oxidative coupling of 1-(phenylsulfonyl)indole and olefins bearing electron-withdrawing groups by palladium acetate.[8)] Since the acylation of 1-(phenylsulfonyl)pyrrole (**10**) with acyl halides and Lewis acids has been reported,[9)] we carried out experiments on the oxidative coupling of **10** and ethyl acrylate. The reaction gave the expected coupling products (**11b**) and (**12b**).

In an effort to elucidate the scope of the oxidative coupling of aromatic heterocyles containing nitrogen atom and alkyl acrylates, the reactions of 1-(2,6-dichlorobenzoyl)pyrazoles and -imidazoles were investigated. The treatment of 1-(2,6-dichlorobenzoyl)pyrazole (**13**) with methyl acrylate and ethyl acrylate in the presence of palladium acetate gave 4-alkenyl-substituted pyrazoles (**14a**) and (**14b**), respectively. Similarly 1-(2,6-dichlorobenzoyl)-3,5-dimethylpyrazole (**15**) reacted with methyl acrylate and ethyl acrylate giving (**16a**) and (**16b**), respectively. On the other hand, the treatment of 1-(2,6-dichlorobenzoyl)-4-methylpyrazole (**17**) with methyl acrylate and palladium acetate gave a 5-alkenyl-substituted pyrazole (**18a**). These results are summarized in Table 1. However, no reaction occurred when the substrate was 1-(2,6-dichlorobenzoyl)-1*H*-indazole (**19**). The attempted oxidative coupling of the imidazoles such as 1-(2,6-dichlorobenzoyl)imidazole (**20**), 1-(2,6-dichlorobenzoyl)-2-methylimidazole (**21**), and 1-(2,6-dichlorobenzoyl)-2-phenyl-imidazole (**22**) and methyl acrylate failed either under our reaction conditions.

The structures of **1**—**22** except for the known compound (**10**)[10)] were determined on the basis of elemental analyses and spectral data. Furthermore, proton NMR spectra showed that all the coupling products have the E stereochemistry.

Table 1 shows an interesting fact that the presence of two methyl groups at the 3- and 5-positions of **15** decreased the conversions and yields of the alkenylation at the 4-position of the pyrazole, although methyl group is an electron-donating substituent. This fact may be interepreted in terms of steric effects. In order to elucidate the steric effects on the alkenylation with methyl acrylate, carboxylation reactions with carbon monoxide of methylbenzenes were also undertaken.

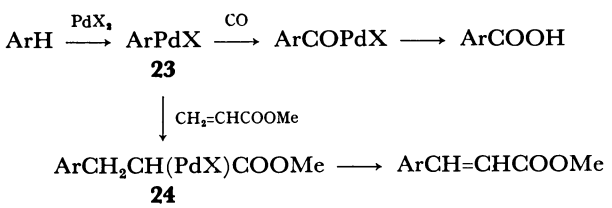
The treatment of *p*-xylene (**25**) under carbon mon-

oxide gave 2,5-dimethylbenzoic acid (**26**) and with methyl acrylate gave methyl 2,5-dimethylcinnamate (**27**). Hydrolysis of **27** gave 2,5-dimethylcinnamic acid (**28**), providing an evidence for the structure of **27**. Mesityrene (**29**) and pentamethylbenzene (**31**) also reacted with carbon monoxide to give 2,4,6-trimethylbenzoic acid (**30**) and pentamethylbenzoic acid (**32**), respectively. However, the reactions of **29** and **31** with methyl acrylate gave complex reaction mixtures under our reaction conditions, and no alkenyl-substituted benzenes such as methyl 2,4,6-trimethylcinnamate and methyl pentamethylcinnamate were obtained, although the oxidative coupling of **29** with styrene had been reported to proceed.[11]

The previous studies concerning the oxidative coupling of arenes and olefins[1] and the carboxylation of arenes with carbon monoxide[12,13] showed that the both reactions proceeded *via* the same intermediate, arylpalladium complex (**23**), as shown in Scheme 1. Therefore, the above results suggest that the formation of the intermediate **24** from **23** is affected by the steric effects of the two methyl groups at 2- and 6-positions of the benzene nucleus or at 3- and 5-positions of **15**, since Watanabe *et al.*[11] have reported that there is a steric hindrance in the transition state involving the palladium–carbon σ-bond on the coupling of styrene and alkylbenzene such as toluene, **25**, and **29**.

Palladium acetate-catalyzed reactions of **1** and **13** with methyl acrylate were carried out using AgOAc,[1] $Cu(OAc)_2$,[1] $Na_2S_2O_8$,[13] and $NaNO_2$[14] as re-oxidants. These results are summarized in Table 2.

