Synthesis of Indole Derivatives from *N*-Alkenyl-*o*-chloroanilines with Zero-valent Nickel Complex

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Reaction of *N*-alkenyl-*o*-chloroanilines in toluene with tetrakis(triphenylphosphine)nickel (0) was carried out mainly to give indole and indoline derivatives in good yields. A detailed analysis of the reaction products has been done and it allows us to confirm the postulated mechanism of the cyclization reaction. Torsional hindrance around the N-C-Csp^2 bond seems to prevent the cyclization reaction.

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Heterocyclic compounds have been obtained using arylnickel [1] and arylpalladium [2] complexes. Zero-valent nickel complexes of the Ni(PPh$_3$)$_n$-type obtained from the divalent nickel complexes with a reducing agent could react with a *N*-alkenyl-*o*-aryl halide in an ethereal solvent forming an arylnickel intermediate complex which cyclizes to provide heterocyclic compounds by an internal reaction between *ortho*-σ-nickel chloride and the double bond of the *N*-alkenyl chain.

We are interested in the general applicability of this reaction to the synthesis of indole derivatives starting from *N*-alkenyl-*o*-chloroaniline derivatives in toluene as the solvent and zero-valent tetrakis(triphenylphosphine)-nickel. The mechanism of the intramolecular cyclization can be deduced from these reaction products.

Results and Discussion.

The *N*-alkenyl-*o*-chloroanilines **1a-7a** used in the cyclization reaction with zero-valent tetrakis(triphenylphosphine)nickel and the products formed are summarized in Table 1.

Compounds **1a, 2a, 3a, 5a** and **6a** were obtained from *o*-chloroaniline, a conveniently functionalized allyl bromide and sodium carbonate following a reported method [3].

Compound **4a** was obtained by reaction in tetrahydrofuran of the *o*-chloroacetanilide with the 4-bromo-2-butenenitrile and a suspension of sodium hydride at room temperature. Only the (*E*)-isomer of **4a** was isolated in pure form and this shows a complex ^{1}H-nmr spectrum of the protons of the *N*-alkenyl chain, the methylene protons being diastereotopics [4].

Compound **7a** was obtained from the *N*-methyl-*o*-chloroanilide of the 3-cyclohexenylacetic acid by reduction with lithium aluminum hydride.

The zero-valent complex tetrakis(triphenylphosphine) nickel was obtained in toluene from anhydrous bis(acetylacetonate)nickel(II) and triethylaluminum as the reducing agent. Bis(acetylacetonate)nickel(II) was obtained from nickel(II) chloride dihydrate by addition of an ethanolic solution of potassium 2,4-pentanedioate and finally recrystallized from benzene. Compounds **1a-7a** were treated in toluene under a helium atmosphere with tetrakis(triphenylphosphine)nickel(0) obtained as indicated above in variable molar ratio of the reducing agent. In general the excess of the reducing agent remains during the reaction.

Thus, **1a** reacts in toluene with tetrakis(triphenylphosphine)nickel(0) to provide the indole **1b** and a product **1d** identified as *N*-methyl-*o*-ethylaniline, which results from

Scheme I

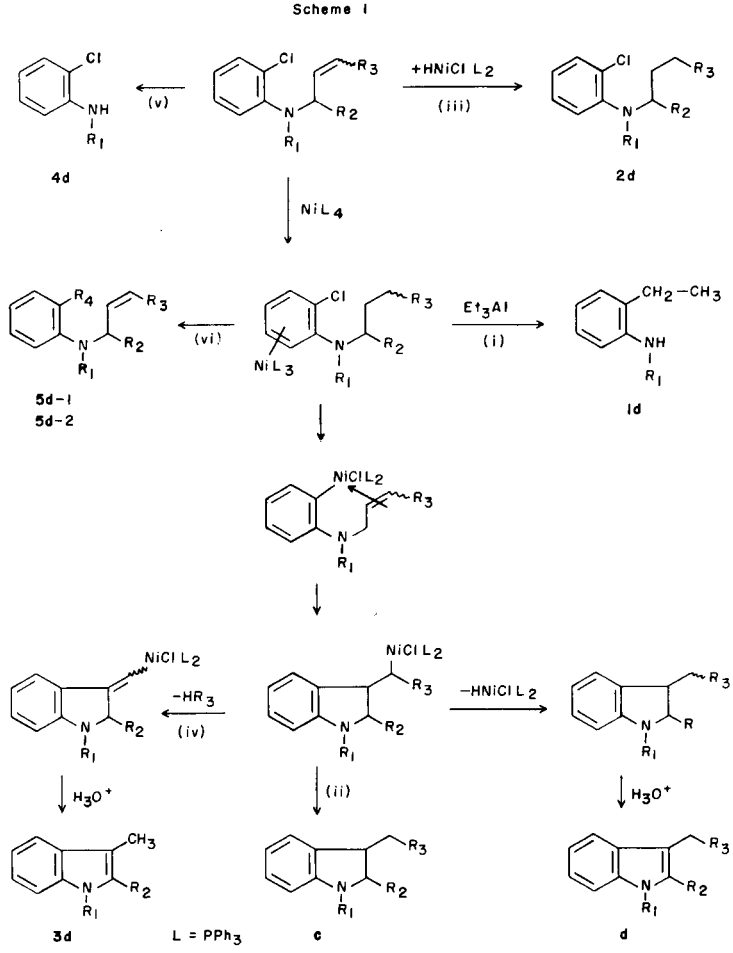
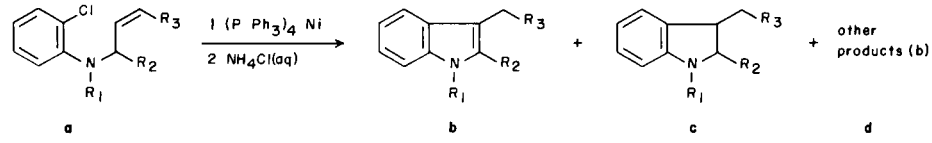
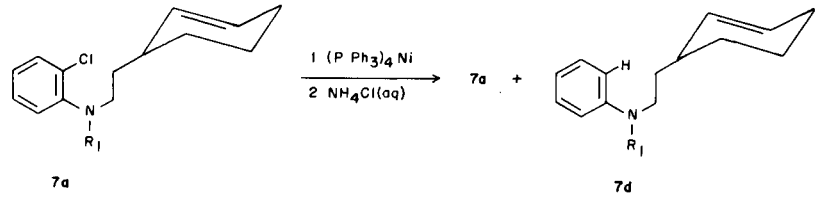


