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Synthesis and Reactions of 1-Aryl-2-nitropyrroles. Structural and Conformational Study of Ethyl N-[2'-[1'-(2-nitropyrrolyl)]phenyl]-N-toluene-4-sulfonamide glycinate

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Dedicated to Hans Suschitzky, with admiration and respect, on the occasion of his eightieth birthday

Abstract: Nitration of 1-aryl(or 1-benzyl)pyrroles **1**, **2** and **7** has provided the corresponding 2- and 3-nitropyrroles **3** and **5**, **4** and **6**, and **8** and **9** in a 1:2 ratio. Reductive cyclisation of **3** and **8**, gave pyrrolo[1,2-a]quinazolines **11** and **12**, and pyrrolo[1,2-b][2,4]benzodiazepine **13**, respectively. A conformational study of **5** in the solid and liquid state using X-ray diffraction analysis, molecular dynamics calculations and NMR spectroscopy, is described.

We are interested in synthesizing novel tricyclic compounds that have structural similarities to the pyrrolo[2,1-c][1,4]benzodiazepine class of antitumour antibiotics[1]. Intramolecular cyclisation of appropriately substituted 2-aminomethyl-1-aryl(or 1-benzyl)pyrroles has given several examples of the corresponding pyrrolo[1,2-a][1,4]benzodiazepine and pyrrolo[2,1-c][1,4]benzodiazocine ring systems[2,3]. We would now like to report our findings on the nitration of 1-aryl(or 1-benzyl)pyrroles as a means of introducing a nitro group at position-2 of the pyrrole ring, which upon reduction, could be used as a nucleophile for intramolecular cyclisation.

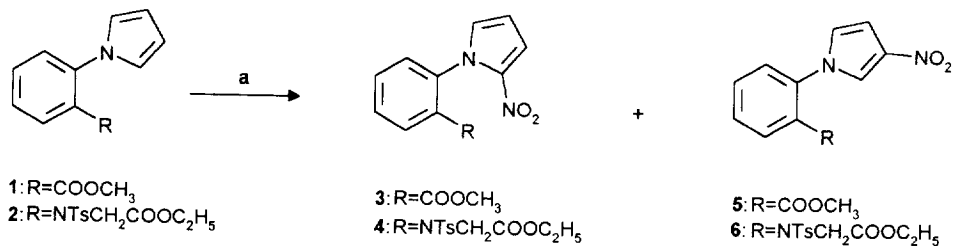
In this context we nitrated pyrroles **1**, **2** and **7** with fuming nitric acid in acetic anhydride at -30°C and obtained the corresponding 2- and 3-nitro isomers **3** and **5**, **4** and **6**, and **8** and **9**, in ratios of approximately 1:2. All compounds were easily separated by flash chromatography. The IR spectra of these compounds show the nitro asymmetric and symmetric absorption bands at around 1500-1520 and 1330-1350 cm^{-1}, respectively. In the ^1H NMR spectra of the 2-nitro isomers the lowest frequency proton signals are in the range of δ= 6.24-6.37 ppm and identified as H-4. The highest frequency proton signals are in the range of δ= 7.54-7.77 ppm and iden-

tified as H-2. In addition the coupling constant between H-3 and H-4 of the 2-nitro compounds is in the range of 4.2-4.3 Hz. This coupling is absent in the corresponding 3-nitro compounds where the largest coupling constant is 3.2 Hz between H-4 and H-5.

Hydrogenation of nitroester **3** in the presence of 5% palladium on carbon followed by heating under reflux for 1 h gave a mixture of pyrrolo[1,2-a]quinazolones **11** and **12** which were separated by column chromatography. Both are known compounds which have been prepared by different routes.[4-8] The postulated intermediate for this cyclisation is the iminopyrrolidine **10**. A similar type of reaction was reported by Grehn[9] who reduced 2-nitro-1-methylpyrrole, trapped the intermediate 2-imino-1-methylpyrrolidine with ethoxycarbonyl isothiocyanate and obtained 2-(3-ethoxycarbonylthioureido)-1-methylpyrrolidine.

Catalytic hydrogenation of nitroester **8** yielded the pyrrolo[1,2-b][2,4]benzodiazepine **13.** Several derivatives of the fully saturated ring system have been synthesised from aminomethylbenzylamine and an appropriate dicarbonyl compound.[10]

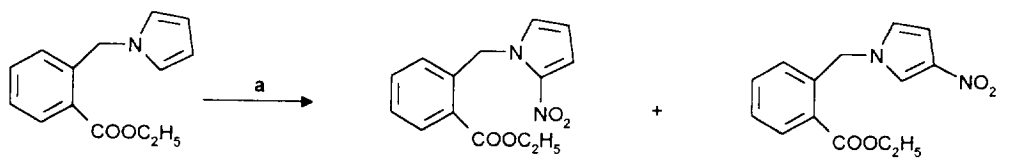
Reduction of nitroester **4** under the same reaction conditions gave an intractable oil composed of three overlapping polar spots on thin layer chromatography. A GC-MS study of this mixture did not help in identifying any products.



