Synthesis of Oxindole Derivatives from *N*-Alkenyl-*o*-Chloroanilides with Zero-Valent Nickel Complex

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Oxindole derivatives have been obtained from *N*-alkenyl-*o*-chloroanilides by reaction with tetrakis(triphenylphosphine)nickel(0) in toluene as solvent in good yields. A detailed analysis of all the products of the reaction allows to confirm the postulated mechanism of the cyclization reaction. The *o*-chloroanilides of the 3-cyclohexenylacetic acid fails in the cyclization reaction, since the torsional hindrance seems to avoid that the endocyclic double bond may be orthogonally to the *ortho*-σ-nickel complex intermediate on the aromatic ring.

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Introduction.

Heterocyclic compounds have been obtained using arylnickel(1) and arylpalladium(2) complexes. Zero-valent nickel complexes, $Ni(PPh_3)_4$-type, obtained from the divalent nickel complex with a reducing agent could react with an *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 the *ortho*-σ-nickel chloride and the double bond of the *N*-alkenyl chain.

In a previous paper [1e] we have analyzed the cyclization reaction between *N*-alkenyl-*o*-chloroanilines and a zero-valent nickel complex. Now we are interested in the general applicability of this reaction to the synthesis of oxindole derivatives starting from *N*-alkenyl-*o*-chloroanilides 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.

N-Alkenyl-*o*-chloroanilides **1a-8a** (Table 1) has been obtained following previously reported methods to the synthesis of similar compounds. Compounds **1a, 2a** and **7a** were obtained by reaction of the *o*-chloroaniline with the respective acid chloride in pyridine as the solvent.

Compounds **3a** and **4a** were prepared from 2'-chloromaleanilic acid (I).

All the attempts to prepare **3a** by esterification of I with methyl alcohol catalyzed by acid were unsuccessful since the main product of this reaction was the *o*-chloro-*N*-phenylmaleiimide (II) together with a mixture of the *(E)* and *(Z)* isomers of **3a**. Compound *(Z)*-**3a** was obtained by the reaction of the carboxylate of I with methyl iodide in hexamethylphosphoric triamide as solvent at room temperature.

Compound **4a** was obtained by reaction of I with isopropyl chloroformate and triethylamine at low temperature followed by addition of dimethylamine in tetrahydrofuran.

Compound **5a** was prepared by treatment of **4a** with sodium hydride and methyl iodide in anhydrous tetrahydrofuran.

Compound **6a** was obtained by reaction of *N*-(3-cyanoethyl)-2-chloromaleanilic acid (III) with isopropyl chloroformate and triethylamine followed by addition of dimethylamine.

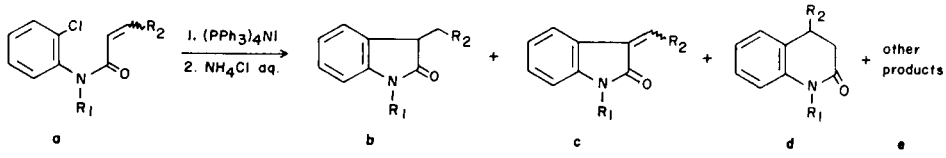
Compound **8a** was prepared by treatment of **7a** with sodium hydride and methyl iodide in anhydrous tetrahydrofuran as the solvent.

Tetrakis(triphenylphosphine)nickel(0) was prepared by reduction of bis(acetylacetonate)nickel(II) with an excess of triethylaluminum in the presence of triphenylphosphine in toluene as the solvent. Pure tetrakis(triphenylphosphine)nickel(0) has been obtained by the above reduction reaction of the bis(acetylacetonate)nickel(II) with triethylaluminum in diethyl ether as the solvent. Zero-valent nickel complex precipitates in this solvent and then it was recovered and washed with diethyl ether to avoid the presence of triethylaluminum. Anhydrous bis(acetylacetonate)nickel(II) was prepared from potassium acetylacetonate and nickel(II) chloride in absolute ethyl alcohol, and finally recrystallized from anhydrous benzene.

In Table 1 are summarized the *N*-alkenyl-*o*-chloroanilides **1a-8a** and the products of their cyclization reaction with zero-valent tetrakis(triphenylphosphine)nickel.

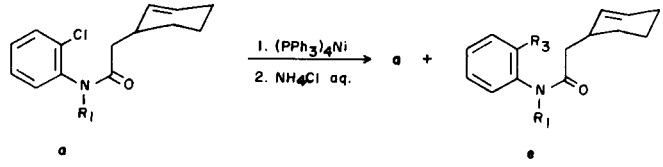
Compound **1a** reacts with the zero-valent nickel complex in the presence of triethylaluminum to give the oxindoles **1b** in a 24% yield and the 2-quinolone **1d** in a 9% yield. Both cyclization compounds agree with the reported literature [3], which has affirmed that the 5-Exo-Trig and the 6-Endo-Trig cyclization products are favoured in the process. Moreover, the main products appearing in this cyclization reaction were *o*-chloropropioanilide (**1e-1**) and *o*-ethylacrylanilide (**1e-2**) which can be generated by the attack of the triethylaluminum (**1e-2**) in excess or of the hy-

Table 1



a b c d e

Compound	R_1	R_2	isomer	X [a]	b	c	d	e
1a	H	H	—	6	24	—	9	31 (**1e-1**) 36 (**1e-2**) [c] (**1e-3**)
1a	H	H	—	[b]	—	—	15	56 (**1e-1**) 29 (**1e-4**)
2a	H	Ph	*(E)*	6	35	7 *(Z)*-**2c** 13 *(E)*-**2c**	—	45 (**2e**)
3a	H	CO_2Me	*(Z)*	[b]	73	26	—	—
4a	H	$CONMe_2$	*(E)*	6	94	[c]	[c]	3.2 (**4e-1**)
5a	CH_3	$CONMe_2$	*(E)*	6	98	—	[c]	1.8 (**4e-2**)
6a	CH_2CH_2CN	$CONMe_2$	*(E)*	6	98	—	[c]	—



a e

7a	H	—	*(Z)*	6	99	[c] (**7e**)		
8a	CH_3	—	*(Z)*	6	74	[c] (**8e-2**)		25 (**8e-1**)

[a] Molar relation of triethylaluminum to bis(acetylacetonate)nickel(II). [b] Crystallized tetrakis(triphenylphosphine)nickel(0). [c] Detected by gc/ms techniques. All the yields were calculated from hplc.

dronickel intermediate complex (**1e-1**) (Figure 1, i and ii).

In contrast with these facts, the cyclization reaction of **1a** was analyzed in absence of triethylaluminum using crystallized tetrakis(triphenylphosphine)nickel(0). This analysis shows a different behaviour between the reagents. Thus the oxindole **1b** was not detected, but the 2-quinolone **1d** was obtained in 15% yield. However, as the main products were obtained *o*-chloropropioanilide (**1e-1**) and propioanilide (**1e-4**) which confirms the double attack of the hydronickel complex on the π-arylnickel intermediate and the double bond respectively (Figure 1, iii). However, in absence of triethylaluminum, the *o*-ethyl derivative **1e-2** was not detected.

