

A Palladium-catalyzed Synthesis of 2-Substituted Indoles.

Akira K_{ASAHARA}^{*}, Taeko I_{ZUMI}^{*}, Hiroshi Y_{ANAI}^{*}, Satoshi M_{URAKAMI}^{*},
Sachiko Y_{USA}^{*}, Hidehiro K_{ON}^{*}, Tokio K_{IKUCHI}^{*}, Shigeo T_{SUDA}^{*},
Naoto K_{UDO}^{*}, Masayuki T_{AKATORI}^{**}, and Takeshi N_{IKAJI}^{**}

^{*} *Department of Applied Chemistry, Faculty of Engineering*

^{**} *Department of Chemistry, Faculty of Education,
Fukushima University*

(Received August 26, 1985)

Abstract

In the presence of palladium (II) acetate, tri-*o*-tolylphosphine, and triethylamine, *o*-bromoaniline derivatives react readily with olefins such as ethylene, 1-hexene, styrene, ethyl acrylate, and acrylonitrile, to produce *o*-alkenylaniline derivatives. A palladium (II)-catalyzed cyclization of *o*-alkenylaniline *p*-toluenesulfonamide led to a formation of a number of 1-tosylindole derivatives.

Introduction

The search for an efficient synthesis of indoles has been a problem for nearly a century in organic synthesis. Beginning with the classical Fischer and Reissert methods, many reports have appeared from practical and academic points of view.¹⁾ On the other hand, a variety of heterocyclic compounds can be synthesized by using palladium-catalyzed intramolecular functionalization of olefins as the ring-forming step.²⁾ In this way, *o*-allylphenols were converted to benzofurans,³⁾ α , β -unsaturated ketoxime to isoxazoles⁴⁾ or pyridines,⁵⁾ 2'-hydroxychalcones to flavones,⁶⁾ and acryloylurea to uracils.⁷⁾ Hegedus *et al.* have recently reported the synthesis of indoles from *o*-allylanilines,⁸⁾ from 2-ethenylaniline,⁸⁾ and from 2-ethenylaniline *p*-toluenesulfonamides⁹⁾

by a palladium-assisted cyclization reaction. Independently of their work, although we also reported a palladium-assisted synthesis of 3-substituted indoles in two steps from *o*-bromoanilines,¹⁰⁾ we wish now to report an efficient synthesis of 2-substituted indoles based on a variety of palladium-catalyzed reaction of *o*-bromoanilines.

Results and Discussion

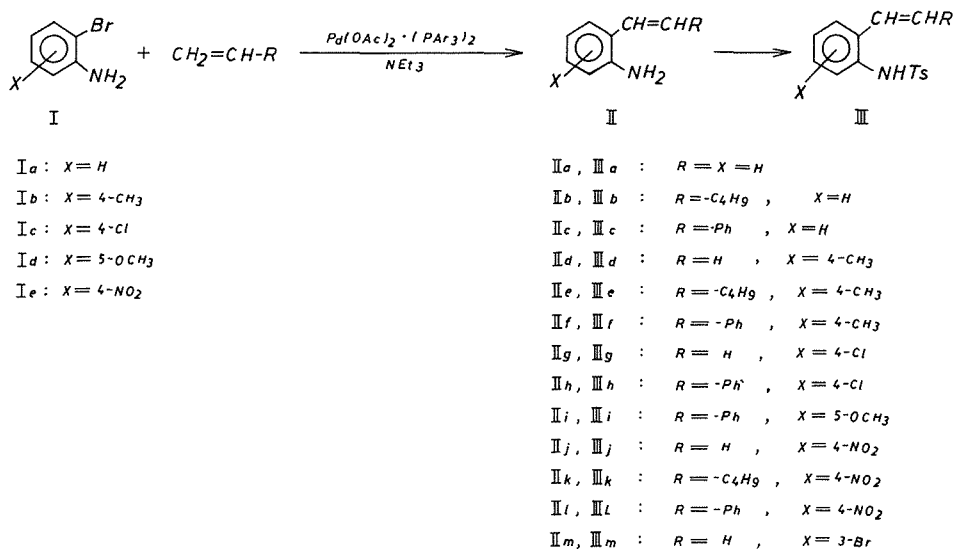
Preparation of 2-alkenylanilines.

General methods for the synthesis of 2-alkenylanilines appear to be the reduction of the corresponding nitro compounds which are in turn prepared from 2-nitrobenzyl bromides and aldehydes. While adequate for the preparation of simple compounds such as 2-ethenylanilines,¹¹⁾

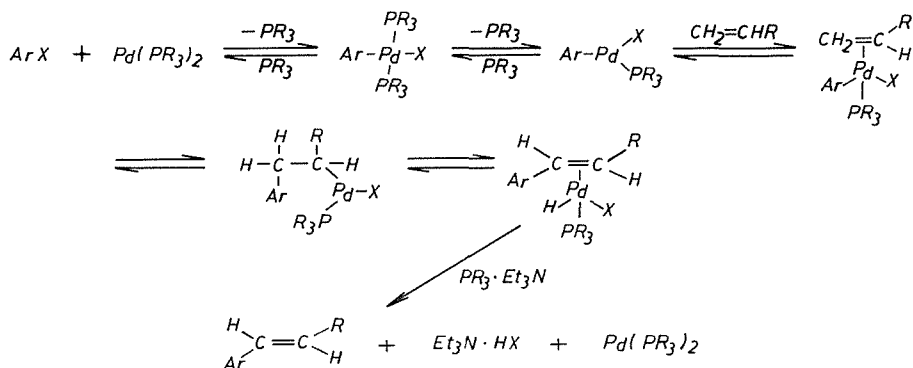
and 3-bromo-2ethenylanilines,⁹⁾ the reaction of 2-nitrobenzyl bromides and aldehydes are severe to tolerate many functional groups. The Heck reaction¹²⁾ of olefins with aromatic halides afforded a more general approach to a variety of 2-alkenylaniline (II) from *o*-bromo-aniline (I) (Scheme 1).

Table 1 summarized our use of the

approach. In the presence of palladium (II) acetate, tri-*o*-tolylphosphine, triethylamine, I reacts readily with olefins such as ethylene, 1-hexene, and styrene to produce II in 65~85% yields. The mechanism of the reaction involves the formation of an organopalladium halide by an oxidative addition followed by addition the olefin and elimination of HPdX.



