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Regiospecific Preparation of γ-Carbolines and Pyrimido[3,4-*a*]indole Derivatives by Intramolecular Ring-Closure of Heterocumulene-Substituted Indoles.[1]

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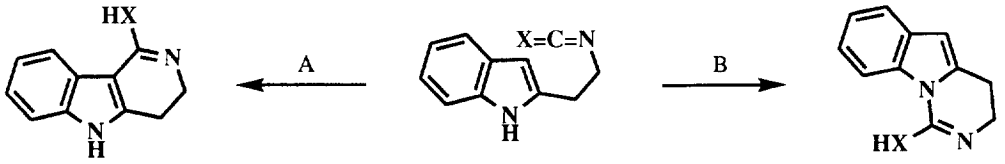
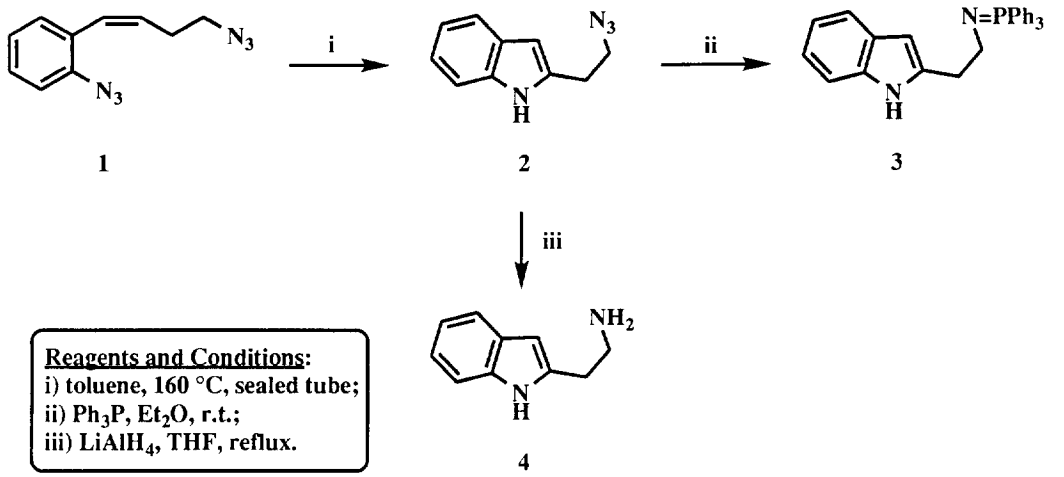
Abstract: Compounds resulting from the aza-Wittig reaction of iminophosphorane derived from 2-(2-azidoethyl)indole and carbon disulfide, diphenylketene, aldehydes and acyl chlorides undergo ring-closure under acidic, basic and thermal conditions to give either dihydro γ-carbolines or dihydropyrimido[3,4-*a*]indoles in a completely regiospecific fashion. The mode of cyclization strongly depends on the cyclizating agent as well as the nature of the reagent. The related carbodiimides **9** undergo regiospecific cyclization to give dihydropyrimido[3,4-*a*]indoles under acidic, basic or thermal conditions.

Conjugated heterocumulenes undergo a variety of interesting reactions, many of them providing examples of intringuing mechanistic challenges, and several are of significant synthetic importance. Heterocyclization reactions of such unsaturated heterocumulenic systems as ketenes, ketenimines, isocyanates, isothiocyanates, and carbodiimides, which have shown a high predictable selectivity, provide an attractive entry to a variety of carbocycles and heterocycles.[2] On the other hand, indoles containing one additional ring fused across the 2,3-positions are widely distributed in Nature. In spite of much work in the synthesis of functionalized pyrido[3,4-*b*]indoles (β-carbolines), due largely to the potent affinity of these compounds for the benzodiazepine receptor,[3] the isomeric series of pyrido[4,3-*b*]indoles (γ-carbolines) has been much less well represented in the literature. The isolation from tryptophan pyrolysates[4] of the highly mutagenic γ-carboline derivatives 3-amino-1,4-dimethyl-5H-pyrido[4,3-*b*]indole (Trp-P-1) and 3-amino-1-methyl-5H-pyrido[4,3-*b*]indole (Trp-P-2) has prompted a renewed interest in the synthesis and biological evaluation of new γ-carboline derivatives.[5]

We have previously reported that β-(indol-2-yl)vinyl heterocumulenes under thermal conditions undergo electrocyclic ring-closure to give γ-carbolines,[6] however when the indole ring is substituted at 3 position, the heterocyclization reaction takes place by nucleophilic attack of the amino group of the indole ring on the central carbon atom of the heterocumulene moiety to give pyrimido[1,6-*a*] indoles.[7] Herein, we wish to report a new regiospecific intramolecular cyclization of heterocumulene-substituted indoles in which the cumulenic portion and the indole ring are linked with a flexible alkyl chain containing two carbon atoms. This class of compounds are capable of undergoing two different modes of cyclization, either on the 3 position of the indole ring (mode A) to give dihydro γ-carbolines or by nucleophilic attack of the indole nitrogen atom on the central carbon atom of the heterocumulene (mode B) to give dihydropyrimido indoles.