It is known that the treatment of 1-substituted pyrazoles and 1-substituted pyrroles with butyllithium gives 1-substituted 5-lithiopyrazoles[15] and 1-substituted α-lithiopyrroles,[16] respectively. On the other hand, it was found that palladium acetate preferentially attacked the 4-position of the pyrazole nucleus, although the palladation of pyrroles occured at α-position of the pyrrole nucleus. The difference between lithiation and palladation of 1-substituted pyrazoles is of interest from the view point of synthetic chemistry utilizing metals.



Scheme 1

Experimental

General. All the melting points are uncorrected. The elemental analyses were performed by the Analytical Center of Kyoto University. The infrared spectra were recorded with a JASCO IRA-1 spectrometer. The proton magnetic resonance spectra were recorded with a JEOL PMX60A spectrometer, using Me_4Si as the internal reference.

Preparation of the Starting 1-(2,6-Dichlorobenzoyl)-Substituted Aromatic Heterocycles (1), (4), (6), (8), (13), (15), (17), (19), (20), (21), and (22). To a stirred solution of 1*H*-aromatic heterocycle and sodium hydride in *N*,*N*-dimethylformamide (DMF), 2,6-dichlorobenzoyl chloride was added dropwise under nitrogen at 0 °C. Then the mixture was stirred at room temperature for 16 h and poured into an excess of ice-cooled water to give 1-(2,6-dichlorobenzoyl)-substituted aromatic heterocycle as a crystalline product, which was collected by suction and recrystallized from ether–hexane. These results are summarized in Table 3. The spectral and analytical data are given below.

1-(2,6-Dichlorobenzoyl)pyrrole (1): Mp 121.5—122.5 °C; IR (Nujol) 1710 cm^{-1}; NMR ($CDCl_3$) δ=6.29 (t, 2H, J=3 Hz), 6.8—7.4 (broad, 2H), 7.33 (s, 3H). Found: C, 55.06; H, 2.91; N, 5.83%. Calcd for $C_{11}H_7NOCl_2$: C, 55.03; H, 2.94; N, 5.83%.

3-Acetyl-1-(2,6-dichlorobenzoyl)-2,4-dimethylpyrrole (4): Mp 127.5—128.5 °C; IR (Nujol) 1720, 1675 cm^{-1}; NMR ($CDCl_3$) δ=2.11 (s, 3H), 2.44 (s, 3H), 2.80 (s, broad, 3H), 6.20 (s, broad, 1H), 7.30 (s, 3H); Mass: *m/z* (rel. intensity) 311 (12), 309 (19), 175 (61), 173 (100). Found: C, 57.94; H, 4.26; N, 4.43%. Calcd for $C_{15}H_{13}NO_2Cl_2$: C, 58.08; H, 4.22; N, 4.52%.

1-(2,6-Dichlorobenzoyl)-2-formylpyrrole (6): Mp 125—126 °C; IR (Nujol) 1720, 1660 cm^{-1}; NMR ($CDCl_3$) δ=6.23 (t, 1H, J=3.5 Hz), 6.63—6.78 (m, 1H), 7.13—7.30 (m, 1H), 7.31 (s, 3H), 10.30 (s, 1H). Found: C, 53.56; H, 2.69; N, 5.21%. Calcd for $C_{12}H_7NO_2Cl_2$: C, 53.76; H, 2.63; N, 5.22%.

1-(2,6-Dichlorobenzoyl)-2,5-dimethylpyrrole (8): Mp 102.5—104.0 °C; IR (Nujol) 1690 cm^{-1}; NMR ($CDCl_3$) δ=2.10 (s, broad, 6H), 6.83 (s, 2H), 7.30 (s, 3H); Mass: *m/z* (rel. intensity) 269 (16), 267 (25), 175 (64), 173 (100). Found: C, 58.19; H, 3.99; N,

Table 2. Palladium acetate-catalyzed alkenylation of **1** and of **13** with methyl acrylate and re-oxidants[a]

Substrate	Re-oxidant (mmol)	Products Yield/%[b]; Yield/%[c] (Conversion/%)
1	AgOAc (2)	**2a**: 534; 68(78), **3a**: 446; 29(78)
1	$Cu(OAc)_2$ (1)	**2a**: 444; 54(83), **3a**: 480; 29(83)
1	$Na_2S_2O_8$ (1)	**2a**: 586; 64(91), **3a**: 470; 26(91)
1	$NaNO_2$ (2)	**2a**: 386; 42(92), **3a**: 353; 19(92)
13	AgOAc (2)	**14a**: 93; 78(12)
13	$Cu(OAc)_2$ (1)	**14a**: 91; 88(11)
13	$Na_2S_2O_8$ (1)	**14a**: 98; 65(15)
13	$NaNO_2$ (1)	**14a**: 89; 71(13)

a) Reaction conditions used in all experiments: substrate (1 mmol), $Pd(OAc)_2$ (0.1 mmol), methyl acrylate (3 mmol), re-oxidant, acetic acid (40 ml), at reflux temperature in air, 16 h reaction. b) Yield based on $Pd(OAc)_2$ used. c) Yield based on the substrate consumed.