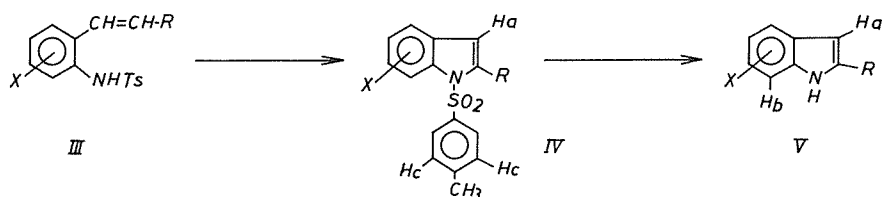
Scheme 1



Scheme 2

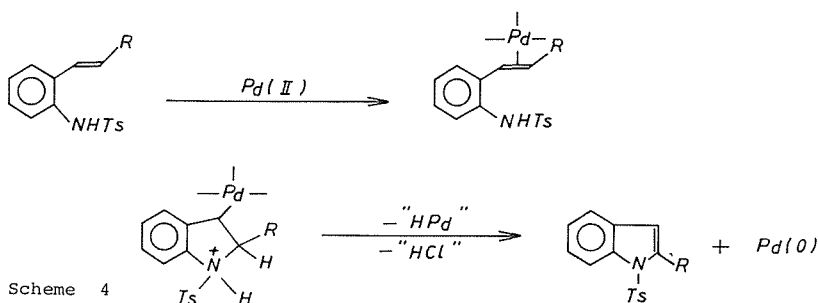
Cyclization reaction of o-alkenylanilines (II). Hegedus *et al.*⁸⁾ have previously reported that 2-ethenylaniline (**IIa**) cyclized smoothly to indole when treated with a catalytic amount of palladium(II) chloride and oxidizing conditions, however, analogous attempts to cyclize 3-bromo-2-ethenylaniline (**IIm**) to 4-bromoindole (**IVo**) were unsuccessful⁹⁾. They have also reported⁹⁾ that palladium(II)-catalyzed closure of acetanilides of **IIm** to 1-acetyl-4-bromoindole was slow, however, an analogous closure of *p*-toluenesulfonamide (**IIIm**) of **IIm** to 4-bromo-1-tosylindole was considerably fast. In our case, a palladium (II)-catalyzed closure

of 4-methyl-2-styrylaniline (**IIf**) to 4-methyl-2-phenylindole (**Vf**) and of N-acetyl derivative of **IIf** to 1-acetyl derivative of **Vf** were unsuccessful, however, *p*-toluenesulfonamide (**IIIf**) was readily converted to 5-methyl-2-phenyl-1-tosylindole (**IVf**), by a palladium-assisted cyclization is shown in Scheme 3, and the results are summarized in Table 2. A possible course of the reaction is shown in Scheme 4, although this route has not been experimentally verified. It is based on analogy to other well-established amination procedures.^{8,13)} Finally, base hydrolysis of the N-tosylindole (**IV**) gave the required indoles (**V**).



$IV_a, V_a :$	$R = X = H$
$IV_b, V_b :$	$R = -C_4H_9, \quad X = H$
$IV_c, V_c :$	$R = -Ph, \quad X = H$
$IV_d, V_d :$	$R = H, \quad X = 5-CH_3$
$IV_e, V_e :$	$R = -C_4H_9, \quad X = 5-CH_3$
$IV_f, V_f :$	$R = -Ph, \quad X = 5-CH_3$
$IV_g, V_g :$	$R = H, \quad X = 5-Cl$
$IV_h, V_h :$	$R = -Ph, \quad X = 5-Cl$
$IV_i, V_i :$	$R = H, \quad X = 6-OCH_3$
$IV_j, V_j :$	$R = -C_4H_9, \quad X = 6-OCH_3$
$IV_k, V_k :$	$R = -Ph, \quad X = 6-OCH_3$
$IV_l, V_l :$	$R = H, \quad X = 5-NO_2$
$IV_m, V_m :$	$R = -C_4H_9, \quad X = 5-NO_2$
$IV_n, V_n :$	$R = -Ph, \quad X = 5-NO_2$
$IV_o, V_o :$	$R = H, \quad X = 4-Br$

Scheme 3



Scheme 4

Table 1 The reaction of *o*-bromoanilines(I) with alkenes

starting materials		product	yield(%)
<i>o</i> -bromoaniline	alkene		
Ia	ethylene	2-vinylaniline (IIa)	82
Ia	1-hexene	2-(1-hexenyl)aniline (IIb)	74
Ia	styrene	2-styrylaniline (IIc)	80
Ib	ethylene	4-methyl-2-vinylaniline (IId)	81
Ib	1-hexene	2-(1-hexenyl)-4-methylaniline (IIe)	75
Ib	styrene	4-methyl-2-styrylaniline (IIf)	77
Ic	ethylene	4-chloro-2-vinylaniline (IIg)	65
Ic	styrene	4-chloro-2-styrylaniline (IIh)	67
Id	styrene	5-methoxy-2-styrylaniline (IIi)	74
Ie	ethylene	4-nitro-2-vinylaniline (IIj)	85
Ie	1-hexene	2-(1-hexenyl)-4-nitroaniline (IIk)	84
Ie	styrene	4-nitro-2-styrylaniline (IIl)	81

Table 2 The properties of 2-alkenylanilines(**IIa-l**).