Table 1



a b c d

Compound	R^1	R^2	R^3	Isomer	X [a]	b	c	d
1a	CH_3	H	H	—	3	73	—	17
2a	CH_3	H	CN	(*Z*) + (*E*)	3	52	18	29
2a	CH_3	H	CN	(*Z*) + (*E*)	6	43	27	30
3a	CH_2CH_2CN	H	CN	(*E*)	3	40	52	6
3a	CH_2CH_2CN	H	CN	(*Z*)	3	35	60	5
4a	$COCH_3$	H	CN	(*E*)	3	—	—	80
4a	$COCH_3$	H	CN	(*E*)	1	50	—	40
5a	H	$-(CH_2)_3-$		(*Z*)	3	—	—	70 [c] 26 [d]
6a	CH_3	$-(CH_2)_3-$		(*Z*)	3	—	—	—



7a 7d

7a	CH_3	—	—	(*Z*)	3	—	—	11

[a] Molar relation of triethylaluminum to bis(acetylacetonate)nickel. [b] See Schemes 1 and 2. [c] Yield of the compound **5d-1**. [d] Yield of the compound **5d-2**.

1a by desallylation and nucleophilic substitution of the aromatic chlorine for an ethyl anion of the triethylalminum in excess, Scheme 1, (i).

Compound **2a** ((*E*) + (*Z*)-isomers) was treated with tetrakis(triphenylphosphine)nickel(0) prepared in a 1:6 molar ratio of bis(acetylacetonate)nickel(II) and triethylaluminum to give indole **2b**, indoline **2c** and a reduction product **2d**, identified as *N*-methyl-*N*-(3-cyanopropyl)-*o*-chloroaniline. When the reaction was carried out in a 1:3 molar ratio of bis(acetylacetonate)nickel(II) and triethylaluminum, indole **2b** and indoline **2c** were also isolated but the ratio of **2b** to **2c** increases while the reduction product **2d** remains constant. This product **2d** would be the result of the reduction of **2a** with the nickel hydride complex appearing in the formation of indole **2b**, Scheme 1, (iii).

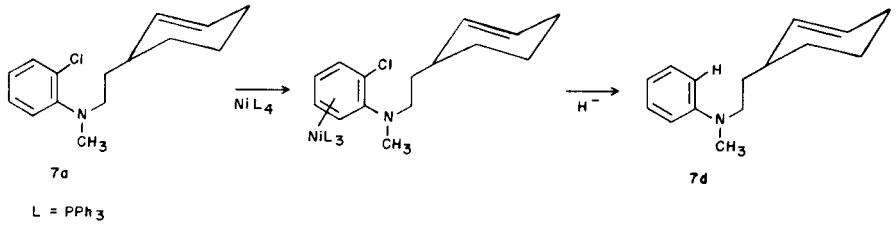
Stereochemistry involvements of the substituents on the terminal carbon of the olefinic bond has been analyzed with the (*E*)-and(*Z*)-isomers of **3a**. Compound (*E*)-**3a** was treated with tetrakis(triphenylphosphine)nickel obtained with molar ratio of 1:3 of bis(acetylacetonate)nickel(II) and triethylaluminum to provide the indole **3b**, the indoline **3c** and the *N*-β-cyanoethyl-3-methylindole, **3d**. This product would be formed by hydrocyanic acid elimination of the nickel σ-intermediate, Scheme 1, (iv).

Isomer (*Z*)-**3a** was treated under the same conditions as that of the (*E*)-isomer with tetrakis(triphenylphosphine)-nickel to give **3b**, **3c** and **3d** in analogous quantitative yield, and thus the (*E*)- and (*Z*)-isomers show the same reactivity with the zero-valent complex. On the other hand, indolines **2c** and **3c** obtained in the reaction of **2a** and **3a** with the zero-valent nickel reagent were transformed by refluxing in toluene with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone quantitatively to the indoles **2b** and **3b** respectively.

Compound (*E*)-**4a** was treated with tetrakis(triphenylphosphine)nickel with molar ratio of 1:3 of bis(acetylacetonate)nickel(II) and triethylaluminum to give only the desallylation product **4d** which was identified as *o*-chloroacetanilide, Scheme 1, (v). Desallylation of the alkenyl chain can occur by implication of the triethylaluminum in excess or the zero-valent nickel complex by coordination of the oxygen atom of the amide group to the metal. Thus, when the tetrakis(triphenylphosphine)nickel was obtained with a molar ratio of 1:1 of bis(acetylacetonate)nickel(II) and triethylaluminum, the desallylation product decreased and the indole **4b** was obtained in moderate yield.

Now, we are interested in the reaction of *N*-cyclohexenyl substrates that have apparently the geometrical requirements for the cyclization reaction. The reaction of com-

Scheme 2



pound **5a** with tetrakis(triphenylphosphine)nickel with a 1:3 molar ratio of bis(acetylacetonate)nickel(II) and triethylaluminum gave two main products **5d-1** and **5d-2**, but the starting product **5a** and cyclization products were not detected. Compounds **5d-1** can be the result of substitution of the chlorine atom of the aromatic ring for an ethyl anion of an excess triethylaluminum. Compound **5d-2** can be produced by direct substitution of the chlorine atom of the aromatic ring with a hydride ion generated from triethylaluminum or nickel hydride complex, Scheme 1, (vi). Compound **6a** was treated with zero-valent tetrakis(triphenylphosphine)nickel in a 1:3 molar ratio of bis(acetylacetonate)nickel(II) and triethylaluminum. Only the starting product **6a** was recovered.

