1-Aryl-2-chloro-5-methoxy-1*H*-3-pyrrolecarbaldehyde as synthons for fused heterocycles: synthesis of pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridine derivatives

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Pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridine derivatives (**6a–f**) were obtained by oxidation of tosylhydrazones of 2-allylamino-5-methoxypyrrole-3-carbaldehydes (**3a–f**) with lead tetraacetate. The nitrilimine intermediates (**5a–f**) underwent intramolecular 1,3-dipolar cycloaddition to yield the tricyclic heterocycles **6a–f** in good yields.

Keywords: fused pyrazoles, pyrroles, pyridines; tosylhydrazones, nitrilimines, intramolecular 1,3-dipolar cycloaddition

Intramolecular 1,3-dipolar cycloaddition reactions offer a useful synthetic strategy for generating several rings in a single step.[1-9] Of the numerous methods of five-membered heterocyclic ring construction, the 1,3-dipolar cycloaddition of carbonyl ylides and azomethine ylides across a C=C bond represents a particularly attractive approach because several stereocentres can be generated in a single step.[1-4] Our recent research efforts have been concerned with the formation of 1,3-dipoles and the application of the resulting 1,3-dipolar moiety to the selective formation of polycyclic skeletons.[1-5] The generation of nitrilimines by oxidation of tosylhydrazones with lead tetraacetate (LTA) provides an important method[6,7] for the assembly of ring systems that are difficult or impossible to prepare by other means. Our intention is to study the scope and generality of this method and apply it toward the synthesis of complex polyheterocycles.[1-5]

Construction of pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridine derivatives through nitrile imides has been a particularly fruitful area of investigation for the synthesis of various types of fused heterocyclic compounds. A recent paper[2] from these laboratories has described a route to isoxazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridine ring systems that involved the intramolecular cycloaddition of nitrones. This kind of reaction is an integral part of our program aimed at developing new cascade reactions and achieving the total syntheses of various nitrogen-containing heterocycles. The dipoles are easily prepared from tosylhydrazones by oxidation with LTA.[10-12] A neighbouring functional group present on the backbone then traps the 1,3-dipole intermediate *via* intramolecular cycloaddition to give cyclic products. The potential for other diverse chemical pathways through the generation and further reaction of this dipole is presently being studied.

Significant effort has been devoted to the synthesis of new and unusual heterocyclic molecules applying 1,3-dipolar cycloaddition reactions including the highly reactive nitrilimine intermediates. A study of 1-aryl-5-methoxy-pyrrolones[2] is designed to expand understanding of the relationship between 1,3-dipolaraddition and the chemical reactivity of the olefinic double bond. These approaches currently are being utilised in an attempt to synthesise pharmaceutically active heterocyclic molecules.

We describe here a novel simple and effective approach to hexahydro derivatives (**6**) of pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]-pyridine. Reaction of the tosylhydrazones of 2-(substituted amino)-1-aryl-5-methoxy-3-carbaldehydes (**3**), bearing an olefinic dipolarophile at the amino moiety, with lead tetraacetate (LTA) leads to the nitrilimine intermediates **5** and hence to the intramolecular 1,3-dipolar cycloadducts **6**.

Since the first report by Fusco *et al.*[13] several intramolecular cycloaddition reactions of nitrilimines have been reported.[14-22] In most cases the nitrilimine and the dipolarophile are situated at *ortho* positions of a benzene ring, and, therefore, their synthetic utility seems to be limited. We have examined the application of the intramolecular cycloaddition reaction of nitrilimines to the synthesis of the pyrazolo[3,4-*d*]pyrrolo[2,3-*b*]pyridine system.