compound	IR (cm ⁻¹), ¹ H-NMR (δ, ppm)
IIa	pale yellow oil, bp 102–104°C/10mmHg (lit. ¹⁸) bp 111.7–111.9°C/28mmHg).
IIb	pale yellow oil, bp 116–118°C/7 mmHg. IR (neat) : 3450, 3350 (NH ₂), 1600, 1500, 750 (<i>o</i> -disubstituted benzene ring), 1620, 970 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 0.89 (t, 3 H, CH ₃), 1.36 (m, 4 H, -CH ₂ CH ₂ -), 2.08 (m, -C=C-CH ₂ -), 3.88 (br-s, 2 H, NH ₂), 6.29 (m, 1 H, -C=CH-CH ₂ -), 6.58 (d, 1 H, -CH=C-CH ₂ -), 6.98–7.18 (m, 4 H, Ar-H). Found : C, 82.05; H, 9.71; N, 7.86%; M ⁺ , 175. Calcd for C ₁₂ H ₁₇ N: C, 82.23; H, 9.78; N, 7.99%; M, 175.
IIc	colorless crystals, mp 105–107°C (lit. ¹⁹) mp 106°C).
IId	pale yellow oil, bp 120–122°C/8 mmHg. IR (neat) : 3450, 3360 (NH ₂), 1600, 1500, 880, 815 (1, 2, 4-trisubstituted benzene ring), 1620, 990, 920 (-CH=CH ₂). ¹ H-NMR (CDCl ₃) : 2.25 (s, 3 H, CH ₃), 3.80 (br-s, 2 H, NH ₂), 5.31, 5.70, 6.60 (ABX type m, 3 H, -CH=CH ₂), 6.94–7.16 (m, 3 H, Ar-H). Found: C, 81.05; H, 8.19; N, 10.44%; M ⁺ , 148. Calcd for C ₉ H ₁₁ N: C, 81.16; H, 8.33; N, 10.52%; M, 148.
IIe	pale yellow oil, bp 125–127°C/7 mmHg. IR (neat) : 3450, 3350 (NH ₂), 1600, 1500, 880, 810 (1, 2, 4-trisubstituted benzene ring), 1620, 970 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 0.88 (t, 3 H, CH ₃), 1.40 (m, 4 H, -CH ₂ CH ₂ -), 2.10 (m, 2 H, -C=C-CH ₂ -), 2.26 (s, 3 H, Ar-CH ₃), 3.94 (br-s, 2 H, NH ₂), 6.34 (m, 1 H, -C=CH-CH ₂ -), 6.71 (d, 1 H, Ar-CH=C-), 7.01–7.23 (m, 3 H, Ar-H). Found: C, 82.27; H, 9.94; N, 7.25%; M ⁺ , 189. Calcd for C ₁₃ H ₁₉ N: C, 82.48; H, 10.12; N, 7.40%; M, 189.

Table 2 (continued- 1)

compound	IR (cm ⁻¹), ¹ H-NMR (δ, ppm)
IIf	colorless crystals, mp 108–109°C. IR (KBr) : 3450, 3350 (NH ₂), 1600, 1500, 890, 820 (1, 2, 4-trisubstituted benzene ring), 760, 690 (monosubstituted benzene ring), 1630, 985 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 2.23 (s, 3H, CH ₃), 3.58 (br-s, 2H, NH ₂), 6.68 (d, 1H, Ar-H, J=8.0 Hz), 6.89–7.62 (m, 9H, Ar-H + -CH=CH-). Found: C, 85.97; H, 7.11; N, 6.76%; M ⁺ , 209. Calcd for C ₁₅ H ₁₅ N: C, 86.08; H, 7.22; N, 6.69%; M, 209.
Ilg	pale yellow oil, bp 144–146 °C/ 4 mmHg. IR (neat) : 3450, 3350 (NH ₂), 1600, 1500, 880, 810 (1, 2, 4-trisubstituted benzene ring). 1620, 990, 920 (-CH=CH ₂). ¹ H-NMR (CDCl ₃) : 4.00 (br-s, 2H, NH ₂), 5.27, 5.65, 6.63 (ABX type m, 3H, -CH=CH ₂), 6.89–7.20 (m, 3H, Ar-H). Found: C, 62.50; H, 5.13; N, 9.04%; M ⁺ , 153. Calcd for C ₈ H ₈ ClN: C, 62.55; H, 5.25; N, 9.12%; M, 153.
IIfh	pale yellow crystals, mp 77–78°C, IR (KBr) : 3450, 3350 (NH ₂), 1600, 1500, 870, 810 (1, 2, 4-trisubstituted benzene ring), 755, 690 (monosubstituted benzene ring), 1630, 970 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 3.78 (br-s, 2H, NH ₂), 6.65 (d, 1H, Ar-H), 6.97–7.60 (m, 9H, -CH=CH- + Ar-H). Found: C, 70.12; H, 5.81; N, 6.73%; M ⁺ , 205. Calcd for C ₁₂ H ₁₂ ClN: C, 70.07; H, 5.88; N, 6.80; M, 205.
III	Colorless crystals, mp 114–115°C. IR (KBr) : 3450, 3350 (NH ₂), 1600, 1500, 880, 820 (1, 2, 4-trisubstituted benzene ring), 760, 690 (monosubstituted benzene ring), 1630, 960 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 3.83 (s, 3H, OCH ₃), 3.98 (br-s, 2H, NH ₂), 6.89–7.24 (m, 10H, Ar-H + -CH=CH-). Found: C, 79.93; H, 6.65; N, 6.03%; M ⁺ , 225. Calcd for C ₁₅ H ₁₅ NO: C, 79.97; H, 6.71, N, 6.22%; M, 225.
IIj	pale yellow crystals, mp 93–94°C. IR (KBr) : 3450, 3350 (NH ₂), 1600, 1500, 900, 830 (1, 2, 4-trisubstituted benzene ring), 1570, 1310 (NO ₂), 1630, 990, 910 (-CH=CH ₂). ¹ H-NMR (CDCl ₃) : 3.87 (br-s, 2H, NH ₂), 5.44, 5.80, 6.71 (ABX type, 3H, -CH=CH ₂), 6.95–8.40 (m, 3H, Ar-H). Found: C, 51.33; H, 5.68; N, 19.85%; M ⁺ , 140. Calcd for C ₆ H ₈ N ₂ O ₂ : C, 51.42; H, 5.75; N, 19.99; M, 140.
IIk	yellow oil, bp 168–169 °C/ 4 mmHg. IR (neat) : 3450, 3350 (NH ₂), 1600, 1500, 900, 830 (1, 2, 4-trisubstituted benzene ring), 1570, 1300 (NO ₂), 1620, 970 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 0.88 (t, 3H, CH ₃), 1.38 (m, 4H, -CH ₂ CH ₂ -), 2.08 (m, 2H, -C=C-CH ₂ -), 3.80 (br-s, 2H, NH ₂), 6.41 (m, 1H, -C=CH-CH ₂ -), 6.92–8.33 (m, 4H, Ar-CH= + Ar-H). Found: C, 65.33; H, 7.21; N, 12.65%; M ⁺ , 220. Calcd for C ₁₂ H ₁₆ N ₂ O ₂ : C, 65.43; H, 7.32; N, 12.72%; M, 220.
III	yellow crystals, mp 134–136°C. IR (KBr) : 3450, 3350 (NH ₂), 1600, 1500, 820, 755, 690 (benzene ring), 1570, 1300 (NO ₂), 1640, 970 (trans-CH=CH-). ¹ H-NMR (CDCl ₃) : 4.08 (br-s, 2H, NH ₂), 6.87–8.40 (m, 10H, -CH=CH- + Ar-H). Found: C, 69.81; H, 4.88; N, 11.60%; M ⁺ , 240. Calcd for C ₁₄ H ₁₂ N ₂ O ₂ : C, 69.99; H, 5.03; N, 11.66; M, 240.