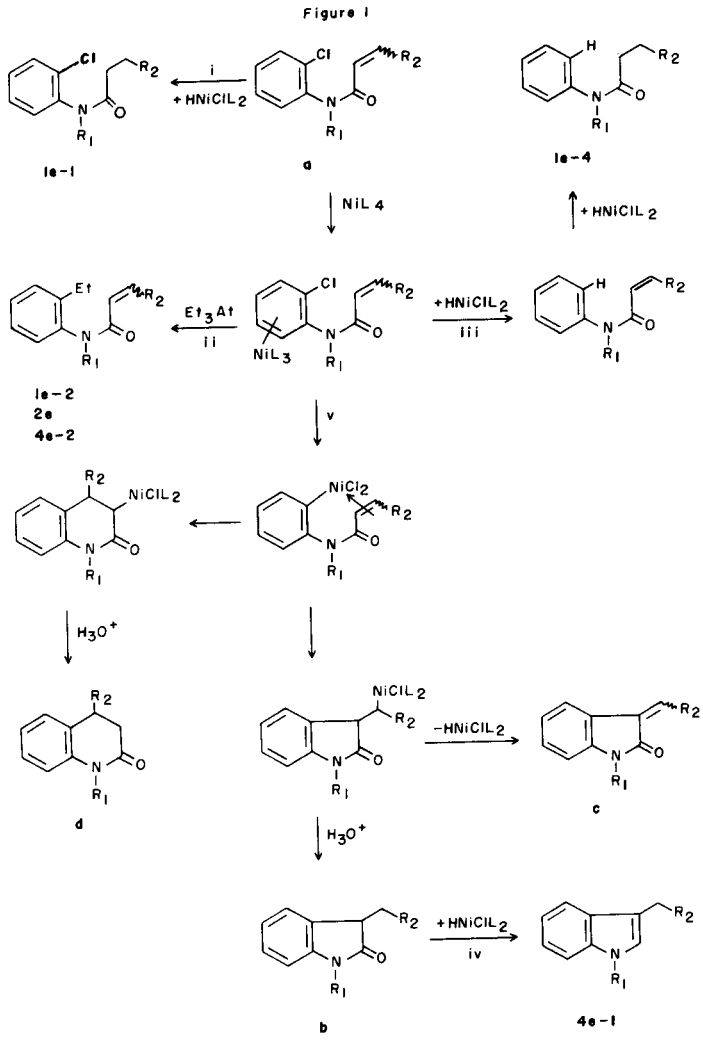
On the other hand, the CH_2-CH_2 fragment of the 2-oxo-1,2,3,4-tetrahydroquinoline (**1d**) shows an AA'BB' system in their ^{1}H-nmr spectrum. This proton system could be produced by the existence of two conformations which interchange slowly by the hindrance to the conformational rotation in the δ-lactam ring [4].

Following the reactive scheme of the *o*-chloroanilide derivatives with tetrakis(triphenylphosphine)nickel(0) in an excess of triethylaluminum, **2a** reacts to give the oxindole **2b** (35%) and the isomeric α,β-unsaturated oxindoles **2c**, *(Z)*-**2c** (7%) and *(E)*-**2c** (13%). Those oxindole derivatives were transformed quantitatively to the saturated oxindole **2b** by reduction with sodium borohydride in absolute ethyl alcohol.

In this cyclization reaction was also obtained *(E)*-*o*-ethylcinnamanilide (**2e**) (45%), by attack of the triethylaluminum in excess on the π-arylnickel intermediate (Figure 1, ii), but the 2-quinolone derivative was not detected.

Compound **3a** reacts with the zero-valent tetrakis(triphenylphosphine)nickel in the absence of triethylaluminum providing the oxindole **3b** (73%) and a *(Z + E)* mixture of the isomeric α,β-unsaturated oxindoles **3c** (26%), which were only possible to isolate by hplc. Unambiguous confirmation of **3b** was obtained by synthesis of this compound by an independent route [5]. Compound **3c** was submitted to reduction with borohydride giving a mixture of products which were identified and compared with the same reduction reaction products of **3b**.

Figure 1



(i) $R_1 = R_2 = H$. (ii) $R_1 = H$; $R_2 = H$, Ph, $CONMe_2$. (iii) $R_1 = R_2 = H$.
(iv) $R_1 = H$; $R_2 = CONMe_2$. (v) $R_1 = H$, CH_3, CH_2CH_2CN; $R_2 = H$, Ph, CO_2Me, $CONMe_2$.

The reaction of **4a** with tetrakis(triphenylphosphine)nickel(0) gave the oxindole **4b** in a good yield (94%) while the presence of the α,β-unsaturated oxindoles **4c** and the 2-quinolone **4d** can be only detected by gc/ms techniques. In this reaction, the *N,N*-dimethyl-3-indolylacetamide (**4e-1**) and the *N,N*-dimethyl-2'-ethylfumaranilide (**4e-2**) appear as side products, generated by reductive attack of the hydronickel complex on the oxindolic carbonyl group and *o*-substitution by triethylaluminium respectively (Figure 1, iv and ii).

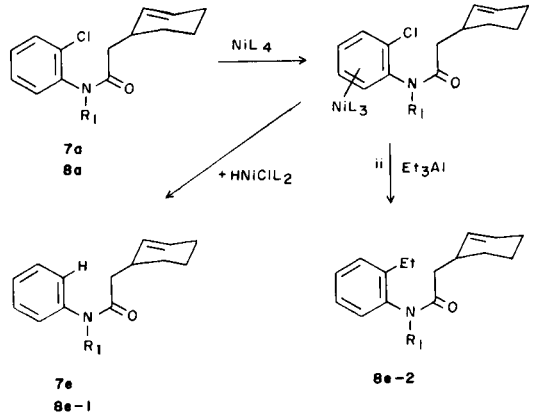
Compounds **5a** and **6a** react with tetrakis(triphenylphosphine)nickel(0) in excess of triethylaluminum to give the oxindoles **5b** and **6b** while the 2-quinolones **5d** and **6d** were only detected by gc/ms techniques as side products. *Ortho*-, ethyl- or hydride substitution were not detected and thus compounds having *N*-alkyl substitution on the NH amido group prevent the formation of these side products.

The cyclization reaction of the *N*-alkenyl-*o*-chloroanilides **1a-6a** with tetrakis(triphenylphosphine)nickel(0) is a good method for the synthesis of oxindole derivatives since this allows the presence in the starting anilide of polar or bulky functional groups without appreciable changes in the yields. The side products obtained seem to confirm the postulated mechanism of the cyclization reaction [1,2] (Figure 1, v).

An interesting structural aspect was observed for the oxindoles **2b-6b** which show a complex ^{1}H-nmr spectrum of the CH-CH_2R fragment with the methylene protons appearing diastereotopically. However, the oxindole **6b** shows an ABCD proton system for both methylenes of the N-CH_2-CH_2-CN fragment. We have analyzed this proton system of the **6b** which is generated by a rigid anchorage of the H_A proton to the carbonyl amido group [6]. The oxindolic proton systems are actually in preparation for publication.

In an extension of the synthesis of oxindole derivatives by cyclization of the *o*-chloroanilides **1a-6a** with tetrakis(triphenylphosphine)nickel(0), we have prepared the *o*-chloroanilides of the 3-cyclohexenylacetic acid [7], **7a** and **8a**, both should be precursors of the 1-benzazepinone derivatives by cyclization reaction with organonickel complex. Moreover, benzazepinones were not obtained and only the side products were isolated in the two cases, **7a** and **8a**, probably due to the endocyclic double bond in the cyclohexene ring which has hindered the conformation with the orthogonal disposition required for the double bond to form the π-complex bond with the *ortho*-σ-nickel complex, Figure 2.

Figure 2



(i) R = H, CH_3. (ii) R = CH_3.