The reaction of 1-aryl-2-chloro-5-methoxy-1*H*-3-pyrrole-carbaldehydes[2] (**1a–c**) with alkenylamines **2a,b** in refluxing ethanol gave the corresponding 2-alkenylamino derivatives (**3a–f**) which were converted into their tosylhydrazones (**4a–f**) by treatment with tosylhydrazine. The nitrilimine intermediates **5** were generated by oxidation of **4a–f** with LTA, resulting in the fused tricyclic products **6a–f** in some 55–70% yields. The analytical and spectroscopic data of the products were consistent with the structures assigned. The IR spectra lacked the NH-stretching vibrations of the hydrazone observed in **4a–f**. The ^{1}H NMR spectrum of **6a** showed a multiplet at 6.92-7.79 for aromatic protons; a singlet at 5.50 for the C8-H proton; a doublet doublet at 4.84 for two protons at C3; a singlet at 3.90 for OCH_3; a multiplet at 3.53 for the C3a proton; a double doublet at 3.48 for two protons of C4; a singlet at 3.27 for NCH_3; and a singlet at 2.33 for one CCH_3. The ^{13}C-NMR revealed signals (see Experimental) which support the suggested structure **6a**.

Attempts to dehydrogenate the 2-pyrazoline ring using various reagents (*N*-bromosuccinimide, chloranil, 2,3-dichloro-5, 6-dicyano-1,4-benzoquinone), were unsuccessful.

In conclusion, intramolecular 1,3-dipolar cycloadditions have provided a simple and effective route for the preparation of the fused pyrazolopyrrolopyridine derivatives.

Experimental

All melting points were determined on a Gallenkamp melting point apparatus. Infrared spectra were measured with a Perkin-Elmer Model 298 spectrophotometer. NMR spectra were recorded on a Varian XL-200 spectrometer with $CDCl_3$ as solvent and TMS as internal reference, chemical shifts are expressed as δ ppm. Analytical data were determined using a Carlo Erba 1106 C,H,N Elemental analyser. Silica gel 60 (Merck, 230–400 mesh) was used for flash chromatography.

2-Amino-1-aryl-5-methoxy-1H-3-pyrrolecarbaldehydes (**3a–f**)*:* A mixture of 2-chloro-5-methoxy-1-phenyl-1*H*-3-pyrrolecarbaldehyde[2] **1** (20 mmol) and *N*-allyl-*N*-methylamine (4.27 g, 60 mmol) or diallylamine (5.83 g 60 mmol) in ethanol (60 ml) was refluxed for 10 h. The ethanol was removed *in vacuo* and the residue was poured into water, then extracted with chloroform (50ml × 4). The organic layer was dried and the chloroform was evaporated off. The residue was purified by flash chomatography to give **3a–f** in 63–75% yield.

2-[Allyl(methyl)amino]-5-methoxy-1-phenyl-1H-3-pyrrolecarbaldehyde (**3a**): yield 71%, pale yellow prisms from ethanol, m.p. 184–185 °C; ν_{max} (KBr) 3050, 2980 and 1690 cm^{-1}; δ_H 9.27 (s, 1H, CHO), 6.35–7.35 (m, 5H, Ph), 5.86–5.96 (m, 1H, CH=), 6.24 (s, 1H, C4-H), 5.06–5.16 (m, 2H, CH_2=), 4.23–4.26 (m, 2H, NCH_2), 3.88 (s, 3H, OCH_3), 3.02 (s, 3H, NCH_3); δ_C (100 MHz, $CDCl_3$) 183.22, 151.83, 146.26, 136.23, 135.84, 134.26, 128.75, 128.23, 126.12,

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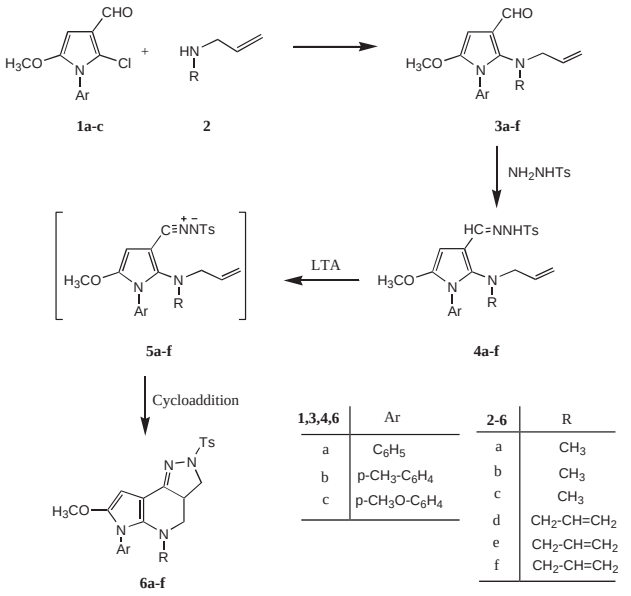

