Synthesis of New Phenylpyrrolylpyrroles

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A series of methyl or ethyl 3-(*N*-arylpyrrol-2-yl)-1*H*-pyrrole-2-carboxylates and 2,4-dicarboxylates has been synthesized using an alkyl isocyanides addition-cyclization to *N*-arylpyrrole derivatives such as carboxaldehydes and nitropropenes.

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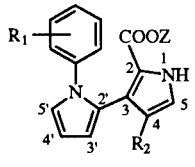
Alkyl isocyanides can be anionized (metalated) in the α-position with the usual bases such as butyllithium, sodium methoxide, DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene) or triethylamine. They contain a nucleophilic center, which can add to polar double bonds, and an electrophilic center, which permits a most useful cyclization to form various heterocycles, such as oxazoles, pyrroles, imidazoles, ... whose nature depends on the attacked double bond one [1].

In the course of our studies on the chemical reactivity of *N*-phenylpyrrole derivatives with potential pharmacological interest, we have carried out the synthesis of several methyl or ethyl 3-(*N*-phenylpyrrol-2-yl)-1*H*-pyrrole-2-carboxylates and 2,4-dicarboxylates, according to a synthetic pathway involving these kinds of reactive agents (Scheme 1).

Scheme 1



	R_1
a	H
b	4-MeO
c	2-NO_2, 4-Cl

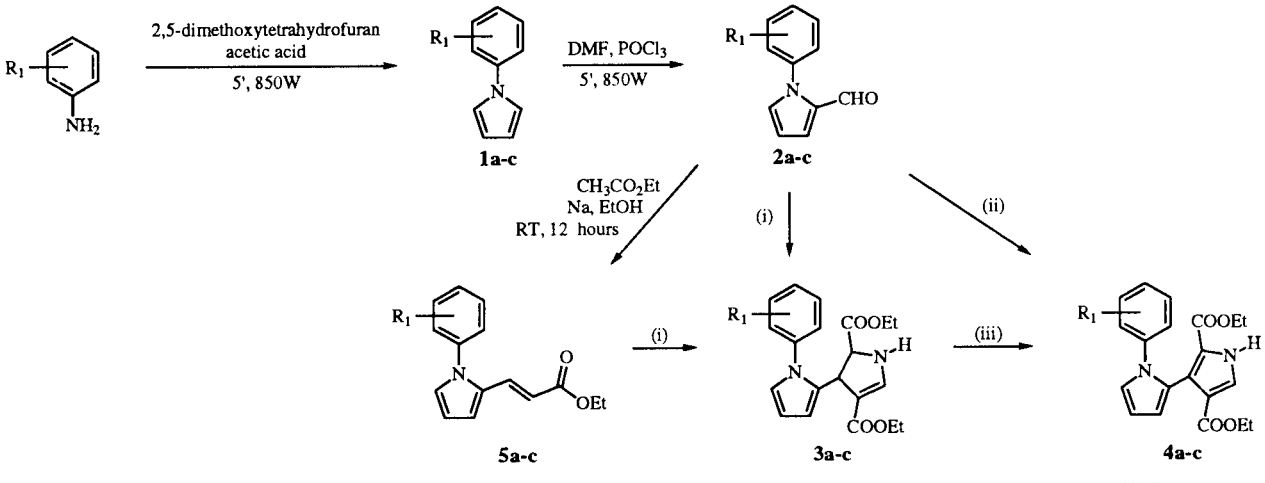
	Z
	CH_3
	C_2H_5

	R_2
	COOEt
	CH_3

The synthesis of such compounds starts from the corresponding anilines and provides the various *N*-phenylpyrroles **1a-c** according to the Clauson-Kaas procedure [2]. Vilsmeier-Haack formylation of 1-arylpyrroles leads predominantly to 2-formylated products **2a-c** [3]. These first two steps were carried out using microwave energy (5 minutes at 850 Watts) with good yields (80% on the average) [4]. Then, the 1-phenylpyrrole-2-carboxaldehydes **2a-c** may be used directly as raw materials to react with ethyl isocyanides in solution in tetrahydrofuran, in the presence of *tert*-butyl alcohol, to form the dicarboxylate compounds either **3a-c** or **4a-c** depending upon the operating conditions [5].