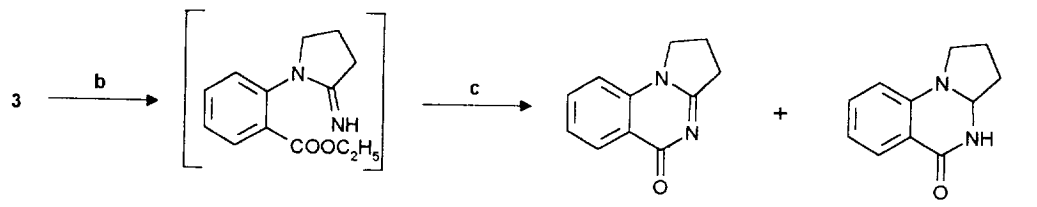
1: R=$COOCH_3$
2: R=$NTsCH_2COOC_2H_5$

3: R=$COOCH_3$
4: R=$NTsCH_2COOC_2H_5$

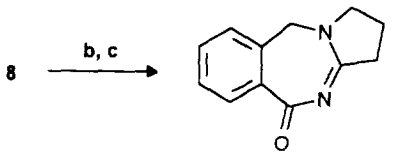
5: R=$COOCH_3$
6: R=$NTsCH_2COOC_2H_5$



7 **8** **9**



10 **11** **12**



13

Reagents: a) $(CH_3CO)_2O$, fuming HNO_3, -30°C to 22°C
b) H_2 / Pd-C, MeOH
c) NaOEt, EtOH, reflux

In the ^1H NMR spectra of **2** and **6** the N-methylene protons appear as singlets at δ= 3.89 and 4.12 ppm respectively. On the other hand the N-methylene protons of compound **4** appear as doublets (J= 17.7 Hz) at δ_a= 3.92 ppm and δ_b= 4.29 ppm. The signals from this group begin to coalesce at 90°. Closely related N-p-tolylsulfonyl methylenes show restricted rotation due to a methyl group ortho to the N-tosyl group. The absence of the ortho methyl group from the ring allows free rotation of the N-methylene group.[11] Furthermore the signal at 4.29 ppm of compound **4** is at higher frequency than the signals for the N-methylene protons in **2** and **6**. These observations merit further investigation. In order to reveal the intrinsic structural features of nitroester **4**, an in depth conformational study both in the solid state and in solution was undertaken. X-ray diffraction, molecular dynamics calculations and NMR spectroscopy were used for this purpose.

Table 1 presents the most important interatomic distances of compound **4**. Some significant torsion angles of the crystal structure are presented in Table 2 along with the corresponding values derived from molecular dynamics simulation. The crystal structure reveals that the interplanar angles between the three aromatic rings A, B, C (Fig. 1) are A/B =112°, A/C=83° and B/C =33°. A study of nitrobiphenyls[12] revealed that the o-nitro group reduces the planarity of the molecules. This is the case for the A-B ring subsystem. The middle benzene ring, B, divides the space into two halves. The nitro group and the ester side chain reside in the same half-space. The ester part is approximately parallel to the tosyl group and interacts with it via C-C, C-H and H-H interactions.The interplanar angle between the nitro group and the pyrrole ring is about 10°. The torsion angle C1-C6-N1-C7 is -71.8° while in other similar compounds this angle has a mean value of -110 + 10°[13]. This deviation reflects the tendancy of nitro group to be placed away from the ester chain. The exocyclic N has essentially sp^2 character with a slight sp^3 component. This is in accord with observations made for analogous compounds containing the sulfonamido group[14]. The crystal packing is essentially governed by Van der Waals interactions. Aromatic rings interact either by stacking or herringbone interactions. The ester chain is positioned between two aromatic rings one belonging to the tosyl group of the same molecule and another, 5-membered ring belonging to a neighbouring molecule. These interactions stabilise the conformation in the solid state.

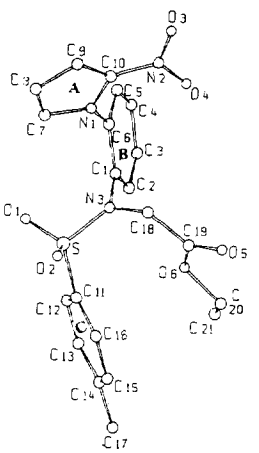


Figure 1. Schakal plot of the X-ray structure of the nitroester **4**, showing the atomic numbering system.