1,3,4,6	Ar
a	C_6H_5
b	p-CH_3-C_6H_4
c	p-CH_3O-C_6H_4

2-6	R
a	CH_3
b	CH_3
c	CH_3
d	CH_2-CH=CH_2
e	CH_2-CH=CH_2
f	CH_2-CH=CH_2

Scheme 1

118.94, 103.59, 91.35, 60.13, 41.38. Found: C, 70.92; H, 6.58; N, 10.18. $C_{16}H_{18}N_2O_2$ requires C, 71.09; H, 6.71; N, 10.36%.

2-[Allyl(methyl)amino]-5-methoxy-1-(4-methylphenyl)-1H-3-pyrrolecarbaldehyde (**3b**): 74%, pale yellow prisms from ethanol, m.p. 194–196 °C; ν_{max} (KBr) 3050, 2980 and 1690 cm^{-1}; δ_H 9.28 (s, 1H, CHO), 6.60–7.22 (m, 4H, Ar), 5.86–5.96 (m, 1H, CH=), 6.16 (s, 1H, C4-H), 5.06–5.12 (m, 2H, CH_2=), 4.18–4.23 (m, 2H, NCH_2), 3.90 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3), 3.05 (s, 3H, NCH_3); δ_C (100 MHz, $CDCl_3$) 183.27, 150.98, 145.97, 136.27, 135.34, 134.20, 133.02, 131.12, 128.29, 118.94, 104.25, 91.21, 59.44, 40.81, 22.04. Found: C, 71.63; H, 6.98; N, 9.64. $C_{17}H_{20}N_2O_2$ requires C, 71.81; H, 7.09; N, 9.85%.

2-[Allyl(methyl)amino]-5-methoxy-1-(4-methoxyphenyl)-1H-3-pyrrolecarbaldehyde (**3c**): 75%, pale yellow prisms from ethanol, m.p. 188–189 °C; ν_{max} (KBr) 3050, 2980 and 1700 cm^{-1}; δ_H 9.30 (s, 1H, CHO), 6.62–7.25 (m, 4H, Ar), 5.86–5.94 (m, 1H, CH=), 6.08 (s, 1H, C4-H), 5.06–5.12 (m, 2H, CH_2=), 4.26–4.28 (m, 2H, NCH_2), 3.90 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.06 (s, 3H, CH_3). Found: C, 67.73; H, 6.69; N, 9.11. $C_{17}H_{20}N_2O_3$ requires C, 67.98; H, 6.71; N, 9.33%.

2-(Diallylamino)-5-methoxy-1-phenyl-1H-3-pyrrolecarbaldehyde (**3d**): 63%, yellow prisms from ethanol, m.p. 179–180 °C; ν_{max} (KBr) 3050, 2980 and 1695 cm^{-1}; δ_H 9.28 (s, 1H, CHO), 6.75–7.78 (m, 5H, Ph), 5.78–5.81 (m, 2H, 2CH=), 6.18 (s, 1H, C4-H), 5.05–5.14 (m, 4H, $2CH_2$=), 4.24–4.27 (m, 4H, 2 NCH_2), 3.85 (s, 3H, OCH_3). δ_C (100 MHz, $CDCl_3$) 184.45, 153.13, 147.12, 136.38, 135.95, 128.71, 128.68, 126.76, 118.65, 105.76, 92.97, 56.77, 55.31. Found: C, 72.74; H, 6.73; N, 9.35. $C_{18}H_{20}N_2O_2$ requires C, 72.95; H, 6.80; N, 9.45%.

