Pergamon

Tetrahedron 54 (1998) 11079–11094

TETRAHEDRON

Synthesis and Reactivity of Substituted 3-([(Trifluoromethyl)sulfonyl]oxy)-1*H*-indole-2-carboxylate in Palladium-Catalyzed Reactions

Béatrice Malapel-Andrieu, Jean-Yves Mérour*

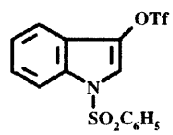
Institut de Chimie Organique et Analytique associé au CNRS, BP 6759, F-45067 Orléans Cédex 2, France

Received 23 March 1998; accepted 2 July 1998

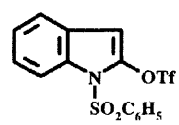
Abstract Palladium-catalysed Suzuki and Stille reactions of substituted 3-indolyltriflate afforded the corresponding 3-substituted indoles. By contrast, the Heck reaction of allyl alcohol with such triflates gave 2-allyloxy-3-oxoindole derivatives rather than the 3-substituted indole products as a result of a nucleophilic attack on an acyliminium intermediate. © 1998 Elsevier Science Ltd. All rights reserved.

Keywords: Indoles; Heck reactions; Suzuki reactions; Coupling reactions

In recent years the palladium(0)-catalysed cross-coupling reaction has evolved into a powerful synthetic tool for the construction of new heterocyclic compounds.[1-3] Especially, numerous reactions have been reported in indole chemistry [4-6] in which the indole moiety is usually introduced *via* indolylboronic acids, [7] *N*-protected 2- and 3-indolylzinc halides[8] or indolylstannanes;[9] little work has been done with 2- or 3- halogenoindole.[10] Recently Gribble *et al.* have reported[11] investigations on the Heck reaction of triflate **1**; we have already described the synthesis and the reactivity of 2-indolyltriflate **2**.[12]



1



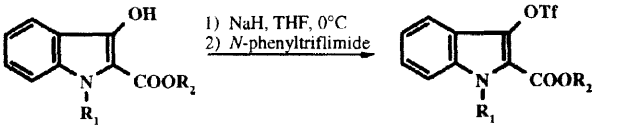
2

Dyker[13] has described the reactivity of 2-bromobenzaldehyde with allylic alcohols in domino-Heck aldol condensation. In order to explore the reactivity of functionalized indolic triflates we have prepared compound **5** and **6**. Non-indolic triflate esters[14] have been reported, for example in carbapenem chemistry,[15] and show a normal reactivity in Heck reactions. The 3-hydroxy esters[16] **3** and **4** were treated with sodium hydride at 0°C followed by addition of *N*-phenyltriflimide to generate the triflate **5** and **6** respectively, in 89% and 95% yields (Scheme 1).

Fax (33) 238417281 E-mail jean-yves.merour@univ-orleans.fr

PII: S0040-4020(98)00649-8

In a preliminary communication[17] we have reported the unexpected reactivity of triflate **6** towards allylic alcohols.

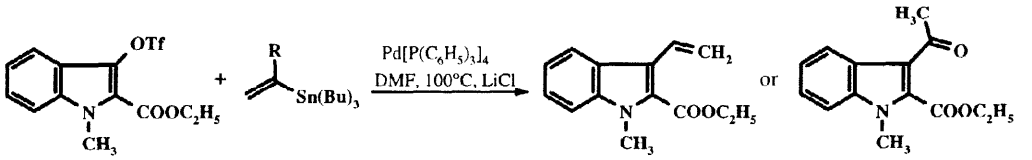


3 $R_1 = H, R_2 = CH_3$
4 $R_1 = CH_3, R_2 = C_2H_5$

5 $R_1 = H, R_2 = CH_3$
6 $R_1 = CH_3, R_2 = C_2H_5$

Scheme 1

In order to test the reactivity of such functionalized triflates we have performed Stille and Suzuki coupling reactions with triflate **6** only since triflate **5** gave degradation products. We have treated first the triflate **6** with vinyltributylstannane **7a** (1.15 eq) to generate the 3-vinylindole **8a** in 89% yield or with 1-ethoxy vinyltributylstannane **7b** (1.15 eq) to obtain the 3-acetylindole **8b** in 65% yield. The conditions used for this Stille coupling reaction was palladium tetrakis(triphenylphosphine) ($Pd[P(C_6H_5)_3]_4$, 3%) as the catalyst with added lithium chloride (3 eq) in DMF at 100°C (Scheme 2). Compound **8a** can be used in Diels Alder reactions.[18]



6

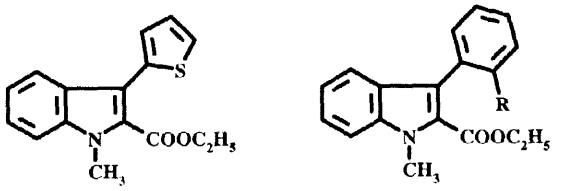
7a R = H
7b R = OC_2H_5

8a

8b

Scheme 2

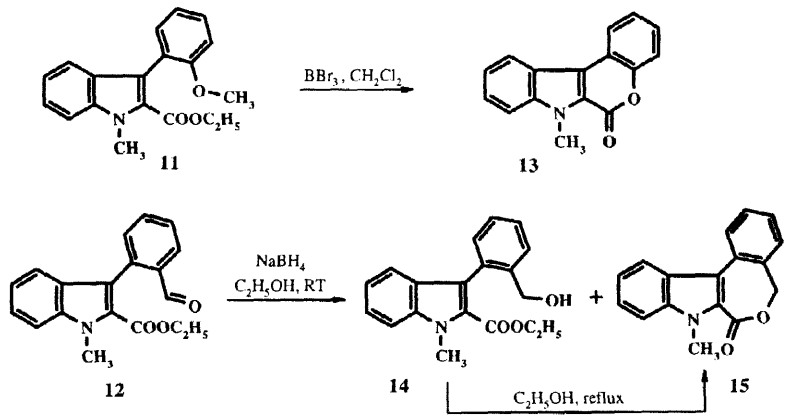
Since 3-phenylindoles have interesting pharmacological structures (as endothelin antagonists), [19] we have treated triflate **6** with phenylboronic acids some of which being functionalized to give access, *inter alia*, to lactonic derivatives. It is well known that an inorganic base is recommended[20] for the Suzuki reaction; in our case however only an organic base[21] such as triethylamine gave satisfactory results. The following conditions were used for the coupling reactions with boronic acids (1.3 eq): $Pd[P(C_6H_5)_3]_4$ (3-5%), triethylamine (1-2 eq) in DMF at 100°C.



9

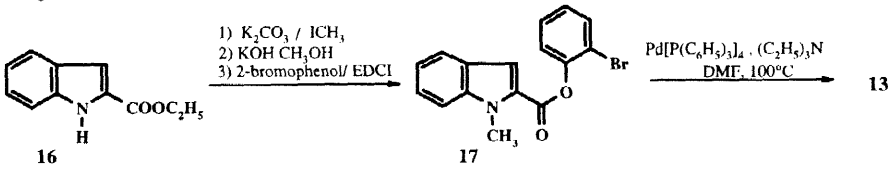
10 R = H
11 R = OCH_3
12 R = CHO

Compound **9** was obtained from thiophene-2-boronic acid and triflate **6** in 73% yield, and compound **10** from phenylboronic acid in 90 % yield. Compound **11** was obtained from 2-methoxyphenylboronic acid in 58% yield and was further demethoxylated with boron tribromide at 0°C to give directly lactone **13** in 83% yield (Scheme 3). Compound **12** was obtained from triflate **6** and 2-formylphenylboronic acid in 30% yield; reduction of the formyl group of **12** with sodium borohydride gave a mixture of alcohol **14** (80% yield) and lactone **15** (19%). Heating **14** in refluxing ethanol afforded quantitatively compound **15**.



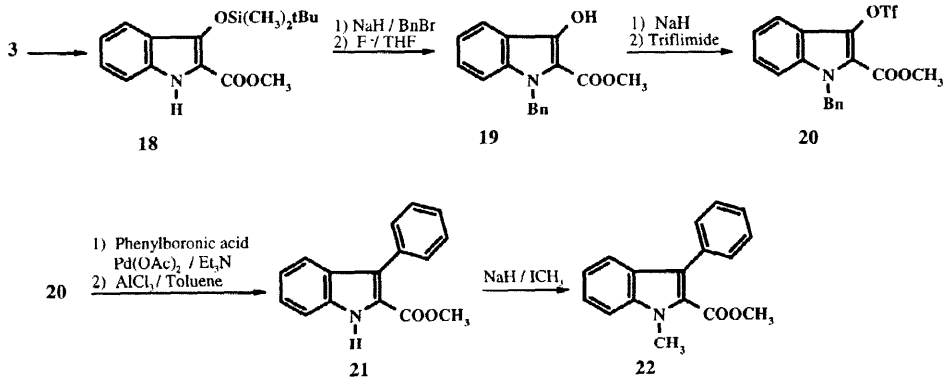
Scheme 3

Compound **13** was also prepared by another route in order to establish its structure: an intramolecular Heck reaction of the 2-bromophenyl ester **17**, synthesized in three steps (52 %) from ethyl indole-2-carboxylate **16**, using $Pd[(P(C_6H_5)_3]_4$ as the catalyst afforded compound **13** in 66% yield (Scheme 4).



Scheme 4

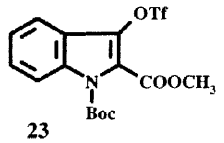
In order to enhance the versatility of the described reactions, we have also prepared the *N*-benzylindolic triflate **20** (Scheme 5). Compound **3** was first protected as a silyloxy derivative **18** (84% yield) and *N*-benzylated with benzyl bromide/NaH (65%). Removal of the silyl group using fluoride anion afforded **19** (60% yield) which was treated with *N*-phenyltriflimide in the presence of sodium hydride in THF at 0°C to afford the triflate **20** in quantitative yield.



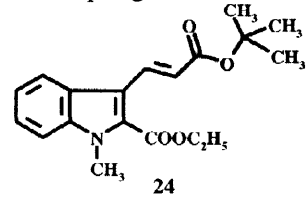
Scheme 5

Suzuki reaction of **20** with phenylboronic acid in the presence of palladium acetate/triethylamine afforded the corresponding 3-phenylindole in 62% yield; this compound was debenzylated in the presence of aluminium chloride/toluene at room temperature to afford **21** in 73 % yield. The nitrogen atom of **21** could be alkylated with an electrophile, such as iodomethane, to give compound **22** in 71% yield. We have also directly

prepared the Boc indolic triflate **23** from compound **5** (Boc_2O/ Et_3N/DMAP) in 40% yield but compound **23** did not give satisfactory results in palladium-catalysed cross-coupling reactions.