The molecular dynamics simulations for $CDCl_3$ solution, presented in Table 2, deduce a structure of **4** that is more compact in comparison to the extended solid state structure. This is mainly reflected by the C1-N3-S-C11 dihedral angle which has an average a value of -100° while in the solid it takes the value 90° . It appears that the methyl group of the ester does not approach the methyl group of the tosyl (average distance 10 Å). The tosyl-benzene ring shows a high degree of mobility in contrast to the relative inertia of the two other aromatic rings. The distance between the N-methylene carbon and the one of the oxygens of the nitro group is relatively constant showing a small variation in the range 2.8 to 3.2 Å.

Table 1. Selected Interatomic Bond Distances (Å) and Bond Angles (°) for Compound **4**.

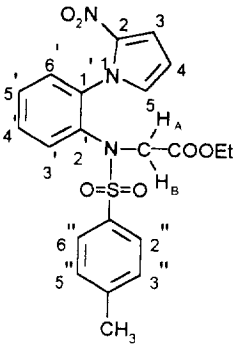
Bond Lengths (Å)		Bond Angles (°)	
C(6)-N(1)	1.437(5)	N(2)-C(10)-C(9)	126.9(4)
C(10)-N(2)	1.407(6)	N(2)-C(10)-N(1)	123.1(4)
N(2)-O(3)	1.237(6)	C(10)-N(1)-C(6)	129.7(3)
N(2)-O(4)	1.228(5)	C(7)-N(1)-C(6)	122.2(4)
C(1)-N(3)	1.431(5)	N(1)-C(6)-C(1)	120.2(3)
N(3)-S	1.642(4)	C(6)-C(1)-N(3)	119.5(4)
O(1)-S	1.431(3)	C(1)-N(3)-S	121.4(3)
O(2)-S	1.430(4)	N(3)-S-C(11)	108.9(2)
C(11)-S	1.762(5)	S-C(11)-C(12)	120.0(4)
N(3)-C18	1.457(6)	C(1)-N(3)-C(18)	117.5(3)
C(18)-C19	1.501(7)	N(3)-C(18)-C(19)	118.2(4)
C(19)-O(6)	1.327(6)	C(19)-O(6)-C(20)	117.4(4)
O(6)-C(20)	1.471(6)	O(6)-C(20)-C(21)	106.6(4)
C(20)-C(21)	1.513(10)		

In the 2D-NOESY spectrum of compound **4** there are significant cross peaks at δ= 3.9 : 7.2 ppm and at δ= 4.3 : 7.2 ppm which indicate that the N-methylene protons are in close proximity (within 4 Å) to either H-3' or H-5 which are coincident at δ= 7.19 ppm. No such peak is observed in the COSY spectrum of this compound. A cross peak at δ= 3.9-7.6 ppm indicates close proximity of one N-methylene proton to the H-2" and H-6" protons. There are no cross peaks to the methyl group of the ethyl ester to any proton apart from the adjacent methylene pair. This was also verified by NOE difference experiments and suggests that the ethyl group is turned away from the tosyl group. The result is contrary to the solid state where X-ray data show

Table 2. Selected Torsion Angles (°) for Compound .

	X-ray structure	MD simulation Average value
C(6)-C(1)-N(3)-S	107	140 ± 20
C(1)-N(3)-S-C(11)	90	-100 ± 50
N(3)-S-C(11)-C(12)	-89	-93 ± 40
N(3)-S-C(11)-C(16)	90	108 ± 50
C(6)-C(1)-N(3)-C(18)	-77	-50 ± 20
C(1)-N(3)-C(18)-C(19)	-84	-60 ± 60
N(3)-C(18)-C(19)-O(6)	-1	-160 ± 20
C(18)-C(19)-O(6)-C(20)	-174	-175 ± 30
C(19)-O(6)-C(20)-C(21)	-166	-140 ± 40

that one of these methyl protons is 3.0 Å away from H-3 proton and 3.3 Å away from either H-2"or H-6"protons. The separation of the coincidental chemical shifts of H-3' and H-5 protons of **5** was achieved by acquiring spectra of the compound in a mixture of 25% MeOD and 75% $CDCl_3$. In these spectra, the H-3 proton appears at δ= 7.06 ppm and the H-5 proton at δ= 7.1 ppm. The two N-methylene protons show signals at δ= 3.8 and 4.1 ppm. In the ^1H NOE difference spectrum of compound **4**, acquired by simultaneous irradiation of both N-methylene protons, there is a strong enhancement of the signals at δ= 7.06 and 7.50 ppm. This confirms



4

Table 3. ^1H NMR Data of Compound **4**.