Table 3. Synthesis of 1-(2,6-dichlorobenzoyl)-substituted aromatic heterocycles from 1*H*-aromatic heterocycles

1*H*-Aromatic heterocycles (mmol)	NaH (mmol)	2,6-$Cl_2C_6H_3COCl$ (mmol)	DMF (ml)	Products (mmol; Yield/%[a])
Pyrrole (48)	48	48	200	**1** (37 mmol; 76%)
3-Acetyl-2,4-dimethylpyrrole (29)	29	29	150	**4** (23 mmol; 78%)
2-Formylpyrrole (52)	52	48	200	**6** (37 mmol; 71%)
2,5-Dimethylpyrrole (53)	53	48	200	**8** (10 mmol; 19%)
Pyrazole (59)	59	48	200	**13** (47 mmol; 79%)
3,5-Dimethylpyrazole (37)	37	37	150	**15** (29 mmol; 78%)
4-Methylpyrazole (18.3)	18.3	18.3	100	**17** (15 mmol; 81%)
Indazole (16.9)	16.9	14.6	100	**19** (15 mmol; 89%)
Imidazole (50)	50	48	200	**20** (28 mmol; 56%)
2-Methylimidazole (59.8)	58.8	47.8	200	**21** (36 mmol; 61%)
2-Phenylimidazole (31)	31	30.1	150	**22** (19 mmol; 62%)

a. Yields based on the 1H-aromatic heterocycles used.

5.05%. Calcd for $C_{13}H_{11}NOCl_2$: C, 58.23; H, 4.14; N, 5.22%.

*1-(2,6-Dichlorobenzoyl)pyrazole (**13**)*: Mp 118.5—119.5 °C; IR (Nujol) 1730 cm^{-1}; NMR ($CDCl_3$) δ=6.46 (d.d, 1H, J= 1 Hz, J=3 Hz), 7.29 (s, 3H), 7.66 (d, 1H, J=1 Hz), 8.30 (d, 1H, J=3 Hz), Found: C, 50.09; H, 2.41; N, 11.74%. Calcd for $C_{10}H_6N_2OCl_2$: C, 49.82; H, 2.51; N, 11.62%.

*1-(2,6-Dichlorobenzoyl)-3,5-dimethylpyrazole (**15**)*: Mp 169.5—170.0 °C; IR (Nujol) 1710—1700 (broad) cm^{-1}; NMR ($CDCl_3$) 2.14 (s, 3H), 2.68 (s, broad, 3H), 6.05 (s, broad, 1H), 7.33 (s, 3H). Found: C, 53.49; H, 3.65; N, 10.37%. Calcd for $C_{12}H_{10}N_2OCl_2$: C, 53.55; H, 3.75; N, 10.41%.

*1-(2,6-Dichlorobenzoyl)-4-methylpyrazole (**17**)*: Mp 165—166 °C; IR (Nujol) 1715—1700 (broad) cm^{-1}; NMR ($CDCl_3$) δ= 2.14 (d, 3H, J=1 Hz), 7.35 (s, 3H), 7.52 (s, 1H), 8.09 (q, 1H, J= 1 Hz). Found: C, 51.97; H, 3.09; N, 11.27%. Calcd for $C_{11}H_8N_2OCl_2$: C, 51.79; H, 3.16; N, 10.98%.

*1-(2,6-Dichlorobenzoyl)indazole (**19**)*: Mp 151.5—152.5 °C; IR (Nujol) 1690 cm^{-1}; NMR($CDCl_3$) δ=7.32 (s, 3H), 7.2—7.8 (m, 3H), 8.07 (s, 1H), 8.55 (broad, d, 1H, J=8 Hz). Found: C, 57.81; H, 2.67; N, 9.61%. Calcd for $C_{14}H_8N_2OCl_2$: C, 57.76; H, 2.77; N, 9.62%.

*1-(2,6-Dichlorobenzoyl)imidazole (**20**)*: Mp 60.5—61.5 °C; IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ=7.06—7.20 (broad, 1H), 7.3—7.5 (broad, 4H), 7.76—7.9 (broad, 1H). Found: C, 49.73; H, 2.43; N, 11.65%. Calcd for $C_{10}H_6N_2OCl_2$: C, 49.82; H, 2.51; N, 11.62%.