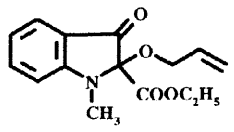


23

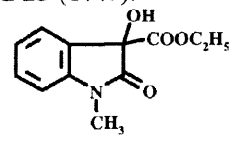


24

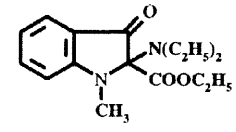
After numerous and unfruitful attempts[17] triflate **6** was reacted in a Heck-type reaction [$Pd(OAc)_2$ 8%, $P(C_6H_5)_3$ 3-10%, Et_3N (1-3 eq)] with *tert*-butyl acrylate (1.3-3 eq) in DMF to afford in moderate yield (32%) the ester **24**.[22] Acrylonitrile did not react under these experimental conditions. Since we could predict the reactivity of triflate **6**, we treated it with allyl alcohol[23,24] in order to obtain a substituted allyl alcohol or an aldehyde. Using the conditions herein reported, [$Pd(OAc)_2$ 6%, $P(C_6H_5)_3$ 3%, Et_3N, 2 eq, DMF 100°C, allyl alcohol, 3 eq], the reaction in the presence of an organic base such as triethylamine did not afford the expected Heck products[25] (**28** or **29**) but rather the 2-allyloxy derivative **25** (45% yield) accompanied with compound **26** (13% yield). After replacement of DMF with acetonitrile, the reaction afforded only compound **25** in 57% yield. Compound **27** was obtained in DMF by increasing the amount of palladium acetate (20%); thus **27** was obtained in 20% yield together with compound **25** (17%).



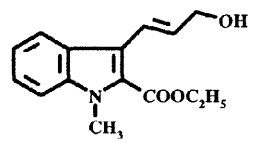
25



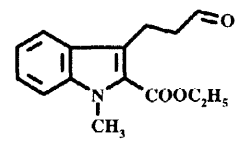
26



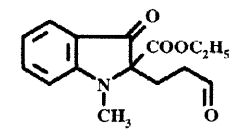
27



28

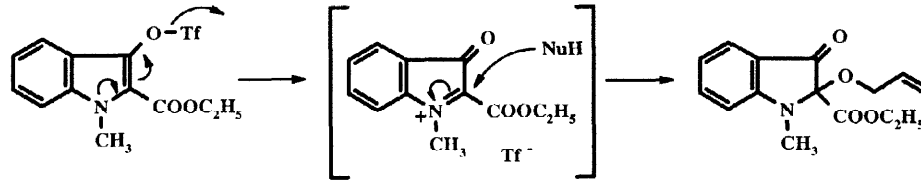


29



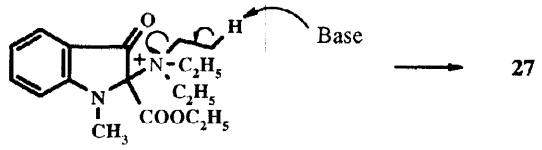
30

The formation of compound **25** can be explained by a nucleophilic attack of the oxygen atom of the allyl alcohol (NuH) on the C-2 carbon atom of an acyliminium species as depicted recently by Edstrom *et al* for pyrido[3,4-*b*]pyrrolizidine triflate.[26] *The formation of the acyliminium species apparently did not require the presence of palladium* but we observed that yields were higher and rates faster in the presence of palladium acetate (Scheme 6).

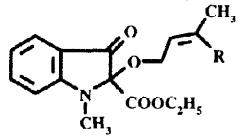


Scheme 6

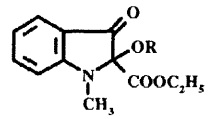
The formation of **27** may be the result of a Hofmann-type elimination on the intermediate resulting from the nucleophilic attack of triethylamine on the acyliminium intermediate.



The formation of **26** is the result of a rearrangement of the non-isolated 2-hydroxy compound **31**; such rearrangement has been described for the NH analogue;[27] the structure of **26** has been confirmed by the synthesis of an authentic sample from *N*-methylaniline and diethyl ketomalonate;[28] the non-isolated product **31** may arise in part from the corresponding acetate. The use of but-2-en-1-ol and 3-methylbut-2-en-1-ol afforded, under similar experimental conditions [$Pd(OAc)_2$ 8%, $P(C_6H_5)_3$ 3%, Et_3N 2eq, DMF 100°C], the corresponding allyloxy derivatives **32** in 20% yield (accompanied with **26** [25%] and **27** [20%]) and **33** in 41% yield (accompanied with **26** [19%]) respectively. Homoallylic alcohol also reacted with triflate **6** to afford **35** and **26** respectively in 19 % and 25% yields. Methanol was able to react with **6** in the absence of palladium to afford the 2-methoxy derivative **34** in 42% yield.

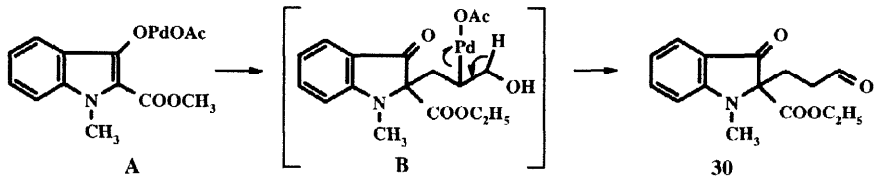


32 R = H
33 R = CH_3



31 R = H
34 R = CH_3
35 R = $CH_2CH_2CH{=}CH_2$

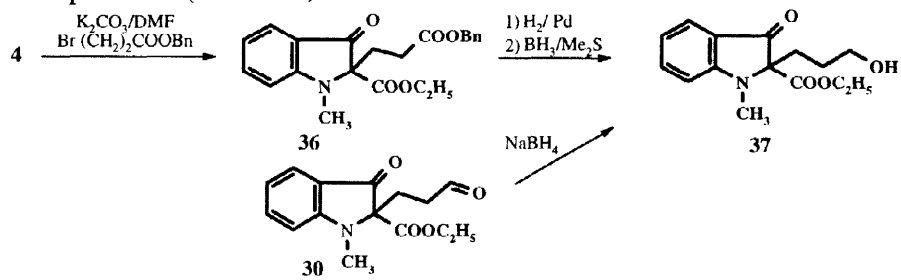
The synthesis of a normal Heck product, such as **28** or **29**, using other experimental conditions has been actively pursued; in particularly the use of sodium hydrogencarbonate and a phase transfer reagent[29] [$Pd(OAc)_2$ 10%, $Et_3N^+Bn\ Cl^-$, 1 eq, allyl alcohol, 1.45 eq, $NaHCO_3$, 2.5 eq, DMF 100°C] gave compound **29** but the yield was low (18%) and the major product was the 2-(3-oxopropyl) derivative **30** (26%-40% yield), again accompanied with compound **26** (18%-6%).



A **B** **30**

Scheme 7

The formation of **30** can be explained by the initial formation of a palladium enolate (**A**) which added on the allyl alcohol to afford the carbopalladiate intermediate (**B**); then a β-elimination between the CH and the C-Pd bonds gave compound **30** (Scheme 7).

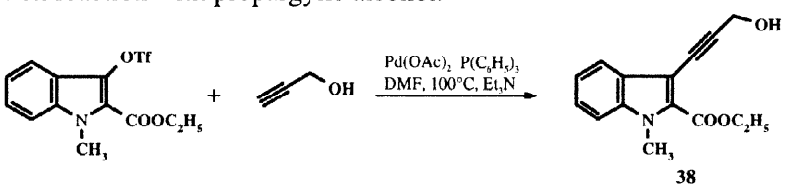


36 **37** **30**

Scheme 8

The structure of compound **30** was confirmed by an alternative synthesis from **4**. Compound **4** was *C*-alkylated in DMF using benzyl 3-bromopropanoate in the presence of potassium carbonate to give compound **36** (87% yield); then hydrogenolysis of the benzyl ester (44% yield) followed by the chemoselective reduction of the acid function using $BH_3.Me_2S$ afforded the alcohol **37** (43% yield); this alcohol was identical to the compound obtained by sodium borohydride reduction (65% yield) of compound **30** (Scheme 8).

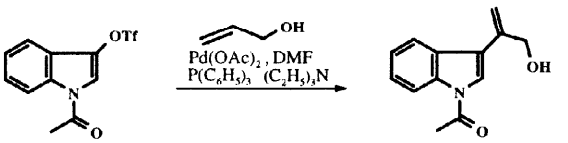
If the Heck reaction with allyl alcohol gave unexpected results by contrast the use of propargylic alcohol (3 eq) cleanly afforded, using a similar catalytic system [$(Pd(OAc)_2$ 8%, $P(C_6H_5)_3$, 2.5%, Et_3N, 2 eq, DMF 100°C], the expected alcohol **38** in good yield (80%) (Scheme 8). By comparison, it is interesting to note that ethyl 3-iodo-1*H*-2-indolecarboxylate or ethyl 3-iodo-1-(methylsulfonyl)-1*H*-2-indolecarboxylate failed to give any detectable product on reaction with propargylic alcohol.[30]



38

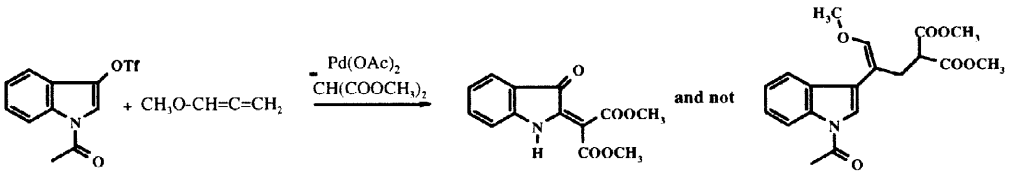
Scheme 9

We wanted to know if it was either the presence of the ester group at position-2 of the indole or if it was an intrinsic property of the indolic triflate which implied such a dualistic behavior. Gribble[11] has described numerous Heck reactions of triflate **1**, which showed the usual reactivity; since the reaction of **1** has not been described with allyl alcohol itself, we have reacted triflate **39** with allyl alcohol (3 eq) [$(Pd(OAc)_2$ 7%, $P(C_6H_5)_3$ 2.5%, Et_3N 2 eq, DMF 100°C]. This led to the unexpected substituted allyl alcohol **40** in 28% yield only; it should be noted that the alcohol **40** might explain the structure of the lactonic derivative formed in an erratic manner from triflate **6** and allyl alcohol.[25] This result indicates that triflates **6** and **39** appear to have a different behavior.



39 40

But, continuing the comparison, we planned a carbopalladiation reaction[31] of triflate **39** with methoxyallene and the dimethyl malonate anion; the postulated π–allyl complex was expected to react with the dimethyl malonate anion in order to generate the substituted malonate **42**; however we obtained only the ketone **41**.



39 41 42

This ketone **41** was also obtained by directly treating triflate **39** with dimethylmalonate anion; that means that a carbon nucleophilic attack in position 2 is also possible with the unsubstituted triflate **39**. This aspect of reactivity is discussed in the following paper.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage and are uncorrected. IR spectra were recorded on Perkin Elmer FT Paragon 1000 PC spectrometer. NMR spectra were obtained on a Bruker advance DPX 250 using TMS as internal standard. Mass spectra were obtained on a Nermag R 10C instrument (chemical ionisation with ammonia) or on a Perkin Elmer API 300 instrument.