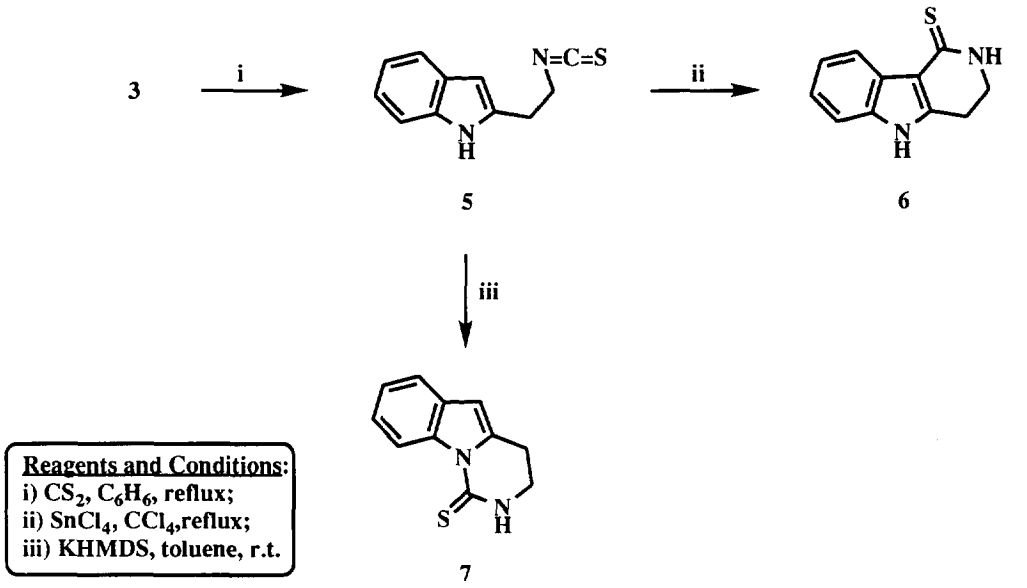


The bis(azide) **1**, the common precursor for this kind of heterocumulene, was prepared in 56% yield by the four-step sequence:[8] (a) reaction of triphenylphosphine with excess of 1,3-dibromopropane, (b) subsequent reaction with excess of sodium azide, (c) conversion of the resulting phosphonium salt to the corresponding ylid by the action of potassium bis(trimethylsilyl)amide and (d) Wittig coupling with *o*-azidobenzaldehyde. When compound **1** was heated at 160 °C in toluene in a sealed tube, 2-(2-azidoethyl)indole **2** was obtained in 61% yield as the only reaction product: no products derived from the decomposition of the alkyl substituted azido group were observed. Staudinger reaction of the azido indole **2** with triphenylphosphine in diethyl ether at room temperature provided the iminophosphorane **3** in 83% yield. From compound **2**, the amine **4** was also obtained in 84% yield by reduction with $LiAlH_4$.

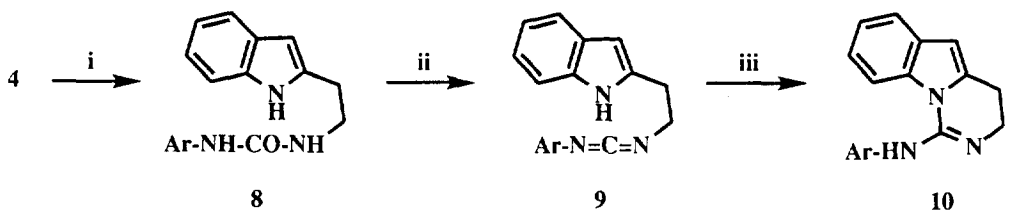


Iminophosphorane **3** reacted with carbon disulfide in benzene at reflux temperature to give the isothiocyanate **5** in almost quantitative yield (97%), which was isolated as a viscous oil. All attemps to promote the thermal cyclization of the isothiocyanate **5** were unsuccessful but, when it was treated with $SnCl_4$ in carbon tetrachloride at room temperature, cyclization took place at the 3 position of the indole ring, to give **6** as the only reaction product, in moderate (45%) yield. However, when **5** was treated with potassium bis(trimethylsilyl)amide in toluene at room temperature cyclization ocurred in a completely regiospecific fashion, to give **7** in moderate yield (50%).