CH_3	1.15 t	H-4	6.37 dd	H-4'	7.37 td	$J_{3,4}$ = 4.2 Hz
CH_3-4"	2.45 s	H-3'	7.19 dd	H-3	7.38 dd	$J_{3,5}$ =1.9 Hz
H_a	3.92 d	H-5	7.19 dd	H-5'	7.43 td	$J_{4,5}$ = 2.8 Hz
CH_2	4.1-3.98 m	H-6'	7.26 dd	H-2", H-6"	7.59 d	J_{AB} =17.76 Hz
H_b	4.29 d	H-3", H-5"	7.30 d			

Table 4. ^{13}C NMR Data of Compound **4**.

CH_3	13.95	C-6'	129.06	C-1"	135.50
CH_3-4"	21.67	C-3", C-5"	129.54	C-2'	136.50
NCH_2	52.23	C-5'	129.64	C-2	137.85
CH_2	61.54	C-4'	129.75	C-1'	138.37
C-4	109.60	C-3'	130.52	C-4"	144.37
C-3	115.12	C-5	132.21	C=O	168.16
C-2", C-6"	128.49				

that the enhancement of the signals of **4** at δ= 7.19 ppm in neat $CDCl_3$ arose from the benzene H-3' proton, rather than from the pyrrolic H-5 proton, although the signal from the latter proton shows a very weak enhancement indicating an interatomic distance of 4-5 Å from one of the methylene protons. Integration of the enhanced peaks shows that the signal from the two α-tosyl protons integrate to approximately the same value as for the single benzene proton, 1.4:1.5, respectively. This suggests that the average distance of the N-methylene protons from proton H-3' is less than the distance of these protons from the α-tosyl protons, both distances being within 4 Å. Separate irradiation of the N-methylene proton signals showed that there was a greater (approx. 40%) NOE of the α-tosyl proton signals when irradiating the higher frequency proton (δ= 4.3 ppm) than the lower frequency one.

The average distance of the nitro group nitrogen to the carbonyl carbon is around 4.8 Å (molecular dyna-

mics trajectory) while from the X-ray (Fig. 1) this distance is 4.2 Å. From the X-ray structure and molecular dynamics calculations we find that in compound **4** the sulfonyl oxygens are at close proximity to one of the methylene hydrogens (about 3.0 Å). The S=O lengths taken from a closely related tosyl sulfonamide have been found to be 1.429(2) Å and 1.427(2) Å[13] whereas in **4** the S=O lengths are 1.431(3) Å and 1.430(4) Å. Although the elongation of S=O bond length in **4** is within experimental error this could be attributed to an attraction between one of the N-methylene hydrogens and the oxygens of the sulfonyl group. Furthermore from atomic charge values derived by MOPAC[15] minimization of the X-ray co-ordinates of **4,** the sulfonyl oxygens appear to have twice the electronegativity when compared to the values of the nitro oxygens (Table 5). This electronegativity difference between the sulfonyl and nitro oxygens explains further why the N-methylene group prefers to reside in the oxygen vicinity of the sulfonyl group.

Table 5 . Atomic Charges from MOPAC Minimization of the Crystal Structure of Compound **4**.

C(10)	-0.08	N(3)	- 0.47	N(1)	-0.14	O(6)	-0.31
N(2)	0.39	S	1.68	C(1)	0.03	C(20)	0.13
O(3)	-0.36	O(1)	-0.67	C(18)	0.09	C(21)	0.02
O(4)	-0.31	O(2)	-0.72	C(5)	-0.27	C(19)	0.32

Table 6. Crystal Data and Intensity Collection Data for compound **4**.

Formula	$C_{21}H_{21}N_3O_6S$	Scan mode	ω-2θ
MW	443.47	Z	4
Space group	$P2_1/c$	dx,Mgm^{-3}	1.399
Cell dimensions a, Å	11.923(2)	Total reflections	4158
b, Å	12.964(3)	Significant reflections	3258
c, Å	13.896(3)	(I>3σ(I))	
β,°	101.48(1)	R	0.067
Diffractometer	CAD4, Cu-Kα	Rw	0.067
	graphite monochromatized	weighting scheme	unit weights
Volume, Å^3	2105.0		

EXPERIMENTAL

Crystals were obtained by recrystallisation from ethanol solution. Crystal and intensity collection data are shown in Table 3. Data reduction was undertaken with an SDP package. The structure was solved by Fourier methods and refined with SHELX 76.