Methyl 3-{[(Trifluoromethyl)sulfonyl]oxy}-1*H*-2-indolecarboxylate (5).

Under a blanket of argon, methyl 3-hydroxy-1*H*-2-indolecarboxylate **3** (200 mg, 1.05 mmol) in THF (2 mL) was added at 0° C to a suspension of sodium hydride (80% weight) (40 mg, 1.33 mmol) in THF (10 ml). After 30 min, *N*-phenylbis(trifluoromethanesulphonimide) (*N*-phenyltriflimide) (560 mg, 1.57 mmol) was added in portions and the mixture was stirred at room temperature for 1h. After evaporation, the residue was dissolved in water (10 mL); the aqueous layer was neutralized to pH 7 with 10% HCl and extracted with dichloromethane (3x10 mL). After drying over $MgSO_4$ the solvent was evaporated and the residue was chromatographed on a silica gel column (eluent dichloromethane/ petroleum ether 80/20) to give compound **5**; m = 302 mg; yield 89 %; mp 168-170°C. IR (KBr) ν = 3300 (NH), 1680 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 3.90 (s, 3H, OCH_3); 7.18-7.23 (m, 2H, Harom); 7.35-7.65 (m, 1H, Harom); 7.61 (d, 1H, Harom; J = 8.1 Hz); 9.15 (s, 1H, NH).^{13}C NMR ($CDCl_3$) δ = 51.9 (CH_3); 111. 9 (CH); 117.3 (C); 118.3 (CH); 118.9 (C); 119.1 (q, J_{C-F} = 320 Hz); 121.8 (CH); 126.4 (CH); 129.6 (C); 132.7 (C); 159.9 (CO). MS (IS): m/z = 324 (M^++1). Anal. Calcd for $C_{11}H_8F_3NO_5S$: C, 40.87; H, 2.49; N, 4.33. Found: C, 41.06; H, 2.63; N, 4.49.

Ethyl 3-{[(Trifluoromethyl)sulfonyl]oxy}-1-methyl-1*H*-2-indolecarboxylate (6).

Same procedure as for compound **5** starting from ethyl 3-hydroxy-1-methyl-1*H*-2-indolecarboxylate **4**; elution dichloromethane/petroleum ether 80/20; yield 95%; mp 82-84°C. IR (KBr) ν = 1680 (CO) cm^{-1}.^1H NMR ($CDCl_3$) δ = 1.45 (t, 3H, CH_3, J= 7.3 Hz); 4.08 (s, 3H, NCH_3); 4.47 (q, 2H, OCH_2, J = 7.3 Hz); 7.23-7.27 (m, 1H, Harom); 7.41-7.43 (m, 2H, Harom); 7.63 (d, 1H, Harom, J = 8.8 Hz).^{13}C NMR ($CDCl_3$) δ = 14.1 (CH_3); 32.0 (NCH_3); 61,7 (OCH_2); 110.6 (CH); 118.7 (q, J_{C-F} = 300Hz); 117.9 (C); 118.6 (C); 119.4 (CH); 122.0 (CH); 126.4 (CH); 130.8 (C); 135.7 (C); 160.3 (CO). MS (CI/NH_3): m/z = 352 (M^++1). Anal.Calcd for $C_{13}H_{12}F_3NO_5S$: C, 44.45; H, 3.44; N, 3.99.Found:C, 44.76; H, 3.50; N, 3.80.

General procedure for Stille reactions

Lithium chloride (70 mg, 1.65 mmol, 3 eq) and palladium tetrakis(triphenylphosphine) (20 mg, 0.017 mmol, 3%) were introduced in a flask; triflate **6** (200 mg, 0.57 mmol) and the stannane derivative (0.66 mmol) in DMF (10 mL) were added dropwise. The mixture was heated at 100°C till complete disappearance of triflate **6** (TLC). Water (10 mL) and dichloromethane (10 mL) were added to the mixture which was extracted with ethyl acetate (3x10 mL); the organic layers were dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (eluent dichloromethane).

Ethyl 3-Vinyl-1-methyl-1*H*-2-indolecarboxylate (8a).

Starting from vinyltributylstannane (0.66 mmol); reaction time 1h30; yield 89%; oil. IR (film) ν = 1670 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.28 (t, 3H, CH_3, J = 7.0 Hz); 3.83 (s, 3H, NCH_3); 4.27 (q, 2H, OCH_2, J = 7.0 Hz); 5.28 (dd, 1H, $CH=CH_2$, J = 1.5 Hz, J = 11 Hz); 5.65 (dd, 1H, $CH=CH_2$, J = 1.5 Hz, J = 17.0 Hz); 6.99-7.04 (m, 1H, Harom); 7.17-7.27 (m, 3H, Harom + $CH=CH_2$); 7.82 (d, 1H, Harom, J = 8.1 Hz). MS (CI/NH_3): m/z = 230 (M^++1). Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.71; H, 6.40; N, 6.22.

Ethyl 3-Acetyl-1-methyl-1*H*-2-indolecarboxylate (8b).

Starting from 1-ethoxyvinyltributylstannane (0.66mmol); reaction time 10 h; yield 65%; oil. IR (film) ν = 1720 (CO); 1640 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.38 (t, 3H, CH_3, J = 7.3 Hz); 2.54 (s, 3H, CH_3); 3.81 (s, 3H, NCH_3); 4.43 (q, 2H, OCH_2, J = 7.3 Hz); 7.20-7.34 (m, 3H, Harom); 7.99 (d, 1H, Harom; J = 8.1 Hz). MS (CI/NH_3): m/z = 246 (M^++1). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.79; H, 6.03; N, 5.85.

General procedure for Suzuki reactions

To a stirred solution of triflate **6** (200 mg, 0.57 mmol) in DMF (3 mL), freshly prepared $Pd(PPh_3)_4$ (20 mg, $1.7.10^{-2}$ mmol, 3%), triethylamine (72 mg, 0.72 mmol, 1.3 eq) and phenylboronic acid (0.72 mmol, 1.3 eq) were added. The mixture was heated at 100°C till the disappearance of triflate **6** (TLC). Water (10 mL) was added and the mixture extracted with ethyl acetate (3x10 mL). After drying over $MgSO_4$, evaporation of the organic layers gave a residue which was chromatographed on a silica gel column (eluent dichloromethane/petroleum ether 50/50).

Ethyl 1-Methyl-3-(2-thienyl)-1*H*-2-indolecarboxylate (9).

Thiophene-2-boronic acid (0.72 mmol); reaction time 1h30; yield 73%; oil. IR (film) ν = 1703 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.16 (t, 3H, CH_3, J = 7.0 Hz); 4.03 (s, 3H, NCH_3); 4.22 (q, 2H, OCH_2, J = 7.0 Hz); 7.10-7.16 (m, 1H, Harom); 7.19-7.23 (m, 1H, Harom); 7.33-7.39 (m, 4H, Harom); 7.62 (d, 1H, Harom, J = 8.2 Hz).^{13}C NMR ($CDCl_3$) δ = 13.8 (CH_3); 31.9 (CH_3); 60.6 (CH_2); 110.0 (CH); 118.9 (C); 120.6 (CH); 121.9 (CH); 123.9 (CH); 124.8 (CH); 125.1 (C); 125.3 (CH); 126.7 (C); 130.2 (CH); 134.2 (C); 138.4 (C); 162.5 (CO). MS (CI/NH_3) 286 (M^++1). Anal. Calcd for $C_{16}H_{15}NO_2S$: C, 67.34; H, 5.30; N, 4.91. Found: C, 67.08; H, 5.24; N, 4.83.

Ethyl 1-Methyl-3-phenyl-1*H*-2-indolecarboxylate (10).

Phenylboronic acid (0.72 mmol); reaction time 4h; yield 90%; oil. IR (film) ν = 1790 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.01 (t, 3H, CH_3, J = 7.3 Hz); 4.05 (s, 3H, NCH_3); 4.16 (q, 2H, OCH_2, J = 7.3 Hz); 7.12 (m, 1H, Harom); 7.31-7,44 (m, 7H, Harom); 7.54 (d, 1H, Harom, J = 8.1 Hz). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.06; H, 5.96; N, 4.89.

Ethyl 3-(2-Methoxyphenyl)-1-methyl-1*H*-2-indolecarboxylate (11).

2-Methoxyphenylboronic acid (0.72 mmol); reaction time 5h; yield 58%; oil. IR (film) ν = 1713 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.00 (t, 3H, CH_3, J = 7.1Hz); 3.72 (s, 3H, OCH_3); 4.08 (s, 3H, NCH_3); 4.12 (q, 2H, OCH_2, J = 7.1 Hz); 6.85-7.04 (m, 3H, Harom); 7.31-7,39 (m, 4H, Harom); 7.47 (d, 1H, Harom, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$) : δ = 12.9 (CH_3); 31.1 (NCH_3); 54.7 (OCH_3); 59.6 (OCH_2); 109.4 (CH); 109.8 (CH); 118.6 (C); 119.3 (CH); 119.4 (CH); 119.7 (CH); 120.7 (C); 123.3 (CH); 124.1 (C); 125.1 (C); 127.6 (CH); 130.8 (CH); 149.3 (C); 156.4 (C); 162.2 (CO). MS (IS): m/z = 310 (M^++1). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 74.02; H, 6.01; N, 4.67.

Ethyl 3-(2-Formylphenyl)-1-methyl-1*H*-2-indolecarboxylate (12).

2-Formylphenylboronic acid (0.72 mmol); reaction time 1h; yield 30%; oil. IR (film) ν = 1680 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 0.84 (t, 3H, CH_3, J = 7.3 Hz); 4,01 (q, 2H, OCH_2, J = 7.3 Hz); 4.09 (s, 3H, NCH_3); 7.28-7.63 (m, 7H, Harom); 8.00 (d, 1H, Harom, J = 7.3 Hz); 9.78 (s, 1H, CHO). Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found: C, 74.48; H, 5.46; N, 4.69.

7-Methyl-6,7-dihydrochromeno[3,4-*b*]indol-6-one (13).

To a solution of compound **11** (150 mg, 0.48 mmol) in dichloromethane (5 mL), boron tribromide (0.7 mL, 1M solution, 0.70 mmol) was added at 0°C; the mixture was stirred for 2h at room temperature and then hydrolyzed at 0°C with water (5mL). Neutralization with 10% NaOH was followed by extraction with dichloromethane (2x10 mL) and drying of the organic layers over $MgSO_4$. Evaporation of the solvent afforded a residue which was chromatographed on a silica gel column (eluent dichloromethane/petroleum ether 50/50) to give **13**; m = 100 mg; yield : 83%.