Thus, in the cyclization reaction of **7a** with zero-valent tetrakis(triphenylphosphine)nickel, the starting product **7a** was recovered unchanged and also by gc/ms the anilide of the 3-cyclohexenylacetic acid **7e** was detected, resulting from the attack of the hydronickel complex on the π-aryl-

nickel intermediate (Figure 2, i).

The cyclization reaction of **8a** with tetrakis(triphenylphosphine)nickel(0) provides the *N*-methylanilide of the 3-cyclohexenylacetic acid (**8e-1**), while the starting product **8a** was recovered in a 74% yield. However, the *N*-methyl-*o*-ethylanilide of the 3-cyclohexenylacetic acid (**8e-2**) was detected by gc/ms techniques.

EXPERIMENTAL

Melting points were measured in a hot stage microscope and are uncorrected. Infrared spectra were recorded on a Pye-Unicam SP1100 spectrophotometer and nuclear magnetic resonance spectra on a Hitachi-Perkin-Elmer R-24A and a Varian XL-100 spectrometers. 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.

o-Chloroacrylanilide (**1a**).

Benzoyl chloride (180 ml) and acrylic acid (30 ml) were refluxed at 110° in presence of hydroquinone as a radical inhibitor under nitrogen. Acrylic acid chloride was removed by continuous distillation at 70° (760 mm Hg). *o*-Chloroaniline (1.651 g, 0.013 mole) in pyridine was carefully added to the cooled acrylic acid chloride (1.17 g, 0.013 mole) to avoid an exothermic reaction. The crude product was washed with 5% hydrochloric acid solution, extracted with diethyl ether and purified by chromatography on silica gel eluting with petroleum ether-ethyl acetate (3:1) to give 2.05 g (87%) of **1a** as a white crystalline solid (mp 63-64°; ir (potassium bromide): 3310 (NH), 1670 (C=O), 1640 (C=C), 760 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 8.48 (m, H-C3, 1H), 7.90 (broad s, NH, 1H), 7.52-6.90 (m, ArH, 3H), 6.50-5.70 (m, CH=CH_2, 3H); ms: (70 eV) 181 (M^+, 5%), 146 (M^+-35, 33%), 127 (M^+-54, 45%), 55 (base peak).

Anal. Calcd. for C_9H_8ClNO: C, 59.51; H, 4.44; N, 7.71; Cl, 19.52. Found: C, 59.25; H, 4.31; N, 7.90; Cl, 19.50.

(E)-*o*-Chlorocinnamanilide (**2a**).

(E)-Cinnamic acid (2.96 g, 0.02 mole) and thionyl chloride (2.38 g, 0.02 mole) were refluxed for 1 hours to give the *(E)*-cinnamic acid chloride which was not isolated. *o*-Chloroaniline (3.175 g, 0.025 mole) in pyridine was carefully added to the *(E)*-cinnamic acid chloride, which was cooled in an ice-water bath to avoid an exothermic reaction. The white crude product was washed with 5% hydrochloric acid solution and recrystallized from ethyl alcohol giving **2a**, 4.28 g (83%), as white crystal plates mp 138-140°; ir (potassium bromide): 3260 (NH), 1655 (C=O), 1630 (C=C); ^{1}H-nmr (deuteriochloroform): δ 8.47 (m, H-C3, 1H), 7.80 (broad s, NH, 1H), 7.71 (d, =CH-Ph, 1H, J = 15 Hz), 7.50-6.82 (m, ArH, 8H), 6.53 (d, NCO-CH=, 1H, J = 15 Hz); ms: (70 eV) 257 (M^+, 4%), 222 (M^+-35, 12%), 131 (M^+-126, base peak), 127 (8%).

Anal. Calcd. for $C_{15}H_{12}ClNO$: C, 69.90; H, 4.69; N, 5.43; Cl, 13.75. Found: C, 69.70; H, 4.50; N, 5.21; Cl, 13.57.

3-Methoxycarbonyl-*N*-(*o*-chlorophenyl)propenamide (**3a**).

(i) 2'-Chloromaleanilic Acid (I).

Solid maleic anhydride (2.31 g, 0.023 mole) was added to a solution of *o*-chloroaniline in anhydrous benzene and the mixture was stirred at room temperature for 30 minutes. The yellow crystalline precipitate of I was collected and recrystallized from ethanol-water giving 4.88 g (92%), mp 134-136°; ir (nujol): 3280 (NH), 3200-2000 (CO*OH*), 1710 (*CO*OH), 1630 (*CO*NH), 1555 (C=C); ^{1}H-nmr (deuterated acetone): δ 10.05 (broad s, NH and COOH, 2H), 8.05 (m, H-C3, 1H), 7.65-7.25 (m, ArH, 3H), 6.90 (d, NCO-CH=, 1H, J = 12 Hz), 6.43 (d, =CH-COOH, 1H, J = 12 Hz); ms: (70 eV) 255 (M^+, 4%), 190 (M^+-35, 25%), 172 (M^+-53, 9%), 149 (4%), 127 (72%), 99 (46%), 81 (37%), 69 (base peak), 55 (28%), 41 (45%).

Anal. Calcd. for $C_{10}H_8ClNO_3$: C, 53.23; H, 3.57; N, 6.20; Cl, 15.71. Found: C, 53.09; H, 3.22; N, 5.97; Cl, 15.65.

(ii) 3-Methoxycarbonyl-*N*-(*o*-chlorophenyl)propenamide (**3a**).

a) 2'-Chloromaleanilic acid (I) (2.25 g, 0.01 mole) was dissolved in a cooled solution of potassium hydroxide (0.56 g, 0.01 mole) in absolute ethyl alcohol. The solvent was removed and then the white potassium salt was dissolved in hexamethylphosphoric triamide. Methyl iodide (2.8 g, 0.02 mole) was added at room temperature and a slightly exothermic reaction occurred. The mixture was stirred at room temperature for 2 hours, diluted with a large excess of water and extracted with ethyl acetate. Chromatography of the crude product on a silica gel column eluting with chloroform-diethyl ether (9:1) gave **3a**, 1.64 g (69%) as a pale-yellow solid, mp 87-88°; ir (potassium bromide): 3230 (NH), 1740 (CO_2Me), 1670 (CONH), 1650 (C=C), 1270 (C-O-C), 755 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 9.55 (broad s, NH, 1H), 8.30 (m, H-C3, 1H), 7.42-6.80 (m, ArH, 3H), 6.39 (d, NCO-CH=, 1H, J = 12.3 Hz), 6.16 (d, =CH-CO_2Me, 1H, J = 12.3 Hz), 3.75 (s, CO_2Me, 3H); ms: (70 eV) 239 (M^+, 6%), 204 (M^+-35, 45%), 180 (M^+-59, 12%), 127 (51%), 113 (base peak), 59 (9%).

Anal. Calcd. for $C_{11}H_{10}ClNO_3$: C, 55.12; H, 4.20; N, 5.48; Cl, 14.79. Found: C, 54.87; H, 4.10; N, 5.71; Cl, 14.83.

b) 2'-Chloromaleanilic acid (I) (2.0 g, 8.87 mmoles) in absolute methyl alcohol (25 ml) was refluxed overnight with sulphuric acid as catalyst. Finally, the mixture was diluted with water and extracted with diethyl ether. The ethereal layer was washed with a 5% sodium carbonate solution, dried over sodium sulphate and ether solvent removed. The crude product was chromatographed on silica gel eluting with chloroform-diethyl ether (20:1) giving *o*-chloro-*N*-phenylmaleiimide (II) as a yellow solid (0.75 g, 40%), mp 63°, and a mixture of the *(E)* and *(Z)* isomers of **3a** (0.82 g, 39%) for which it was not possible to separate and isolate and to determine their spectroscopic data.