2-(Diallylamino)-5-methoxy-1-(4-methylphenyl)-1H-3-pyrrolecarbaldehyde (**3e**): 69%, yellow prisms from ethanol, m.p. 211–212 °C; ν_{max} (KBr) 3050, 2980 and 1700 cm^{-1}; δ_H 9.26 (s, 1H, CHO), 6.63–7.29 (m, 4H, Ar), 5.79–5.86 (m, 2H, 2CH=), 6.22 (s, 1H, C4-H), 5.02–5.10 (m, 4H, $2CH_2$=), 4.25–4.27 (m, 4H, $2NCH_2$), 3.85 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 185.15, 151.64, 145.12, 135.64, 135.49, 133.88, 131.21, 128.75, 119.42, 103.23, 90.84, 57.35, 56.51, 22.12. Found: C, 73.47; H, 7.00; N, 8.89. $C_{19}H_{22}N_2O_2$ requires C, 73.52; H, 7.14; N, 9.03%.

2-(Diallylamino)-5-methoxy-1-(4-methoxyphenyl)-1H-3-pyrrolecarbaldehyde (**3d**): 72%, yellow prisms from ethanol, m.p. 228–229 °C; ν_{max} (KBr) 3050, 2980 and 1700 cm^{-1}; δ_H 9.30 (s, 1H, CHO), 6.84–7.35 (m, 4H, Ar), 5.80–5.89 (m, 2H, 2CH=), 6.18 (s, 1H, C4-H), 5.06–5.13 (m, 4H, $2CH_2$=), 4.29–4.32 (m, 4H, $2NCH_2$), 3.85 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3). Found: C, 69.79; H, 6.64; N, 8.46. $C_{19}H_{22}N_2O_3$ requires C, 69.92; H, 6.79; N, 8.58%.

Tosylhydrazones (**4a-f**): Tosylhydrazine (1.90 g, 10 mmol) in methanol (10 ml) containing a few drops of conc. hydrochloric acid was added to a stirred and cooled solution of **3a** (2.7g, 10 mmol) in methanol (20 ml) at 0°C. After 3 h, the resultant precipitate was collected by filtration. Recrystallisation from ethanol gave 2.94 g, (67%) of the tosylhydrazone **4a**. Compounds **4b–f** were prepared analogously.

N′-[[2-[Allyl(methyl)amino]-5-methoxy-1-phenyl-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4a**): yield 67%, m.p. 183–185 °C; ν_{max} (KBr) 3140, 3050, 2980 and 1630, 1340 and 1160 cm^{-1}; δ_H 11.54 (s, 1H, NH), 6.80–8.31 (m, 10H, Ph, Ar and CH=N), 6.29 (s, 1H, C4-H), 6.11 (m, 1H, CH=), 5.14–5.28 (m, 2H, CH_2=), 4.18–4.21 (m, 2H, NCH_2), 3.86 (s, 3H, OCH_3), 2.95 (s, 3H, NCH_3), 2.42 (s, 3H, CH_3).δ_C (100 MHz, $CDCl_3$) 152.43, 151.05, 145.35, 137.08, 134.34, 131.52, 130.05, 129.17, 136.84, 135.18, 126.78, 128.15, 106.52, 117.49, 96.85, 59.76, 58.25, 41.32, 21.23. Found: C, 62.78; H, 5.87; N, 12.63; S, 7.23. $C_{23}H_{26}N_4O_3S$ requires C, 62.99; H, 5.98; N, 12.78; S, 7.31%.