*1-(2,6-Dichlorobenzoyl)-2-methylimidazole (**21**)*: Mp 120.5—121.0 °C; IR (Nujol) 1730 cm^{-1}; NMR ($CDCl_3$) δ=2.68 (s, 3H), 6.64—6.90 (m, 2H), 7.32(s, 3H). Found: C, 51.51; H, 3.32; N, 10.99%. Calcd for $C_{11}H_8N_2OCl_2$: C, 51.79; H, 3.16; N, 10.98%.

*1-(2,6-Dichlorobenzoyl)-2-phenylimidazole (**22**)*: Mp 102.5—104.0 °C; IR (Nujol) 1710 cm^{-1}; NMR ($CDCl_3$) δ=7.10—7.63 (m, 10H). Found: C, 60.39; H, 3.10; N, 8.73%. Calcd for $C_{16}H_{10}N_2OCl_2$: C, 60.59; H, 3.18; N, 8.83%.

*1-(Phenylsulfonyl)pyrrole (**10**).* To a stirred solution of pyrrole (149 mmol) and sodium hydride (149 mmol) in *N,N*-dimethylformamide (200 ml), benzenesulfonyl chloride (149 mmol) was added dropwise under nitrogen at 0 °C. Then the mixture was stirred at room temperature for 3 h and poured into an excess of ice-cooled water to give **10** (80.5 mmol; 54% yield based on pyrrole used): Mp 88—89 °C (lit,[8] 89.0—89.5 °C).

*General Procedure for the Stoichiometric Alkenylation of Pyrroles (**1**), (**2a**), (**4**), (**6**), (**8**), and (**10**), and Pyrazoles (**13**), (**15**), and (**17**) with palladium Acetate and Alkyl Acrylates.* A solution of the pyrroles or the pyrazoles (1 mmol), alkyl acrylates (3 mmol), and palladium acetate (1 mmol) in acetic acid (40 ml) was heated at reflux temperature in air. The reaction mixture was evaporated to give a brown residue which was then chromatographed on a silica-gel plate, developed by benzene or chloroform, to give alkyl 3-(2-pyrrolyl)- or 3-(4-pyrazolyl)acrylates. The results are summarized in Table 1. The spectral and analytical data are given below.

*Methyl (E)-3-[1-(2,6-Dichlorobenzoyl)-2-pyrrolyl]acrylate (**2a**)*: Mp 110.5—111.5 °C; IR (Nujol) 1720, 1700, 1630 cm^{-1}; NMR ($CDCl_3$) δ=3.79 (s, 3H), 6.23 (t, 1H, J=3.5 Hz), 6.27 (d, 1H, J=16 Hz), 6.5—6.9 (m, 2H), 7.35 (s, 3H), 8.45 (d, broad, 1H, J=16 Hz); Mass: m/z (rel. intensity) 325 (13), 323 (19), 175 (65), 173 (100). Found: C, 55.62; H, 3.46; N, 4.56%. Calcd for $C_{15}H_{11}NO_3Cl_2$: C, 55.58; H, 3.42; N, 4.32%.

*(E)-Ethyl 3-[1-(2,6-Dichlorobenzoyl)pyrrol-2-yl]acrylate (**2b**)*: Mp 133—134 °C; IR (Nujol) 1710, 1705, 1620 cm^{-1}; NMR ($CDCl_3$) δ=1.31 (t, 3H, J=7 Hz), 4.22 (q, 2H, J=7 Hz), 6.23 (t, 1H, J=3.5 Hz), 6.26 (d, 1H, J=16 Hz), 6.5—6.9 (m, 2H), 7.34 (s, 3H), 8.4 (d, broad, 1H, J=16 Hz); Mass: m/z (rel. intensity) 339 (7), 337 (11), 175 (65), 173 (100). Found: C, 56.74; H, 3.93; N, 4.19%. Calcd for $C_{16}H_{13}NO_3Cl_2$: C, 56.82; H, 3.87; N, 4.14%.

*Dimethyl (E,E)-3,3'-[1-(2,6-Dichlorobenzoyl)pyrrole-2,5-diyl]diacrylate (**3a**)*: Mp 166—168 °C; IR (Nujol) 1710 (broad), 1615 cm^{-1}; NMR ($CDCl_3$) δ=3.67 (s, 6H), 6.08 (d, 2H, J= 16 Hz), 6.63 (s, 2H), 7.30 (s, 3H), 7.50 (d, 2H, J=16 Hz). Mass: m/z (rel. intensity) 409 (8), 407 (12), 175 (65), 173 (100). Found: C, 56.15; H, 3.65; N, 3.42%. Calcd for $C_{19}H_{15}NO_5Cl_2$: C, 55.90; H, 3.70; N, 3.43%.