The failure of the cyclization of **5a** and **6a** with the zero-valent complex suggested the preparation of **7a** which has torsional possibilities of the chain in order to close the double bond to the σ-nickel aromatic bond, Scheme 1. Compound **7a** was treated with tetrakis(triphenylphosphine)nickel in a 1:3 molar ratio of bis(acetylacetonate)-nickel(II) and triethylaluminum. The starting product was recovered in 74% and *N*-methyl,*N*-2-(Δ^2-cyclohexenyl)-ethylaniline (**7d**) was obtained in 11% yield. The product **7d** can result from the substitution of the chlorine atom of the aromatic ring for a hydride ion from triethylaluminum or the nickel hydride complex, Scheme 2.

Nucleophilic substitution of the chlorine atom of the aromatic ring with an ethyl or a hydride ion under the conditions required in those reaction can occur through the π-aryl nickel complex intermediate [5], Scheme 1 (i,vi) and Scheme 2.

On the basis of these results, the theory can be advanced that the cyclization reaction fails because of the torsional hindrance around the N-C-Csp^2 bond of the cyclohexenyl ring which avoids the π-effective orthogonal positioning of the double bond of the cyclohexenyl ring to the σ-nickel aromatic bond, Scheme 1.

EXPERIMENTAL

Melting points were measured on a hot stage microscope and are uncorrected. Infrared spectra were recorded on a Pye-Unicam SP-1100 spectrophotometer and nuclear magnetic resonance spectra on a Hitachi Perkin-Elmer R-24 A. Elemental analyses have been obtained with a Perkin-Elmer 240 analyzer. Mass spectra were recorded on a Hewlett-Packard 5985 gc/ms system. The solvents and reagents were purified and dried rigorously.

N-Allyl-*N*-methyl-*o*-chloroaniline (**1a**).

A mixture of *N*-methyl-*o*-chloroaniline [3] (2.83 g, 20 mmoles), allyl bromide (3.59 g, 29 mmoles) and solid sodium carbonate (1.73 g, 16 mmoles) in ethanol-water (4:1) was refluxed for 48 hours. After the ethanol was removed, the reaction mixture was diluted with water and the resultant aqueous layer was extracted with diethyl ether. The ethereal layer was dried (anhydrous sodium sulphate) and evaporated and the residual oil was purified by chromatography on silicagel eluting with *n*-hexane-diethyl ether (96:4) to give **1a** (2.43 g, 65%) as a colourless liquid which darkens upon standing, mp 84° (picrate); ir (film): 1650 (C=C); 930 (CH=CH$_2$); nmr (carbon tetrachloride): δ 7.35-6.75 (m, aromatic H, 4H), 6.25-5.60 (m, CH=, 1H), 5.30-5.00 (m, =CH$_2$, 2H), 3.60 (d, CH$_2$N, J = 6 Hz, 2H), 2.70 (s, CH$_3$N, 3H); ms: 154 (M$^+$ -27, 100), 138, 111.

Anal. Calcd. for $C_{16}H_{15}ClN_4O_7$(picrate): C, 46.7; H, 3.6; N, 13.6; Cl, 8.6. Found: C, 46.9; H, 3.3; N, 13.2; Cl, 8.6.

N-Methyl-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**2a**).

A mixture of *N*-methyl-*o*-chloroaniline (1.2 g, 8.4 mmoles), 4-bromo-2-butenenitrile [6] (2.0 g, 13 mmoles) and solid sodium carbonate (0.9 g, 8.4 mmoles) in ethanol-water (4:1) was refluxed for 48 hours. When ethanol was removed, the reaction mixture was diluted with water and the aqueous solution was extracted with diethyl ether. The ethereal layer was dried (anhydrous sodium sulphate) and evaporated and the residual oil was purified by chromatography on silicagel eluting with toluene-chloroform (7:3) to give **2a** (0.98 g, 82%) as a 2:1 ratio of the (*E*) + (*Z*) isomers as a yellow oil. It was not possible to separate the mixture of *E* and *Z* isomers by distillation, therefore the physical data on the *E* and *Z* isomers were obtained on samples obtained by chromatographic separation.

The (*E*)-isomer had nmr (carbon tetrachloride): δ 7.40-6.77 (m, aromatic H, 4H), 6.6 (dt, HC=C-CN, 1H, J = 18 and 5 Hz), 5.70 (dt, C=CH-CN, 1H, J = 18 and 2 Hz), 3.69 (dd, CH$_2$N, 2H, J = 5 and 2 Hz), 2.70 (s, CH$_3$N, 3H), ms: 206 (M$^+$), 171, 154 138 (100), 111, 91.

The (*Z*)-isomer had nmr (carbon tetrachloride): δ 7.40-6.77 (m, aromatic H, 4H), 7.40-6.77 and 6.6 (dt, HC=C-CN, 1H, J = 12 and 6 Hz), 5.45 (dt, C=CH-CN, 1H, J = 12 and 1 Hz), 3.95 (dd, CH$_2$N, 2H, J = 6 and 1 Hz), 2.75 (s, CH$_3$N, 3H); ms: 206 (M$^+$), 171, 154, 138 (100), 111, 91.

N-(β-Cyanoethyl)-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**3a**).

A mixture of *N*-(β-cyanoethyl)-*o*-chloroaniline [7] (1.8 g, 10 mmoles), 4-bromo-2-butenenitrile (2.17 g, 14 mmoles) and solid sodium carbonate (0.87 g, 8.2 mmoles) dissolved in ethanol-water (4:1) was refluxed for 52 hours. When the ethanol was removed, the reaction mixture was diluted with water and the resultant aqueous solution was extracted with chloroform. The chloroform layer was dried (anhydrous sodium sulphate) and evaporated and the residual oil was purified by chromatography on silica gel eluting with toluene-ethyl acetate (6:1) to give the two isolated (*E*)-(*Z*) isomers, (*E*) (0.46 g, 19%) and (*Z*) (0.24 g, 10%). The (*E*)-isomer of **3a** was a fluorescent yellow oil; ir (film): 2270 (CN), 2245 (CNα,β-unsaturated),

1645 (C=C); nmr (deuteriochloroform): δ 7.50-7.00 (m, aromatic H, 4H), 6.71 (dt, CH=, 1H, J = 16.8 and 6 Hz), 5.74 (dt, CH=, 1H, J = 16.8 and 2 Hz), 3.85 (dd, CH_2N, 2H, J = 6 and 2 Hz), 3.35 (t, CH_2N, 2H, J = 7 Hz) 2.38 (t, CH_2CN, 2H, J = 7 Hz); ms: 245 (M^+), 205, 139 (100), 138, 130, 111, 102.