Because the reactants provide the ester groups, at least two equivalents of alkyl isocyanides are required. To synthesize the pyrroles **4a-c**, two equivalents of alkyl isocyanides, four equivalents of DBU and an eight-hour heating period are needed. However, this reaction may be

Scheme 2



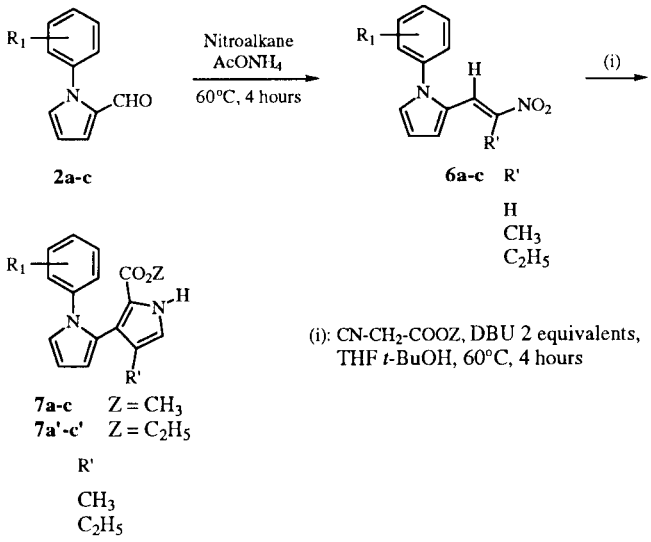
(i): CN-CH_2-COOEt 2 equivalents, DBU 2 equivalents, THF *t*-BuOH, 60°C, 4 hours
(ii): CN-CH_2-COOEt 2 equivalents, DBU 4 equivalents, THF *t*-BuOH, 60°C, 8 hours
(iii): DBU 2 equivalents, THF *t*-BuOH, 60°C, 4 hours

stopped at a pyrroline intermediate stage **3a-c** stable enough to be isolated. Only two equivalents of the base are employed to prevent the ultimate proton-extracting step which would lead to the pyrroles **4a-c**. These could be isolated from **3a-c** by treatment with two equivalents of DBU and a four-hours heating period. The α,β-unsaturated carbonyl compounds **5a-c**, synthesized themselves from the corresponding carboxaldehydes according to a Claisen condensation, lead to the same results when they were treated with alkyl isocyanides and DBU as in the process described above (Scheme 2) [6].

Primary amines may displace the carbonyl group of pyrrolecarboxaldehydes when refluxed in ethanol and the imines are then isolated. These, according to Schöllkopf and Gerhart results, should react to form an imidazoline ring [1]. In any case, our imines lead, with alkyl isocyanides, first to a pyrroline ring **3a-c** and then to a pyrroledicarboxylate *i.e.* **4a-c**. We supposed that the imines, in spite of their stability, return to the aldehyde stage and then, the *N*-phenylpyrrolecarboxaldehydes react as above.

Synthesis of arylpyrrolylpyrroles bearing just one ester moiety **7a-c** cannot be obtained directly from **2a-c**. It is necessary to use the nitrovinyl derivatives **6a-c**. These are easily obtained from the corresponding carboxaldehydes *via* a base-catalyzed condensation of nitroalkanes (nitromethane, nitroethane or nitropropane). The *E* isomers are always the major products. Few traces of *Z* isomers can be detected. In order to react, R' must include at least one carbon. If R' = H (nitromethane adducted), no further reaction with alkyl isocyanides seems to occur. Most of our work has been carried out using nitroethane. As usual, 20 minutes at room temperature are required to anionize 1 equivalent of alkyl isocyanide with 1 equivalent of DBU in a mixture of tetrahydrofuran and *tert*-butyl alcohol before heating four hours at 60° [7]. Yields are generally better with the ethyl ester group (70%) than with the methyl group (60%) (Scheme 3).

Scheme 3



EXPERIMENTAL

General Methods.

Melting points were taken on a Köfler bank and are uncorrected. Infrared spectra were recorded on a Philips PU 9716 apparatus and only noteworthy absorptions (reciprocal centimeters) are listed. Nmr spectra were recorded on a Jeol Lambda 400 using TMS as an internal standard. Chemical shifts are reported in ppm downfield (δ) from TMS.

N-Arylpyrroles **1a-c**. General Procedure.

A solution of the appropriate aniline with 2,5-dimethoxytetrahydrofuran (1.2 equivalents) in acetic acid (100 ml) is refluxed for 5 minutes at 850 Watts after which the solvent is removed under reduced pressure and the oily residue taken up with diethyl ether. The organics were washed sequentially with water and saturated sodium bicarbonate solution, then dried over magnesium sulfate and evaporated. Water vapor purification gives the *N*-phenylpyrroles **1a-c** analytically pure.