Strain-energy calculations were performed using Chem3D Plus v3 package[16] which contained a module for MM2 (molecular mechanics version 2), the parameters used are as in Cobb *et al*[13]. A sampling of the conformational space was performed using a small scale molecular dynamics (MD) of the sulfamido compound in a solvent 'bath' of $CDCl_3$ molecules at a target temperature of 300K. A trajectory of 60 psec was obtained after a 10 psec equilibration period.

Solvents and reagents were used as received from the manufacturers except for acetic anhydride, which was freshly distilled, and dichloromethane, ethanol, ethyl acetate, methanol and petroleum ether (bp 40-60°C), which were purified according to methods described by Perrin *et al*[17]. Silica gel Merck (230-400 mesh) was used throughout for purification by flash chromatography, and Fluka silica gel 60 F_{254} was used for thin layer

chromatography. Melting points were measured with a Büchi 510 apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 257 spectrometer. Solids were taken as Nujol mulls and liquids as thin films between sodium chloride discs. All NMR spectra were obtained from a 40.4 mg/ml solution in $CDCl_3$, or the same concentration in 75% $CDCl_3$ / 25% MeOD solvent mixture. The 1-D proton spectra were acquired at 360.1 MHz and the carbon spectra at 90 MHz on a Brüker AM 360 spectrometer at 294 K. The routine spectra were acquired with a 20 degree flip angle, 3.9 seconds aquisition and a digital resolution of 0.254 Hz/data point. NOE difference spectra were acquired with the same digital resolution but a flip angle of 30 degrees and a 2 second delay between acquisitions plus a 0.8 sec irradiation time. When processing the NOE difference spectra a line broadening of 0.7 Hz was used[18]. The 2-D proton spectra were acquired at 400.1 spectra on a Brüker AMX 400 spectrometer. The spectral width for the 2-D spectra was 7.3 ppm and the digital resolution was 2.8 Hz/data point. The phase sensitive NOESY was recorded with a 2 second acquisition delay and 0.5 second irradiation time. Mass spectra were obtained with a JEOL JMS-AX 505W machine. Elemental analyses were performed by the European Environmental Research Institute of Ioannina on a Perkin-Elmer 2400 elemental analyser and by the School of Pharmacy, University of London, on a Carlo Erba 1106 elemental analyser.

Ethyl N-[2'-[1'-(pyrrolyl)]phenyl]-N-toluene-4-sulfonyl glycinate **2** and 1-(2-ethoxycarbonylbenzyl)pyrrole **7** were prepared according to the methods of Cheeseman and Varvounis[19] and Corelli *et al*[20], respectively.

General Procedure for the Preparation of 2-Nitro- and 3-Nitro-1-arylpyrroles (3) and (5), (4) and (6), and (8) and (9).

Fuming nitric acid (0.32 ml, 8 mmol) was added dropwise to acetic anhydride (30 ml) at -10°C while stirring. The resulting mixture was added dropwise to a stirred solution of pyrrole **1**, **2** or **7** (5 mmol) in acetic anhydride (30 ml) at -30 to -40°C. The temperature was maintained at -30 to -40°C for 1h, left to rise to 0°C and then stirred at that temperature for a further 2h. The mixture was poured onto ice (180 g) and extracted with chloroform (3 × 50 ml). The combined organic layers were washed with brine (3 × 20 ml), dried over anhydrous sodium sulfate, and filtered. Chloroform was evaporated and the remaining acetic acid in the mixture removed by codistillation with toluene. The crude solid was chromatographed on a silica gel column and eluted with ethyl acetate/petroleum ether (bp 40-60°C) (1:4) to afford **3** and **5**, and **4** and **6**. Elution with ethyl acetate/petroleum ether (bp 40-60°C) (1:8) gave **8** and **9**.

1-(2-Methoxycarbonylphenyl)-2-nitropyrrole 3: (31%), m.p. 124-125°C (yellow needles from ethanol); (Found: C, 58.35 ; H, 3.90 ; N, 11.39. $C_{12}H_{10}N_2O_4$ requires: C, 58.54; H, 4.10; N, 11.38); i.r. (Nujol) 1715 (COOEt), 1520 asym (NO_2) and 1350 sym (NO_2) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$) 3.70 (s, 3H, CH_3), 6.36 (dd, $J_{4,5}$= 2.7 Hz, H-4), 6.18 (dd, $J_{5,3}$= 2.0 Hz, H-5), 7.32 (dd, $J_{3,4}$= 4.2 Hz, H-3), 7.34 (dd, J= 7.35, 1.9 Hz, H-6'), 7.56 (td, J= 7.75, 1.7 Hz, H-5'), 7.65 (td, J= 7.68, 1.8 Hz, H-4'), 8.12 (dd, J= 7.68, 1.8 Hz, H-3'); ^{13}C n.m.r. δ ($CDCl_3$): 52.5 (CH_3), 109.5 (C-4), 113.7 (C-3), 127.8 (C-2'), 128.6 (C-6'), 129.3 (C-5, C-4'), 131.5 (C-3'), 133.2 (C-5'), 139.0 (C-1'), 164.8 (CO); m/z (%): 246 (M^+, 41), 200 (100), 185 (82), 169 (30).