Anal. Calcd. for $C_{13}H_{12}ClN_3$: C, 63.5; H, 4.9; N, 17.1; Cl, 14.4. Found: C, 63.4; H, 4.7; N, 16.8; Cl, 14.3.

The (*Z*)-isomer of **3a** was a brown oil; ir (film): 2270 (CN) 2240 (CN α,β-unsaturated), 1625 (C=C); nmr (deuteriochloroform): δ 7.5-7.0 (m, aromatic H, 4H), 6.6 (dt, CH=, 1H, J = 11 and 6 Hz), 5.45 (dt, CH=, 1H, J = 11 and 1.5 Hz), 4.15 (dd, CH_2N, 2H, J = 6 and 1.5 Hz), 3.40 (t, CH_2N, 2H, J = 7 Hz), 2.50 (t, CH_2CN, 2H, J = 7 Hz); ms: 245 (M^+), 205, 139 (100), 138, 129, 111, 102.

Anal. Calcd. for $C_{13}H_{12}ClN_3$: C, 63.5; H, 4.9; N, 17.1; Cl, 14.4. Found: C, 63.3; H, 4.6; N, 17.0; Cl, 14.3.

In the same reaction, when the time of reaction was 72 hours, the (*E*)-(*Z*)-isomers of **3a** were (*E*) (22%) and (*Z*) (11%).

N-Acetyl-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**4a**).

To a suspension of sodium hydride (0.24 g, 0.01 mole) in anhydrous tetrahydrofuran was added a solution of *o*-chloroacetanilide (1.69 g, 0.01 mole) in tetrahydrofuran under a stream of nitrogen. After the evolution of hydrogen ceased, a solution of 4-bromo-2-butenenitrile (1.46 g, 0.01 mole) in tetrahydrofuran was added and the mixture was stirred for 2 hours at room temperature. Finally, a mixture of tetrahydrofuran-water (1:1) was added and the organic layer was separated, dried (anhydrous sodium sulphate) and evaporated. The residual oil was purified by chromatography on silicagel eluting with toluene-ethyl acetate (6:1). The (*E*)-isomer of **4a** was isolated (0.54 g, 26%) as a yellow oil; ir (film): 2240 (CN), 1670 (CON), 1650 (C=C); nmr (deuteriochloroform): δ 7.63-7.23 (m, aromatic H, 4H), 6.738 (dd of doublets, HC=C-CN, 1H, J = 16.3, 5.9 and 6.8 Hz); 5.438 (dd of doublets, C=CH-CN, 1H, J = 16.3, 1.5 and 1.4 Hz); 4.723 (dd of doublets, CH(1)-N, 1H, J = 15.8, 1.9 and 1.5 Hz); 4.034 (dd, of doublets, CH(2)-N, 1H, J = 15.8, 6.8 and 1.4 Hz); 1.846 (s, CH_3CO, 3H); ms: 234 (M^+), 192, 157, 140, 111, 99, 43 (100%).

Anal. Calcd. for $C_{12}H_{11}ClN_2O$: C, 61.4; H, 4.7; N, 11.9; Cl, 15.1. Found: C, 61.2; H, 4.5; N, 12.02; Cl, 15.0.

A mixture was obtained of the (*Z*)-isomer, the (*E*)-isomer and *o*-chloroacetanilide. It was not possible to isolate pure samples of either isomer.

N-(Δ²-Cyclohexenyl)-*o*-chloroaniline (**5a**).

A mixture of *o*-chloroaniline (1.27 g, 0.01 mole), 3-bromocyclohexene (3.2 g, 0.02 mole) and solid sodium carbonate (1.06 g, 0.01 mole) in ethanol-water (4:1) was refluxed for 6 days. After the ethanol was removed, the reaction mixture was diluted with water and the resultant aqueous layer was extracted with diethyl ether. The ethereal layer was separated and dried with anhydrous sodium sulphate and evaporated. The residual oil was purified by chromatography on silicagel eluting with cyclohexane-diethyl ether to give 1.5 g (77%) of **5a** as a yellow oil; ir (film): 3430 (NH), 1650 (C=C), 1600 (aromatic C=C), 735 (*o*-substitution); nmr (carbon tetrachloride): δ 7.28-6.83 (m, H-C4 and H-C6 of the aromatic ring, 2H), 6.78-6.28 (m, H-C3 and H-C5 of the aromatic ring, 2H), 5.78 (m, CH=CH, 2H), 4.58 (m, NH and CH-N, 2H), 2.28-1.48 (m, $(CH_2)_3$, 6H); ms: 207 (M^+), 172, 144, 127 (100%), 117, 91, 81.

Anal. Calcd. for $C_{12}H_{14}ClN$: C, 69.4; H, 6.8; N, 6.7; Cl, 17.0. Found: C, 69.2; H, 6.5; N, 6.3; Cl, 16.9.

N-(Δ²-Cyclohexenyl)-*N*-methyl-*o*-chloroaniline (**6a**).

A mixture of *N*-methyl-*o*-chloroaniline (1.41 g, 0.01 mole), 3-bromocyclohexene (3.2 g, 0.02 mole) and solid sodium carbonate (1.06 g, 0.01 mole) in ethanol-water (4:1) was refluxed for 6 days. After the ethanol was removed, the mixture was diluted with water and extracted with diethyl ether. The ethereal layer was dried with anhydrous sodium sulphate, the solvent was removed and the residual oil was purified by chromatography on silica gel eluting with cyclohexane-diethyl ether (24:1) to give 0.48 g (22%) of the **6a** as a dark yellow oil; (ir film): 1650 (C=C), 1600 (aromatic C=C), 750 (*o*-substitution); nmr (deuteriochloroform): δ 7.30-6.90 (m, aromatic H, 4H), 5.7 (m, CH=CH, 2H), 3.95 (m, CH-N, 1H), 2.64 (s, CH_3-N, 3H), 2.2-1.5 (m, $(CH_2)_3$, 6H); ms: 221 (M^+); 193 186, 178, 158, (100%), 143, 141, 125, 111, 91.