*Diethyl (E,E)-3,3'-[1-(2,6-Dichlorobenzoyl)pyrrole-2,5-diyl]diacrylate (**3b**)*: Mp 153—154 °C; IR (Nujol) 1710 (broad), 1615 cm^{-1}; NMR ($CDCl_3$) δ=1.28 (t, 6H, J=7 Hz), 4.14 (q, 4H, J=7 Hz), 6.13 (d, 2H, J=16 Hz), 6.68 (s, 2H), 7.37 (s, 3H), 7.53 (d, 2H, J=16 Hz); Mass: 437 (5), 435 (7), 175 (63), 173 (100). Found: C, 58.07; H, 4.47; N, 3.41%. Calcd for $C_{21}H_{19}NO_5Cl_2$: C, 57.81; H, 4.39; N, 3.21%.

*Methyl (E)-3-[4-Acetyl-1-(2,6-dichlorobenzoyl)-3,5-dimethyl-2-pyrrolyl]acrylate (**5a**)*: Mp 121—123 °C; IR (Nujol) 1720, 1660 1625 cm^{-1}; NMR ($CDCl_3$) δ=2.21 (s, 3H), 2.48 (s, 3H), 2.53 (s, 3H), 3.65 (s, 3H), 5.68 (d, 1H, J=16 Hz), 7.18 (d, 1H, J= 16 Hz), 7.30 (s, 3H); Mass: m/z (rel. intensity) 395 (9), 393 (14), 175 (63), 173 (100). Found: C, 57.59; H, 4.63; 3.70%. Calcd for $C_{19}H_{17}NO_4Cl_2$: C, 57.88; H, 4.35; N, 3.55%.

*Ethyl (E)-3-[4-Acetyl-1-(2,6-dichlorobenzoyl)-3,5-dimethyl-2-pyrrolyl]acrylate (**5b**)*: Mp 114—116 °C; IR (Nujol) 1710 (broad),

1660, 1625 cm^{-1}; NMR ($CDCl_3$) δ=1.26 (t, 3H, J=7 Hz), 2.22 (s, 3H), 2.50 (s, 3H), 2.56 (s, 3H), 4.12 (q, 2H, J=7 Hz), 5.68 (d, 1H, J=16 Hz), 7.16 (d, 1H, J=16 Hz), 7.33 (s, 3H); Mass: m/z (rel. intensity) 409 (8), 407 (13), 175 (63), 173 (100). Found: C, 58.65; H, 4.71; N, 3.20%. Calcd for $C_{20}H_{19}NO_4Cl_2$: C, 58.84; H, 4.69; N, 3.43%.

*Methyl (E)-3-[1-(2,6-Dichlorobenzoyl)-5-formyl-2-pyrrolyl]acrylate (**7a**)*: Mp 182.0—183.5 °C; IR (Nujol) 1720, 1705, 1675, 1630 cm^{-1}; NMR ($CDCl_3$) δ=3.70 (s, 3H), 6.19 (d, 1H, J=16 Hz), 6.65 (d, 1H, J=3.5 Hz), 7.10—7.55 (m, 2H), 7.33 (s, 3H), 9.72 (s, 1H); Mass: m/z (rel. intensity) 353 (4), 351 (6), 175 (62), 173 (100). Found: C, 54.67; H, 3.06; N, 4.12%. Calcd for $C_{16}H_{11}NO_4Cl_2$: C, 54.41; H, 3.14; N, 3.97%.

*Ethyl (E)-3-[1-(2,6-Dichlorobenzoyl)-5-formyl-2-pyrrolyl]acrylate (**7b**)*: Mp 145—147 °C; IR (Nujol) 1710 (broad), 1675, 1630 cm^{-1}; NMR ($CDCl_3$) δ=1.26 (t, 3H, J=7 Hz), 4.13 (q, 2H, J=7 Hz), 6.20 (d, 1H, J=16 Hz), 6.63 (d, 1H, J=3.5 Hz), 7.06—7.53 (m, 2H), 7.33 (s, 3H), 9.73(s, 1H); Mass: m/z (rel. intensity) 367 (4), 365 (6), 175 (64), 173 (100). Found: C, 55.56; H, 3.50; N, 3.89%. Calcd for $C_{17}H_{13}NO_4Cl_2$: C, 55.61; H, 3.57; N, 3.81%.