1-(2-Methoxycarbonylphenyl)-3-nitropyrrole 5: (58%), m.p. 114-115°C (yellow needles from iso-propyl alcohol); (Found: C, 58.41; H, 3.95; N, 11.36. $C_{12}H_{10}N_2O_4$ requires: C, 58.54; H, 4.10; N, 11.38); i.r. (Nujol) 1715 (COOEt), 1525 asym (NO_2) and 1355 sym (NO_2) cm^{-1} ; ^1H n.m.r. δ ($CDCl_3$): 3.77 (s, 3H, CH_3),

6.71 (dd, $J_{5,2}$= 2.5 Hz, H-5), 6.85 (dd, 1H, $J_{4,5}$= 3.2 Hz, H-4), 7.40 (dd, 1H, J= 7.7, 1.5 Hz, H-6'), 7.57 (td, 1H, J= 7.4, 1.4, H-4') 7.65 (dd, 1H, $J_{2,4}$= 1.8 Hz, H-2), 7.67 (td, 1H, J= 7.4, 1.7 Hz, H-5'), 8.00 (dd, 1H, J= 7.6, 1.4 Hz, H-3'); ^{13}C n.m.r. δ ($CDCl_3$) : 52.7 (CH_3), 105.8 (C-4), 122.9 (C-5), 123.3 (C-2), 127.5 (C-6'), 127.6 (C-2'), 129.3 (C-4'), 131.5 (C-3'), 133.1 (C-5'), 138.7 (C-1'), 165.6 (CO); m/z (%): 246 (M^+, 60), 200 (100), 185 (70), 169 (26).

Ethyl N-[2'-[1'-(2-nitropyrrolyl)]phenyl]-N-toluene-4-sulfonyl glycinate 4: (22%), m.p.110-111°C, (yellow prisms from ethanol). (Found: C, 56.91; H, 4.81; N, 9.39.$C_{21}H_{21}N_3O_6S$ requires C, 56.87; H, 4.77; N, 9.48); i.r. (Nujol) 1730 (COOEt), 1490 asym (NO_2), 1350 sym (NO_2), 1310 asym (SO_2) and 1150 sym (SO_2) cm^{-1}; m/z (%): 443 (M^+, 12), 370 (10), 324 (15), 288 (100), 169 (100).

Ethyl N-[2'-[1'-(3-nitropyrrolyl)]phenyl]-N-toluene-4-sulfonyl glycinate 6: (43%), m.p. 45-46°C (yellow prisms from ethanol). (Found: C, 56.77; H, 4.85; N, 9.28. $C_{21}H_{21}N_3O_6S$ requires C, 56.87; H, 4.77; N, 9.48; i.r. (Nujol) 1700 (COOEt), 1510 asym (NO_2), 1340 sym (NO_2), 1355 (asym) (SO_2) and 1160 (sym) (SO_2) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$) 1.63 (t, 3H, CH_3-CH_2O), 2.45 (s, 3H, CH_3-tosyl), 4.07 (q, 2H, CH_3-CH_2O), 4.12 (s, 2H, N-CH_2), 6.85 (dd, 1H, $J_{4,5}$=3.2 Hz, H-4), 7.05 (dd, 1H, $J_{5,2}$=2.4 Hz, H-5), 7.25 (dd, 1H, H-3'), 7.30 (d, 2H, H-3", H-5"), 7.36 (td, 1H, H-4'), 7.37 (dd, 1H, H-6'), 7.46 (td, 1H, H-5'), 7.53 (d, 2H, H-2", H-6"), 7.77 (dd, 1H, $J_{2,4}$=1.7 Hz, H-2); ^{13}C n.m.r. δ ($CDCl_3$): 13.97 (CH_3), 21.62 (CH_3-tosyl), 51.80 (N-CH_2), 61.73 (CH_2), 106.07 (C-4), 123.58 (C-5), 127.45 (C-6'), 128.20 (C-2", C-6"), 129.29 (C-4'), 129.49 (C-2), 129.85 (C-5'), 129.93 (C-3", C-5"), 130.13 (C-3'), 134.41 (C-2'), 135.13 (C-1"), 138.25 (C-1'), 144.78 (C-4"), 167.84 (CO); m/z (%): 443 (M^-, 2.8), 370 (2.2), 324 (3.2), 242 (89), 214 (75), 169 (100).