Anal. Calcd. for $C_{13}H_{16}ClN$: C, 70.4; H, 7.2; N, 6.3; Cl, 16.0. Found: C, 70.3; H, 7.0; N, 6.1; Cl, 15.9.

N-Methyl-*N*-2-(Δ²-cyclohexenyl)ethyl-*o*-chloroaniline (**7a**).

(i) *o*-Chloroanilide of the 3-Cyclohexenylacetic Acid (I).

A mixture of the 3-cyclohexenylacetic acid [8] (1.3 g, 9.25 mmoles) and thionyl chloride (2.2 g, 18.5 mmoles) was refluxed for 3 hours and the excess of thionyl chloride was removed by distillation under reduced pressure. *o*-Chloroaniline (2.35 g, 18.5 mmoles) was added with ice-cooling and a white solid precipitate which was recrystallized from diethyl ether and identified as I mp 124-125° (1.64 g, 71%) was obtained; ir (potassium bromide): 3300 (NH), 1660 (C=O), 1590 (aromatic C=C), 755 (*o*-substitution); nmr (deuteriochloroform): δ 8.42 (broad d, H-C3, 1H, J = 8 Hz), 7.7 (broad s, NH, 1H), 7.5-6.7 (m, aromatic H, 3H), 5.68 (m, CH=CH, 2H), 2.90-2.30 (m, CH_2CO and CH, 3H), 2.15-1.20 (m, $(CH_2)_3$, 6H); ms: 249 (M^+), 214, 169, 134, 127 (100%), 81.

Anal. Calcd. for $C_{14}H_{16}ClNO$: C, 67.3; H, 6.4; N, 5.6; Cl, 14.2. Found: C, 67.0; H, 6.3; N, 5.2; Cl, 14.1.

(ii) *N*-Methyl-*o*-chloroanilide of the 3-Cyclohexenylacetic Acid (II).

To a suspension of sodium hydride (0.37 g, 8.5 mmoles, 55% in mineral oil) in anhydrous tetrahydrofuran was added a solution of I (1.41 g, 5.67 mmoles) in anhydrous tetrahydrofuran under a stream of nitrogen and the mixture was stirred at room temperature until the evolution of hydrogen ceased. Methyl iodide (1.6 g, 11.6 mmoles) was added and the mixture stirred at room temperature overnight. Saturated ammonium chloride was added and the mixture extracted with diethyl ether. The organic layer was dried with anhydrous sodium sulphate and the residual oil was purified by chromatography on silicagel eluting with ethyl acetate-petroleum ether yielding an oily product which was identified as II (1.41 g, 95%); ir (film): 1665 (CON), 1585 (aromatic C=C), 760 (*o*-substitution); nmr (carbon tetrachloride): δ 7.6-7.05 (m, aromatic H, 4H); 5.45 (m, CH=CH, 2H), 3.12 (s, CH_3N, 3H), 2.5 (m, CH_2CO, 2H), 2.10-1.35 (m, CH and $(CH_2)_3$, 7H); ms: 263 (M^+), 228, 183, 148, 141 (100%), 81.

Anal. Calcd. for $C_{15}H_{18}ClNO$: C, 68.3; H, 6.9; N, 5.3; Cl, 13.4. Found: C, 68.0; H, 6.7; N, 5.0; Cl, 13.2.

(iii) *N*-Methyl-*N*-2-(Δ²-cyclohexenyl)ethyl-*o*-chloroaniline (**7a**).

The amide II (1.42 g, 5.4 mmoles) dissolved in anhydrous diethyl ether was added to a suspension of lithium aluminum hydride (0.41 g, 10 mmoles) in anhydrous diethyl ether with ice-cooling over a period of 30 minutes. Then the mixture was stirred at room temperature for 1 hour. Afterwards, water was carefully added and the solid was filtered off. The resulting salt was washed and refluxed with diethyl ether and the combined ethereal layers were dried with anhydrous sodium sulphate and evaporated. Chromatography on silica-gel eluting with chloroform-petroleum ether (4:1) gave an oil, 1.07 g (80%) which was identified as **7a**; ir (film): 1650 (C=C), 1590 (aromatic C=C), 750 (*o*-substitution); nmr (carbon tetrachloride): δ 7.40-6.65 (m, aromatic H, 4H), 5.52 (m, CH=CH, 2H), 3.02 (t, CH_2N, 2H, J = 7 Hz), 2.70 (s, CH_3N, 3H), 2.4-1.3 (M, CH,CH_2 and $(CH_2)_3$, 9H); ms: 249 (M^+), 214, 206, 154 (100), 141, 119, 111, 91.

Anal. Calcd. for $C_{15}H_{20}ClN$: C, 72.1; H, 8.0; N, 5.6; Cl, 14.2. Found: C, 72.0; H, 7.8; N, 5.3; Cl, 14.3.

Bis(acetylacetonate)nickel(II).

To a solution of potassium acetylacetonate prepared from acetylacetone (2.0 g, 0.02 mole) and potassium hydroxide (1.12 g, 0.02 mole) in absolute ethyl alcohol was added nickel(II) chloride (2.37 g, 0.01 mole) in absolute ethyl alcohol. The mixture was stirred at room temperature for 30 minutes. The white solid was filtered off and the solvent evaporated. An emerald green solid was obtained which was recrystallized from anhydrous benzene (2.0 g, 78%) mp 230°.

Anal. Calcd. for $C_{10}H_{14}O_4Ni$: Ni, 22.87. Found: Ni, 22.61.

Cyclization Reaction of the *N*-Alkenyl-*o*-chloroanilines **1a-7a** with Tetrakis(triphenylphosphine)nickel(0).

General Procedure.

To a solution of bis(acetylacetonate)nickel(II) (0.25 g, 1 mmole) and triphenylphosphine (1.05 g, 4 mmoles) in anhydrous toluene (10 ml) was added triethylaluminum (0.34 g, 3 mmoles, 0.81 ml of a solution 50% in toluene), under a stream of helium while cooling the mixture in an ice-ammonium chloride bath. The mixture, after a vigorous initial reaction, was stirred at room temperature for 30 minutes to acquire a characteristic dark red colouring of tetrakis(triphenylphosphine)nickel(0). Afterwards, a solution of the *N*-β-alkenyl-*o*-chloroaniline derivative (1 mmole) in toluene was added and the mixture was warmed at 60-70° for 4-5 hours. Finally, the complex was hydrolyzed with a saturated ammonium chloride solution. The organic layer was extracted and dried and the product was purified by chromatography on silicagel eluting with the adecuate solvent.