Table 3 The tosylation of 2-alkenylanilines (**IIa-1**)

2-alkenylanilines	product	yield (%)
IIa	N-tosyl-2-vinylaniline (IIIa)	78
IIb	N-tosyl-2-(1-hexenyl)aniline (IIb)	82
IIc	N-tosyl-2-styrylaniline (IIc)	85
IId	N-tosyl-4-methyl-2-vinylaniline (IId)	75
IIf	N-tosyl-2-(1-hexenyl)-4-methylaniline (IIf)	72
IIg	N-tosyl-4-methyl-2-styrylaniline (IIg)	80
IIh	N-tosyl-4-chloro-2-vinylaniline (IIh)	65
IIi	N-tosyl-4-chloro-2-styrylaniline (IIi)	73
IIj	N-tosyl-5-methoxy-2-styrylaniline (IIj)	76
IIk	N-tosyl-4-nitro-2-vinylaniline (IIk)	73
III	N-tosyl-4-nitro-2-vinylaniline (III)	65
	N-tosyl-4-nitro-2-vinylaniline (III)	68

Table 4 The properties of N-tosyl-2-alkenylanilines (**IIIa-1**).

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
IIIa	colorless crystals, mp 119–120°C. IR: 3200 (NH), 1600, 1500, 820, 750 (benzene ring), 1620, 980, 910 ($-\text{CH}=\text{CH}_2$), 1330, 1160 (SO_2-NH). $^1\text{H-NMR}$: 2.37 (s, 3 H, CH_3), 5.27, 5.50, 6.70 (ABX type, 3 H, $-\text{CH}=\text{CH}_2$), 6.78 (br-s, 1 H, NH), 6.93–7.60 (m, 8 H, Ar-H). Found: C, 65.82; H, 5.44; N, 4.97%; M^+ , 273. Calcd for $\text{C}_{15}\text{H}_{15}\text{NO}_2\text{S}$: C, 65.91; H, 5.53; N, 5.12%; M , 273.
IIIb	colorless crystals, mp 40–42°C. IR: 3200 (NH), 1600, 1500, 820, 750 (benzene ring), 1630, 975 (trans- $-\text{CH}=\text{CH}-$), 1335, 1160 ($-\text{SO}_2-\text{NH}-$). $^1\text{H-NMR}$: 0.89 (t, 3 H, CH_3), 1.38 (m, 4 H, $-\text{CH}_2\text{CH}_2-$), 2.17 (m, 2 H, $-\text{C}=\text{CH}-\text{CH}_2-$), 2.29 (s, 3 H, Ar- CH_3), 6.28 (m, 1 H, $-\text{C}=\text{CH}-\text{CH}_2-$), 6.51 (br-s, 1 H, NH), 6.82–7.38 (m, 9 H, Ar-H + Ar-CH-), Found: C, 69.14; H, 6.88; N, 4.07%; M^+ , 329. Calcd for $\text{C}_{19}\text{H}_{23}\text{NO}_2\text{S}$: C, 69.26; H, 7.03; N, 4.25%; M , 329.
IIIc	colorless crystals, mp 144–146°C. IR: 3270 (NH), 1500, 1500, 820, 760, 745, 690 (benzene ring), 1620, 970 (trans- $-\text{CH}=\text{CH}-$), 1330, 1160 ($-\text{SO}_2-\text{NH}-$). $^1\text{H-NMR}$: 2.27 (s, 3 H, CH_3), 6.67–7.64 (m, 16 H, Ar-H + NH + $-\text{CH}=\text{CH}-$). Found: C, 72.05; H, 5.37; N, 3.95%; M^+ , 349. Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}_2\text{S}$: C, 72.18; H, 5.48; N, 4.00%; M , 349.
IIId	colorless crystals, mp 118–119°C. IR: 3250 (NH), 1600, 1500, 890, 820 (benzene ring). $^1\text{H-NMR}$: 2.27 (s, 3 H, CH_3), 2.37 (s, 3 H, CH_3), 5.21, 5.47, 6.66 (ABX type, 3 H, $-\text{CH}=\text{CH}_2$), 6.77 (br-s, 1 H, NH), 6.93–7.60 (m, 7 H, Ar-H). Found: C, 66.79; H, 5.90; N, 4.83%; M^+ , 287. Calcd for $\text{C}_{16}\text{H}_{17}\text{NO}_2\text{S}$: C, 66.87; H, 5.96; N, 4.87%; M , 287.

Table 4 (continued-1)