Heck reaction of compound **17**. To a stirred solution of compound **17** (100 mg, 0.30 mmol) in DMF (5 mL) palladium acetate (8 mg, 0.036 mmol), triphenylphosphine (2 mg, 0.008 mmol), triethylamine (36 mg, 0.36 mmol) were added. The mixture was heated for 26 h at 100°C. Water (10mL) was added and the mixture was neutralized and extracted with ethyl acetate (3x 10 mL). Organic layers were dried over $MgSO_4$ and evaporated. The residue was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 1/9); m = 50 mg; yield 66%; mp 184-186°C. IR (KBr) ν = 1725 (CO) cm^{-1}.^1H NMR ($CDCl_3$) δ = 4.16 (s, 3H, NCH_3); 7.30-7.44 (m, 6H, Harom); 8.14-8.17 (m, 2H, Harom); ^{13}C NMR ($CDCl_3$) δ = 29.3 (CH_3); 108.7 (2xCH); 114.9 (CH); 116.7 (C); 118.7 (C); 118.9 (C); 119.0

(CH); 119.6 (CH); 120.4 (CH); 122.3 (CH); 125.1 (C); 125.2 (CH); 138.9 (C); 148.9 (C); 154.0 (CO). MS (CI/NH_3) : m/z = 250 (M^+ + 1). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 77.10; H, 4.45; N, 5.62. Found: C, 76.89; H, 4.62; N, 5.46.

Ethyl [2-(Hydroxymethyl)phenyl]-1-methyl-1*H*-2-indolecarboxylate (14).

Compound **12** (100 mg, 0.326 mmol) was dissolved in ethanol (0.65 mL)/chloroform (2 mL) containing SiO_2 (160 mg); sodium borohydride (31 mg, 0.81 mmol) was added at 0°C and the mixture was stirred for one day at room temperature; evaporation of the solvent, addition of water (10 mL), filtration, extraction with ethyl acetate (3x10 mL), drying over $MgSO_4$ and evaporation leave a residue which was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 1/9); m = 80 mg; yield: 80%; mp 108-110°C. IR (KBr) ν = 3476 (OH), 1702 (CO) cm^{-1}.^{1}H NMR ($CDCl_3$) δ = 0.92 (t, 3H, CH_3, J = 7.2 Hz); 2.03 (br s, 1H, OH); 4.04-4.17 (m, 5H, NCH_3, OCH_2); 4.42 (m, 2H, OCH_2); 7.05-7.13 (m, 1H, Harom); 7.17-7.44 (m, 6H, Harom); 7.58 (d, 1H, Harom, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$) δ = 19.9 (CH_3); 38.4 (NCH_3); 67.1 (OCH_2); 70.1 (CH_2O); 116.6 (CH); 127.2 (CH); 127.8 (CH); 129.4 (C); 131.9 (C); 132.3 (CH); 133.5 (CH); 133.6 (CH); 134.3 (CH); 134.6 (C); 137.3 (CH); 140.2 (C); 144.8 (C); 146.4 (C); 168.6 (CO). MS (CI/NH_3): m/z = 310 (M^++1). Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.53. Found: C, 74.01; H, 6.30; N, 4.45.

8-Methyl-7,8-dihydro-5*H*-benzo[5,6]oxapino[3,4-*b*]indol-7-one (15).

This product was obtained during the reduction of compound **12**. Elution ethyl acetate/petroleum ether 1/9; yield 19%; oil. IR (film) ν = 1707 (CO) cm^{-1}.^{1}H NMR ($CDCl_3$) δ = 4.04 (s, 3H, NCH_3); 5.06 (s, 2H, OCH_2); 7.27-7.64 (m, 7H, Harom); 8.00 (d, 1H, Harom; J = 7.3 Hz). MS (CI/NH_3): m/z = 264 (M^++1). Anal. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.24; H, 5.15; N, 5.21.

2-Bromophenyl 1-Methyl-1*H*-2-indolecarboxylate (17).

To a 0°C solution of 1-methyl-1*H*-2-indolecarboxylic acid[32](100 mg, 0.57 mmol) in dichloromethane (5 mL)/ DMF (8 drops) were added EDCI (120 mg, 0.63 mmol), dimethylaminopyridine (115 mg, 0.94 mmol) and 2-bromophenol (108 mg, 0.63 mmol). The mixture was stirred for 24 h at room temperature; the organic layer was washed with 5% NaOH (3x5 mL), water (2x5 mL) and dried over $MgSO_4$. Evaporation leave a residue which was chromatographed on a silica gel column (eluent dichloromethane/petroleum ether 50/50); m = 165 mg; yield 88%; mp 116-118°C. IR (KBr) ν = 1738 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ = 4.11 (s, 3H, NCH_3); 7.13-7.45 (m, 6H, Harom); 7.65-7.68 (m, 2H, Harom); 7.77 (d, 1H, Harom, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$) δ = 30.6 (NCH_3); 109.3 (CH); 111.3 (CH); 115.5 (C); 119.8 (CH); 121.9 (CH); 123.1 (CH); 124.7 (CH); 124.8 (C); 125.1 (CH); 126.3 (CH); 127.4 (CH); 127.5 (C); 139.2 (C); 146.9 (C); 158.6 (CO). MS (CI/NH_3): m/z = 330 (M^++1), 332 (M^+ +3). Anal. Calcd for $C_{16}H_{12}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.47; H, 3.74; N, 4.33.

Methyl 3-(*tert*-Butyldimethylsilyloxy)-1*H*-2-indolecarboxylate (18).

To a solution of methyl 3-hydroxy-1*H*-2-indolecarboxylate **3** (200 mg, 1.04 mmol) in THF (10 mL) were added imidazole (142 mg, 2.08 mmol) and *tert*-butyldimetylsilyl chloride (312 mg, 2.08 mmol) which was refluxed for 24h under an argon atmosphere; after cooling, the mixture was evaporated and water (10mL) was added to the residue; extraction with ethyl acetate (3x20 mL), drying over $MgSO_4$, and evaporation leave a residue which was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 1/9) to give **18**; m = 270 mg; yield 84%; mp 140-142°C. IR (KBr) ν = 3334 (NH), 1672 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ = 0.23 (s, 6H, $Si(CH_3)_2$); 1.11 (s, 9H, $C(CH_3)_3$); 3.95 (s, 3H, OCH_3); 7.04-7.11 (m, 1H, Harom); 7.29-7.31 (m, 2H, Harom); 7.64 (d, 1H, Harom, J = 8.2 Hz); 8.69 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ = -4.90 ($Si(CH_3)_2$); 17.3 (C); 24.7 ($C(CH_3)_3$); 50.2 (OCH_3); 110.9 (CH); 112.7 (C); 118.4 (CH); 119.3 (CH); 120.6 (C); 124.8 (CH); 133.6 (C); 139.1 (C); 161.5 (CO). MS (IS): m/z = 306 (M^++1). Anal. Calcd for $C_{16}H_{23}NO_3Si$: C, 62.92; H, 7.59; N, 4.59. Found: C, 63.13; H, 7.45; N, 4.41.

Methyl 1-Benzyl-3-hydroxy-1*H*-2-indolecarboxylate (19).

Methyl 1-Benzyl-3-(*tert*-butyldimethylsilyloxy)-1*H*-2-indolecarboxylate:

To a suspension of sodium hydride (60%, 34 mg, 0.85 mmol) in THF (10 mL) compound **18** (200 mg, 0.65 mmol) was portionwise added at 0°C; the mixture was stirred for 30 mn and benzyl bromide (144 mg, 0.84 mmol) was dropwise added; the mixture was stirred for 16h at room temperature; the solvent was evaporated and water (10mL) and ethyl acetate (10 mL) were added to the residue; the aqueous layer was neutralized to pH 7 with 10% HCl; extraction with ethyl acetate (2x20 mL), drying over $MgSO_4$, and evaporation leave a residue which was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 1/9); m = 170 mg; yield: 65%; oil. IR (film) ν = 1703 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 0.22 (s, 6H, $Si(CH_3)_2$); 1.13 (s, 9H, $C(CH_3)_3$); 3.85 (s, 3H, OCH_3); 5.76 (s, 2H, CH_2); 7.01 (d, 1H, Harom, J = 8.0 Hz); 7.07-7.14 (m, 2H, Harom); 7.17-7.30 (m, 5H, Harom); 7.68 (d, 1H, Harom, J = 8.0 Hz). ^{13}C NMR ($CDCl_3$) δ = -4.8 ($Si(CH_3)_2$); 17.4 (C); 24.8 ($C(CH_3)_3$); 46.7 (CH_2); 49.9 (OCH_3); 109.4 (CH); 113,9 (C); 118,5 (CH); 119.4 (CH); 125.1 (CH); 125.9 (CH); 127.4 (CH); 127.6 (C); 113.1 (C); 137.6 (C); 140.5 (C); 161.3 (CO).

Methyl 1-Benzyl-3-hydroxy-1*H*-2-indolecarboxylate (**19**).

To a 0°C solution of methyl 1-benzyl-3-(*tert*-butyldimethylsilyloxy)-1*H*-2-indolecarboxylate (320 mg, 0.81 mmol) in THF (20 mL) was added tetrabutylammonium fluoride (1M solution in THF, 1.60 mmol, 1.6 mL). The mixture was stirred for 2 h at room temperature. Dichloromethane (2 mL) was added and after addition of isopropanol a solid was obtained; this solid was dissolved in ethyl acetate (10 mL) and the organic layer was washed with water (2x5 mL) and dried over $MgSO_4$. After evaporation, the desilylated compound **19** was obtained; m = 134 mg; yield 60%; mp 122-124°C. IR (KBr) ν = 3436 (OH), 1706 (CO) cm^{-1}.^1H NMR ($CDCl_3$) δ = 3.89 (s, 3H, OCH_3); 5.58 (s, 2H, CH_2); 6.98-7.01 (m, 2H, Harom); 7.01-7.06 (m, 1H, Harom); 7.19-7.28 (m, 4H, Harom); 7.31-7.38 (m, 1H, Harom); 7.78 (d, 1H, Harom, J = 8.2 Hz); 8.66 (br s, 1H, OH). ^{13}C NMR ($CDCl_3$) δ = 48.0 (CH_2); 51.5 (CH_3); 108.8 (C); 110.3 (CH); 116.8 (C); 119.5 (CH); 120.4 (CH); 126.1 (CH); 127.1 (CH); 127.6 (CH); 128.6 (CH); 137.7 (C); 138.5 (C); 149.1 (C); 164.3 (CO).). Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.77; H, 5.50; N, 4.89.

Methyl 1-Benzyl-3-{[(trifluoromethyl)sulfonyl]oxy-1*H*-2-indolecarboxylate (20).