*Methyl (E)-3-[1-(2,6-Dichlorobenzoyl)-2,5-dimethyl-3-pyrrolyl]acrylate (**9a**)*: Mp 117—118 °C; IR (Nujol) 1725, 1700, 1635 cm^{-1}; NMR ($CDCl_3$) δ=2.07 (s, broad, 3H), 2.26 (s, broad, 3H), 3.76 (s, 3H), 6.05 (d, 1H, J=16 Hz), 6.14 (s, 1H), 7.33 (s, 3H), 7.60 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 353 (11), 351 (17), 175 (65), 173 (100). Found: C, 58.14; H, 4.43; N, 3.96%. Calcd for $C_{17}H_{15}NO_3Cl_2$: C, 57.92; H, 4.29; N, 3.98%.

*Ethyl (E)-3-[1-(2,6-Dichlorobenzoyl)-2,5-dimethyl-3-pyrrolyl]acrylate (**9b**)*: Mp 126.5—127.5 °C; IR (Nujol) 1715, 1635 cm^{-1}; NMR ($CDCl_3$) δ=1.30 (t, 3H, J=7 Hz), 2.07 (s, broad, 3H), 2.25 (s, broad, 3H), 4.23 (q, 2H, J=7 Hz), 6.05 (d, 1H, J=16 Hz), 6.14 (s, 1H), 7.35 (s, 3H), 7.58 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 367 (12), 365 (17), 175 (65), 173 (100). Found: C, 58.77; H, 4.73; N, 3.76%. Calcd for $C_{18}H_{17}NO_3Cl_2$: C, 59.03; H, 4.68; N, 3.82%.

*Ethyl (E)-3-[1-(Phenylsulfonyl)-2-pyrrolyl]acrylate (**11b**)*: Mp 78—79 °C; IR (Nujol) 1705, 1625, 1370, 1185 (broad) cm^{-1}; NMR ($CDCl_3$) δ=1.32 (t, 3H, J=7 Hz), 4.24 (q, 2H, J=7 Hz), 6.12 (d, 1H, J=16 Hz), 6.35 (t, 1H, J=3.5 Hz), 6.4—6.8 (m, 1H), 7.2—7.9 (m, 6H), 8.07 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 305 (33), 141 (25), 136 (26), 119 (47), 77 (100). Found: C, 58.90; H, 4.83; N, 4.59%. Calcd for $C_{15}H_{15}NO_4S$: C, 59.00; H, 4.95; N, 4.89%.

*Diethyl (E,E)-3,3'-[1-(Phenylsulfonyl)pyrrole-2,5-diyl]diacrylate (**12b**)*: Mp 85—86 °C; IR (Nujol) 1705, 1620, 1380, 1370, 1175 (broad) cm^{-1}; NMR ($CDCl_3$) δ=1.32 (t, 6H, J=7 Hz), 4.25 (q, 4H, J=7 Hz), 6.16 (d, 2H, J=16 Hz), 6.64 (s, 2H), 7.2—8.0 (m, 5H), 8.24 (d, 2H, J=16 Hz); Mass: m/z (rel. intensity) 404 (25), 403 (100), 262 (63). Found: C, 59.54; H, 5.25; N, 3.56%. Calcd for $C_{20}H_{21}NO_6S$: C, 59.57; H, 5.25; N, 3.47%.

*Methyl (E)-3-[1-(2,6-Dichlorobenzoyl)-4-pyrazolyl]acrylate (**14a**)*: Mp 164—166 °C; IR (Nujol) 1730, 1700, 1660 cm^{-1}; NMR ($CDCl_3$) δ=3.75 (s, 3H), 6.27 (d, 1H, J=16 Hz), 7.32 (s, 3H), 7.52 (d, 1H, J=16 Hz), 7.82 (s, 1H), 8.42 (s, 1H); Mass: m/z (rel. intensity) 326 (6), 324 (8), 291 (10), 289 (28), 175 (66), 173 (100). Found: C, 51.85; H, 2.91; N, 8.56%. Calcd for $C_{14}H_{10}N_2O_3Cl_2$: C, 51.72; H, 3.10; N, 8.62%.

*Ethyl (E)-3-[1-(2,6-Dichlorobenzoyl)-4-pyrazolyl]acrylate (**14b**)*: Mp 133—134 °C; IR (KBr) 1725, 1695, 1660, 1620 cm^{-1}; NMR ($CDCl_3$) δ=1.33 (t, 3H, J=7 Hz), 4.27 (q, 2H, J=7 Hz), 6.32 (d, 1H, J=16 Hz), 7.38 (s, 3H), 7.58 (d, 1H, J=16 Hz), 7.89 (s, 1H), 8.49 (s, 1H); Mass: m/z (rel. intensity) 340 (6), 338 (9), 305 (11), 303 (32), 175 (63), 173 (100). Found: C, 53.32; H, 3.49; N, 8.14%. Calcd for $C_{15}H_{12}N_2O_3Cl_2$: C, 53.12; H, 3.57; N, 8.26%.