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
IIIe	colorless crystals, mp 91–93°C. IR : 3275(NH), 1600, 1500, 895, 815(benzene ring), 1630, 970(trans-CH=CH-), 1330, 1170(-SO ₂ -NH). $^1\text{H-NMR}$: 0.86(t, 3H, CH ₃), 1.35(m, 4H, -CH ₂ -), 2.73(m, 2H, -C=C-CH ₂ -), 2.31(s, 3H, Ar-CH ₃), 6.58(m, 1H, C=CH-C), 6.75–7.00(m, 8H, NH + Ar-CH=C- + Ar-H). Found: C, 69.87; H, 7.25; N, 3.96%; M ⁺ , 343. Calcd for C ₂₀ H ₂₅ NO ₂ S: C, 69.93; H, 7.33; N, 4.07%; M, 343.
IIIf	colorless crystals, mp 123–125°C. IR : 3250(NH), 1600, 1500, 890, 810, 760, 690(benzene ring), 1620, 950(trans-CH=CH-), 1320, 1140(SO ₂ -NH-). $^1\text{H-NMR}$: 2.24(s, 3H, CH ₃), 2.31(s, 3H, CH ₃), 6.57(s, 1H, NH), 6.76–7.70(m, 14H, -CH=CH- + Ar-H). Found: C, 72.61; H, 5.75; N, 3.68%; M ⁺ , 363. Calcd for C ₂₂ H ₂₁ NO ₂ S: C, 72.69; H, 5.84; N, 3.85%; M, 363.
IIIg	colorless crystals, mp 122–123°C. IR : 3250(NH), 1600, 1500, 880, 815(benzene ring), 1620, 980, 910(-CH=CH ₂), 1330, 1160(SO ₂ -NH-). $^1\text{H-NMR}$: 2.37(s, 3H, CH ₃), 5.27, 5.62, 6.63(ABX type, 3H, -CH=CH ₂), 7.06–7.62(m, 8H, -NH + Ar-H). Found: C, 58.45; H, 4.51; N, 4.47%; M ⁺ , 308. Calcd for C ₁₅ H ₁₄ ClNO ₂ S: C, 58.53; H, 4.58; N, 4.55%; M, 308.
IIIh	colorless crystals, mp 161–163°C. IR : 3270(NH), 1600, 1500, 890, 820, 755, 690(benzene ring), 1630, 960(trans-CH=CH-), 1330, 1160(SO ₂ -NH-). $^1\text{H-NMR}$: 2.22(s, 3H, CH ₃), 6.28–7.62(m, 15H, NH + -CH=CH- + Ar-H). Found: C, 65.45; H, 4.58; N, 3.53%; M ⁺ , 384. Calcd for C ₂₁ H ₁₈ ClNO ₂ S: C, 65.57; H, 4.72; N, 3.64%; M, 384.
IIIi	colorless crystals, mp 96–97°C. IR : 3225(NH), 1600, 1500, 890, 820, 760, 690(benzene ring), 1630, 960(trans-CH=CH-), 1320, 1150(SO ₂ -NH-). $^1\text{H-NMR}$: 2.25(s, 3H, CH ₃), 3.83(s, 3H, OCH ₃), 6.65–7.58(m, 15H, NH + -CH=CH- + Ar-H). Found: C, 69.54; H, 5.46; N, 3.60%; M ⁺ , 379. Calcd for C ₂₂ H ₂₁ NO ₃ S: C, 69.63; H, 5.57; N, 3.69%; M, 379.
IIIj	colorless crystals, mp 135–137°C. IR : 3320(NH), 1600, 1500, 895, 820 (benzene ring), 1620, 985, 930(-CH=CH ₂), 1520, 1350(NO ₂), 1340, 1170 (SO ₂ -NH-). $^1\text{H-NMR}$: 2.27(s, 3H, CH ₃), 5.35, 5.68, 6.63(ABX type, 3H, -CH=CH ₂), 6.98–8.35(m, 8H, NH + Ar-H). Found: C, 56.41; H, 4.34; N, 8.65%; M ⁺ , 318. Calcd for C ₁₅ H ₁₄ N ₂ O ₄ S: C, 56.59; H, 4.43; N, 8.79%; M, 318.
IIIk	colorless crystals, mp 95–96°C. IR : 3275(NH), 1600, 1500, 890, 815(benzene ring), 1620, 970(trans-CH=CH-), 1510, 1345(NO ₂), 1340, 1170 (SO ₂ -NH-). $^1\text{H-NMR}$: 0.89(t, 3H, CH ₃), 1.31(m, 4H, -CH ₂ -), 2.18(m, 2H, -C=C-CH ₂ -), 2.31(s, 3H, CH ₃), 6.54(m, 1H, Ar-C=CH-), 6.88–8.35(m, 9H, NH + Ar-CH=C- + Ar-H). Found: C, 60.91; H, 5.79; N, 7.45%; M ⁺ , 374. Calcd for C ₁₉ H ₂₂ N ₂ O ₄ S: C, 60.94; H, 5.92; N, 7.48%; M, 374.

Table 4 (continued-- 2)

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
III	colorless crystals, mp 162–164°C. IR : 3250(NH), 1600, 1500, 890, 820, 750, 690(benzene ring), 1630, 970(trans-CH=CH-), 1510, 1350(NO_2), 1330, 1160($\text{SO}_2\text{-NH-}$). $^1\text{H-NMR}$: 2.33(s, 3H, CH_3), 6.87–8.40(m, 15H, $\text{NH} + \text{-CH=CH-} + \text{Ar-H}$). Found: C, 63.88; H, 4.48; N, 7.02%; M^+ , 394. Calcd for $\text{C}_{21}\text{H}_{18}\text{N}_2\text{O}_4\text{S}$: C, 63.94; H, 4.59; N, 7.10%; M, 394.

Table 5 The Palladium-assisted cyclization of **IIIa-1**.

starting material	product	yield (%)
IIIa	1-tosylindole (IVa)	70
IIIb	2-butyl-1-tosylindole (IVb)	64
IIIc	2-phenyl-1-tosylindole (IVc)	62
IIId	5-methyl-1-tosylindole (IVd)	60
IIIe	2-butyl-5-methyl-1-tosylindole (IVe)	54
IIIf	5-methyl-2-phenyl-1-tosylindole (IVf)	65
IIIg	5-chloro-1-tosylindole (IVg)	74
IIIh	5-chloro-2-phenyl-1-tosylindole (IVh)	72
IIIi	6-methoxy-2-phenyl-1-tosylindole (IVi)	65
IIIj	5-nitro-1-tosylindole (IVj)	58
IIIk	2-butyl-5-nitro-1-tosylindole (IVk)	55
IIIl	5-nitro-2-phenyl-1-tosylindole (IVl)	62

Table 6 The properties of 1-tosylindoles (**IVa-1**).

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
IVa	colorless crystals, mp 78–79°C. IR : 1600, 1500, 820, 750(benzene ring), 1370, 1170($\text{SO}_2\text{N-}$). $^1\text{H-NMR}$: 2.29(s, 3H, CH_3), 6.67(d, 1H, Ha, $J=4.0\text{Hz}$), 7.05–7.67(m, 6H, benzene ring + indole $\text{C}_2\text{-H}$), 7.78(d, 2H, Hc, $J=8.0\text{Hz}$), 8.24(d, 1H, Hb). Found: C, 66.22; H, 4.75; N, 5.01%; M^+ , 271. Calcd for $\text{C}_{15}\text{H}_{13}\text{NO}_2\text{S}$: C, 66.39; H, 4.82; N, 5.16%; M, 271.
IVb	colorless crystals, mp 92–93°C. IR : 1600, 1500, 745(benzene ring), 1370, 1170($\text{SO}_2\text{N-}$). $^1\text{H-NMR}$: 0.94(t, 3H, CH_3), 1.31–1.80(m, 4H, $-\text{CH}_2\text{CH}_2-$), 2.39(s, 3H, Ar-CH_3), 2.93(t, 2H, indole- CH_2-), 6.36(s, 1H, Ha), 7.08–7.44(m, 5H, Ar-H), 7.59(d, 2H, Hc), 8.11–8.21(m, 1H, Hb). Found: C, 69.55; H, 6.41; N, 4.19%; M^+ , 327. Calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{S}$: C, 69.69; H, 6.46; N, 4.27%; M, 327.