Same procedure as for compound **6** starting from compound **19**; elution ethyl acetate/petroleum ether 1/9; yield 97%; mp 92-94°C. IR (KBr) ν = 1721 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 3.93 (s, 3H, OCH_3); 5.83 (s, 2H, CH_2); 7.02-7.05 (m, 2H, Harom); 7.24-7.31 (m, 5H, Harom); 7.37-7.42 (m, 1H, Harom); 7.68 (d, 1H, Harom, J = 8.0 Hz).^{13}C NMR ($CDCl_3$) δ = 48.0 (CH_2); 51.9 (CH_3); 111.1 (CH); 118.2 (C); 118.6 (q, J_{C-F} = 321 Hz); 118.8 (CH); 121.9 (C); 122.3 (CH); 126.1 (2xCH); 126.7 (CH); 127.4 (CH); 128.7 (2xCH); 129.9 (C); 135.7 (C); 137.0 (C); 160.2 (CO). MS (CI/NH_3): m/z = 414 (M^++1). Anal. Calcd for $C_{18}H_{14}F_3NO_5S$: C, 52.30; H, 3.41; N, 3.39. Found: C, 52.70; H, 3.56; N, 3.45.

Methyl 3-Phenyl-1*H*-2-indolecarboxylate (21).

Methyl 1-Benzyl-3-phenyl-1*H*-2-indolecarboxylate:

Same procedure as for compound **10** starting from compound **20** and phenylboronic acid; reaction time 2h30; elution dichloromethane/petroleum ether 3/7; m = 45 mg; yield: 62%; oil. IR (film) ν = 1703 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 3.62 (s, 3H, OCH_3); 5.82 (s, 2H, CH_2); 7.09-7.13 (m, 3H, Harom); 7.21-7.28 (m, 4H, Harom); 7.33-7.42 (m, 3H, Harom); 7.45-7.49 (m, 3H, Harom); 7.61 (d, 1H, Harom, J = 7.5 Hz). MS (CI/NH_3): m/z = 342 (M^++1).

Methyl 3-Phenyl-1*H*-2-indolecarboxylate **21**

Methyl 1-Benzyl-3-phenyl-1*H*-2-indolecarboxylate (30 mg, 0.088 mmol) was added to a suspension of aluminium chloride (25 mg, 0.19 mmol) in toluene (2 mL). The solution was stirred for 1 h, under a nitrogen atmosphere, at room temperature. After evaporation of toluene, ethyl acetate (10 mL) was added and the mixture was treated with a solution of 5% NaOH (5 mL). The organic layer was dried over $MgSO_4$ and evaporated; the residue was chromatographed on silica gel column (eluent dichloromethane/petroleum ether 1/1); m = 16 mg; yield 73%; oil. IR (film) ν = 3338 (NH), 1676 (CO) cm^{-1} ^1H NMR ($CDCl_3$) δ = 3.82 (s, 3H, OCH_3); 7.12-7.18 (m, 2H, Harom); 7.33-7.50 (m, 4H, Harom); 7.54-7.58 (m, 2H, Harom); 7.64 (d, 1H, Harom, J = 8.2 Hz); 8.01 (br s, 1H, NH). ^{13}C NMR ($CDCl_3$) δ = 50.9 (OCH_3); 110.8 (CH); 120.1 (CH); 120.9 (CH); 121.5 (C); 123.6 (C); 125.1 (CH); 126.4 (CH); 126.8 (CH); 127.9 (C); 135.2 (CH);

135.4 (CH); 133.7 (C); 134.9 (C); 161.6 (CO). Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57. Found: C, 76.81; H, 5.16; N, 5.69.

Methyl 1-Methyl-3-phenyl-1*H*-2-indolecarboxylate (22).

Compound **21** (16 mg, 0.063 mmol) was added to a suspension of sodium hydride (60% weight, 3 mg, 0.078 mmol) in THF (3 mL). The mixture was stirred for 30 min at 0°C and iodomethane (23 mg, 0.16 mmol) was added. After stirring for 16 h at room temperature the solvent was evaporated; water (5mL) and ethyl acetate (5mL) were added to the residue; the mixture was extracted with ethyl acetate (3x3 mL); drying over $MgSO_4$ and evaporation leave a residue which was chromatographed on a silica gel column (eluent : dichloromethane/petroleum ether 50/50); m = 12 mg; yield 71%; oil. IR (film) ν = 1705 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 3.69 (s, 3H, OCH_3); 4.14 (s, 3H, NCH_3); 7.13-7.17 (m, 2H, Harom); 7.35-7.44 (m, 6H, Harom); 7.57 (d, 1H, Harom, J = 8.2 Hz). ^{13}C NMR ($CDCl_3$) δ = 30.3 (NCH_3); 31.4 (OCH_3); 109.5 (CH); 120.1 (CH); 121.0 (CH); 124.0 (C); 124.7 (CH); 125.9 (C); 126.2 (CH); 127.2 (CH); 127.3 (CH); 128.3 (C); 129.7 (CH); 129.8 (CH); 134.0 (C); 137.9 (C); 162.5 (CO). MS (CI/NH_3) m/z = 266 (M^++1).Anal. Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.72; H, 5.63; N, 5.32.

1-(*tert*-Butyl) and 2-Methyl 3-[(Trifluoromethylsulfonyl)oxy]-1*H*-1,2-indoledicarboxylate (23).

To a solution of triflate **5** (600 mg, 1.85 mmol) in DMF (10 mL) were added triethylamine (185 mg, 1.85 mmol), dimethylaminopyridine (226 mg, 1.85 mmol) and di-*tert*-butyldicarbonate (600 mg, 2.77 mmol); the mixture was stirred for 24h at room temperature. Water (20 mL) was added and the mixture was extracted with ethyl acetate (3x15 ml). Organic layers were washed with water (3x10mL), dried over $MgSO_4$ and evaporated. The residue was purified by column chromatography on silica gel (eluent dichloromethane/petroleum ether 80/20) to give compound **23**; m = 313 mg; yield 40%; oil. IR (film) ν = 1747 (CO), 1640 (NCO) cm^{-1}.^1H NMR ($CDCl_3$) δ = 1.66 (s, 9H, $C(CH_3)_3$); 4.00 (s, 3H, OCH_3); 7.40 (t, 1H, Harom, J = 8.0 Hz); 7.55 (t, 1H, Harom, J = 8.0 Hz); 7.64 (d, 1H, Harom, J = 8.0 Hz); 8.18 (d, 1H, Harom, J = 8.0 Hz). MS (CI/NH_3) m/z = 424 (M^++1). Anal. Calcd for $C_{16}H_{16}F_3NO_7S$: C, 45.39; H, 3.81; N, 3.31. Found: C, 45.24; H, 4.00; N, 3.44.

Ethyl 1-Methyl 3-[(E)-3-(*tert*-butoxy)-3-oxo-1-propenyl]-1*H*-2-indolecarboxylate (24).

Compound **6** (200mg, 0.57 mmol), triethylamine (58mg, 0.57 mmol, 1 eq), *tert*-butyl acrylate (96mg, 0.75 mmol, 1.3 eq), palladium acetate (10mg, 0.045 mmol, 8%) triphenylphosphine (15mg, 0.057 mmol, 10%) were added to DMF (6mL) and the mixture was heated for 20h at 100°C. Water (5mL) was added, then 10% HCl till pH 7; the mixture was extracted with ethyl acetate (3x10 mL); the organic layers were washed with water (10 mL) and dried over $MgSO_4$. Evaporation leave a residue which was chromatographed on a silica gel column (eluent dichloromethane/petroleum ether 75/25; m = 60 mg; yield 32%; mp 114°C. IR (film) ν = 1680 large (CO) cm^{-1}. ^1H NMR ($CDCl)_3$ δ = 1.50 (t, 3H, CH_3, J = 7.0 Hz); 1.56 (s, 9H, CH_3); 4.02 (s, 3H, NCH_3); 4.47 (q, 2H, OCH_2, J = 7.0 Hz); 6.51 (d, 1H, =CH, J = 16.0 Hz); 7.23-7.26 (m, 1H, Harom); 7.39-7.42 (m, 2H, Harom); 8.02 (m, 1H, Harom, J = 8.2 Hz); 8.38 (d, 1H, =CH, J = 16.0 Hz). ^{13}C NMR ($CDCl)_3$: δ = 14.4 (CH_3); 28.3 (3xCH_3); 32.1 (CH_3); 61.5 (CH_2); 80.0 (C); 110.6 (CH); 117.3 (C); 120.6 (CH); 122.0, (CH); 122.2 (CH); 125.2 (CH); 128.5 (C); 135.5 (C); 137.0 (CH); 139.0 (C); 162.1 (CO); 167.0 (CO). MS (IS) m/z = 330 (M^++1). Anal. Calcd for $C_{19}H_{23}NO_4$: C, 69.28; H, 7.04; N, 4.25. Found: C, 69.39; H, 7.12; N, 4.43.

2-(Allyloxy)-1-methyl-3-oxo-2-indolinecarboxylate (25).

Typical procedure reaction between the indolic triflate **6** and allylic alcohol: to $Pd(OAc)_2$ (8 mg, 0.035 mmol, 6%) and triphenylphosphine (4-5 mg, 0.015-0.018 mmol, 3%) were added under a nitrogen atmosphere a solution of the triflate **6** (200 mg, 0.57 mmol), allylic alcohol (3 eq) and triethylamine (2 eq) in DMF (10 mL). The solution was stirred at 100°C and the reaction was monitored by TLC. When all the starting material has disappeared (5h), water (20 mL) was added and the aqueous layer was neutralized with 10% HCl and twice extracted with ethyl acetate (2x10 mL). The organic layers were washed with water, brine and dried ($MgSO_4$). After filtration and evaporation the residue was purified on a silica gel column using ethyl acetate/petroleum ether (2/8) as eluent; m = 75 mg; yield 45%; oil. IR (film) ν=1760, 1715

cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.14 (t, 3H, CH_3, J=7.3Hz); 2.85 (s, 3H, NMe); 3.78-3.92 (m, 2H, OCH_2); 4.10-4.19 (m, 2H, OCH_2); 5.05-5.19 (m, 2H, $=CH_2$); 5.79-5.92 (m, 1H, CH=); 6.69-6.76 (m, 2H, Harom); 7.43-7.49 (m, 2H, Harom); ^{13}C NMR ($CDCl_3$) δ=14.1 (CH_3); 28.0 (CH_3); 62.4 (CH_2); 65.6 (CH_2); 95.3 (C-2); 108.6 (CH=); 117.9 (C); 118.1 (CH) 118.8 ($=CH_2$); 118.9 (C); 125.1 (CH); 113.4 (CH); 138.6 (CH); 161.1 (C); 165.1 (CO); 194.7 (CO). **MS (CI/NH_3) m/z** = 276 (M^++1). Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.57; H, 6.30; N, 4.93.

Ethyl 3-Hydroxy-1-methyl-2-oxo-3-indolinecarboxylate (26).