*Methyl (E)-3-[1-(2,6-Dichlorobenzoyl)-3,5-dimethyl-4-pyrazolyl]acrylate (**16a**)*: Mp 176—178 °C; IR (KBr) 1725, 1705, 1660, 1620 cm^{-1}; NMR ($CDCl_3$) δ=2.28 (s, 3H), 2.80 (s, 3H), 3.79 (s, 3H), 6.20 (d, 1H, J=16 Hz), 7.32 (s, 3H), 7.62 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 354 (7), 352 (10), 319 (17), 317 (49), 175 (65), 173 (100). Found: C, 54.33; H, 3.89; N, 7.80%. Calcd for $C_{16}H_{14}N_2O_3Cl_2$: C, 54.40; H, 4.00; N, 7.93%.

*Ethyl (E)-3-[1-(2,6-Dichlorobenzoyl)-3,5-dimethyl-4-pyrazolyl]acrylate (**16b**)*: Mp 161—163 °C; IR (KBr) 1725, 1710, 1660, 1620 cm^{-1}; NMR ($CDCl_3$) δ=1.32 (t, 3H, J=7 Hz), 2.27 (s, 3H), 2.81 (s, 3H), 4.27 (q, 2H, J=7 Hz), 6.21 (d, 1H, J=16 Hz), 7.33 (s, 3H), 7.62 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 368 (10), 366 (14), 333 (25), 331 (69), 175 (65), 173 (100). Found: C, 55.77; H, 4.37; N, 7.52%. Calcd for $C_{17}H_{16}N_2O_3Cl_2$: C, 55.60; H, 4.39; N, 7.63%.

*Methyl (E)-3-[2-(2,6-Dichlorobenzoyl)-4-methyl-2H-pyrazol-3-yl]acrylate (**18a**)*: Mp 161—162 °C; IR (Nujol) 1730—1710 (broad), 1660 cm^{-1}; NMR($CDCl_3$) δ=2.24 (s,3H), 3.83 (s, 3H), 6.30 (d, 1H, J=16 Hz), 7.33 (s, 3H), 7.52 (s, 1H), 8.40 (d, 1H, J=16 Hz); Mass: m/z (rel. intensity) 340 (10), 338 (14), 305 (9), 303(25), 175 (64), 173 (100); High-resolution Mass: m/z 338.0206 (M^+). Found: C, 52.62; H, 3.46; N, 8.21%. Calcd for $C_{15}H_{12}N_2O_3Cl_2$: C, 53.12; H, 3.57; N, 8.26%.

*Palladium Acetate-catalyzed Alkenylation of **1** and of **13** with Methyl Acrylate.* A solution of **1** or **13** (1 mmol), methyl acrylate (3 mmol), re-oxidants (listed in Table 2), and palladium acetate (0.1 mmol) in acetic acid (40 ml) was heated at reflux temperature in air for 16 h. The reaction mixture was evaporated to give a brown residue which was chromatographed on a silica-gel plate, developed by benzene or chloroform, to give alkenyl-substituted pyrroles (**2a**) and (**3a**) and pyrazole (**14a**). The results are summarized in Table 2.

Carboxylation of Methylbenzenes with Carbon Monoxide and Palladium Acetate. Carbon monoxide was bubbled through the stirred solution of methylbenzenes (10 mmol) in acetic acid (40 ml) containing palladium acetate (1 mmol) at reflux temperature for 7 h. The reaction mixture was evaporated and chromatorgaphed on a silica-gel column with benzene/ether to give methylbenzoic acids: 2,5-dimethylbenzoic acid (**26**) (0.16 mmol, 16% yield based on palladium acetate used); 2,4,6-trimethylbenzoic acid (**30**) (0.43 mmol, 43% yield); pentamethylbenzoic acid (**32**) (0.21 mmol, 21% yield): Mp 207—210 °C (lit,[17] 211 °C); IR (Nujol) 3300—2300, 1700 cm^{-1}; NMR ($CDCl_3$) δ=2.19 (s, broad, 9H), 2.27 (s, broad, 6H), 10.0 (s, broad, 1H). The structures of **26** and **30** were confirmed by comparing the IR spectra with those of the commercially available samples.

*Methyl (E)-2,5-Dimethylcinnamate (**27**).* A solution of *p*-xylene (**25**) (10 mmol), methyl acrylate (3 mmol), and palladium acetate (1 mmol) in acetic acid (40 ml) was stirred at reflux temperature in air for 7 h. The mixture was evaporated to give a brown residue which was chromatographed on a silica-gel plate, developed by a mixture of hexane and ether (1:1) to give **27** (0.50 mmol, 50% yield based on palladium acetate used): Bp 100 °C/10 Torr. (1 Torr=133.322 Pa); IR (Nujol) 1745, 1725, 1640 cm^{-1}; NMR($CDCl_3$) δ=2.32 (s, 3H), 2.36 (s, 3H), 3.78 (s, 3H), 6.29 (d, 1H, J=16 Hz), 7.00—7.35 (m, 3H), 3H), 7.91 (d, 1H, J=16 Hz). Found: C, 75.53; H, 7.63%. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42%.