Table 6 (continued-1)

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
IVc	colorless crystals, mp 149–150°C. IR : 1600, 1500, 820, 770, 760, 700 (benzene ring), 1370, 1170 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.24 (s, 3 H, CH_3), 6.51 (s, 1 H, Ha), 7.02–7.42 (m, 10H, Ar-H), 7.58 (d, 2 H, Hc), 8.33 (d, 1 H, Hd). Found: C, 72.50; H, 4.85; N, 3.94%; M^+ , 347. Calcd for $\text{C}_{21}\text{H}_{17}\text{NO}_2\text{S}$: C, 72.59; H, 4.93; N, 4.03%; M, 347.
IVd	colorless oil. IR : neat : 1600, 1500, 880, 810 (benzene ring), 1370, 1170 ($\text{SO}_2\text{N}-$), $^1\text{H-NMR}$: 2.28 (s, 3 H, CH_3), 2.38 (s, 3 H, CH_3), 6.58 (d, 1 H, Ha, $J=4.0\text{Hz}$), 7.04–7.38 (m, 3 H, Ar-H), 7.51 (d, 1 H, indole $\text{C}_2\text{-H}$, $J=4.0\text{Hz}$), 7.68 (d, 2 H, Hc, $J=8.0\text{Hz}$), 8.28 (m, 1 H, Hb). Found: C, 67.22; H, 5.16; N, 4.78%; M^+ , 285. Calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_2\text{S}$: C, 67.34; H, 5.29; N, 4.90%; M, 285.
IVe	colorless crystals, mp 85–86°C. IR: 1600, 1500, 890, 810 (benzene ring), 1370, 1170 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 0.90 (t, 3 H, CH_3), 1.17–1.75 (m, 4 H, $-\text{CH}_2\text{CH}_2-$), 2.20 (s, 3 H, Ar- CH_3), 2.31 (s, 3 H, Ar- CH_3), 2.96 (t, 2 H, indole $-\text{CH}_2-$), 6.28 (s, 1 H, Ha), 6.92–7.22 (m, 4 H, Ar-H), 7.58 (d, 2 H, Hc), 8.03 (d, 1 H, Hb). Found: C, 70.24; H, 6.65; N, 3.87%; M^+ , 341. Calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_2\text{S}$: C, 70.34; H, 6.78; N, 4.10%; M, 341.
IVf	colorless crystals, mp 111–112°C. IR : 1600, 1500, 890, 810, 760, 690 (benzene ring), 1375, 1175 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.21 (s, 3 H, Ar- CH_3), 2.37 (s, 3 H, Ar- CH_3), 6.46 (s, 1 H, Ha), 6.96 (m, 9 H, Ar-H), 7.56 (d, 2 H, Hc), 8.18 (d, 1 H, Hb). Found: C, 72.97; H, 5.20; N, 3.81%; M^+ , 361. Calcd for $\text{C}_{22}\text{H}_{19}\text{NO}_2\text{S}$: C, 73.10; H, 5.29; N, 3.87%; M, 361.
IVg	colorless crystals, mp 82–83°C. IR : 1600, 1500, 880, 820 (benzene ring), 1370, 1170 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.28 (s, 3 H, CH_3), 6.58 (d, 1 H, Ha, $J=4.0\text{Hz}$), 7.11–7.48 (m, 4 H, Ar-H), 7.58 (d, 1 H, indol $\text{C}_2\text{-H}$, $J=4.0\text{Hz}$), 7.67 (d, 2 H, Hc, $J=8.0\text{Hz}$), 8.21 (m, 1 H, Hc). Found: C, 58.84; H, 3.85; N, 4.51%; M^+ , 306. Calcd for $\text{C}_{15}\text{H}_{12}\text{ClNO}_2\text{S}$: C, 58.92; H, 3.95; N, 4.58%; M, 306.
IVh	colorless crystals, mp 141–142°C. IR : 1600, 1500, 890, 820, 770, 690 (benzene ring), 1360, 1170 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.26 (s, 3 H, CH_3), 6.58 (s, 1 H, Ha), 6.99–7.42 (m, 9 H, Ar-H), 7.56 (d, 2 H, Hc), 8.24 (m, 1 H, Hb). Found: C, 65.91; H, 4.13; N, 3.57%; M^+ , 382. Calcd for $\text{C}_{21}\text{H}_{16}\text{ClNO}_2\text{S}$: C, 66.05; H, 4.22; N, 3.66; M, 382.
IVi	colorless crystals, mp 135–136°C. IR : 1600, 1500, 830, 810, 760, 690 (benzene ring), 1360, 1160 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.28 (s, 3 H, Ar- CH_3), 3.94 (s, 3 H, OCH_3), 6.48 (s, 1 H, Ha), 7.06–7.38 (m, 9 H, Ar-H), 7.50 (d, 2 H, Hc), 7.93 (s, 1 H, Hb). Found: C, 69.87; H, 4.93; N, 3.60%; M^+ , 377. Calcd for $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{S}$: C, 70.00; H, 5.07; N, 3.71%; M, 377.
IVj	colorless crystals, mp 82–83°C. IR : 1600, 1500, 890, 810 (benzene ring), 1510, 1340 (NO_2), 1390, 1170 ($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.32 (s, 3 H, CH_3), 6.81 (d, 1 H, Ha, $J=4.0\text{Hz}$), 7.28 (d, 2 H, tosyl-H, $J=8.0\text{Hz}$), 7.74 (d, 1 H, indol $\text{C}_2\text{-H}$, $J=4.0\text{Hz}$), 7.80 (d, 2 H, Hc), 8.07–8.11 (m, 3 H, indol-H + Hb). Found: C, 56.84; H, 3.71; N, 8.70%; M^+ , 316. Calcd for $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$: C, 56.95; H, 3.82; N, 8.83%; M, 316.