N′-[[2-[Allyl(methyl)amino]-5-methoxy-1-(4-methylphenyl)-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4b**): 65%, m.p. 174–176 °C; ν_{max} (KBr) 3140, 3050, 2980, 1635, 1340 and 1160 cm^{-1}; δ_H 11.56 (s, 1H, NH), 6.79–8.26 (m, 9H, 2Ar and CH=N), 6.12 (s, 1H, C4-H), 5.89–5.94 (m, 1H, CH=), 5.11–5.17 (m, 2H, CH_2=), 3.95–4.12 (m, 2H, NCH_2), 3.90 (s, 3H, OCH_3), 2.97 (s, 3H, NCH_3), 2.36 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 153.78, 152.19, 146.89, 137.87, 137.49, 136.28, 135.43, 132.67, 131.84, 129.35, 127.6, 125.57, 118.87, 106.56, 98.05, 58.90, 57.44, 42.32, 22.00, 21.45. Found: C, 63.52; H, 6.21; N, 12.21; S, 7.12. $C_{24}H_{28}N_4O_3S$ requires C, 63.69; H, 6.24; N, 12.38; S, 7.08%.

N′-[[2-[Allyl(methyl)amino]-5-methoxy-1-(4-methoxyphenyl)-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4c**): 69%, m.p. 197–198 °C; ν_{max} (KBr) 3140, 3050, 2980, 1635, 1345 and 1160 cm^{-1}; δ_H 11.58 (s, 1H, NH), 7.04–8.01 (m, 9H, 2Ar and CH=N), 6.12 (s, 1H, C4-H), 5.82–5.91 (m, 1H, CH=), 5.10–5.16 (m, 2H, CH_2=), 4.16–4.24 (m, 2H, NCH_2), 3.88 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.06 (s, 3H, NCH_3), 2.43 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 161.27, 154.22, 152.77, 145.49, 136.18, 135.18, 131.43, 129.69, 128.83, 127.16, 125.51, 117.79, 117.55, 105.28, 98.65, 58.24, 57.98, 56.23, 41.84, 22.06, 21.89. Found: C, 61.43; H, 6.00; N, 11.79; S 6.53. $C_{24}H_{28}N_4O_4S$ requires C, 61.52; H, 6.02; N, 11.96; S, 6.84%.

N′-[[2-(Diallylamino)-5-methoxy-1-phenyl-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4d**): 69%, m.p. 163–165 °C; ν_{max} (KBr) 3140, 3050, 2980, 1640, 1320 and 1150 cm^{-1}; δ_H 11.60 (s, 1H, NH), 6.65–8.71 (m, 10H, Ph, Ar and CH=N), 5.76–5.85 (m, 2H, 2CH=), 6.13 (s, 1H, C4-H), 5.02–5.11 (m, 4H, $2CH_2$=), 4.12–4.22 (m, 4H, 2 NCH_2), 3.90 (s, 3H, OCH_3), 2.38 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 153.56, 151.68, 146.55, 136.94, 136.62, 135.14, 133.23, 129.28, 128.53, 128.36, 127.56, 124.43, 116.68, 104.33, 97.05, 60.20, 58.27, 21.23. Found: C, 64.43; H, 6.02; N, 11.98; S, 6.75. $C_{25}H_{28}N_4O_3S$ requires C, 64.63; H, 6.07; N, 12.06; S, 6.90%.

N′-[[2-(Diallylamino)-5-methoxy-1-(4-methylphenyl)-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4e**): 71%, m.p. 185–186 °C; ν_{max} (KBr) 3150, 3050, 2980, 1640, 1320 and 1150 cm^{-1}; δ_H 11.72 (s, 1H, NH), 6.79–7.88 (m, 9H, 2Ar and CH=N), 6.16 (s, 1H, C4-H), 5.81–5.89 (m, 2H, 2CH=), 5.07–5.13 (m, 4H, $2CH_2$=), 4.01–4.07 (m, 4H, $2NCH_2$), 3.88 (s, 3H, OCH_3), 2.40 (s, 3H, CH_3), 2.44 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 153.98, 152.78, 147.82, 136.88, 136.56, 135.47, 134.31, 130.52, 129.03, 128.57, 126.86, 126.53, 116.85, 105.72, 97.92, 60.94, 59.39, 22.00, 21.55; (Found: C, 65.12; H, 6.30; N, 11.57; S, 6.53. $C_{26}H_{30}N_4O_3S$ requires C, 65.25; H, 6.32; N, 11.71; S, 6.70%).