N-Phenylpyrrole (**1a**).

This compound was obtained as colorless crystals (92%), mp 62°; ^{1}H-nmr (deuteriochloroform): δ 7.34-7.45 (m, 5H, phenyl protons), 7.10 (dd, 2H, J = 1.95 Hz, H-2,5), 6.39 (dd, 2H, J = 1.95 Hz, H-3,4); ms: (m/z, %) 143 (M^+, 100), 77 (52).

Anal. Calcd. for $C_{10}H_9N$: C, 83.88; H, 6.34; N, 9.78. Found: C, 83.73; H, 6.32; N, 9.79.

N-(4-Methoxyphenyl)pyrrole (**1b**).

This compound was obtained as yellow crystals (83%), mp 57°; ^{1}H-nmr (deuteriochloroform): δ 6.69-7.13 (m, 4H, phenyl protons), 6.74 (dd, 2H, J = 1.95 Hz, H-2,5), 6.13 (dd, 2H, J = 1.95 Hz, H-3,4), 3.72 (s, 3H, OMe); ms: (m/z, %) 173 (M^+, 100), 107 (71).

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.28; H, 6.40; N, 8.09. Found: C, 76.30; H, 6.39; N, 8.10.

N-(4-Chloro-2-nitrophenyl)pyrrole (**1c**).

This compound was obtained as red crystals (89%), mp 56°; ^{1}H-nmr (DMSO-d_6): δ 7.65-8.18 (m, 3H, phenyl protons), 6.93 (dd, 2H, J = 1.95 Hz, H-2,5), 6.29 (dd, 2H, J = 1.95 Hz, H-3,4); ms: (m/z, %) 222 (M^+, 100), 156 (68).

Anal. Calcd. for $C_{10}H_7N_2O_2Cl$: C, 53.95; H, 3.17; N, 12.58. Found: C, 53.83; H, 3.16; N, 12.61.

N-Arylpyrrole-2-carboxaldehydes **2a-c**. General Procedure.

To cooled *N*,*N*-dimethylformamide (1.2 equivalents) was added dropwise phosphorus oxychloride (1.2 equivalents). A solution of the appropriate *N*-arylpyrrole in 1,2-dichloroethane (100 ml) was then added. The mixture was brought to room temperature, heated for 5 minutes at 850 Watts and then, poured into ice. The organic layer was washed with water and saturated sodium bicarbonate solution, dried over calcium chloride and evaporated to give predominantly the 2-isomer as crystals.

Recrystallization from ethyl ether/petroleum ether gave analytically pure **2a-c**.

N-Phenylpyr role-2-carboxaldehyde (**2a**).

This compound was obtained as yellow crystals (87%), mp 98°; ir (potassium bromide): ν 1690 (CO) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 9.54 (s, 1H, CHO), 7.34-7.40 (m, 5H, phenyl protons), 7.22 (dd, 1H, $J_{H5\ H3}$ = 0.95 Hz, $J_{H5\ H4}$ = 1.98 Hz, H5), 7.03 (dd, 1H, $J_{H3\ H4}$ = 3.41 Hz, $J_{H3\ H5}$ = 0.95 Hz, H3), 6.03 (dd, 1H, $J_{H4\ H3}$ = 3.41 Hz, $J_{H4\ H5}$ = 1.98 Hz, H4); ms (m/z, %) 171 (M^+, 88), 142 (79), 65 (43).

Anal. Calcd. for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18. Found: C, 76.98; H, 5.29; N, 8.21.

N-(4-Methoxyphenyl)pyrrole-2-carboxaldehyde (**2b**).

This compound was obtained as yellow crystals (84%), mp 116°; ir (potassium bromide): ν 1650 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.14 (s, 1H, CHO), 6.67-7.02 (m, 4H, phenyl protons), 6.85 (dd, 1H, $J_{H5\ H3}$ = 0.96 Hz, $J_{H5\ H4}$ = 2.00 Hz, H5), 6.75 (dd, 1H, $J_{H3\ H4}$ = 3.42 Hz, $J_{H3\ H5}$ = 0.96 Hz, H3), 6.12 (dd, 1H, $J_{H4\ H3}$ = 3.42 Hz, $J_{H4\ H5}$ = 2.00 Hz, H4), 3.72 (s, 3H, OMe); ms: (m/z, %) 201 (M^+, 62), 172 (47), 65 (32).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.41; H, 5.49; N, 6.97.