Table 6 (continued-2)

compound	IR (KBr), cm^{-1} , $^1\text{H-NMR}$ (CDCl_3), δ , ppm
IVk	colorless crystals, mp 108–109°C. IR : 1600, 1500, 895, 810(benzene ring), 1510, 1350(NO_2), 1370, 1170($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 0.94(t, 3 H, CH_3), 1.22–1.85(m, 4 H, $-\text{CH}_2\text{CH}_2-$), 2.34(s, 3 H, Ar-CH_3), 3.02(t, 2 H, indole- CH_2-), 6.54(s, 1 H, Ha), 7.27(d, 2 H, tosyl-H adjacent to CH_3 , $J=8.0\text{Hz}$), 7.69(d, 2 H, Hc, $J=8.0\text{Hz}$), 8.02–8.38(m, 3 H, $\text{Ar-H} + \text{Hb}$). Found: C, 61.13; H, 5.29; N, 7.39%; M^+ , 372. Calcd for $\text{C}_{19}\text{H}_{20}\text{N}_2\text{O}_4\text{S}$: C, 61.27; H, 5.41; N, 7.52%; M, 372.
IVl	colorless crystals, mp 108–109°C. IR : 1600, 1500, 905, 820, 770, 715(benzene ring), 1515, 1350(NO_2), 1380, 1180($\text{SO}_2\text{N}-$). $^1\text{H-NMR}$: 2.31(s, 3 H, CH_3), 6.67(s, 1 H, Ha), 7.09(d, 2 H, tosyl-H adjacent to CH_3 , $J=8.0\text{Hz}$), 7.44(br-s, 5 H, Ar-H), 7.69(d, 2 H, Hc, $J=8.0\text{Hz}$), 8.11–8.56(m, 3 H, indol-H + Hb). Found: C, 64.18; H, 3.95; N, 7.06%; M^+ , 392. Calcd for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$: C, 64.27; H, 4.10; N, 7.13%; M, 392.

Table 7 Hydrolysis of **IVa-1**.

starting material	product	yield (%)
IVa	Indole (Va)	78
IVb	2-butylindole (Vb)	74
IVc	2-phenylindole (Vc)	80
IVd	5-methylindole (Vd)	75
IVe	2-butyl-5-methylindole (Ve)	86
IVf	5-methyl-2-phenylindole (Vf)	75
IVg	5-chloroindole (Vg)	78
IVh	5-chloro-2-phenylindole (Vh)	88
IVi	6-methoxy-2-phenylindole (Vi)	82
IVj	5-nitroindole (Vj)	85
IVk	2-butyl-5-nitroindole (Vk)	82
IVl	5-nitro-2-phenylindole (VI)	77

Table 8 The properties of indoles (**V**).

compound	IR (cm^{-1}), $^1\text{H-NMR}$ (δ , ppm)
Va	colorless crystals, mp 51–52°C, (lit. ²⁰), mp 52–53°C).
Vb	colorless crystals, mp 35–36°C, (lit. ²¹), mp 35–36°C).
Vc	colorless crystals, mp 187–189°C (lit. ²²), mp 186–188°C).
Vb	colorless crystals, mp 60°C (lit. ²³), mp 58.5°C).

Table 8 (continued-1)

compound	IR (cm ⁻¹), ¹ H-NMR (δ, ppm)
Ve	colorless crystals, mp 57–59°C. IR (KBr) : 3375(NH), 1600, 1500, 880, 815 (benzene ring). ¹ H-NMR (CDCl ₃) : 0.89(t, 3 H, CH ₃), 1.20–1.68(m, 4 H, –CH ₂ CH ₂ –), 2.38(s, 3 H, Ar-CH ₃), 2.59(t, 2 H, indole-CH ₂ –), 6.12(s, 1 H, Ha), 6.93–7.38(m, 3 H, Ar-H), 7.48(br-s, 1 H, NH). Found: C, 83.25; H, 9.07; N, 7.40%; M ⁺ , 187. Calcd for C ₁₃ H ₁₇ N: C, 83.37; H, 9.15; N, 7.48%; M, 187.
Vf	colorless crystals, mp 212–213°C, (lit. ²⁴), mp 213°C).
Vg	colorless crystals, mp 70–72°C, (lit. ²⁵), mp 71–72°C).
Vh	colorless crystals, mp 190–191°C, (lit. ²⁶), mp 191°C).
Vi	colorless crystals, mp 170–171°C. IR (KBr) : 3370(NH), 1600, 1500, 900, 815, 760, 700(benzene ring). ¹ H-NMR (CDCl ₃) : 3.87(s, 3 H, OCH ₃), 6.76(s, 1 H, Ha), 6.96–7.69(m, 9 H, Ar-H + NH). Found: C, 80.60; H, 5.81; N, 6.20%; M ⁺ , 223. Calcd for C ₁₅ H ₁₃ NO: C, 80.69; H, 5.87; N, 6.27%; M, 223.
Vj	yellow crystals, mp 132–134°C, (lit. ²⁷), mp 133–136°C).
Vk	yellow crystals, mp 105–105°C. IR (KBr) : 3300(NH), 1600, 1500, 890, 820, 770, 750(benzene ring), 1550, 1320(NO ₂). ¹ H-NMR (CDCl ₃) : 0.94(t, 3 H, CH ₃), 1.33–1.84(m, 4 H, –CH ₂ CH ₂ –), 2.80(t, 2 H, indole-CH ₂ –), 6.42(s, 1 H, Ha), 7.32(d, 1 H, Hb), 8.06(d-d, 1 H, indole-6 H), 8.39(br-s, 1 H, NH), 8.48(d, 1 H, indole-4 H). Found: C, 65.91; H, 6.37; N, 12.69%; M ⁺ , 218. Calcd for C ₁₂ H ₁₄ N ₂ O ₂ : C, 66.03; H, 6.47; N, 12.84%; M, 218.
VI	yellow crystals, mp 200–202°C, (lit. ²⁸), mp 201–203°C).

Experimental

Materials. All melting points are uncorrected. 2-Bromo-4-methylaniline (**Ib**),¹⁴⁾ 2-bromo-4-chloroaniline(**Ic**),¹⁵⁾ 2-bromo-5-methoxyaniline (**Id**),¹⁶⁾ and 2-bromo-4-nitroaniline (**Ie**)¹⁷⁾ were prepared by the method described in the literature.

Measurements. The IR spectra were measured on KBr disks with Hitachi 260-10 spectrometer, and ¹H NMR spectra were obtained by means of a Hitachi R-22 spectrometer in CDCl₃, using TMS as the internal standard. The mass spectra were obtained on a Hitachi RMU-6 M

mass spectrometer, using a direct insertion probe at an ionization energy of 70 eV.