1-(2-Ethoxycarbonylbenzyl)-2-nitropyrrole 8: (20%), m.p. 96-97°C (pale yellow needles from ethanol). (Found: C, 61.41; H, 5.29; N, 10.44. $C_{14}H_{14}N_2O_4$ requires: C, 61.30; H, 5.15; N, 10.22); i.r. (Nujol) 1715 (COOEt), 1520 asym (NO_2) and 1330 sym (NO_2) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.41 (t, 3H, CH_3-CH_2O), 4.39 (q, 2H, CH_3-CH_2O), 5.99 (s, 2H, N-CH_2), 6.26 (dd, 1H, $J_{4,5}$= 2.8 Hz, H-4), 6.59 (dd, 1H, J=7.3, 0.8Hz, H-6'), 6.86 (dd, 1H, $J_{5,3}$=2.02 Hz, H-5), 7.30 (dd, 1H, $J_{3,4}$=4.32 Hz, H-3), 7.34 (td, 1H, J= 7.4, 1.5 Hz, H-4'), 7.39 (td, 1H, J= 7.4, 1.7 Hz, H-5'), 8.06 (dd, 1H, J= 7.5, 1.4 Hz, H-3'); ^{13}C n.m.r. δ ($CDCl_3$): 14.3 (CH_3), 52.5 (N-CH_2), 61.3 (CH_2), 108.9 (C-4), 114.8 (C-3), 126.5 (C-4'), 127.6 (C-6'), 128.3 (C-2'), 129.8 (C-5), 131.1 (C-3'), 132.9 (C-5'), 138.9 (C-1'), 166.7 (CO); m/z (%): 292 [$(M+NH_4)^+$, 100], 275 [$(M+H)^+$, 4], 242 (11), 160 (10), 130 (38).

1-(2-Ethoxycarbonylbenzyl)-3-nitropyrrole 9: (42%), m.p. 43-45°C (oil gradually solidifies). (Found: C, 61.39; H, 5.24; N, 10.35. $C_{14}H_{14}N_2O_4$ calc. for: C, 61.30; H, 5.15; N, 10.22); i.r. (Nujol) 1710 (COOEt), 1530 asym (NO_2) and 1335 sym (NO_2) cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.39 (t, 3H, CH_3 -CH_2O), 4.36 (q, 2H, CH_3 -CH_2O), 5.52 (s, 2H, N-CH_2), 6.62 (dd, 1H, $J_{5,2}$= 2.5 Hz, H-5), 6.73 (dd, 1H, $J_{4,5}$= 3.2 Hz, H-4), 6.99 (dd, 1H, J= 7.1, 1.3 Hz, H-6'),), 7.43 (td, 1H, J= 7.6, 1.4 Hz, H-4'), 7.52 (td, 1H, J= 7.5, 1.6 Hz, H-5'), 7.54 (dd, 1H, $J_{2,4}$= 1.8 Hz, H-2), 8.06 (dd, 1H, J= 7.7, 1.5 Hz, H-3');^{13}C n.m.r. δ ($CDCl_3$): 14.2 (CH_3), 52.6 (N-CH_2), 61.4 (CH_3), 105.8, (C-4), 122.3 (C-2), 122.5 (C-5), 128.6 (C-4'), 129.0 (C-5'), 131.4 (C-3'), 133.0 (C-2'), 137.4 (C-1'), 166.5 (CO); m/z (%): 292 [$(M+NH_4)^+$, 100], 275 [$(M+H)^+$, 12], 242 (25), 160 (16), 130 (43).

5-Oxo-1,2,3-tetrahydropyrrolo[1,2-a]quinazoline (11) and 6-oxo-1,2,3,4-tetrahydropyrrolo[1,2a]-quinazoline (12).

A suspension of nitroester **3** (1.73 g, 7 mmol) in absolute methanol (150 ml) containing a few drops of glacial acetic acid, was hydrogenated at 3 atmospheres pressure in the presence of 10% Pd-C (0.1 g). After 12h the catalyst was filtered off and the solution was concentrated to give an oil which was chromatographed on a silica gel column. Elution with ethyl acetate and then methanol gave compounds **11** and **12** as crystalline solids.