N-(2-Nitro-4-chlorophenyl)pyrrole-2-carboxaldehyde (**2c**).

This compound was obtained as brown crystals (66%), mp 94°; ir (potassium bromide): ν 1660 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.44 (s, 1H, CHO), 7.93-8.30 (m, 3H, phenyl protons), 7.45 (dd, 1H, $J_{H5\ H3}$ = 0.96 Hz, $J_{H5\ H4}$ = 2.00 Hz, H5), 7.29 (dd, 1H, $J_{H3\ H4}$ = 3.41 Hz, $J_{H3\ H5}$ = 0.96 Hz, H3), 6.52 (dd, 1H, $J_{H4\ H3}$ = 3.41 Hz, $J_{H4\ H5}$ = 2.00 Hz, H4); ms: (m/z, %) 250 (M^+, 78), 221 (54), 65 (30).

Anal. Calcd. for $C_{11}H_7N_2O_3Cl$: C, 52.71; H, 2.81; N, 11.18. Found: C, 52.63; H, 2.79; N, 11.20.

Ethyl (*E*)-3-(*N*-Arylpyrrol-2-yl)prop-2-enecarboxylates **5a-c**. General Procedure.

To a solution of the corresponding arylpyrrole-2-carboxaldehyde **2a-c** in 50 ml of ethanol were added 1 equivalent of ethyl acetate and 1 equivalent of sodium. The mixture was stirred for 4 hours at room temperature after which, 10 ml of acetic acid then 10 ml of water was added. The aqueous layer was extracted with diethyl ether. The organics were washed with water and saturated sodium bicarbonate solution, dried over magnesium sulfate and evaporated to give **5a-c**.

Ethyl (*E*)-3-(*N*-Phenylpyrrol-2-yl)prop-2-enecarboxylate (**5a**).

This compound was obtained as an oil (76%); ir (potassium bromide): ν 1690 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.53-7.70 (m, 5H, phenyl protons), 7.31 (d, $J_{H3\ H2}$ = 14.74, H3 propene), 7.21 (dd, 1H, $J_{H5'\ H4'}$ = 1.97 Hz, $J_{H5'\ H3'}$ = 0.93 Hz, H5'), 7.04 (dd, 1H, $J_{H3'\ H5'}$ = 0.93 Hz, $J_{H3'\ H4'}$ = 3.38 Hz, H3'), 6.55 (dd, 1H, $J_{H4'\ H5'}$ = 1.97 Hz, $J_{H4'\ H3'}$ = 3.38 Hz, H4'), 6.30 (dd, $J_{H2\ H3}$ = 14.74, H2 propene), 4.31 (m, 2H, OCH_2 ester), 1.31 (m, 3H, CH_3); ms: (m/z, %) 241 (M^+, 82), 182 (61), 154 (38), 143, 77.

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.80. Found: C, 74.67; H, 6.27; N, 5.79.

The ir and ^{1}H-nmr data of compounds **5b-c** are not listed here but are in accordance with those for **5a.**

Ethyl 3-(*N*-Arylpyrrol-2-yl)-1*H*-pyrroline-2,4-dicarboxylates **3a-c**. General Procedure.

To a solution of the appropriate arylpyrrole-2-carboxaldehyde or α,β-unsaturated compound in tetrahydrofuran (50 ml) and *tert*-butyl alcohol (20 ml) were added DBU (2.1 equivalents) and ethyl isocyanide (2 equivalents). The mixture was stirred for 20 minutes at room temperature then heated for 4 hours at 60°. Concentration of the solvents gave an oil which was washed with water. The oily residue was taken up in diethyl ether. The organic layer was dried over magnesium sulfate and removed under reduced pressure to give **3a-c**.

Ethyl 3-(*N*-Phenylpyrrol-2-yl)-4,5-dihydro-1*H*-pyrroline-2,4-dicarboxylate (**3a**).

This compound was obtained as an oil (58%); ir (potassium bromide): ν 3300 (NH), 1680, 1660 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.45 (s, 1H, NH), 7.04-7.39 (m, 5H, phenyl protons), 7.27 (s, 1H, H5), 6.92 (dd, 1H, $J_{H5'\ H4'}$ = 1.98 Hz, $J_{H5'\ H3'}$ = 0.93 Hz, H5'), 6.23 (dd, 1H, $J_{H3'\ H5'}$ = 0.93 Hz, $J_{H3'\ H4'}$ = 3.36 Hz, H3'), 6.15 (dd, 1H, $J_{H4'\ H5'}$ = 1.98 Hz, $J_{H4'\ H3'}$ = 3.36 Hz, H4'), 4.28 (m, 2H, OCH_2), 4.10 (m, 2H, OCH_2), 3.61 (d, 1H, CH), 3.57 (d, 1H, CH), 1.22 (m, 6H, 2 x CH_3); ms: (m/z, %) 354 (M^+, 86), 309 (72), 281 (54).