The ^{13}C-NMR spectrum of compound **6** shows five quaternary carbon atoms, whereas in the spectrum of **7** only four quaternary carbon atoms appear and the C-3 of the indole ring appears now at δ 104.75 ppm. In addition, the ^{1}H-NMR spectrum of **7** shows a singlet a δ 6.34 ppm due to the H-3 of the indole ring, whereas in compound **6** this signal is absent.

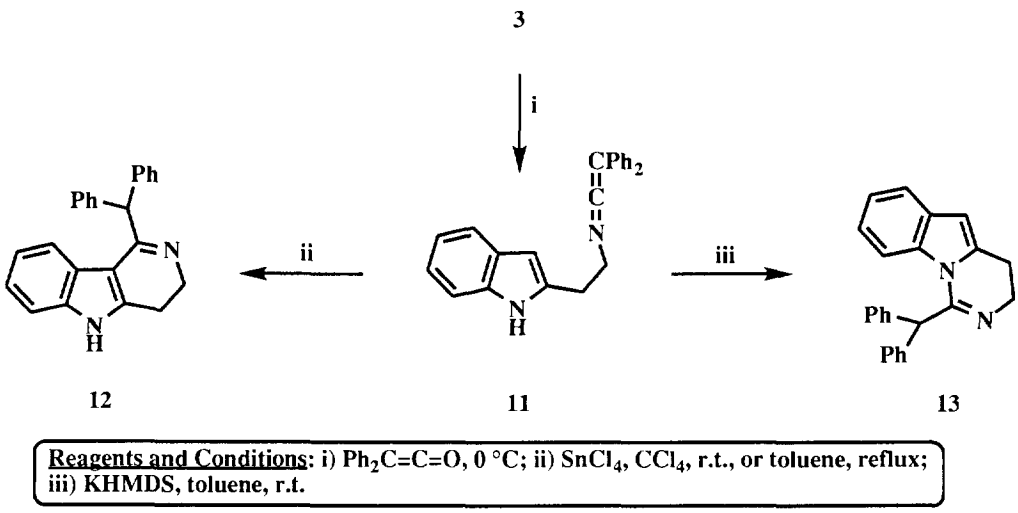


In order to investigate the scope of these processes, variations were considered. At first it was of interest to see what would happen with other types of heterocumulenes, such as carbodiimides and ketenimines. Direct conversion of iminophosphorane **3** into carbodiimide **9**, by reaction with aryl isocyanates failed. However, when amine **4** was treated with aryl isocyanates, the corresponding ureas **8** were obtained in 77-83% yields. Compounds **8** were converted into carbodiimides **9** by the action of triphenylphosphine in the presence of triethylamine and carbon tetrachloride: these carbodiimides were used for the next step without further purification. Regioselective cyclization of carbodiimides **9** to give **10** was achieved either by the action of $SnCl_4$ (30-38%), potassium bis(trimethylsilyl)amide (66-80%) or thermal treatment at 160 °C (43-67%). This behaviour is in sharp contrast with that observed for the closely related 2-(2-indolyl)phenyl aryl carbodiimides, which undergo cyclization at the 3 position of the indole ring to give indolo[3,2-*c*]quinolines.[7]



	Yield % 8	Yield % 10		
		Method A	Method B	Method C
a Ar= Ph-	83	32	80	43
b Ar= $4MeC_6H_4$-	77	38	72	67
c Ar= $4MeOC_6H_4$-	83	30	66	51
d Ar= PhCH=CH-	74			

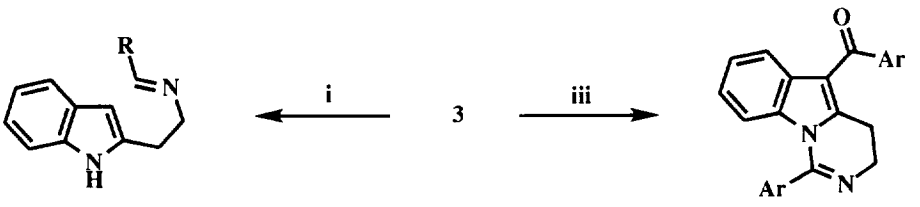
On the other hand, reaction of iminophosphorane **3** with diphenylketene provided ketenimine **11**, isolated as viscous oil, which was cyclized either by the action of $SnCl_4$, or thermal treatment, to give **12** albeit in low yields (20-25%), whereas treatment with potassium bis(trimethylsilyl)amide afforded a complex mixture from which compound **13** only could be isolated as an unstable oil in yield lower than 10%.



Reagents and Conditions: i) $Ph_2C=C=O$, 0 °C; ii) $SnCl_4$, CCl_4, r.t., or toluene, reflux; iii) KHMDS, toluene, r.t.