11: (0.54 g, 42%), m.p. 223-224°C (lit[4] 222°C) (colourless needles from isopropyl alcohol; (Found: C, 70.86; H, 5.34; N, 14.95). $C_{11}H_{10}N_2O$ calc. for: C, 70.95; H, 5.41; N, 15.04); i.r. (Nujol) 1630 (CO) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$/drops DMSO-d_6): 2.40 (qui, 2H, J= 9 Hz, H-2), 3.13 (t, 2H, J= 9 Hz, H-3), 4.23 (t, 2H, J= 9 Hz, H-1), 7.1-7.75 (m, 3H, H-7, H-8 and H-9), 8.18 (dd, 1H, J= 7.2, 2.75 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$/ few drops DMSO-d_6): 18.6 (C-2), 32.6 (C-3), 48.8 (C-1), 14.7 (C-9), 118.6 (C-10a), 125.7 (C-8), 128.5 (C-7), 133.6 (C-6), 138.7 (C-6a), 166.5 (CN), 170.1 (C=O); m/z (%): 186 (M^+, 100), 158 (97), 132 (64), 77 (71).

12: (0.3g, 22%) m.p. 168-169°C (lit[6] 168°C) (colourless needles from ethanol); (Found: C, 69.95; H, 6.54; N, 14.67; $C_{11}H_{12}N_2O$ calc. for: C, 70.19; H, 6.42; N, 14.88); i.r. (Nujol) 3180 NH and 1660 (CO) cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.95-2.37 (m, 4H, H-2a, H-2b, H-3a and H-3c), 3.28-3.54 (m, 2H, H-1a and H-1b), 4.86-4.89 (m, 1H, H-4), 6.58 (d, 1H, J=8.1Hz, H-10), 6.81 (t, 1H, J=7.5Hz, H-9), 7.34 (s, br, 1H, NH), 7.37 (td, 1H, J=8.2, 1.5Hz, H-8), 7.90 (dd, 1H, J=7.8, 1.4Hz, H-7); ^{13}C n.m.r. δ ($CDCl_3$): 21.8 (C-2), 32.2 (C-2), 46.0 (C-3), 69.3 (C-4), 112.8 (C-10), 118.1 (C-9), 118.1 (C-10a), 129.0 (C-8), 134.2 (C-7), 147.0 (C-6a), 166.2 (CO); m/z(%): 188 (M^+, 36), 187 (M^+-1, 100), 158 (47), 132 (42), 105 (31), 77 (65).

5-Oxo-1,2,3-trihydro-5H-pyrrolo[1,2-b][2,4]benzodiazepine (13).

A solution of nitroester **8** (1 g, 3.6 mmol) in dry methanol (100 ml) was hydrogenated at 3 atmospheres pressure in the presence of 10% Pd-C (0.05 g). After 16h the catalyst was filtered off and the solution concentrated to dryness. To the residual material was added a solution containing sodium (0.23 g) in dry ethanol (30 ml). The reaction mixture was heated under reflux for 4h and then concentrated to dryness. Water (30 ml) was added and the mixture extracted with dichloromethane (3 × 10 ml). The combined organic layers were washed with brine (3 × 10 ml), dried over anhydrous sodium sulfate, and filtered. Concentration to dryness yielded a crude material which was chromatographed on a silica gel column. Elution with ethyl acetate and then with ethyl acetate/methanol (1:1) gave **13** (0.4 g, 55%), m.p. 156-158°C (colourless needles from ethanol). (Found: C, 65.78; H, 6.55; N, 12.61. $C_{12}H_{12}N_2O$ calc. for: C, 66.03; H, 6.46; N, 12.83); i.r. (Nujol) 1730 (CO) cm^{-1}; ^1H n.m.r. δ (DMSO-d_6): 1.96 (qui, 2H, J= 7 Hz, H-2a and H-2b), 2.30 (t, 2H, J= 7.6 Hz, H-1a and H-1b), 3.24 (t, 2H, J= 7 Hz, H-3a and H-3b), 4.55(s, 2H, H-5a and H-5b), 7.16-7.46 (m, 4H, benzenoid); ^{13}C n.m.r. δ (DMSO - d_6) : 17.5 (C-2), 30.2 (C-1), 43.1(C-3), 46.6 (C-5), 126.8 (C-6), 127.3 and 127.4 (C-7 and C-8), 129.7 (C-9), 134.9 (C-5a), 136.2 (C-9a), 170.4 (C-12), 174.3 (C=O); m/z (%) : 219 [$(M+2+NH_3)^+$, 100], 217 [$(M+NH_3)^+$, 10], 201 [$(M+1)^+$, 3], 173 (1).

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