Anal. Calcd. for $C_{20}H_{22}N_2O_4$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.63; H, 6.24; N, 7.91.

Ethyl 3-(*N*-(4-methoxyphenyl)pyrrol-2-yl)-4,5-dihydro-1*H*-pyrroline-2,4-dicarboxylate (**3b**).

This compound was obtained as an oil (61%); ir (potassium bromide): ν 3250 (NH), 1680, 1670 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.44 (s, 1H, NH), 6.65-7.22 (m, 4H, phenyl protons), 6.92 (s, 1H, H5), 6.65 (dd, 1H, $J_{H5'\ H4'}$ = 1.99 Hz, $J_{H5'\ H3'}$ = 0.93 Hz, H5'), 6.25 (dd, 1H, $J_{H3'\ H5'}$ = 0.93 Hz, $J_{H3'\ H4'}$ = 3.39 Hz, H3'), 6.22 (dd, 1H, $J_{H4'\ H5'}$ = 1.99 Hz, $J_{H4'\ H3'}$= 3.39 Hz, H4'), 4.26 (m, 2H, OCH_2), 4.13 (m, 2H, OCH_2), 3.73 (s, 3H, OMe), 3.58 (d, 1H, CH), 3.57 (d, 1H, CH), 1.25 (m, 6H, 2 x CH_3); ms: (m/z, %) 384 (M^+, 63), 339 (58), 311 (20).

Anal. Calcd. for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.59; H, 6.28; N, 7.31.

Ethyl 3-(*N*-(4-Chloro-2-nitrophenyl)pyrrol-2-yl)-4,5-dihydro-1*H*-pyrroline- 2,4-dicarboxylate (**3c**).

This compound was obtained as white crystals (diethyl ether) (48%), mp 62°; ir (potassium bromide): ν 3300 (NH), 1680, 1660 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 9.52 (s, 1H, NH), 7.25-7.60 (m, 3H, phenyl protons), 7.37 (s, 1H, H5), 6.96 (dd, 1H, $J_{H5'\ H4'}$ = 1.98 Hz, $J_{H5'\ H3'}$ = 0.94 Hz, H5'), 6.41 (dd, 1H, $J_{H3'\ H5'}$ = 0.94 Hz, $J_{H3'\ H4'}$ = 3.37 Hz, H3'), 6.32 (dd, 1H, $J_{H4'\ H5'}$ = 1.98 Hz, $J_{H4'\ H3'}$ = 3.37 Hz, H4'), 4.19 (m, 2H, OCH_2), 4.10 (m, 2H, OCH_2), 3.48 (d, 1H, CH), 3.05 (d, 1H, CH), 1.26 (m, 6H, 2 x CH_3); ms: (m/z, %) 433 (M^+, 68), 388 (59), 360 (56).

Anal. Calcd. for $C_{20}H_{20}N_3O_6Cl$: C, 55.37; H, 4.65; N, 9.69. Found: C, 55.27; H, 4.63; N, 9.70.

Ethyl 3-(*N*-Arylpyrrol-2-yl)-1*H*-pyrrole-2,4-dicarboxylates **4a-c**. General Procedure.

If using a large excess of DBU (4 equivalents at least) in the reaction described above and heating for 8 hours at 60°, the pyrroline ring undergoes an ultimate proton-extracting step to give the pyrrole. Poured into water, the (*N*-arylpyrrol-2-yl)pyrrolyldicarboxylates compounds are extracted with ethyl ether. The organic layer is dried over magnesium sulfate, passed through a silica gel pad and removed *in vacuo* to give **4a-c** as oils.

Ethyl 3-(*N*-Phenylpyrrol-2-yl)-1*H*-pyrrole-2,4-dicarboxylates (**4a**).

This compound was obtained as an oil (76%); ir (potassium bromide): ν 3300 (NH), 1680, 1660 (CO) cm^{-1}; ^1H-nmr (deuteriochloroform): δ 9.45 (s, 1H, NH), 6.99-7.17 (m, 5H, phenyl protons), 7.02 (s, 1H, H5), 6.90 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 6.17 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.36 Hz, H3'), 6.14 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.36 Hz, H4'), 4.26 (m, 2H, OCH_2), 4.18 (m, 2H, OCH_2), 1.25 (m, 6H, 2 x CH_3); ms: (m/z, %) 352 (M^+, 82), 262 (71), 206 (68).