Cyclization of *N*-allyl-*N*-methyl-*o*-chloroaniline (**1a**).

To a solution of the tetrakis(triphenylphosphine)nickel(0) obtained from bis(acetylacetonate)nickel(II) (0.77 g, 3 mmoles), triphenylphosphine (3.19 g, 0.012 mole) and triethylaluminum (1.0 g, 9 mmoles, 2.4 ml of a solution 50% in toluene) was added a solution of **1a** (0.55 g, 3 mmoles) in toluene. The mixture was stirred at room temperature for 90 minutes, warmed to 80-90° for 2 hours and finally refluxed for one hour. The crude product was purified by chromatography on silicagel eluting with *n*-hexane-diethyl ether (96:4) to give **1b** (0.311 g, 73%) and **1d** (68.2 mg, 17%).

1,3-Dimethylindole (**1b**).

This compound was isolated as a yellow oil (picrate mp 143-144° [9]); ir (film): 1600 (C=C); nmr (carbon tetrachloride): δ 7.49-6.84 (m, aromatic H, 4H), 6.62 (q, H-C2, 1H, J = 1 Hz), 3.62 (s, CH_3N, 3H), 2.26 (d, CH_3-Ar, 3H, J = 1 Hz); ms: 144 (M^+-1), 130 (100), 117, 103, 89.

Anal. Calcd. for $C_{16}H_{14}N_4O_7$ (picrate): C, 51.3; H, 3.7; N, 15.0. Found: C, 50.85; H, 3.80; N, 15.3.

N-Methyl-*o*-ethylaniline (**1d**).

This compound was isolated as a brown oil; ir (film): 3475 (NH), 750 (*o*-substitution); nmr (carbon tetrachloride): δ 7.40-6.38 (m, aromatic H, 4H), 3.40 (broad s, NH, 1H), 2.80 (s, CH_3N, 3H), 2.39 (q, CH_2-Ar, 2H, J = 7 Hz), 1.16 (t, CH_3-3H, J = 7 Hz); ms: 135 (M^+), 134, 120 (100), 119, 104.

Anal. Calcd. for $C_9H_{13}N$: C, 79.9; H, 9.7; N, 10.3. Found: C, 80.1; H, 9.5; N, 10.0.

Cyclization of *N*-Methyl-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**2a**).

To a solution of the tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene, prepared from bis(acetylacetonate)nickel(II) (0.128 g, 0.5 mmole), triphenylphosphine (0.524 g, 2 mmoles) and triethylaluminum (0.171 g, 1.5 mmoles, 0.41 ml of a solution 50% in toluene) was added a solution of **2a** (0.10 g, 0.5 mmole) in anhydrous toluene. The mixture was warmed at 70-80° for 5 hours. The crude product was purified by chromatography on silicagel eluting with petroleum ether-ethyl acetate to give 1-methylindole-3-acetonitrile (**2b**) (44.5 mg, 52%), 1-methyl-2,3-dihydroindole-3-acetonitrile (**2c**) (15.5 mg, 18%) and *N*-methyl-*N*-(3-cyanopropyl)-*o*-chloroaniline (**2d**) (30 mg, 29%).

1-Methylindole-3-acetonitrile (**2b**).

Compound **2b** [9] was isolated as a white solid recrystallized from diethyl ether-petroleum ether, mp 58°; ir (nujol): 2260 (CN), 1620 (C=N), 740 (*o*-substitution); nmr (deuteriochloroform): δ 7.78-7.08 (m, aromatic H, 4H), 7.03 (t, H-C2, 1H, J = 1 Hz), 3.73 (d, CH_2CN, 2H, J = 1 Hz), 3.68 (s, CH_3N, 3H); ms: 170 (M^+), 169 (100), 155, 144, 128, 115, 101, 87.

1-Methyl-2,3-dihydroindole-3-acetonitrile (**2c**).

This compound was isolated as a yellow oil; ir (film): 2260 (CN) 750 (*o*-substitution); nmr (carbon tetrachloride): δ 7.10-6.90 (m, H-C4 and H-C6, 2H), 6.70-6.30 (m, H-C5 and H-C7, 2H), 3.40-3.0 (m, CH_2N and CH, 3H), 2.73 (s, CH_3N, 3H), 2.43 (d, CH_2CN, 2H, J = 7 Hz); ms: 172 (M^+), 144, 132 (100), 117, 103, 91.

Anal. Calcd. for $C_{11}H_{12}N_2$: C, 76.7; H, 7.0; N, 16.2. Found: C, 76.5; H, 6.9; N, 16.0.

N-Methyl-*N*-(3-cyanopropyl)-*o*-chloroaniline (**2d**).

This compound was isolated as a yellow oil; ir (film): 2280 (CN); 1600 (aromatic C=C), 750 (*o*-substitution); nmr (carbon tetrachloride): δ 7.32-6.88 (m, aromatic H, 4H), 3.05 (t, CH_2N, 2H, J = 6.7 Hz), 2.67 (s, CH_3N, 3H), 2.39 (t, CH_2CN, 2H, J = 7.29 Hz), 1.82 (quintuplet, CH_2, 2H, J = 6.98 Hz); ms: 208 (M^+), 154 (100), 138, 118, 91.

Anal. Calcd. for $C_{11}H_{13}ClN_2$: C, 63.3; H, 6.2; N, 13.4; Cl, 17.0. Found: C, 63.1; H, 6.0; N, 13.1; Cl, 16.9.

Cyclization of the (*E*)-Isomer of *N*-(β-Cyanoethyl)-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**3a**).