(E)-2,5-Dimethylcinnamic Acid (28). A solution of **27** (1.85 mmol) and sodium hydroxide (52.5 mmol) in a mixture of methanol (50 ml) and water (50 ml) was heated at reflux temperature in air for 7 h. The mixture was poured into an excess of ice-cooled water and neutralized with dilute hydrochloric acid to give **28** as a crystalline product (1.70 mmol, 92% yield): Mp 130—132°C; IR (Nujol) 1690, 1620, 1610 cm^{-1}; NMR ($CDCl_3$) δ=2.32 (s, 3H), 2.39 (s, 3H), 6.32 (d, 1H, J=16 Hz), 7.06 (s, broad, 2H), 7.35 (s, broad, 1H), 8.03 (d, 1H, J=16 Hz), 10.14 (s, broad, 1H). Found: C, 74.97; H, 6.86%. Calcd for $C_{11}H_{12}O_2$: C, 74.72; H, 6.87%.

The authors wish to thank Professors Tsunao Hase and Tsutomu Sakakibara of Kagoshima University for their support throughout the study, and Dr. Tetsuo Iwagawa for his mass-spectrometric analyses.

References

1) For a review; I. Moritani and Y. Fujiwara, *Synthesis*, **1973**, 524.
2) R. Asano, I. Moritani, Y. Fujiwara, and S. Teranishi, *Bull. Chem. Soc. Jpn.*, **46**, 663 (1973).
3) Y. Fujiwara, O. Maruyama, M. Yoshidomi, and H. Taniguchi, *J. Org. Chem.*, **46**, 851 (1981).
4) T. Itahara, M. Ikeda, and T. Sakakibara, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1361.
5) T. Itahara, *J. Chem. Soc., Chem. Commun.*, **1981**, 254.
6) T. Itahara, M. Hashimoto, and H. Yumisashi, *Synthesis*, **1984**, 255.
7) T. Itahara and F. Ouseto, *Synthesis*, **1984**, 488.
8) T. Itahara, K. Kawasaki, and F. Ouseto, *Synthesis*, **1984**, 236.
9) R. X. Xu, H. J. Anderson, N. J. Gogan, C. E. Loader, and R. McDonald, *Tetrahedron Lett.*, **1981**, 4899; J. Rokach, P. Hamel, and M. Kakushima, *Tetrahedron Lett.*, **1981**, 4901.
10) E. P. papadopoulos and N. F. Haider, *Tetrahedron Lett.*, **1968**, 1721.
11) M. Watanabe, M. Yamamura, I. Moritani, Y. Fujiwara, and A. Sonoda, *Bull. Chem. Soc. Jpn.*, **47**, 1035 (1974).
12) P. M. Henry, *Tetrahedron Lett.*, **1968**, 2285; Ger. Pat. Dos 2340592; Y. Fujiwara, T. Kawauchi, and H. Taniguchi, *J. Chem. Soc., Chem. Commun.*, **1980**, 220; Y. Fujiwara, I. Kawata, H. Sugimoto, and H. Taniguchi, *J. Organomet. Chem.*, **256**, C35 (1983).
13) T. Itahara, *Chem. Ind. (London)* **1982**, 599.
14) T. Tisue and W. J. Downs, *J. Chem. Soc., Chem. Commun.*, **1969**, 410; P. M. Henry, *J. Org. Chem.*, **36**, 1886 (1971); R. O. C. Norman, W. J. E. Parr, and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 1*, **1974**, 369.
15) P. W. Alley and D. A. Shirley, *J. Am. Chem. Soc.*, **80**, 6271, (1958); R. Huttel and M. E. Schön, *Justus Liebigs Ann. Chem.*, **625**, 55 (1959); D. E. Butler and S. M. Alexander, *J. Org. Chem.*, **37**, 215 (1972).
16) D. A. Shirley, B. H. Gross, and P. A. Roussel, *J. Org. Chem.*, **20**, 225 (1955); D. J. Chadwick and C. Willbe, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 887; D. J. Chadwick and I. A. Cliffe, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 2845; D. J. Chadwick and S. T. Hodgson, *J. Chem. Soc., Perkin Trans. 1*, **1982**, 1833.
17) O. Jacobson, *Ber.*, **19**, 1214 (1886).