N-(*o*-Chlorophenyl)maleiimide (II).

This compound had ir (potassium bromide): 1775 and 1715 (CO-N-CO); ^{1}H-nmr (deuteriochloroform): δ 7.50-7.05 (m, ArH, 4H), 6.70 (s, CH=CH, 2H); ms: (70 eV) 207 (M^+, 11%), 172 (M^+-35, base peak), 144 (12%), 125, (5%), 55 (7%).

Anal. Calcd. for $C_{10}H_6ClNO_2$: C, 57.85; H, 2.91; N, 6.74; Cl, 17.07. Found: C, 57.61; H, 2.97; N, 6.53; Cl, 17.12.

N,N-Dimethyl-2'-chlorofumaranilide (**4a**).

Ethyl chloroformate (2.59 g, 0.024 mole) in anhydrous tetrahydrofuran was added in a solution of triethylamine (2.50 g, 0.024 mole) and 2'-chloromaleanilic acid (I) (5.60 g, 0.024 mole) in tetrahydrofuran at −12 to −15°. After 30 minutes, 30 ml of a solution of dimethylamine in anhydrous tetrahydrofuran (15%) was added at the same temperature. The mixture was stirred at room temperature overnight. Triethylamine hydrochloride was filtered off and the solvent evaporated and the residual oil was crystallized from diethyl ether as a white solid, 2.72 g (45%), mp 143-145°, identified as **4a**; ir (nujol): 3290 (NH), 1620 (broad, CONH and $CONMe_2$), 1555 (C=C); ^{1}H-nmr (deuteriochloroform): δ 8.92 (broad s, NH, 1H), 8.44 (m, H-C3, 1H), 7.75-7.10 (m, ArH and CH=CH, 5H), 3.20 (s, CH_3N, 3H), 3.07 (s, CH_3N, 3H); ms: (70 eV) 252 (M^+, 11%), 217 (M^+-35, 40%), 180 (M^+-72, 17%), 143 (55%), 127 (89%), 126 (base peak), 98 (85%), 72 (72%).

Anal. Calcd. for $C_{12}H_{13}ClN_2O_2$: C, 57.03; H, 5.18; N, 11.08; Cl, 14.02. Found: C, 57.55; H, 5.41; N, 11.18; Cl, 13.75.

N,N',N'-Trimethyl-2'-chlorofumaranilide (**5a**).

Compound **4a** (1.23 g, 4.8 mmoles) in anhydrous tetrahydrofuran was added to a cooled suspension of sodium hydride 55% in mineral oil (0.3 g, 7 mmoles) in tetrahydrofuran under nitrogen. When the evolution of hydrogen had ceased, methyl iodide (1.5 g, 10 mmoles) was added and the mixture was stirred at room temperature for 3 hours. Hydrolysis with a mixture of tetrahydrofuran-water (2:1), extraction with ethyl acetate and elimination of the solvent gave an oil, which was chromatographed on a silica gel column eluting with toluene-ethyl acetate (1:1) to obtain **5a** after crystallization of diethyl ether as a white solid, 0.63 g (49%), mp 115-116°; ir (nujol): 1630 (broad, CONMe and $CONMe_2$), 1580 (C=C);

^{1}H-nmr (deuteriochloroform): δ 7.55-7.26 (m, ArH and NCO-CH=, 5H), 6.63 (d, =CH-CONMe$_2$, 1H, J = 15 Hz), 3.30 (s, CH$_3$N-Ar, 3H), 3.10 (s, CH$_3$N, 3H), 2.96 (s, CH$_3$N, 3H); ms: (70 eV) 231 (M$^+$-35, base peak), 222 (M$^+$-44, 4%), 194 (M$^+$-72, 12%), 160 (8%), 141 (45%), 126)37), 111 (10%), 98 (75%), 72 (42%).

Anal. Calcd. for $C_{13}H_{15}ClN_2O_2$: C, 58.54; H, 5.66; N, 10.50; Cl, 13.29. Found: C, 58.27; H, 5.88; N, 10.44; Cl, 12.96.

N-(3-Cyanoethyl),*N*,*N*'-dimethyl-2'-chlorofumaranilide (**6a**).

(i) *N*-(3-Cyanoethyl)-2'-chloromaleanilic Acid (III).

Treatment of the *N*-(3-cyanoethyl)-*o*-chloroaniline (3.42 g, 0.019 mole) with maleic anhydride (1.86 g, 0.019 mole) and sulphuric acid as catalyst has been made in anhydrous dioxane. The mixture was refluxed for 48 hours and the solvent was removed to give a residual oil which was chromatographed on silica gel column and eluted with ethyl acetate-chloroform (1:1) yielding III after crystallization from diethyl ether as a colorless solid, 2.32 g (44%), mp 102-130°; ir (potassium bromide): 2260 (C≡N), 1715 (COOH), 1635 (CON); ^{1}H-nmr (deuteriochloroform) [6]: δ 11.97 (broad s, OH, 1H), 7.58-7.45 (m, ArH, 4H), 6.32 (d, NCO-CH=, 1H, J = 12.9 Hz), 5.93 (d, =CH-COOH, 1H, J = 12.9 Hz), 4.29 (m, H_A, 1H), 3.75 (m, H_B, 1H), 2.91 (m, H_C, 1H), 2.71 (m, H_D 1H); ms: (70 eV) 243 (M$^+$-35, 40%), 180 (13%), 140 (base peak), 111 (23%), 99 (46%).

Anal. Calcd. for $C_{13}H_{11}ClN_2O_3$: C, 56.02; H, 3.97; N, 10.05; Cl, 12.72. Found: C, 55.93; H, 3.91; N, 10.23; Cl, 12.53.

(ii) *N*-(3-Cyanoethyl),*N*,*N*'-dimethyl-2'-chlorofumaranilide (**6a**).

Ethyl chloroformate (0.92 g, 8.6 mmoles) in anhydrous tetrahydrofuran was added to a solution of III (2.39 g, 8.6 mmoles) and triethylamine (0.98 g, 9.15 mmoles) in tetrahydrofuran at −12 to −15° under a nitrogen stream. After 30 minutes dimethylamine 15% in tetrahydrofuran was added and the mixture was stirred overnight at room temperature. The solid was filtered off and the solvent evaporated to give a residual oil which was chromatographed on a silica gel column and eluted with ethyl acetate-toluene-chloroform (9:1:1) giving after crystallization from diethyl ether **6a** as a colourless solid, 0.76 g (29%), mp 107-109°; ir (potassium bromide): 2250 (C≡N), 1675 (broad, NCO and CONMe$_2$); ^{1}H-nmr (deuteriochloroform) [6]: δ 7.63-7.36 (m, ArH, 4H), 7.44 (d, NCO-CH=, 1H, J = 15.3 Hz), 6.55 (d, =CH-CONMe$_2$, 1H, J = 15.3 Hz), 4.27 (m, H_A, 1H), 3.74 (m, H_B, 1H), 3.10 and 2.96 (s, CH$_3$N, 6H), 2.91 (m, H_C, 1H), 2.64 (m, H_D 1H); ms: (70 eV) 305 (M$^+$, 4%), 270 (M$^+$-35, 67%), 261 (M$^+$-44, 2%), 233 (M$^+$-72, 4%), 180 (26%), 140 (38%), 126 (base peak), 111 (14%), 98 (78%), 72 (30%).