Compound obtained during the reaction of allyl alcohol with triflate **6**; m = 17 mg; yield 13%; mp=136-138°C (litt.[28] mp=130°C). IR (KBr) ν=3302, 1756, 1708 cm^{-1}. ^1H NMR ($CDCl_3$) δ=1.10 (t, 3H, CH_3, J=7.3 Hz); 3.18 (s, 3H, NMe); 4.10-4.20 (m, 3H, OCH_2CH_3, OH); 6.81 (d, 1H, Harom, J=8.1 Hz); 7.03 (t, 1H, Harom, J=7.3 Hz); 7.21 (d, 1H, Harom, J=8.1 Hz); 7.32 (t, 1H, Harom, J=7.3 Hz); ^{13}C NMR (DMSO-d6) δ=15.2 (CH_3); 27.5 (CH_3); 62.7 (CH_2); 78.6 (C-3); 110.5 (CH); 124.1 (CH); 124.8 (CH); 129.7 (C); 131.7 (CH); 145.5 (C); 170.4 (CO); 174.4 (CO). MS (CI/NH_3) m/z = 236 (M^++1). Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.52; H, 5.38; N, 5.90.

Ethyl 2-(Diethylamino)-1-methyl-3-oxo-2-indolinecarboxylate (27).

Compound obtained during the reaction of allyl alcohol (3 eq) with palladium acetate (20% mole), triphenylphosphine (10% mole), triethylamine (2 eq) and triflate **6** (0.57 mmol, 1 eq) in DMF at 100°C; m = 33 mg; yield 20%; oil. IR (film) ν = 1745 (CO), 1713 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.10 (6H, CH_3, J = 7,3 Hz); 1.24 (t, 3H, CH_3, J = 7.1 Hz); 2,69-2.84 (m, 4H, NCH_2); 3.01 (s, 3H, NCH_3); 4.23 (q, 2H, OCH_2, J = 7.1 Hz); 6.70-6.84 (m, 2H, Harom); 7.45-7.56 (m, 2H, Harom). ^{13}C NMR ($CDCl_3$) δ = 14.1 (CH_3); 15.3 (2xCH_3); 28.6 (CH_3); 43.6 (2xNCH_2); 61.9 (OCH_2); 88.5 (C-2); 108.1 (CH); 117.7 (CH); 119.2 (C); 124.5 (CH); 137.9 (CH); 160.0 (C); 167.0 (CO); 198.8 (CO). MS (CI/NH_3) m/z = 291 (M^++1). Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.19; H, 7.64; N, 9.65. Found: C, 66.26; H, 7.73; N, 9.54.

1-Methyl-3-(2-oxoethyl)-1*H*-2-indolecarboxylate (29).

To a solution of triflate **6** (500 mg, 1.42 mmol) in DMF (10mL), palladium acetate (32 mg, 0.142 mmol, 10%) sodium hydrogencarbonate (298 mg, 3.55 mmol), benzyltriethylammonium chloride (323 mg, 1.42 mmol, 1 eq) allyl alcohol (120mg, 2.05 mmol, 1.45 eq) were successively added. The mixture was heated for 4h at 100°C. After cooling, water (10mL) was added and the mixture extracted with ethyl acetate (3x10 mL); organic layers were washed with water (3x10 mL), dried over $MgSO_4$, and evaporated; the residue was chromatographed on a silica gel column (eluent/dichloromethane). Compound **29** (m = 66 mg; yield 18%), was first eluted, then compound **30** (m = 101 mg; yield 26%) and finally compound **26** (m = 60 mg, yield 18%); oil. IR (film) ν = 1742 (CO), 1704 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.46 (t, 3H, CH_3, J = 7.3 Hz); 2.83 (t, 2H, CH_2, J = 7.3 Hz); 3.43 (t, 2H, CH_2, J = 7.3 Hz); 4.03 (s, 3H, NCH_3); 4.42 (q, 2H, OCH_2, J = 7.3 Hz); 7.04-7.12 (m, 1H, Harom); 7.29-7.33 (m, 2H, Harom); 7.68-7.72 (d, 1H, Harom, J = 8.0 Hz); 9.88 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$) δ = 13.3 (CH_3); 17.2 (CH_2); 31.1 (CH_3); 44.1 (CH_2); 59.6 (CH_2); 109.2 (CH); 119.1 (CH); 119.3 (CH); 121.8 (C); 123.8 (C); 124.4 (CH); 125.1 (C); 137.6 (C); 161.4 (CO); 201.2 (CHO). MS (CI/ NH_3) m/z = 260 (M^++1). Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40. Found: C, 69.23; H, 6.49; N, 5.50.

Ethyl 1-Methyl-3-oxo-2-(3-oxopropyl)-2-indolinecarboxylate (30).

Compound **30** has been isolated during the synthesis of **29**; yield 26%; oil. IR (film) ν = 1745 (CO), 1705 (CO), 1694 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.22 (t, 3H, CH_3, J = 7.1 Hz); 2.21-2.31 (m, 2H, CH_2CHO); 2.49-2.53 (m, 1H, CH_2); 2.62-2.68 (m, 1H, CH_2); 2.95 (s, 3H, NCH_3); 4.13-4.25 (m, 2H, OCH_2); 6.79-6.87 (m, 2H, Harom); 7.54 (t, 1H, Harom, J = 7.8 Hz); 7.62 (d, 1H, Harom, J = 7.8Hz). ^{13}C NMR ($CDCl_3$) δ = 13.0 (CH_3); 22.8 (CH_2); 28.3 (NCH_3); 36.3 (CH_2); 61.3 (CH_2); 75.5 (C-2): 107.9 (CH); 117.3 (CH); 118.6 (C); 124.1 (CH); 137.2 (CH); 161.1 (C); 165.7 (CO); 199.4 (CHO). MS (CI/NH_3): m/z = 276 (M^++1). Anal. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.26; H, 6.34; N, 5.00.

Ethyl 2-[2-Butenyloxy]-1-methyl-3-oxo-2-indolinecarboxylate (32).

Same procedure as for compound **25** starting from triflate **6**, palladium acetate (8%) and 2-buten-1-ol; elution ethyl acetate/petroleum ether 1/9; yield 20%; oil. IR (film) ν = 1760 (CO); 1715 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.24 (t, 3H, CH_3, J = 7.2 Hz); 1.64 (d, 3H, CH_3, J = 3.9 Hz); 2.96 (s, 3H, NCH_3); 3.88 (m, 2H, OCH_2); 4.18-4.29 (m, 2H, OCH_2); 5.62-5.65 (m, 2H, CH=CH); 6.78-6.85 (m, 2H, Harom); 7.51-7.59 (m, 2H, Harom). MS (CI/NH_3): m/z = 307 (M^++18). Anal. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.56; H, 6.50; N, 4.71.

Ethyl 2-[(3-Methyl-2-butenyl)oxy]-3-oxo-2-indolinecarboxylate (33).

Same procedure as for compound **25** starting from triflate **6**, palladium acetate (8%) and 3-methyl-2-buten-1-ol; elution: ethyl acetate/petroleum ether 1/9; yield 41%; oil. IR (film) ν = 1756 (CO); 1712 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.18 (t, 3H, CH_3, J = 7.2 Hz); 1.45 (s, 3H, CH_3); 1.62 (s, 3H, CH_3); 2.92 (s, 3H, NCH_3); 3.89-3.93 (m, 2H, OCH_2); 4.15-4.21 (m, 2H, OCH_2CH_3); 5.27-5.41 (m, 1H, CH=); 6.73-6.80 (m, 2H, Harom); 7.45-7.53 (m, 2H, Harom). ^{13}C NMR ($CDCl_3$) : δ = 12.1 (CH_3); 15.8 (CH_3); 23.6 (CH_3); 26.0 (CH_3); 57.3 (C); 59.4 (CH_2); 60.4 (CH_2); 91.2 (C); 106.5 (CH); 116.6 (CH); 118.3 (CH); 121.6 (C); 122.8 (CH); 136.3 (CH); 158.8 (C); 163.2 (CO); 193.2 (CO). Anal. Calcd for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62. Found: C, 67.55; H, 7.05; N, 4.68.

Ethyl 2-Methoxy-1-methyl-3-oxo-2-indolinecarboxylate (34).

To a stirred solution of triflate **6** (200 mg, 0.57 mmol) in DMF (3 mL) methanol (27 mg, 0.85 mmol) was added and the mixture was heated for 6 h at 80°C. After cooling water (5mL) was added and the solution was extracted with ethyl acetate (2x5 mL). The organic layers were washed with water and dried over $MgSO_4$; evaporation leave a residue which was chromatographed on a silica gel column (eluent dichloromethane); m = 60 mg; yield 42%; oil. IR (film) ν = 1760 (CO); 1715 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.17 (t, 3H, CH_3, J = 7.3 Hz); 2.86 (s, 3H, NCH_3); 3.17 (s, 3H, OCH_3); 4.10-4.21 (m, 2H, CH_2); 6.71-6.76 (m, 2H, Harom); 7.43-7.50 (m, 2H, Harom). ^{13}C NMR ($CDCl_3$) δ = 13.1 (CH_3); 26.9 (CH_3); 50.6 (CH_3); 61.5 (CH_2); 92.7 (C-2); 107.5 (CH); 117.7 (CH); 117.8 (C); 124.0 (CH); 137.7 (CH); 160.3 (C); 164.0 (CO); 193.7 (CO). MS(CI/NH_3): m/z = 250 (M^++1). Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 62.33; H, 6.15; N, 5.48.

Ethyl 2-(3-Butenyloxy)-1-methyl-3-oxo-2-indolinecarboxylate (35).

Same procedure as for compound **25** starting from triflate **6** and 3-buten-1-ol; elution ethyl acetate/petroleum ether 1/9. yield 19%; oil. IR (film) ν = 1760 (CO); 1715 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.24 (t, 3H, CH_3, J = 7.1 Hz); 2.43 (m, 2H, CH_2); 3.01 (s, 3H, NCH_3); 3.33-3.51 (m, 2H, OCH_2); 4.18-4.31 (m, 2H, OCH_2); 5.03-5.15 (m, 2H, $CH=CH_2$); 5.73-5.89 (m, 1H, $CH=CH_2$); 6.78-6.86 (m, 2H, Harom); 7.52-7.59 (m, 2H, Harom). ^{13}C NMR ($CDCl_3$) δ = 13.1 (CH_3); 27.0 (NCH_3); 32.9 (CH_2); 61.4 (OCH_2); 62.7 (OCH_2); 92.4 (C-2); 107.5 (CH=); 115.9 (=CH_2); 117.6 (CH); 117.8 (CH); 124.1 (CH); 133.3 (C); 137.6 (CH); 160.2 (C); 164.1 (CO); 193.8 (CO). MS(CI/NH_3) : m/z = 290 (M^++1). Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.12; H, 6.80; N, 4.79.

Ethyl 2-[3-(Benzyloxy)-3-oxopropyl]-1-methyl-3-oxo-2-indolinecarboxylate (36).