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 67.95; H, 5.71; N, 7.96.

Ethyl 3-(*N*-(4-Methoxyphenyl)pyrrol-2-yl)-1*H*-pyrrole-2,4-dicarboxylate (**4b**).

This compound was obtained as an oil (81%); ir (potassium bromide): ν 3300 (NH), 1680, 1660 (CO) cm^{-1}; ^1H-nmr (deuteriochloroform): δ 9.45 (s, 1H, NH), 6.71-7.20 (m, 4H, phenyl protons), 7.05 (s, 1H, H5), 6.58 (dd, 1H, $J_{H5' H4'}$ = 1.99 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 6.24 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.39 Hz, H3'), 6.22 (dd, 1H, $J_{H4' H5'}$ = 1.99 Hz, $J_{H4' H3'}$ = 3.39 Hz, H4'), 4.24 (m, 2H, OCH_2), 4.15 (m, 2H, OCH_2), 3.74 (s, 3H, OMe), 1.24 (m, 6H, 2 x CH_3); ms: (m/z, %) 382 (M^+, 82), 292 (76), 236 (68).

Anal. Calcd. for $C_{21}H_{22}N_2O_5$: C, 65.96; H, 5.80; N, 7.33. Found: C, 65.95; H, 5.78; N, 7.31.

Ethyl 3-(*N*-(4-Chloro-2-nitrophenyl)pyrrol-2-yl)-1*H*-pyrrole-2,4-dicarboxylates (**4c**).

This compound was obtained as an oil (78%); ir (potassium bromide): ν 3300 (NH), 1670, 1660 (CO) cm^{-1}; ^1H-nmr (deuteriochloroform): δ 9.50 (s, 1H, NH), 7.28-7.56 (m, 3H, phenyl protons), 7.36 (s, 1H, H5), 6.96 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.94 Hz, H5'), 6.38 (dd, 1H, $J_{H3' H5'}$ = 0.94 Hz, $J_{H3' H4'}$ = 3.37 Hz, H3'), 6.36 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.37 Hz, H4'), 4.20 (m, 2H, OCH_2), 4.16 (m, 2H, OCH_2), 1.25 (m, 6H, 2 x CH_3); ms: (m/z, %) 431 (M^+, 71), 341 (58), 285 (46).

Anal. Calcd. for $C_{20}H_{18}N_3O_6Cl$: C, 55.63; H, 4.20; N, 9.73. Found: C, 55.61; H, 4.18; N, 9.71.

(*E*)-1-(*N*-Arylpyrrol-2-yl)-2-nitroprop-2-enes **6a-c**. General Procedure.

To a suspension of ammonium acetate (2.5 equivalents) in nitroalkane, here nitroethane, (50 ml) is added a solution of the appropriate *N*-phenylpyrrolecarboxaldehyde readily soluble in nitroethane (100 ml). The mixture is heated for 4 hours at 60° after which the solvent is evaporated. The oily residue is washed with water and taken up in diethyl ether. The organics are dried over magnesium sulfate then removed under reduced pressure to give a yellow solid which was recrystallized from diethyl ether/petroleum ether to give analytically pure **6a-c**.

(*E*)-2-Nitro-1-(*N*-phenylpyrrol-2-yl)prop-2-ene (**6a**).

This compound was obtained as yellow crystals (73%), mp 92°; ^1H-nmr (deuteriochloroform): δ 7.88 (d, 1H, CH), 7.28-7.88 (m, 5H, phenyl protons), 7.14 (dd, 1H, $J_{H5' H4'}$ = 1.99 Hz, $J_{H5' H3'}$ = 0.95 Hz, H5), 6.80 (dd, 1H, $J_{H3' H5'}$ = 0.95 Hz, $J_{H3' H4'}$ = 3.38 Hz, H3'), 6.48 (dd, 1H, $J_{H4' H5'}$ = 1.99 Hz, $J_{H4' H3'}$ = 3.38 Hz, H4'), 2.52 (s, 3H, Me); ms: (m/z, %) 228 (M^+, 24), 143 (52), 77 (40).

Anal Calcd. for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found C, 68.39; H, 5.29; N, 12.27.