N′-[[2-(Diallylamino)-5-methoxy-1-(4-methoxyphenyl)-1H-pyrrol-3-yl]methylene]-4-methylbenzenesulfonhydrazide (**4f**), 70%, m.p. 242–243 °C; ν_{max} (KBr) 3150, 3050, 2980, 1640, 1320 and 1150 cm^{-1}; δ_H 11.70 (s, 1H, NH), 6.89–7.85 (m, 9H, 2Ar and CH=N), 6.22 (s, 1H, C4-H), 5.90–5.96 (m, 2H, 2CH=), 5.15–5.23 (m, 4H, $2CH_2$=), 4.18–4.25 (m, 4H, $2NCH_2$), 3.89 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.39 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 154.02, 153.21, 147.24, 141.24, 136.89, 136.25, 130.18, 129.57, 128.38, 127.24, 126.30, 115.27, 116.56,104.91, 98.14, 58.82, 60.02, 21.76, 21.62. Found: C, 63.03; H, 6.03; N, 11.08; S, 4.32. $C_{26}H_{30}N_4O_4S$ requires C, 63.14; H, 6.11; N, 11.33; S, 6.48%.

Pyrazolopyrrolopyridines (**6a–f**): LTA (2.3 g, 5.21 mmol) in dry acetonitrile (30ml) was added dropwise to a stirred and cooled solution of 4 (3.5 mmol) in dry acetonitrile (100 ml) at –5 °C during 1h. After complete of the addition, the reaction mixture was allowed to stand at the same temperature for 3h. The resultant precipitate was filtered off and the filtrate was evaporated to dryness. The residue was poured into water and extracted with dichloromethane (3 × 50 ml). The organic layer was washed with water several times, dried, and evaporated to afford a residue. Crystallisation of the residue from ethanol gave **6a–f** in 55–69% yield.

7-Methoxy-5-methyl-2-[(4-methylphenyl)sulfonyl]-6-phenyl-2,3,3a,4,5,6-hexahydropyrazolo[3,4-d]-pyrrolo[2,3-b]pyridine (**6a**): yield 63%, m.p. 224–225 °C; ν_{max} (KBr) 3050, 2980 and 1635 cm^{-1};

δ_H 6.92–7.79 (m, 9H, Ph and Ar), 5.50 (s, 1H, C8-H), 4.84 (dd, 2H, *J* = 15, 8 Hz, C3-H), 3.90 (s, 3H, OCH_3), 3.53 (m, 1H, C3a-H), 3.48 (dd, 2H, *J* = 9, 4 Hz, C4-H), 3.27 (s, 3H, NCH_3), 2.33 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 160.98, 150.33, 144.55, 136.41, 135.71, 135.43, 130.35, 128.65, 127.76, 127.24, 126.64, 107.51, 98.87, 60.38, 58.98, 57.77, 55,35, 40.35, 22.56. Found: C, 63.21; H, 5.53; N, 12.74; S, 7.12. $C_{23}H_{24}N_4O_3S$ requires C, 63.28; H, 5.54; N, 12.83; S, 7.34%.

7-Methoxy-5-methyl-6-(4-methylphenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,3a,4,5,6-hexahydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridine (**6b**): 64%, m.p. 186–187 °C; δ_{max} (KBr) 3050, 2980 and 1635 cm^{-1}; δ_H 6.73–7.79 (m, 8H, 2Ar), 5.56 (s, 1H, C8-H), 4.90 (dd, 2H, J = 14, 8 Hz, C3-H), 3.92 (s, 3H, OCH_3), 3.84 (dd, 2H, J = 9, 4, C4-H), 3.30 (s, 2H, NCH_3), 3.38 (s, 3H, CH_3), 233 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 161.27, 149.22, 143.49, 136.18, 135.63, 131.43, 129.69, 127.58, 126.16, 124.43, 117.79, 105.28, 98.65, 59.66, 58.24, 56.23, 52.87, 41.84, 22.06, 21.89. Found: C, 63.77; H, 5.73; N, 12.32; S, 7.01. $C_{24}H_{26}N_4O_3S$ requires C, 63.98; H, 5.82; N, 12.44; S, 7.12%.