Anal. Calcd. for $C_{15}H_{16}ClN_3O_2$: C, 58.92; H, 5.27; N, 13.74; Cl, 11.59. Found: C, 58.99; H, 5.42; N, 13.44; Cl, 11.79.

o-Chloroanilide of the 3-Cyclohexenylacetic Acid (**7a**).

A mixture of the 3-cyclohexenylacetic acid (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 at 0° and a white solid precipitated, which was recrystallized from diethyl ether giving **7a**, 1.64 g (71%), mp 124-125°; ir (potassium bromide): 3300 (NH), 1660 (CON), 1590 (C=C), 755 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 8.42 (broad d, H-C3, 1H, J = 8 Hz), 7.7 (broad s, NH, 1H), 7.5-6.7 (m, ArH, 3H), 5.68 (m, CH=CH, 2H), 2.90-2.30 (m, CH$_2$CO and CH, 3H), 2.15-1.20 (m, (CH$_2$)$_3$, 6H); ms: (70 eV) 249 (M$^+$, 15%), 214 (M$^+$-35, 4%), 169 (M$^+$-84, 19%), 134 (21%), 127 (base peak), 81 (30%).

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.

N-Methyl-*o*-chloroanilide of the 3-Cyclohexenylacetic Acid (**8a**).

To a suspension of sodium hydride (0.37 g, 8.5 mmoles, 55% in mineral oil) in anhydrous tetrahydrofuran was added a solution of **7a** (1.41 g, 5.67 mmoles) in 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 silica gel column eluting with ethyl acetate-petroeum ether yielding **8a** as an oil, 1.41 g (95%); ir (film): 1665 (CON), 1585 (aromatic C=C), 760 (*o*-substitution); ^{1}H-nmr (carbon tetrachloride): δ 7.6-7.05 (m, ArH, 4H), 5.45 (m, CH=CH, 2H), 3.12 (s, CH$_3$N, 3H), 2.5 (m, CH$_2$CO, 2H), 2.10-1.35 (m, CH and (CH$_2$)$_3$, 7H); ms: (70 eV) 263 (M$^+$, 18%), 228 (M$^+$-35, 29%), 183 (M$^+$-80, 11%), 168 (M$^+$-95, 9%), 148 (61%), 141 (base peak), 81 (35%).

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.

Anhydrous bis(Acetylacetonate)nickel(II).

To a solution of potassium acetylacetonate in absolute ethyl alcohol prepared from acetylacetone (2.0 g, 0.02 mole) and potassium hydroxide (1.12 g, 0.02 mole) was added nickel(II) chloride (2.37 g, 0.01 mole) in absolute ethyl alcohol and the mixture was stirred at room temperature for 30 minutes. The white solid was filtered off and the solvent evaporated, providing an emerald green solid 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 *N*-Alkenyl-*o*-chloroanilides **1a-8a** 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, was added triethylaluminum (0.68 g, 6 mmoles, 1.62 ml of a solution 50% in toluene) at −15° with an external bath and under a stream of helium. The mixture, after a vigorous initial reaction, was stirred at room temperature for 30 minutes and acquired the characteristic dark red colour of tetrakis(triphenylphosphine)nickel(0). A solution of the *N*-alkenyl-*o*-chloroanilide derivative (1 mmole) in toluene was added and the mixture was warmed within a range of 60-80° for 4-5 hours. Finally the mixture was hydrolyzed with a saturated ammonium chloride solution. The organic layer was extracted and dried and then was purified by chromatography on a silica gel column.

Cyclization of **1a**. a) In a 6:1 Molar Ratio of Triethylaluminum to Substrate.

To a solution of tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene prepared from bis(acetylacetonate)nickel(II) (0.51 g, 2 mmoles), triphenylphosphine (2.09 g, 8 mmoles) and triethylaluminum (1.36 g, 12 mmoles, 3.2 ml of a solution 50% in toluene) was added a solution of **1a** (0.35 g, 2 mmoles) in toluene at 60°. The mixture was stirred at 60-80° for 5.5 hours and hydrolyzed with a saturated solution of ammonium chloride. The crude product was purified by chromatography on silica gel by using first a column and finally thick-layer methods with petroleum ether-ethyl acetate (3:1) as the eluent in both cases. In order of the elution there was obtained the following products:

o-Chloropropioanilide (**1e-1**).

This compound was a colourless solid, mp 87-88°, 0.11 g (31%); ir (potassium bromide): 3230 (NH), 1670 (CON), 760 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 8.37 (dd, H-C3, 1H, J = 8.0 and 1.5 Hz), 7.65 (broad s, NH, 1H), 7.43-6.92 (m, ArH, 3H), 2.46 (a, CH$_2$CO, 2H, J = 7.65 Hz), 1.26 (t, CH$_3$, 3H, J = 7.65 Hz); ms: (70 eV) 183 (M$^+$, 5%), 148 (M$^+$-35, 19%), 127 (M$^+$-56, base peak).

Anal. Calcd. for $C_9H_{10}ClNO$: C, 58.86; H, 5.48; N, 7.62; Cl, 19.30. Found: C, 58.63; H, 5.23; N, 7.61; Cl, 19.22.

o-Ethylacrylanilide (**1e-2**).

This compound was a colourless solid, mp 105-106°, 0.125 g (36%); ir (potassium bromide): 3300 (NH), 1665 (CON), 1640 (C=C), 760 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 7.79 (broad s, NH, 1H), 7.62-7.06 (m, ArH, 4H), 6.39-6.27 (m, HC=, 1H), 5.78-5.52 (m, CH$_2$=, 2H), 2.60 (q, CH$_2$Ar, 2H, J = 7.6 Hz), 1.19 (t, CH$_3$, 3H, J = 7.6 Hz); ms: (70 eV) 175 (M$^+$, 30%), 160 (M$^+$-15, 18%), 146 (M$^+$-29, 26%), 557 (base peak).

Anal. Calcd. for $C_{11}H_{13}ClNO$: C, 75.40; H, 7.47; N, 7.99. Found:

C, 75.27; H, 7.32; N, 7.83.

3-Methoxyindole (**1b**).

This compound was a colourless solid, mp 124° [8], 71 mg (24%); ir (potassium bromide): 3240 (NH), 1720 (CON oxindole); ^{1}H-nmr (deuteriochloroform): δ 8.70 (broad s, NH, 1H), 7.35-6.82 (m, ArH, 4H), 3.38 (broad q, CH, 1H, J = 7.6 Hz), 1.48 (d, CH_3, 3H, J = 7.6 Hz); ms: (70 eV) 147 (M^+, 60%), 132 (M^+-15, 19%), 118 (M^+-29, base peak), 104 (28%).

Anal. Calcd. for C_9H_9NO: C, 73.44; H, 6.16; N, 9.51. Found: C, 73.21; H, 6.12; N, 9.33.

2-Oxo-1,2,3,4-tetrahydroquinoline (**1d**).

This compound was a colourless solid, mp 167° [9], 27 mg (9%); ir (potassium bromide): 3240 (broad, NH), 1685 (CON); ^{1}H-nmr (deuteriochloroform): δ 8.73 (broad s, NH, 1H), 7.78-6.75 (m, ArH, 4H), 2.97 (m, CH_2CO, 2H), 2.63 (m, CH_2Ar, 2H); ms: (70 eV) 147 (M^+, base peak), 118 (M^+-29, 74%), 92 (21%).