(*E*)-2-Nitro-1-(*N*-(4-methoxyphenyl)pyrrol-2-yl)prop-2-ene (**6b**).

This compound was obtained as yellow crystals (77%), mp 89°; ^1H-nmr (deuteriochloroform): δ 7.55 (d, 1H, CH), 7.02-7.24 (m, 4H, phenyl protons), 7.13 (dd, 1H, $J_{H5' H4'}$ = 2.01 Hz, $J_{H5' H3'}$ = 0.95 Hz, H5'), 6.94 (dd, 1H, $J_{H3' H5'}$ = 0.95 Hz, $J_{H3' H4'}$ = 3.40 Hz, H3'), 6.37 (dd, 1H, $J_{H4' H5'}$ = 2.01 Hz, $J_{H4' H3'}$ = 3.40 Hz, H4'), 3.74 (s, 3H, OMe), 2.51 (s, 3H, Me); ms: (m/z, %) 258 (M^+, 32), 173 (30), 141 (10).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.10; H, 5.45; N, 10.87.

(*E*)-2-Nitro-1-(*N*-(4-chloro-2-nitrophenyl)pyrrol-2-yl)prop-2-ene (**6c**).

This compound was obtained as yellow crystals (69%), mp 101°; ^1H-nmr (deuteriochloroform): δ 7.88 (d, 1H, CH), 7.28-7.88 (m, 3H, phenyl protons), 7.14 (dd, 1H, $J_{H5' H4'}$ = 1.99 Hz, $J_{H5' H3'}$ = 0.95 Hz, H5'), 6.80 (dd, 1H, $J_{H3' H5'}$ = 0.95 Hz, $J_{H3' H4'}$ = 3.38 Hz, H3'), 6.48 (dd, 1H, $J_{H4' H5'}$ = 1.99 Hz, $J_{H4' H3'}$ = 3.38 Hz, H4'), 2.52 (s, 3H, Me); ms: (m/z, %) 307 (M^+, 49), 222 (48), 190 (28).

Anal. Calcd. for $C_{13}H_{10}N_3O_4Cl$: C, 50.75; H, 3.28; N, 13.66. Found: C, 50.73; H, 3.29; N, 13.67.

Alkyl 4-Methyl-3-(*N*-arylpyrrol-2-yl)-1*H*-pyrrole-2-carboxylates **7a-c**. General Procedure.

To a solution of the appropriate arylpyrrole nitrovinyl derivative in tetrahydrofuran (50 ml) and *tert*-butanol (20 ml) were added DBU (1.1 equivalents) and alkyl isocyanide (methyl or ethyl, 1 equivalent). The mixture was stirred for 20 minutes at room temperature then heated for 4 hours at 60°. Concentration of the solvents gave an oil which was washed with water. The oily residue was taken up in diethyl ether. The organic layer was dried over magnesium sulfate and removed under reduced pressure to give **7a-c**.

Methyl 4-Methyl-3-(*N*-phenylpyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7a**).

This compound was obtained as an oil (66%); ir (potassium bromide): ν 3300 (NH), 1670 (CO) cm^{-1}; ^1H-nmr (DMSO-d_6): δ 11.35 (s, 1H, NH), 7.51-7.68 (m, 5H, phenyl protons), 7.48 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 7.39 (s, 1H, H5), 6.68 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.36 Hz, H3'), 6.49 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.36 Hz, H4'), 3.72 (s, 3H, OMe), 2.09 (m, 3H, Me); ms: (m/z, %) 280 (M^+, 100), 249 (23), 221 (7).

Anal. Calcd. for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.84; H, 5.74; N, 10.01.

Ethyl 4-Methyl-3-(*N*-phenylpyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7a'**).

This compound was obtained as an oil (69%); ir (potassium bromide): ν 3300 (NH), 1670 (CO) cm^{-1}; ^1H-nmr (DMSO-d_6): δ 11.33 (s, 1H, NH), 7.50-7.67 (m, 5H, phenyl protons), 7.47 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 7.40 (s, 1H, H5), 6.66 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.36 Hz, H3'), 6.51 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.36 Hz, H4'), 3.95 (m, 2H, OCH_2 ester), 1.97 (m, 3H, Me), 1.32 (m, 3H, CH_3 ester); ms: (m/z, %) 294 (M^+, 100), 249 (28), 221 (15).

Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.43; H, 6.14; N, 9.53.

Methyl 4-Methyl-3-(*N*-(4-methoxyphenyl)pyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7b**).