To a solution of tetrakis(triphenylphosphine)nickel(0) which was prepared from bis(acetylacetonate)nickel(II) (0.77 g, 3 mmoles), triphenylphosphine (3.14 g, 12 mmoles) and triethylaluminum (1.03 g, 9 mmoles, 2.4 ml of a solution 50% in toluene) in anhydrous toluene was added a solution of the (*E*)-isomer of **3a** (0.74 g, 3 mmoles) in toluene. The mixture was warmed at 65° for 5 hours. The crude product was purified by chromatography on silicagel eluting with toluene-ethyl acetate (6:1) to give a first fraction with 1-(β-cyanoethyl)-3-methylindole (**3d**) (35.2 mg, 6%) and a second fraction with 1-(β-cyanoethyl)indole-3-acetonitrile (**3b**) and 1-(β-cyanoethyl)-2,3-dihydroindole-3-acetonitrile (**3c**) (92% of yield, **3b**, 43% and **3c** 57% by ^{1}H-nmr and gc-ms).

1-(β-Cyanoethyl)-3-methylindole (**3d**).

This compound was isolated as a white solid recrystallized from diethyl ether-petroleum ether, mp 72-73°; ir (nujol): 2270 (CN); 1610 (C=N), 745 (*o*-substitution); nmr (carbon tetrachloride): δ 7.83-7.08 (m, aromatic H, 4H), 6.88 (q, H-C2, 1H, J = 1 Hz), 4.20 (t, CH_2N, 2H, J = 7 Hz), 2.55 (t, CH_2CN, 2H, J = 7 Hz), 2.25 (d, CH_3-Ar, 3H, J = 1 Hz); ms: 184 (M^+), 144 (100), 130, 128, 115, 103, 102.

Anal. Calcd. for $C_{12}H_{12}N_2$: C, 78.2; H, 6.5; N, 15.2. Found: C, 78.4; H, 6.3; N, 15.0.

Oxidation of the Mixture of **3b** and **3c** with 2,3-Dichloro-5,6-dicyano-*p*-benzoquinone.

A mixture 30.6 mg of **3b** and **3c** was refluxed in toluene with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (34.0 mg) for 3 hours. After filtration and removing of the solvent, the residual oil was purified by chromatography on silica-gel eluting with toluene-ethyl acetate (6:1) and **3b** was isolated in quantitative yield as a white solid recrystallized from diethyl ether-petroleum ether, mp 85-86°; ir (nujol): 2250 (CN); 1610 (C=N); 740 (*o*-substitution); nmr (deuteriochloroform): δ 7.50-7.0 (m, aromatic H, 5H), 4.30 (t, CH_2N, 2H, J = 7 Hz); 3.70 (d, CH_2CN, 2H, J = 1 Hz), 2.70 (t, CH_2CN, 2H, J = 7 Hz); ms: 209 (M^+), 169 (100), 155, 140, 128, 115, 101, 89.

Anal. Calcd. for $C_{19}H_{14}N_6O_7$ (picrate): C, 52.0; H, 3.2; N, 19.1. Found: C, 51.7; H, 3.3; N, 19.3.

Cyclization of the (*Z*)-Isomer of *N*-(β-Cyanoethyl)-*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**3a**).

To a solution of the tetrakis(triphenylphosphine)nickel(0) obtained from bis(acetylacetonate)nickel(II) (0.26 g, 1 mmole), triphenylphosphine (1.05 g, 4 mmoles) and triethylaluminum (0.31 g, 3 mmoles, 0.81 ml of a solution 50% in toluene) in anhydrous toluene was added a solution of the (*Z*)-isomer of **3a** (0.24 g, 1 mmole) in toluene. The mixture was warmed at 70° for 5 hours. The crude product was purified by chromatography on silicagel eluting with benzene-ethyl acetate (6:1) to give a first fraction with **3d** (29.3 mg, 5%) and **3b** and **3c** in the same fraction (0.20 g 95%, **3b** 37% and **3c** 63% by ^{1}H-nmr and gc-ms).

Cyclization of the *N*-Acetyl,*N*-(*o*-chlorophenyl)-4-amino-2-butenenitrile (**4a**).

(a) To a solution of tetrakis(triphenylphosphine)nickel(0) obtained from bis(acetylacetonate)nickel(II) (0.69 g, 2.3 mmoles), triphenylphosphine (2.43 g, 9.2 mmoles) and triethylaluminum (0.79 g, 6.9 mmoles, 1.8 ml of a solution 50% in toluene) in anhydrous toluene was added a solution of **4a** (0.54 g, 2.3 mmoles) in toluene. The mixture was warmed at 60-70° for 5 hours. The crude product was purified by chromatography on silicagel eluting with toluene-ethyl acetate (6:1) to give *o*-chloroacetanilide **4d** (0.30 g, 80%), mp 88° (identified as the *o*-chloroacetanilide by comparison with an authentic sample); ir (nujol): 3300 (NH); 1660 (CONH); 750 (*o*-substitution); nmr (deuteriochloroform): δ 8.25 (broad d, H-C_3, 1H, J = 8 Hz), 7.60 (broad s, NH, 1H); 7.40-6.80 (m, aromatic H, 3H); 2.20 (s, CH_3CO, 3H).

(b) A solution of the bis(acetylacetonate)nickel(II) (0.3 g, 1.2 mmoles), triphenylphosphine (1.26 g, 4.8 mmoles) and triethylaluminum (0.14 g, 1.2 mmoles, 0.3 ml of a solution 50% in toluene) in anhydrous toluene was stirred at room temperature for one hour. Afterwards, was added a solution in toluene of the (*E*)-isomer of **4a** (0.28 g, 1.2 mmoles). The mixture was warmed at 60-70° for 5 hours. Two products were isolated by chromatography on silicagel. *o*-Chloroacetanillide (**4d**) (82 mg, 40%) was isolated as before and 1-acetylindole-3-acetonitrile (**4b**) (0.113 g, 50%) was isolated as a white solid recrystallized from carbon tetrachloride, mp 114-115° [11]; ir (nujol): 2270 (CN), 1710 (CON); nmr (deuteriochloroform): δ 7.58-7.13 (m, aromatic H, 5H), 3.80 (d, CH_2CN, 2H, J = 1 Hz), 2.67 (s, CH_3CON, 3H); ms: 198 (M^+), 155 (100), 130, 115, 102, 89.

Cyclization of the *N*-(Δ²-Cyclohexenyl)-*o*-chloroaniline (**5a**).