7-Methoxy-6-(4-methoxyphenyl)-5-methyl-2-[(4-methylphenyl)sulfonyl]-2,3,3a,4,5,6-hexahydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridine (**6c**): 69%, m.p. 215–216 °C; ν_{max} (KBr) 3050, 2980 and 1635 cm^{-1}; δ_H 6.79–8.26 (m, 8H, 2Ar), 5.53 (s, 1H, C8-H), 5.90 (dd, 2H, J = 14, 8 Hz, C3-H), 3.92 (s, 3H, OCH_3), 3.84 (m, 1H, C3a-H), 3.74 (s, 3H, OCH_3), 3.77 (s, 3H, CH_3), 3.50 (dd, 2H, J = 9, 4 Hz, C4-H), 3.27 (s, 3H, NCH_3), 2.30 (s, 3H, CH_3). δ_C (100 MHz, $CDCl_3$) 162.78, 148.19, 144.98, 137.87, 137.49, 135.43, 132.67, 131.84, 136.23, 133.98, 130.18, 126.75, 118.78, 106.98, 98.05, 58.90, 57.44, 42.32, 22.00, 21.045. Found: C, 61.58; H, 5.58; N, 11.89; S 6.68. $C_{24}H_{26}N_4O_4S$ requires C, 61.79; H, 5.62; N, 12.01; S, 6.87%.

5-Allyl-7-methoxy-2-[(4-methylphenyl)sulfonyl]-6-phenyl-2,3,3a,4,5,6-hexahydropyrazolo[3,4-d]pyrrolo[2,3-b]pyridine (**6d**): 0.254 g, 55%, m.p. 231–232 °C; ν_{max} (KBr) 3050, 2980 and 1640 cm^{-1}; δ_H 6.69–7.82 (m, 9H, Ph and Ar), 5.87–5.97 (m, 1H, C3a-H), 5.28 (s, 1H, C8-H), 5.06–5.16 (dd, 2H, *J* = 17, 10 Hz, C3a-H), 3.90 (s, 3H, OCH_3), 3.82 (d, 2H, *J* = 6Hz, NCH_2), 3.53–3.64 (m, 2H, $=CH_2$), 2.34 (s, 3H, CH_3); δ_C (100 MHz, $CDCl_3$) 162.44, 145.21, 142.66, 136.68, 134.57, 133.74, 133.12, 130.70, 128.84, 127.88, 126.76, 116.49, 105.43, 97.88, 60.43, 58.96, 57.89, 56.91, 55.75, 54.31, 22.76; (Found: C, 64.87; H, 5.62; N, 12.01; S, 6.88. $C_{25}H_{26}N_4O_3S$ requires C, 64.92; H, 5.67; N, 12.11; S, 6.93%).

5-Allyl-7-methoxy-6-(4-methylphenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,3a,4,5,6-hexahydro-pyrazolo[3,4-d]pyrrolo[2,3-b]pyridine (**6e**): 0.266 g, 56%, m.p. 254–256 °C; ν_{max} (KBr) 3050, 2980 and 1640 cm^{-1}; δ_H 6.80–7.94 (m, 8H, 2Ar), 5.84-5.93 (m, 1H, C3a-H), 5.31 (s, 1H, C8-H), 5.01–5.09 (dd, 2H, *J* = 10, 2 Hz, C3-H), 5.11–5.19 (dd, 2H, *J* = 9, 4 Hz, C4-H), 3.95 (s, 3H, OCH_3), 3.83 (d, 2H, *J* = 6Hz, NCH_2) 3.74 (d, 2H, *J* = 6Hz, $=CH_2$), 3.53 (m, 1H, CH=), 2.35 (s, 3H, CH_3), 2.44 (s, 3H, CH_3). Found: C, 65.43; H, 5.85; N, 11.63; S, 6.52. $C_{26}H_{28}N_4O_3S$ requires C, 65.52; H, 5.92; N, 11.76; S, 6.73%.