To a solution of ethyl 3-hydroxy-1-methyl-1*H*-2-indolecarboxylate **4** (438mg, 2 mmol) in DMF (10 mL) were added benzyl 3-bromopropanoate (632 mg, 2.6 mmol) and potassium carbonate (360 mg, 2.6 mmol); the mixture was heated for 3h at 90°C and then evaporated under reduced pressure. Water (10 mL) was added and the mixture was neutralized with 10% HCl; extraction with ethyl acetate (3x10 mL), drying over $MgSO_4$ and evaporation leave a residue which was chromatographed on a silica gel colum (elution dichloromethane); m = 662 mg; yield 87%; oil. IR (film). ν = 1720 large (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 1.20 (t, 3H, CH_3, J = 6.6 Hz); 2.01-2.25 (m, 2H, CH_2); 2.42-2.52 (m, 1H, CH_2); 2.66-2.76 (m, 1H, CH_2); 2.90 (s, 3H, NCH_3); 4.11-4.19 (m, 2H, OCH_2); 5.03 (s, 2H, CH_2); 6.76 (t, 1H, Harom, J = 8.1 Hz); 7.26-7.33 (m, 6 H, Harom); 7.47 (m, 1H, Harom); 7.56 (d, 1H, Harom, J = 7.3 Hz). ^{13}C NMR ($CDCl_3$) δ = 14.1 (CH_3); 26.3 (CH_2); 28.0 (CH_2); 29.2 (NCH_3); 62.2 (CH_2); 66.4 (CH_2); 78.9 (C-2); 108.8 (CH); 118.1 (CH); 119.6 (C); 125.1 (CH); 126.9 (CH); 128.0 (CH); 135.6 (C); 138.1 (CH); 162.2 (C); 166.7 (CO); 172.3 (CO); 195.4 (CO). Anal. Calcd for $C_{22}H_{23}NO_5$: C, 69.28; H, 6.08; N, 3.67. Found: C, 69.32; H, 6.12; N, 3.74.

Ethyl 2-(3-Hydroxypropyl)-1-methyl-3-oxo-2-indolinecarboxylate (37).

3-[2-(ethoxycarbonyl)-1-methyl-3-oxo-2,3-dihydro-1*H*-2-indolyl] propanoic acid :

A solution of compound **36** (300 mg, 0.79 mmol) in methanol (10 mL) was stirred for 45 mn under one atmosphere of hydrogen in presence of palladium on carbon 10% (30 mg). The catalyst was filtered and the solvent evaporated. Water (10 mL) was added to the mixture and then an aqueous solution of sodium hydroxide till pH 10-11. The aqueous layer was extracted with dichloromethane (10mL), acidified till pH 1 with 10% HCl; extraction with ethyl acetate (2x20 mL), drying over $MgSO_4$ and evaporation gave the acid; m = 100 mg; yield 44%; oil. IR (film) ν = 3420 (OH), 1740 (CO), 1710 (CO), 1680 (CO) cm^{-1}.^{1}H NMR (DMSO-d6) δ = 1.07 (t, 3H, CH_3, J = 6.3 Hz); 1.79-1.88 (m, 2H, CH_2); 2.32-2.37 (m, 2H, CH_2COOH); 2.89 (s, 3H, NCH_3); 3.97-4.17 (m, 2H, OCH_2); 6.74 (t, 1H, Harom, J = 7.8 Hz); 7.01 (d, 1H, Harom, J = 7.8 Hz); 7.43 (d, 1H, Harom, J = 7.8 Hz); 7.53-7.58 (t, 1H, Harom, J = 7.8 Hz). ^{13}C NMR (DMSO-d6) δ = 16.5 (CH_3); 28.5 (CH_2); 30.2 (CH_2); 31.6 (CH_3); 64.6 (CH_2); 79.2 (C-2); 111.2 (CH); 120.7 (CH); 121.9 (C); 127.5 (CH); 140.6 (CH); 164.6 (C); 169.1 (CO); 180.7 (CO); 197.8 (CO).

Ethyl 2-(3-Hydroxypropyl)-1-methyl-3-oxo-2-indolinecarboxylate (**37**).

To a solution of 3-[2-(ethoxycarbonyl)-1-methyl-3-oxo-2,3-dihydro-1*H*-2-indolyl] propanoic acid (170 mg, 0.58 mmol) in THF (10 mL) was added $BH_3.Me_2S$ (2M solution in THF, 0.6 mL, 1.2 mmol). The mixture was refluxed for 2h30, then water (10 mL) was added. Extraction with ethyl acetate (3x10 mL), drying over $MgSO_4$, and evaporation leave a residue which was chromatographed on silica gel column (eluent dichloromethane/methanol 99/1); m = 70 mg; yield 43%.

From compound **30**. To a solution of compound **30** (20 mg, 0.073 mmol) in chloroform (1 mL) and ethanol (0.2 mL) were added at 0°C SiO_2 (40 mg) and sodium borohydride (8 mg, 0.2 mmol). The mixture was stirred overnight at room temperature and then evaporated. Water (5mL) and ethyl acetate (10 mL) were added; the organic layer was washed with water (5mL), brine (5mL), and dried over $MgSO_4$. Evaporation leave a residue which was chromatographed on a silica gel column (eluent dichloromethane/methanol 99/1) to give the alcohol **35**; m = 13 mg; yield 65%; oil. IR (film) ν = 3462 (OH), 1739 (CO), 1694 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ = 1.22 (t, 3H, CH_3, J = 7.1 Hz); 1.26-1.37 (m, 2H, CH_2); 1.66 (br s, 1H, OH); 2.18-2.24 (m,1H, CH_2); 2.41-2.51 (m, 1H, CH_2); 3.01 (s, 3H, NCH_3); 3.53-3.63 (m, 2H, CH_2O); 4.13-4.24 (m, 2H, OCH_2); 6.74 (t, 1H, Harom, J = 8.0 Hz); 6.83 (d, 1H, Harom, J = 8.0 Hz); 7.51 (t, 1H, Harom, J = 8.0 Hz); 7.58 (d, 1H, Harom, J = 8.0 Hz). 13.6 (CH_3); 25.5 (CH_2); 27.3 (CH_2); 28.3 (CH_3); 61.6 (CH_2); 61.7 (CH_2); 77.0 (C-2); 107.8 (CH); 117.1 (CH); 118.7 (C); 124.5 (CH); 137.5 (CH); 161.4 (C); 166.8 (CO); 195.4 (CO). MS (CI/ NH_3) : m/z = 278 (M^++1). Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 65.11; H, 7.07; N, 4.95.

Ethyl 3-(3-Hydroxy-1-propynyl)-1-methyl-1*H*-2-indolinecarboxylate (38).

Under an argon atmosphere triflate **6** (200 mg, 0.57 mmol), propargyl alcohol (95 mg, 1.7 mmol, 3 eq), triethylamine (115 mg, 1.14 mmol, 2 eq) in DMF (6 mL) were added to a suspension of palladium acetate (10 mg, 0.045 mmol, 10%) and triphenylphosphine (4 mg, 0.015 mmol). The mixture was stirred for 6h at 100°C. After cooling, water (10mL) was added, then 10% HCl till pH 7; extraction with ethyl acetate (3x15 mL), drying over $MgSO_4$, evaporation afforded an oil. This oil was chromatographed on a silica gel column (eluent dichloromethane) to give **36**; m = 117 mg; yield 80%; oil. IR (film) ν = 3500 (OH), 2300 (triple bond), 1694 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ = 1.49 (t, 3H, CH_3, J = 7.2 Hz); 1.86 (m, 1H, OH, exchangeable with D_2O); 4.15 (s, 3H, CH_3); 4.87 (q, 2H, OCH_2, J = 7.2 Hz); 4.64 (s, 2H, CH_2OH); 7.24-7.28 (m, 2H, Harom); 7.40-7.42 (m, 1H, Harom); 7.82 (d, 1H, Harom, J = 8.2 Hz). MS (CI/ NH_3) : m/z = 258 (M^++1). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 69.83; H, 5.69; N, 5.36.

Acetyl-1*H*-3-indolyle trifluoromethanesulfonate (39).

To a -78°C solution of 1-acetyl-1*H*-indol-3(2*H*)-one (130 mg, 0.74 mmol) in THF (10 mL) was added, under an argon atmosphere, lithium diisopropylamide (2M solution in THF, 0.75 mL, 1.5 mmol). The mixture was stirred for 20min at -78°C and *N*-phenyltriflimide (800 mg, 2.23 mmol) in THF (5 mL) was added. The mixture was stirred for 16 h at room temperature. The solvent was evaporated, water (5 mL), and ethyl acetate (10 mL) were added. After neutralization with

10% HCl the aqueous layer was extracted with ethyl acetate (3x10 mL); the organic layers were washed with brine and dried over $MgSO_4$. Evaporation leave an oil which was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 1/9). A solidl was obtained; m = 175 mg; yield 76%; mp 68-70°C. IR (KBr) ν = 1710 (CO) cm^{-1}.^{1}H NMR ($CDCl_3$) δ = 2.65 (s, 3H, CH_3); 7.34-7.43 (m, 2H, Harom); 7.46 (s, 1H, H-2); 7.48-7.59 (m, 1H, Harom); 8.44 (d, 1H, Harom, J = 8.2 Hz).^{13}C NMR ($CDCl_3$) δ = 23.8 (CH_3); 115.2 (CH); 116.8 (CH); 117.1 (CH); 118.7 (q, J_{C-F} = 321Hz);122.2 (C); 124.6 (CH); 127.1 (CH); 133.1 (C); 133.3 (C); 168.2 (CO). MS (IS) : m/z = 307 (M^++1) Anal. Calcd for $C_{11}H_8F_3NO_4S$: C, 43.00; H, 2.62; N, 4.56. Found: C, 42.81; H, 2.83; N, 4.69.

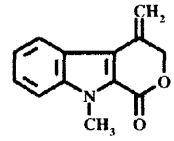
1-{3-[1-Hydroxymethyl)vinyl]-1*H*-1-indolyl}-1-ethanone (40).