This compound was obtained as yellow crystals (petroleum ether) (54%); ir (potassium bromide): ν 3300 (NH), 1680 (CO) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 11.17 (s, 1H, NH), 6.54-7.01 (m, 4H, phenyl protons), 6.89 (dd, 1H, $J_{H5' H4'}$ = 1.99 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 6.73 (s, 1H, H5), 6.35 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.39 Hz, H3'), 6.09 (dd, 1H, $J_{H4' H5'}$ = 1.99 Hz, $J_{H4' H3'}$ = 3.39 Hz, H4'), 3.86 (s, 3H, OMe ester), 3.54 (s, 3H, OMe), 1.96 (m, 3H, Me); ms: (m/z, %) 310 (M^+, 100), 279 (34), 251 (27).

Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.65; H, 5.83; N, 9.01.

Ethyl 4-Methyl-3-(*N*-(4-methoxyphenyl)pyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7b'**).

This compound was obtained as yellow crystals (petroleum ether) (57%), mp 61°; ir (potassium bromide): ν 3300 (NH), 1680 (CO) cm^{-1}; ^{1}H-nmr (DMSO-d_6): δ 11.15 (s, 1H, NH), 6.55-7.00 (m, 4H, phenyl protons), 6.88 (dd, 1H, $J_{H5' H4'}$ = 1.99 Hz, $J_{H5' H3'}$ = 0.93 Hz, H5'), 6.71 (s, 1H, H5), 6.30 (dd, 1H, $J_{H3' H5'}$ = 0.93 Hz, $J_{H3' H4'}$ = 3.39 Hz, H3'), 6.10 (dd, 1H, $J_{H4' H5'}$ = 1.99 Hz, $J_{H4' H3'}$ = 3.39 Hz, H4'), 3.90 (m, 2H, OCH_2 ester), 3.51 (s, 3H, OMe), 1.95 (m, 3H, Me), 1.10 (m, 3H, CH_3 ester); ms: (m/z, %) 324 (M^+, 100), 279 (56), 251 (37).

Anal. Calcd. for $C_{19}H_{20}N_2O_3$: C, 70.35; H, 6.21; N, 8.64. Found: C, 70.36; H, 6.20; N, 8.66.

Methyl 4-Methyl-3-(*N*-(4-chloro-2-nitrophenyl)pyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7c**).

This compound was obtained as an oil (58%); ir (potassium bromide): ν 3300 (NH), 1680 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.37 (s, 1H, NH), 7.54-7.81 (m, 3H, phenyl protons), 6.98 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.94 Hz, H5'), 6.73 (s, 1H, H5), 6.51 (dd, 1H, $J_{H3' H5'}$ = 0.94 Hz, $J_{H3' H4'}$ = 3.37 Hz, H3'), 6.39 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.37 Hz, H4'), 3.82 (s, 3H, OMe ester), 1.96 (m, 3H, Me); ms: (m/z, %) 359 (M^+, 100), 328 (58), 300 (32).

Anal. Calcd. for $C_{17}H_{14}N_3O_4Cl$: C, 56.76; H, 3.92; N, 11.68. Found: C, 56.74; H, 3.91; N, 11.69.

Ethyl 4-Methyl-3-(*N*-(4-chloro-2-nitrophenyl)pyrrol-2-yl)-1*H*-pyrrole-2-carboxylate (**7c'**).

This compound was obtained as yellow crystals (diethyl ether/petroleum ether) (73%), mp 52°; ir (potassium bromide): ν 3300 (NH), 1670 (CO) cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.29 (s, 1H, NH), 7.51-7.86 (m, 3H, phenyl protons), 6.96 (dd, 1H, $J_{H5' H4'}$ = 1.98 Hz, $J_{H5' H3'}$ = 0.94 Hz, H5'), 6.73 (s, 1H, H5), 6.53 (dd, 1H, $J_{H3' H5'}$ = 0.94 Hz, $J_{H3' H4'}$ = 3.37 Hz, H3'), 6.33 (dd, 1H, $J_{H4' H5'}$ = 1.98 Hz, $J_{H4' H3'}$ = 3.37 Hz, H4'), 4.04 (m, 2H, OCH_2 ester), 1.93 (m, 3H, Me), 1.30 (m, 3H, CH_3 ester); ms: (m/z, %) 373 (M^+, 94), 328 (74), 300 (42).

Anal. Calcd. for $C_{18}H_{16}N_3O_4Cl$: C, 57.84; H, 4.31; N, 11.24. Found: C, 57.82; H, 4.31; N, 11.26.

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