General procedure for the palladium-catalysed reaction of o-bromoanilines (I**) with alkenes.** A mixture of 20 mmol of **I**, 25 mmol alkene, 0.044 g (0.2 mmol) of palladium(II) acetate, 0.364 g (1.2 mmol) of tri-*o*-tolylphosphine and 2.5 g (25 mmol) of triethylamine in 15 cm³ of acetonitrile was heated under nitrogen in a sealed tube at 100°C for 20 h. In the case of the reaction with ethylene, a mixture of 20 mmol of **I**, 0.2 mmol of palladium(II) acetate, 1.2 mmol of tri-*o*-tolylphosphine, and 25 mmol of triethylamine in 30 cm³ of

acetonitrile was stirred at 120°C under an ethylene pressure (15 atm) for 24 h. The cooled reaction mixture was diluted with ether and water. The ether phase was separated, washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated. The residue was then purified by column chromatography (silica gel, benzene-hexane (1:1)), followed by recrystallization from ethanol or benzene. The structure of the products was confirmed by a mixed-melting point determination with an authentic sample and by the observation of the IR, ¹H NMR and mass spectra. The results and the properties of the products (**II-1**) are summarized in Tables 1 and 2, respectively.

Preparation of N-tosyl-2-alkenylaniline (IIIa-1)

To a solution of *p*-toluenesulfonylchloride (3.0 g, 15.8 mmol) in dry pyridine (30 cm³), the compound (**IIa-1**, 14 mmol) in dry pyridine (20 cm³) was added at room temperature. After stirring for 36 h, the resulting mixture was poured into 450 cm³ of ice water. The precipitate was filtered, washed with water, and air-dried to afford tan solid. Recrystallization from ethanol afforded colorless crystals of **IIIa-1**. The results and the properties of **IIIa-1** are summarized in Tables 3 and 4, respectively.

The palladium assisted cyclization of IIIa-1 to N-tosylindoles (IVa-1).

A mixture of **IIIa-1** (10 mmol) and lithium chloropalladate(II) (10 mmol) in ethanol (80 cm³) was refluxed for 36 h with stirring. After cooling to room temperature, the solvent was removed *in vacuo*. The resulting residue was taken up in 200 cm³ of CHCl₃, washed with H₂O 3 times, dried (MgSO₄), filtered, and concentrated *in vacuo* to afford shiny beige crystals.

Purification by column chromatography (silica gel, benzene) followed by the recrystallization from ethanol afforded **IVa-1** as shiny colorless crystals. The results and the properties of **IV** are summarized in Tables 5 and 6, respectively.

Hydrolysis of IVa-1 to indoles (Va-1).

A mixture of **IVa-1** (6.0 mmol), ethanol (40 cm³), and 20% aqueous sodium hydroxide solution (30 cm³) was refluxed for 24 h under a nitrogen atmosphere. The resulting solution was cooled to room temperature and concentrated *in vacuo* until the solution became cloudy. The suspension was neutralized with 1 M HCl and then extracted with ether 3 times. The combined extracts were dried (MgSO₄), filtered, concentrated *in vacuo*, and recrystallized from ethanol or benzene to afford pale yellow crystals of **Va-1**.

References

- 1) Reviews: a) R.K.Brown: "Indoles, Part 1, Chemistry of Heterocyclic Compounds", W.J.Houlchan, Ed., Wiley-Interscience, New York, 1972, vol. 25, p 232-317.
b) R.J.Sundberg: "The Chemistry of Indoles", Academic Press, New York, 1970.
- 2) J.Tsuji: "Organic Synthesis with Palladium Compounds" Berlin, Springer-Verlag, 1980.
- 3) T.Hosokawa, S.Miyagi, S-I. Murahashi, and A.Sonoda: *J.Org. Chem.* **43**, 2752 (1978).
- 4) K.Maeda, T.Hosokawa, S-I. Murahashi, and I.Moritani: *Tetrahedron Lett.* **1973**, 5075.
- 5) T.Hosokawa, N.Shino, K.Maeda, A.Sonoda, and S-I. Murahashi: *Tetrahedron Lett.* **1976**, 383.

- 6) A.Kasahara, T.Izumi, and M.Ooshima: *Bull. Chem. Soc. Jpn.* **47**, 2526 (1974).
- 7) A.Kasahara and N.Fukuda: *Chem. Ind. (London)*, **1976**, 485.
- 8) L.S.Hegedus, G.F.Allen, J.J.Bozell, and E.L.Waterman: *J. Am. Chem. Soc.* **100**, 5800 (1978).
- 9) P.J.Harrington and L.S.Hegedus: *J. Org. Chem.* **49**, 2657 (1984).
- 10) A.Kasahara, T.Izumi, S.Murakami, and H.Yanai: *Bull. Chem. Soc. Jpn.*, **59** (1986), in Press.
- 11) M.Butcher, R.J.Mathews, and S.Middleton: *Aust. J. Chem.* **26**, 2067 (1973).
- 12) C.B.Ziegler, Jr. and R.F.Heck: *J. Org. Chem.* **43**, 2941 (1978).
- 13) B.Akermark, J.E.Backvall, L.S.Hegedus, K.Zetterberg, K.Siirala-Hansen, and K.Sjoberg: *J. Organometal. Chem.* **72**, 124 (1974).
- 14) J.R.Johnson and L.T.Sandobn: *Org. Synth.* coll vol. *II*, 111 (1956).
- 15) F.D.Chattawy and K.J.P.Orton: *Chem. Ber.* **33**, 2396 (1900).
- 16) H.H.Hodgson and R.J.H.Dyson: *J. Chem. Soc.* **1935**, 946.
- 17) B.H.Nicolet and W.L.Ray: *J. Am. Soc.* **49**, 1801 (1927).
- 18) W.S.Johnson and B.G.Buell: *J. Am. Chem. Soc.* **74**, 4517 (1952).
- 19) F.Sachs and S.Hilpert: *Chem. Ber.* **39**, 899 (1906).
- 20) F.T.Tyson: *Org. Synth.* coll. vol. **III**, 479 (1955).
- 21) L.S.Hegedus, P.M.Winton and S.Varaprath: *J. Org. Chem.* **46**, 2215 (1981).
- 22) R.L.Shriner, W.C.Ashley, and E.Welch: *Org. Synth.* coll. vol. **III**, 725 (1955).
- 23) O.Kruber: *Chem. Ber.* **59**, 2759 (1926).
- 24) C.Hansch, D.G.Crosby, M.Sadvski, A.Leo, and D.Percivil: *J. Am. Chem. Soc.* **73**, 704 (1951).
- 25) H.N.Rydon and J.C.Tweddle: *J. Chem. Soc.* **1955**, 3499.
- 26) F.Brown and F.G.Mann: *J. Chem. Soc.* **1948**, 858.
- 27) W.G.Goll, B.D.Astill, and V.Boekelheide: *J. Org. Chem.* **20**, 1538 (1955).
- 28) W.E.Noland, K.R.Rush, and L.R.Smith: *J. Org. Chem.* **31**, 65 (1966).