Anal. Calcd. for C_9H_9NO: C, 73.45; H, 6.17; N, 9.51. Found: C, 73.63; H, 6.28; N, 9.32.

By gc/ms techniques also was detected *o*-ethylpropioanilide (**1e-3**); ms: (70 eV) 177 (M^+, 12%), 148 (M^+-29, 15%), 121 (M^+-56, 47%), 106 (base peak), 91 (23%), 57 (41%).

b) With Crystalline Tetrakis(triphenylphosphine)nickel(0).

To a mixture of bis(acetylacetonate)nickel(II) (0.7 g, 2.76 mmoles) and triphenylphosphine (4.12 g, 0.015 moles) in anhydrous diethyl ether was added triethylaluminum (0.94 g, 3 mmoles, 1.57 ml) at −15° and the mixture was stirred at room temperature under nitrogen for 15 minutes. The brick red slurry was filtered through a sintered glass in nitrogen atmosphere and the crystalline solid tetrakis(triphenylphosphine)nickel(0) was washed two times with cold anhydrous diethyl ether. After the complex was dissolved in anhydrous toluene and this solution was warmed at 60°, then **1a** (0.5 g, 2.76 mmoles) in toluene was added to the solution of tetrakis(triphenylphosphine)nickel(0) at 60° and the mixture was stirred at 60-80° for 5 hours. The crude product was purified as described in part a) and there was obtained the following products:

o-Chloropropioanilide (**1e-1**).

This compound was obtained in 56% yield (0.28 g), mp 87-88°.

Propioanilide (**1e-4**).

This compound was a colourless solid, mp 104°, 0.116 g (29%); ir (potassium bromide): 3280 (NH), 1670 (CON), 750, 690 (monosubstitution); ^{1}H-nmr (deuteriochloroform): δ 7.50-6.95 (m, ArH, 5H), 2.30 (q, CH_2CO, 2H, J = 6.6 Hz), 1.13 (t, CH_3, 3H, J = 6.6 Hz); ms: (70 eV) 149 (M^+, 15%), 93 (M^+-56, base peak), 57 (16%).

Anal. Calcd. for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.38. Found: C, 72.20; H, 7.15; N, 9.27.

2-Oxo-1,2,3,4-tetrahydroquinoline (**1d**).

This compound was obtained in 15% yield (60 mg) mp 167°.

The spectral data of **1d** and **1e-1** are given in part a).

Cyclization of **2a**.

To a solution of tetrakis(triphenylphosphine)nickel(0) prepared from bis(acetylacetonate)nickel(II) (0.641 g, 2.5 mmoles), triphenylphosphine (2.62 g, 0.01 mole) and triethylaluminum (1.71 g, 0.015 mole, 4.0 ml of a solution 50% in toluene) in anhydrous toluene was added **2a** (0.645 g, 2.5 mmoles) in anhydrous toluene at 60° and the mixture was stirred at 105° for 5.75 hours. Then it was hydrolyzed with a saturated solution of ammonium chloride. The crude product was purified first by column and finally by thick-layer chromatography on silica gel with a mixture of hexane-ethyl aceate (3:1) as the eluent in both cases. The four products obtained in the order of the elution were:

(E)-o-Ethylcinnamanilide (**2d**).

This compound was a white solid when recrystallized from ethyl alcohol, mp 160-161°, 0.28 g (45%); ir (potassium bromide): 3280 (NH), 1660 (CON), 750 (*o*-substitution); ^{1}H-nmr (deuteriochloroform): δ 7.75 (d, CO-CH=, 1H, J = 15.55 Hz), 7.53-7.14 (m, ArH, 9H), 6.59 (d, =CH-Ar, 1H, J = 15.55 Hz), 2.66 (q, CH_2Ar, 2H, J = 7.4 Hz), 1.25 (t, CH_3, 3H, J = 7.4 Hz); ms: (70 eV) 251 (M^+, 4%), 222 (M^+-29, 1%), 160 (M^+-91, 18%), 131 (base peak), 121 (27%), 103 (72%), 91 (13%).

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.81; N, 5.57. Found: C, 81.20; H, 6.73; N, 5.31.

(Z)-Benzylidene-1,3-dihydroindole-2-one (*(Z)*-**2c**).

This compound was deep orange needles, mp 180-181° [10], 39 mg (7%); ir (potassium bromide): 3210 (NH), 1701 (CON); ^{1}H-nmr (deuteriochloroform): δ 8.28 (m, H-*ortho* of the phenyl ring, 2H), 8.16 (broad s, NH, 1H), 7.56 (s, vinylic H, 1H), 7.52-6.79 (m, ArH, 7H); ms: (70 eV) 221 (M^+, base peak), 193 (M^+-28, 50%), 165 (M^+-56, 75%), 144 (M^+-77, 94%).

Anal. Calcd. for $C_{15}H_{11}NO$: C, 81.42; H, 5.01; N, 6.33. Found: C, 81.05; H, 4.87; N, 6.03.

(E)-Benzylidene-1,3-dihydroindole-2-one (*(E)*-**2c**).

This compound was yellow needles, mp 175-176° [10], 72 mg (13%); ir (potassium bromide): 3200 (NH), 1710 (CON); ^{1}H-nmr (deuteriochloroform): δ 8.90 (broad s, NH, 1H), 7.84 (s, vinylic H, 1H), 7.72-6.69 (m, ArH, 9H); ms: (70 eV) 221 (M^+, base peak), 193 (M^+-28, 50%), 165 (M^+-56, 67%), 144 (M^+-77, 82%).

Anal. Calcd. for $C_{15}H_{11}NO$: C, 81.42; H, 5.01; N, 6.33. Found: C, 81.10; H, 5.21; N, 6.23.

3-Benzyloxindole (**2b**).

This compound was a colourless solid, mp 131° [11], 0.195 g (35%); ir (potassium bromide): 3220 (NH), 1720 (CON oxindole); ^{1}H-nmr (deuteriochloroform): δ 8.25 (broad, s, NH, 1H), 7.27-6.70 (m, ArH, 9H), 3.76 (dd, H-C3, 1H, J = 4.604 and 9.285 Hz), 3.05 (dd, CH_M-Ph, 1H, J = −13.739 and 4.604Hz), 2.96 (dd, CH_A-Ph, 1H, J = −13.739 and 9.285 Hz); ms: (70 eV) 223 (M^+, 29%), 205 (M^+-18, 2%), 146 (M^+-77, 5%), 132 (M^+-91, 21%), 117 (2%), 104 (4%), 91 (base peak).

Anal. Calcd. for $C_{15}H_{13}NO$: C, 80.69; H, 5.86; N, 6.27. Found: C, 81.13; H, 5.57; N, 6.31.

Reduction of *(Z)*-**2c** and *(E)*-**2c** to **2b** with Sodium Borohydride.

A solution of the *(Z)* or *(E)* isomer of **2c** (30 mg, 0.135 mmole) in absolute ethyl alcohol was added to a suspension of sodium borohydride (10.26 mg, 0.27 mmole) in absolute ethyl alcohol while cooling with an ice bath. The mixture was stirred at room temperature for 3 hours and was then hydrolyzed with a saturated ammonium chloride solution and extracted with ethyl acetate. The 3-benzyloxindole (**2b**) was recovered quantitatively in both cases after chromatography on silica gel eluting with hexane-ethyl acetate (3:1).