To a solution of tetrakis(triphenylphosphine)nickel(0) obtained from bis(acetylacetonate)nickel(II) (0.61 g, 2.3 mmoles), triphenylphosphine (2.5 g, 9.56 mmoles) and triethylaluminum (0.81 g, 7.17 mmoles, 1.9 ml of a solution 50% in toluene) in anhydrous toluene was added **5a** (0.496 g, 2.39 mmoles) in anhydrous toluene at 70°. The mixture was stirred at 80-100° for 5 hours. The products were separated by chromatography on silicagel eluting with benzene. They were **5d-1** (0.33 g, 70%) and **5d-2** (0.108 g, 26%).

N-(Δ²-Cyclohexenyl)-2-ethylaniline (**5d-1**).

Compound **5d-1** was isolated as brown oil; ir (film): 3480 (NH), 1615 (C=C); 735 (*o*-substitution); nmr (deuteriochloroform): δ 7.6-6.9 (m, H-C3 and H-C5 of the aromatic ring, 2H), 6.8-6.4 (m, H-C4 and H-C6 of the aromatic ring, 2H), 5.72 (m, CH=CH, 2H), 3.95 (broad s, NH, 1H), 3.4 (m, CHN, 1H), 2.4 (q, CH_2-Ar, 2H, J = 7 Hz), 2.1-1.48 (m, $(CH_2)_3$, 6H), 1.15 (t, CH_3, 3H, J = 7 Hz); ms: 201 (M^+), 173, 158, 144, 132, 121, 106, 40 (100).

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.5; H, 9.5; N, 6.9. Found: C, 83.4; H, 9.3; N, 6.7.

N-(Δ²-Cyclohexenyl)aniline (**5d-2**).

Compound **5d-2** was isolated as a yellow oil; ir (film): 3450 (NH), 1610 (C=C), 735, 710 (monosubstituted); nmr (deuteriochloroform): δ 7.3-6.9 (m, H-C (*meta*), 2H), 6.8-6.4 (m, H-C (*ortho*) and H-C (*para*), 3H), 5.70 (m, CH=CH, 2H), 3.90 (broad s, NH, 1H), 3.3 (m, CHN, 1H), 2.20-1.40 (m, $(CH_2)_3$, 6H); ms: 173 (M^+), 145, 130, 117, 93 (100).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.2; H, 8.7; N, 8.0. Found: C, 83.0; H, 8.5; N, 8.1.

Cyclization of *N*-(Δ²-Cyclohexenyl)-*N*-methyl-*o*-chloroaniline (**6a**).

To a solution of tetrakis(triphenylphosphine)nickel(0) prepared from bis(acetilacetonate)nickel(II) (0.25 g, 1 mmole), triphenylphosphine (1.04 g, 4 mmoles) and triethylaluminum (0.34 g, 3 mmoles, 0.81 ml of a solution 50% in toluene) in anhydrous toluene was added **6a** (0.221 g, 1 mmole) in anhydrous toluene and the mixture was stirred at 80-100° for 5 hours. The purification of the crude product by chromatography on silicagel eluting with benzene-hexane (2:1) gave quantitatively the starting material unchanged, which was identified by ir, nmr and ms.

Cyclization of *N*-Methyl-*N*-2-(Δ²-cyclohexenyl)ethyl-*o*-chloroaniline (**7a**).

To a solution of tetrakis(triphenylphosphine)nickel(0) obtained from bis(acetylacetonate)nickel(II) (0.82 g, 3.2 mmoles), triphenylphosphine (3.35 g, 12.8 mmoles) and triethylaluminum (1.09 g, 9.6 mmoles, 2.6 ml of a solution 50% in toluene) in anhydrous toluene was added **7a** (0.8 g, 3.2 mmoles) and the mixture was stirred at 110° for 5 hours. The purification of the crude product by chromatography on silica gel eluting with petroleum ether-chloroform (1:1) gave the starting material unchanged **7a** (0.59 g, 74%) and *N*-methyl,*N*-2-(Δ²-cyclohexenyl)ethylaniline (**7d**) (73 mg, 11%) as an oil; ir (film): 1610 (C=C); nmr (deuteriochloroform): δ 7.5-7.0 (m, H-C (*meta*) and H-C (*para*), 3H), 6.9-6.4 (m, H-C (*ortho*), 2H), 5.65 (s, CH=CH, 2H), 3.38 (broad t, CH_2N, 2H, J = 8 Hz), 2.90 (s, CH_3N, 3H), 2.30-1.10 (m, CH, CH_2 and $(CH_2)_3$, 9H); ms: 215 (M^+), 172, 120 (100), 107, 91.

Anal. Calcd. for $C_{15}H_{21}N$: C, 83.6; H, 9.8; N, 6.5. Found: C, 83.4; H, 9.7; N, 6.3.

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REFERENCES AND NOTES

[1a] M. Mori and Y. Ban, *Tetrahedron Letters*, 1803 (1976); [b] M. Mori and Y. Ban, *Tetrahedron Letters*, 1807 (1976); [c] M. Mori, S. Kudo and Y. Ban, *J. Chem. Soc., Perkin Trans. I*, 771 (1979); [d] M. Mori, Y. Hashimoto and Y. Ban, *Tetrahedron Letters*, 631 (1980).

[2] M. Mori, K. Chiba and Y. Ban, *Tetrahedron Letters*, 1037 (1977).

[3] A. J. Beckwith and W. B. Gara, *J. Chem. Soc., Perkin Trans II*, 795 (1975).

[4] J. G. Rodriguez and L. Canoira, submitted for publication.

[5] S. G. Davies, "Organotransition Metal Chemistry: Applications to Organic Synthesis", Pergamon Press, Oxford, 1982, p 166.

[6] J. W. E. Glattfeld and E. Reitz, *J. Am. Chem. Soc.*, **62**, 974 (1940).

[7] A. Heininger, *J. Org. Chem.*, **22**, 1213 (1957).

[8] H. O. House, R. G. Calson and H. Babad, *J. Org. Chem.*, **28**, 3359 (1963).

[9] H. R. Snyder and E. L. Eliel, *J. Am. Chem. Soc.*, **70**, 1703 (1948).

[10] C. D. Nenitzescu und D. Raileanu, *Chem. Ber.*, **91**, 1141 (1958).