5-Allyl-7-methoxy-6-(4-methoxyphenyl)-2-[(4-methylphenyl)sulfonyl]-2,3,3a,4,5,6-hexahydro-pyrazolo[3,4-d]pyrrolo[2,3-b]pyridine (**6f**): 0.295 g, 60%, m.p. 276–277 °C; ν_{max} (KBr) 3050, 2980 and 1640 cm^{-1}; δ_H 6.95–7.95 (m, 8H, 2Ar), 5.89 (m, 1H, CH=), 5.31 (s, 1H, C8-H), 5.04–5.12 (m, 2H, CH_2=), 3.94 (s, 3H, OCH_3), 3.84–3.92 (m, 2H, NCH_2), 3.84–3.86 (dd, 2H, *J* = 9, 4Hz, C4-H), 3.77 (s, 3H, OCH_3), 3.49–3.65 (m, 2H, $=CH_2$), 3.47–3.54 (m, 1H, C3a-H), 2.39 (s, 3H, CH_3). Found: C, 63.31; H, 5.68; N, 11.65; S, 6.44. $C_{26}H_{28}N_4O_4S$ requires C, 63.40; H, 5.73; N, 11.73; S, 6.51%.

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References

1 H.A. Abd El-Nabi, *Tetrahedron*, 2002, 58, 135-141.
2 H.A. Abd El-Nabi, *Tetrahedron*, 2000, 56, 3013-3020.
3 H.A. Abd El-Nabi, *Tetrahedron*, 1997, 53, 1813-1822.
4 H.A. Abd El-Nabi, *J. Chem. Res.* (S), 1996, 466-467.
5 A.M. Nour El-Din, A.E. Mourad and H.A. Abdel Nabi, *J. Chem. Eng. Data*, 1986, 31, 259-269.
6 A.S. Shawali, *Chem. Rev*., 1993, 93, 2731-2777.
7 M. Nogachi, S. Nagata and S. Kajigaeshi, *Chem. Pharm. Bull.*, 1986, 34, 3994-4000.
8 M. Gotoh, B. Sun, K. Hirayama and M. Noguchi, *Tetrahedron*, 1996, 52, 887-900.
9 B. Sun, K. Adachi and M. Noguchi, *Tetrahedron*, 1996, 52, 901-914.
10 R.N. Butler, *Chem. Ind. (London)* 1968, 437.
11 W.A.F. Gladstone, *J. Chem. Soc., Chem. Commun.*, 1969, 179.
12 T. Sasaki and T. Yoshioka, *Bull. Chem. Soc. Jap*. 1970, 43, 1254.
13 R. Fusco, L. Garanti and G. Zecchi, *Tetrahedron Lett.*, 1974, 269.
14 L. Garanti and G. Zecchi, *Tetrahedron Lett.*, 1976, 1339.
15 L. Garanti and G. Zecchi, *J. Org. Chem.*, 1977, 42, 1389.
16 L. Garanti and G. Zecchi, *J. Org. Chem.*, 1978, 43, 2077.
17 A. Padwa, S. Nahm and E. Sato, *J. Org. Chem.*, 1978, 43, 1664.
18 H. Meir, H. Heimgartner and H. Schmidt, *Helv. Chim. Acta*, 1978, 60, 1078.
19 H. Meir and H. Heimgartner, *Helv. Chim. Acta*, 1978, 60, 3035.
20 T. Shimizu, Y. Hayashi, Y. Nagano and K. Teramura, *Bull. Chem. Soc. Jpn*., 1980, 53, 429.
21 T. Shimizu, Y. Hayashi, Y. Kitora and K. Teramura, *Bull. Chem. Soc. Jpn*., 1982, 55, 2450.
22 T. Shimizu, Y. Hayashi, S. Ishikawa and K. Terashima, *Bull. Chem. Soc. Jpn*., 1982, 55, 2456.