Cyclization of **3a**.

To a mixture of bis(acetylacetonate)nickel(II) (0.685 g, 2.67 mmoles) and triphenylphosphine (3.98 g, 15.2 mmoles), in anhydrous diethyl ether was added triethylaluminum (0.89 g, 7.87 mmoles, 1.5 ml) at −15° under a nitrogen atmosphere and the mixture was stirred at room temperature for 15 minutes. The brick-red slurry was filtered through sintered glass under a nitrogen atmosphere and the crystalline brick-red solid was washed with two portions of cold anhydrous diethyl ether. The solid tetrakis(triphenylphosphine)nickel(0) was solved in anhydrous toluene and this solution warmed to 70° and then **3a** (0.64 g, 2.67 mmoles) in anhydrous toluene was added to this solution. The mixture was warmed at 90° for 5 hours and then it was hydrolyzed with a saturated ammonium chloride solution. The crude product was chromatographed in silica gel (column and thick-layer), eluting with ethyl acetate-chloroform (2:1). Two compounds were isolated.

Methyl Oxindolylacetate (**3b**).

This compound was obtained as a colourless solid, mp 185-186°, 0.39 g (73%); ir (potassium bromide): 3200 (NH), 1735 (CO_2Me), 1720 (CON ox-

indole); ^{1}H-nmr (deuteriochloroform): δ 9.20 (broad s, NH, 1H), 7.68-6.84 (m, ArH, 4H), 3.81 (dd, H-C3, 1H, J = 4.525 and 8.017 Hz), 3.69 (s, CH_3O, 3H), 3.08 (dd, CH_M-CO_2Me, 1H, J = −16.841 and 4.525 Hz), 2.82 (dd, CH_A-CO_2Me, 1H, J = −16.841 and 8.017 Hz); ms: (70 eV) 205 (M^+, 18%), 173 (M^+-32, 14%), 162 (M^+-43, 2%), 145 (M^+-60, base peak), 132 (13%), 117 (18%), 104 (4%), 90 (8%).

Anal. Calcd. for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.82. Found: C, 64.15; H, 5.23; N, 6.57.

Methyl Isatinylidene-3-acetate (**3c**).

This compound was obtained as an oil, 0.136 g (26%). It was a mixture of the *(Z)* and *(E)* isomers. It was not possible to separate them by chromatographic or recrystallization methods; ir (potassium bromide): 3550 (NH), 1715 CO_2Me), 1700 (CON); ^{1}H-nmr (deuteriochloroform): δ 7.59-6.99 (m, ArH and vinylic H, 5H), 2.90 (s, CH_3O, 3H), 2.87 (s, CH_3O, 3H); ms: (70 eV) 203 (M^+, 50%), 185 (M^+-18, 9%), 174 (M^+-29, base peak), 158 (M^+-45, 20%), 144 (M^+-59, 72%), 132 (47%), 120 (20%), 104 (15%), 55 (57%).

Cyclization of **4a**.

To a solution of tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene, prepared from bis(acetylacetonate)nickel(II) (1.3 g, 5.24 mmoles) triphenylphosphine (5.50 g, 0.02 mole) and triethylaluminum (3.6 g, 0.31 mmole, 8.5 ml of a solution 50% in toluene) was added **4a** (1.34 g, 5.24 mmoles) in anhydrous tetrahydrofuran at 70° under a nitrogen atmosphere. The mixture was warmed at 80° for 5 hours and then it was hydrolyzed with 0.01*N* hydrochloric acid. The crude product was purified, first on a silica gel column and finally by thick layer chromatography with ethyl acetate-methylene chloride (20:3) as the eluent in both cases. The following products were isolated:

N,N-Dimethyl-3-indolylacetamide (**4e-1**).

This compound was obtained in 3.2% yield (34 mg); ^{1}H-nmr (deuteriochloroform): δ 8.8 (broad s, NH, 1H), 7.65-7.10 (m, ArH, 4H), 7.01 (t, H-C2, 1H), 3.80 (d, CH_3CON, 2H, J = 0.8 Hz), 2.99 (s, CH_3N, 3H), 2.96 (s, CH_3N, 3H); ms: (70 eV) 202 (M^+, 12%), 169 (M^+-33, 1%), 130 (M^+-72, base peak), 72 (10%).

N,N-Dimethyl-2′-ethylfumaranilide (**4e-2**).

This compound was obtained in 1.8% yield (23.2 mg); ^{1}H-nmr (deuteriochlorof): δ 8.58 (broad s, NH, 1H), 7.65-7.10 (m, ArH, and olefinic protons, 6H), 3.08 (s, CH_3N, 3H), 2.98 (s, CH_3N, 4H), 2.95 (q, CH_2-Ar, 2H, J = 8.0 Hz), 1.12 (t, CH_3, 3H, J = 8.0 Hz); ms: (70 eV) 246 (M^+, 7%), 231 (M^+-15, 3%), 174 (M^+-72, 36%), 126 (86%), 121 (55%), 106 (58%), 72 (24%), 46 (base peak).

The products **4e-1** and **4e-2** were mixed in the same fraction and it was not possible to isolate them by chromatographic or recrystallization methods.

N,N-Dimethyl-3-oxindolylacetamide (**4b**).

This compound was obtained as an oil, 1.0 g (94%); ir (potassium bromide): 3440 (sharp, free NH), 3230 (broad, associated NH), 1725 (CON oxindole), 1650 (CON); ^{1}H-nmr (deuteriochloroform): δ 9.02 (broad s, NH, 1H), 7.29-6.82 (m, ArH, 4H), 3.92 (dd, H-C3, 1H, J = 3.175 and 8.938 Hz), 3.09 (dd, CH_M-$CONMe_2$, 1H, J = −16.51 and 3.175 Hz), 2.97 (s, CH_3N, 3H), 2.95 (s, CH_3N, 3H), 2.72 (dd, CH_A-$CONMe_2$, 1H, J = −16.513 and 8.937 Hz); ms: (70 eV) 218 (M^+, 29%), 173 (M^+-45, 8%), 146 (M^+-72, 74%), 145 (base peak), 128 (41%), 117 (70), 104 (11%), 90 (28%), 72 (57%), 46 (96%).

Anal. Calcd. for $C_{12}H_{14}N_2O_2$: C, 66.03; H, 6.46; N, 12.83. Found: C, 65.84; H, 6.21; N, 12.59.

However, by gc/ms techniques, two minor products were detected:

4-(*N,N*-Dimethylcarbamoyl)-2-oxo-1,2,3,4-tetrahydroquinoline (**4d**).

This compound had ms: (70 eV) 218 (M^+, 5%), 173 (M^+-45, 2%), 146 (M^+-72, 15%), 145 (20%), 128 (base peak), 117 (16%), 100 (22%), 72 (50%).

N,N-Dimethylisatylidene-3-acetamide (**4c**).

This compound had ms: (70 eV) 216 (M^+, 12), 172 (M^+-44, 62%), 145 (M^+-71, 36%), 116 (91%), 89 (53%), 72 (27%), 44 (base peak).

Cyclization of **5a**.

To a solution of tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene, prepared from bis(acetylacetonate)nickel(II) (0.256 g, 1 mmole), triphenylphosphine (1.05 g, 4 mmoles) and triethylaluminum (0.69 g, 6 mmoles, 1.62 ml of a solution 50% in toluene) was added **5a** (0.27 g, 1 mmole) in anhydrous tetrahydrofuran under nitrogen and the mixture was stirred at 50-60° for 4 hours. The crude product was purified first by column and finally by thick-layer chromatography with ethyl acetate-benzene as the eluent.