Under an argon atmosphere, triflate **39** (200 mg, 0.65 mmol), allyl alcohol (110 mg, 1.90 mmol), triethylamine (130 mg, 1.30 mmol) dissolved in DMF (5 mL) were added to a suspension of palladium acetate (10 mg, 0.045 mmol, 7% mole) and triphenylphosphine (5 mg, 0.019 mmol). The mixture was stirred for 18h at 100°C. After cooling, water (10mL) was added and 10% HCl till pH 7. Extraction with ethyl acetate (3x15 mL), drying over $MgSO_4$ and evaporation afforded an oil. This oil was chromatographed on a silica gel column (eluent ethyl acetate/petroleum ether 4/6) to give **40**; m = 40 mg; yield 28%; oil. IR (film) ν = 3453 (OH), 1703 (CO) cm^{-1}. ^{1}H NMR ($CDCl_3$) δ = 1.85 (br s, 1H, OH); 2.63 (s, 3H, CH_3); 4.49 (br s, 2H, OCH_2); 5.54 (br d, 1H, =CH, J= 1.2 Hz); 5.66 (br s, 1H, =CH); 7.30-7.37 (m, 2H, Harom); 7.53 (s, 1H, H-2); 7.77 (d, 1H, Harom, J=7.6 Hz); 8.44 (d, 1H, Harom, J=7.6 Hz). ^{13}C NMR ($CDCl_3$) δ = 23.0 (CH_3); 65.3 (OCH_2); 113.3 (CH_2); 115.7 (CH); 119.5 (CH); 119.6 (C); 121.7 (CH); 122.9 (CH); 124.8 (CH); 127.8 (C); 135.1 (C); 139.0 (C); 167.6 (CO). MS (CI / NH_3): m/z = 216 (M^++1). Anal. Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.80; H, 6.17; N, 6.68.

REFERENCES and NOTES

1. Tsuji, J. *Palladium Reagents and Catalysts*, Wiley, New York, **1995**. Malleron, J.L.; Fiaud, J.C.; Legros, J.-Y. *Handbook of Palladium-Catalyzed Organic Reactions*, Academic Press, San Diego, **1997**.
2. Heuman, A.; Reglier, M.; *Tetrahedron* **1996**, *52*, 9289-9346; Mitchell, T.N. *Synthesis* **1992**, 803-815.
3. de Meijere A.; Meyer, F.E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2379-2411. Kanilin, V.N. *Synthesis*, **1992**, 413-432.
4. Grigg, R. *J. Heterocycl. Chem.* **1994**, *31*, 631-639
5. Hegedus, L.S. *Angew Chem, Int. Ed.* **1988**, *27*, 1113-1126. Harrington, P.J.; Hegedus, L.S.; Mc Daniel, K.F. *J. Am. Chem. Soc.* **1987**, *109*, 4335-4338. Zembower, D.E.; Ames, M.M. *Synthesis* **1994**, 1433-1436. Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. *Synlett* **1990**, 47-48
6. Martin, A.R.; Zheng, Q. in *Advances in Nitrogen Heterocycles*, Moody C.J. Ed., Jai Press Inc., Londres, **1995**, vol. 1, p 71-172.
7. Zheng, Q.; Yang, Y.; Martin, A.R. *Heterocycles* **1994**, *37*, 1761-1772. Kawasaki, I.; Yamashita, M.; Ohta, S.; *Chem. Pharm. Bull.* **1996**, *44*, 1831.
8. Amat, M.; Hadida, S.; Pshenichnyi, G.; Bosch, J. *J. Org. Chem.* **1997**, *62*, 3158-3175 and references therein. Choshi, T.; Yamada, S.; Sugino, E.; Kuwada, T.; Hibino, S. *Synlett* **1995**, 147-148. Fisher, L.E.; Labadie, S.S.; Reuter, D.C.; Clark, R.D. *J. Org. Chem.* **1995**, *60*, 6224-6225.
9. Palmisano, G.; Santagostino, M. *Synlett* **1993**, 771-773. Palmisano, G.; Santagostino, M. *Helv. Chim. Acta*, **1993**, 76, 2356-2366. Fukuyama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, 116, 3127-3128. Hudkins, R.L.; Diebold, J.L.; Marsh, F.D. *J. Org. Chem.* **1995**, 60, 6218-6220.
10. Yokoyama, Y.; Ikeda, M.; Saito, M.; Yoda, T.; Suzuki, H.; Murakami,Y. *Heterocycles*, **1990**, *31*, 1505-1511. Somei, M.M.; Saïda, Y. *Heterocycles* **1985**, *12*, 3113-3114. Gilchrist, T.L.; Kemmitt, P.D. *Tetrahedron* **1997**, *12*, 4447-4456. Chu, L.; Fisher, M.H.; Goulet, M.T.; Wyvratt, M.J. *Tetrahedron Lett.* **1997**, *38*, 3871-3874. Choshi, T.; Fujimoto, H.; Sugino, E.; Hibino, S. *Heterocycles* **1996**, *43*, 1847-1854. Harrington, P.J.; Hegedus, L.S. *J. Org. Chem.* **1984**, *49*, 2657-2662. Somei, M.; Saïda, Y.; Komura, N. *Chem. Pharm. Bull.* **1986**, *34*, 4116-4125. Choshi, T.; Takuya, S.; Fujimoto, H.; Nagayama, C.; Sugino, E.; Hibino, S. *Tetrahedron Lett.* **1996**, 37, 2593-2596.

11. Conway, S.C.; Gribble, G.W. *Synth. Comm.* **1992**, *22*, 2129-2124. Conway, S.C;. Gribble, G.W. *Heterocycles* **1990**, *30*, 627-633. Conway, S.C.; Gribble, G.W. *Synth. Comm.* **1992**, *22*, 2987-2995.
12. Bourlot, A.-S.; Desarbre, E.; Mérour, J.-Y. *Synthesis* **1994**, 411-416. Joseph, B.; Malapel, B.; Mérour, J.-Y.; *Synth. Comm.* **1996**, 3289-3295.
13. Dyker, G.; Grundt, P. *Tetrahedron Lett.* **1996**, *37*, 619-622.
14. Houpis, I.N.; *Tetrahedron Lett.* **1991**, *32*, 6675-6678. Cappelli, A.; Anzini, M.; Vomero, S.; De Benedetti, P.G.; Menziani, M.C.; Giorgi, G.; Manzoni, C. *J. Med. Chem.* **1997**, *40*, 2910-2921. Paquette, L.A.; Wang, T.-Z.; Sivik, M.R. *J. Am. Chem. Soc* **1994**, *116*, 2665-2666.
15. Nishi, K., Nakurawa,Y.; Onoue, H. *Tetrahedron Lett.* **1989**, 37, 2987-2988. Farina, V.; Baker, S.R.; Benigni, D.A.; Hauck. S.I.; Sapino, Jr.C. *J. Org. Chem.* **1990**, *55*, 5833-5847. Elliott, R.L.; Nicholson, N.H.; Peaker, F.E.; Takle. A.K., Richardson, C.M.; Tyler, J.W.; White, J.; Pearson, M. J.; Eggleston, D.S.; Haltiwanger, R.C. *J. Org. Chem.* **1997**, *62*, 4998-5016.
16. Unangst, P.C.; Connor. D.T.; Miller, S.R. *J. Heterocycl. Chem.* **1996**, *33*, 1627-1630. Unangst, P.C.; Brown, R.E. *J. Heterocycl. Chem.* **1984**, *21*, 283-285. Unangst, P.C.; Brown, R.E.; Herzig, D.J. *J. Med. Chem.* **1980**, *23*, 1251-1255.
17. Malapel-Andrieu, B.; Mérour, J.Y. *Tetrahedron Lett.*, **1998**, *39*, 39-42.
18. Pindur, U. *Heterocycles* **1988**, *27*, 1253-1268. Pindur, U.; Pfeuffer, L.; Kim, M.-H. *Helv. Chim. Acta* **1989**, *72*, 65-72. Schuster, H.F.; Coppola, G.-M. *J. Heterocycl. Chem.* **1994**, *31*, 1381-1384.
19. Mederski, W.W.K.R.; Osswald, M.; Dorsch, D.; Anzali, S.; Christadler, M.; Schmitges, C-J.; Wilm, C. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 17-22. Morin, D.; Zini, R.; Ledewyn, S.; Tillement. J.P. *J. Pharm. Sci.* **1986**, 75, 883-885.
20. Chu, L.; Fisher, M.H.; Goulet, M.T.; Wyvratt, M.J. *Tetrahedron Lett.* **1997**, *38*, 3871-3874.
21. Genêt, J.P.; Linquist, A.; Blart, E.; Mouriès, V.; Savignac, M.; Vaultier, M. *Tetrahedron. Lett.* **1995**, *36*, 1443-1446.
22. Di Fabio, R., Pentassuglia, G. *Synth. Commun.* **1998**, *28*, 51-60 and references therein.
23. Melpolder, J.B.; Heck, R.F. *J. Org. Chem.* **1976**, *41*, 265-272. Tamaru, Y.; Yamada, Y.; Yoshida,Y. *Tetrahedron* **1979**, *35*, 329. Kao, L.-C.; Stakem, F.G.; Patel, B.A.; Heck, R.F. *J. Org. Chem.* **1982**, *47*, 1267-1277. Jeffery, T. *J. Chem. Soc., Chem. Comm.* **1991**, 324-325. Jeffery, T. *Tetrahedron Lett.* **1991**, *32*, 2121-2124. Bernocchi, E.; Cacchi, S.; Ciattini, P.G.; Morera, E.; Ortar, G. *Tetrahedron Lett.* **1992**, 33, 3073-3076.
24. Kang, S.-K.; Lee, H.-W.; Jang, S.-B.; Kim, T.-H.; Puyn, S.-J. *J. Org. Chem.* **1996**, *61*, 2604-2605.
25. We obtained in an erratic manner in some experiments the compound **9-Methyl-4-methylene-1,3,4,9-tetrahydropyrano[3,4-*b*]indol-1-one:** This product is obtained in the same experimental conditions as for compound **25**; yield 45%; oil. IR (film) ν = 1730 (CO) cm^{-1}. ^1H NMR ($CDCl_3$) δ = 4.12 (s, 3H, NCH_3); 5.08 (m, 2H, OCH_2); 5.32 (m, 1H, =CH); 5.74 (s, 1H, =CH); 7.27-7.30 (m, 1H, Harom); 7.45-7.47 (m, 2H, Harom); 7.92 (d, 1H, Harom, J = 8.5 Hz). MS (CI/NH_3) : m/z = 214 (M^++1).



26. Edstrom, E.D.; Yu, T. *J. Org. Chem.* **1995**, *60*, 5382-5383.
27. Acheson, R. M. Booth, S. R. G. *J. Chem. Soc.* **1968**, 30-32.
28. Guyot, A.; Martinet, J. *C. R. Hebd. Séances Acad. Sci.* **1913**, *156*, 1625-1628.
29. Busacca, C.A.; Johnson, R.E.; Swestock, J. *J. Org. Chem.* **1993**, *58*, 3299-3303.
30. Sakamoto, T.; Nagano, T.; Kondo, Y.; Yamanaka, H. *Chem. Pharm. Bull.* **1988**, *36*, 2248-2252.
31. Gauthier, V. Cazes, B.. Goré, J *Bull. Soc. Chim. Fr.* **1996**, *133*, 563579. Chaptal, N.; Colovray-Gotteland, V. Grandjean, C.; Cazes, B.; Goré, J. *Tetrahedron Lett.* **1995**, *36*, 5015-5018.
32. Johnson, J.R.; Habsbrouck, R.B.; Duchter, J.D.; Bruce, W.F. *J. Am. Chem. Soc.* **1945**, *67*, 423-430.