N,N-Dimethyl-(*N*-methyloxyindolyl)-3-acetamide (**5b**).

This compound was isolated as a colourless solid, mp 135-136°, 0.224 g (98%); ir (nujol): 1725 (CON oxindole), 1635 (CON amide); ^{1}H-nmr (deuteriochloroform): δ 7.42-6.77 (m, ArH, 4H), 3.95 (dd, H-C3, 1H, J = 3.167 and 9.345 Hz), 3.23 (s, CH_3N, 6H), 3.13 (dd, CH_M-CO, 1H, J = −16.312 and 3.167 Hz), 2.99 (s, CH_3N, 3H), 2.66 (dd, CH_A-CO, 1H, J = 16.312 and 9.345 Hz); ms: (70 eV) 232 (M^+, 27%), 160 (M^+-72, 96%), 146 (M^+-86, 22%), 130 (base peak), 117 (64%), 103 (22%), 91 (50%), 72 (76%), 42 (88%).

Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 67.22; H, 6.94; N, 12.06. Found: C, 67.13; H, 6.63; N, 12.15.

1-Methyl-4-(*N,N*-dimethylcarbamoyl)-2-oxo-1,2,3,4-tetrahydroquinoline (**5d**).

This compound was detected by gc/ms techniques.

Cyclization of **6a**.

To a solution of the complex tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene prepared from bis(acetylacetonate)nickel(II) (0.31 g, 1.22 mmoles), triphenylphosphine (1.24 g, 48 mmoles) and triethylaluminum (0.70 g, 6.1 mmoles, 1.6 ml of a solution 50% in toluene) was added **6a** (0.37 g, 1.22 mmoles) in anhydrous tetrahydrofuran under nitrogen and the mixture was stirred at 60° for 5 hours. The crude product was purified by chromatography on silica gel (column and thick-layer) eluting with ethyl acetate-toluene (9:1).

N,N-Dimethyl-*N*-(3-cyanoethyloxindolyl)-3-acetamide (**6b**).

This compound was isolated as the main product as a colourless solid, mp 113-15°, 0.31 g (98%); ir (nujol): 2270 (C≡N), 1725 (CON oxindole), 1655 (CON amide); ^{1}H-nmr (deuteriochloroform): δ 7.38-6.85 (m, ArH, 4H), 4.11 (m, N-CH_A, 1H, J = −13.967, 7.391 and 7.029 Hz), 4.01 (m, N-CH_B, 1H, J = −13.967, 8.857 and 5.568 Hz), 3.87 (dd, H-C3, 1H, J = 3.282 and 8.178 Hz), 3.13 (dd, CH_M-CON, 1H, J = −16.677 and 3.282 Hz), 3.00 (s, CH_3N, 3H), 2.93 (s, CH_3N, 3H), 2.85 (dd, CH_A-CON, 1H, J = −16.677 and 8.178 Hz), 2.785 (m, CH_C-CN, 1H, J = −16.151, 7.391 and 8.857 Hz), 2.780 (m, CH_D-CN, 1H, J = −16.151, 7.029 and 5.568 Hz); ms: (70 eV) 271 (M^+, 53%), 225 (M^+-46, 15%), 199 (M^+-72, 21%), 158 (base peak), 146 (17%), 130 (26%), 117 (11%), 103 (7%), 72 (26%).

Anal. Calcd. for $C_{15}H_{17}N_3O_2$: C, 66.40; H, 6.31; N, 15.48. Found: C, 66.21; H, 6.35; N, 15.70.

N-3-Cyanoethyl-4-(*N,N*-dimethylcarbamoyl)-2-oxo-1,2,3,4-tetrahydroquinoline (**6d**).

This compound was detected by gc/ms techniques; ms: (70 eV) 271 (M^+, 17%), 199 (M^+-72, 9%), 128 (base peak), 100 (20%), 72 (33%).

Cyclization of **7a**.

To a solution of tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene prepared from bis(acetylacetonate)nickel(II) (0.195 g, 0.761 mmoles), triphenylphosphine (0.797 g, 3 mmoles) and triethylaluminum (0.52 g, 4.56 mmoles, 1.24 ml of a solution 50% in toluene) was added **7a** (0.190 g, 0.761 mmole) in anhydrous tetrahydrofuran under nitrogen and the mixture was refluxed at 120° for 5 hours. The crude product was purified by chromatography on silica gel eluting with benzene and identified as the starting product **7a** unchanged. However, by gc/ms techni-

ques was detected the anilide of the 3-cyclohexenylacetic acid (**7e**); ms: (70 eV) 215 (M^+, 17%), 148 (M^+-67, 14%), 141 (M^+-74, 18%), 93 (base peak), 81 (50%).

Cyclization of **8a**.

N-Methyl-*o*-chloroanilide of the 3-cyclohexenylacetic acid (**8a**) (0.76 g, 2.9 mmoles) in anhydrous tetrahydrofuran was added to a solution of tetrakis(triphenylphosphine)nickel(0) in anhydrous toluene, prepared from bis(acetylacetonate)nickel(II) (0.75 g, 2.9 mmoles), triphenylphosphine (3.03 g, 11.6 mmoles) and triethylaluminum (1.98 g, 17.4 mmoles, 4.72 ml of a solution 50% in toluene). The mixture was refluxed at 120° for 5 hours. The crude product was purified by a combination of column and thick-layer chromatography on silica gel with chloroform-petroleum ether (5:1) and ethyl acetate-petroleum ether (2:1) as the eluents. The main products obtained were:

N-Methyl-*o*-chloroanilide of 3-Cyclohexenylacetic Acid (**8a**).

This compound was obtained unchanged, 0.55 g (74%).

N-Methylanilide of 3-Cyclohexenylacetic Acid (**8e-1**).

This compound was obtained as an oil, 0.175 g (25%); ir (potassium bromide): 1660 (CON), 765 and 695 (monosubstitution); ^{1}H-nmr (deuteriochloroform): δ 7.39-7.19 (m, H *ortho* and H *para*, 3H), 7.12-7.05 (m, H *meta*, 2H), 5.53 (dd of doublets, =C*H*-CH_2, 1H, J = 10.0, 5.68 and 3.43 Hz), 5.39 (dd, CH-C*H*=, 1H, J = 10.00 and 2.02 Hz), 3.20 (s, CH_3N, 3H), 1.93 (d, CH_2-CO, 2H, J = 8.0 Hz), 1.88-1.61 (m, CH-C= and CH_2-CH=, 3H), 1.54-1.35 (m, CH_2-C, 2H), 1.13-0.94 (m, CH_2-CH_2-CH_2, 2H); ms: (70 eV) 229 (M^+, 37%), 228 (M^+-1, 3%), 200 (M^+-29, 2%), 134 (M^+-95, 11%), 107 (base peak), 95 (4%).

Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.10. Found: C, 78.41; H, 8.17; N, 6.20.

N-Methyl-*o*-ethylanilide of 3-Cyclohexenylacetic Acid (**8e-2**).

This compound was detected by gc/ms techniques; ms: (70 eV) 257 (M^+, 23%), 228 (M^+-29, 2%), 177 (M^+-80, 30%), 162 (M^+-95, base peak), 148 (13%), 135 (61%), 120 (77%), 95 (11%), 81 (36%).

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