The aza-Wittig reactions of iminophosphorane **3** with aldehydes and acyl chlorides have also been studied. Aldimines **14** prepared from iminophosphorane **3** and aldehydes were cyclized by the action of $SnCl_4$ to give the dihydro γ-carbolines **15** in low yields (20-35%), better yields (42-61%) were obtained when the potassium bis(trimethylsilyl)amide was used as cyclizating agent. Aldimines **14** were recovered unaltered after prolonged heating at 160° C.

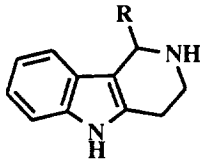
Direct reaction of iminophosphorane **3** with acyl chlorides provided the corresponding aminophosphonium chlorides, however when compound **3** was treated with potassium bis(trimethylsilyl)amide and then with two equiv of acyl chloride the corresponding 3-aroyldihydropyrimidoindoles **16** were isolated in modest yields (21-26%). When 1:1 molar ratio iminophosphorane/acyl chloride was used the same products were obtained although in lower yields.



14 16

	Yield % 16
a R= Ph-	25
b R= $4MeC_6H_4$-	21
c R= $4ClC_6H_4$-	26

ii



15

	Yield % 15	
	Method A	Method B
a R= Ph-	20	56
b R= $4MeC_6H_4$-	35	49
c R= $4MeOC_6H_4$-		61
d R= $2N_3C_6H_4$-		39
e R= PhCH=CH-		52
f R= Et		42

Reagents and Conditions:
i) R-CHO, toluene, reflux;
ii) $SnCl_4$, CCl_4, r.t., or KHMDS, toluene, r.t.
iii) KHMDS, toluene, -78 °C, then 2 Ar-COCl, r.t.

Several trends have surfaced from this study. First, isothiocyanate **5** and ketenimines **11** show identical behaviour towards different cyclizating agents. They undergo cyclization at the 3 position of the indole ring under Lewis acid-catalysed conditions, whereas under strongly basic conditions cyclization takes place at the indole nitrogen atom. Second, carbodiimides **9** undergo regiospecific ring closure to give dihydropyrimido indoles under acidic and basic conditions as well as by thermal treatment. In contrast the aldimines **14** undergo regiospecific ring closure to give dihydro-γ-carbolines under acid or basic conditions. Finally, iminophosphorane **3** undergoes cyclization to give dihydropyrimidoindoles by the action of acyl chlorides in the presence of a base. These results show a detailed picture of the ability of the aza-Wittig product derived from the readily available iminophosphorane **3** to undergo two different types of cyclization reactions under a wide variety of conditions; simply by changing either the nature of the reagent or the cyclizating agent the reaction may be driven towards the formation of dihydro γ-carbolines, or dihydropyrimido indoles. These latter compounds have been shown to be useful as analgesic and antiinflammatory agents.[9]

Experimental.

The solvents have been dried by the usual procedures[10] and, all reactions were conducted under an atmosphere of dry nitrogen. All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions or films on a Nicolet 5DX spectrophotometer. NMR spectra were recorded on a Brucker AC-200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin-Elmer 240C instrument.

Z-4-(2-Azidophenyl)-3-butenylazide 1. The previously unreported bis-azide **1** has been prepared according to the method described in the literature:[8] (56%), colourless oil; (Found: C, 56.07; H, 4.79; N, 39.40. $C_{10}H_{10}N_6$ requires: C, 56.07; H, 4.71; N, 39.23); IR (film) 2112 (N_3), 1574, 1483, 1450, 759 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.47 (dq, 2H, J= 1.5, 6.9 Hz, $C\underline{H}_2CH$=), 3.32 (t, 2H, J= 6.9 Hz, $C\underline{H}_2N_3$), 5.71 (dt, 1H, J= 6.9, 11.6 Hz, $CH_2C\underline{H}$=), 6.55 (d, 1H, J= 11.6 Hz, =C<u>H</u>Ar), 7.06-7.32 (m, 4H, H_{arom}); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 28.29, 50.92, 118.33, 124.38, 126.66 (q), 127.28, 128.54, 128.96, 130.19, 137.98 (q); m/z (%) 214 (M^+,4), 130 (100).

2-(2-Azidoethyl)indole 2. A solution of the bis-azide **1** (0.7 g, 3.2 mmol) in dry toluene (20 ml) was heated at 160 °C in a sealed tube for 6 h. After cooling, the solvent was removed under reduced pressure and the residual material was chromatographed on a silica gel column eluting with diethyl ether/n-hexane (1/1), affording the azido indole **2**: (61%), as a colourless oil; (Found: C, 64.36; H, 5.56; N, 30.00. $C_{10}H_{10}N_4$ requires: C, 64.50; H, 5.41; N, 30.09); IR (film) 3392, 2107 (N_3), 1455, 789, 750 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.78 (t, 2H, J= 6.6 Hz, $C\underline{H}_2CH_2N_3$), 3.43 (t, 2H, J= 6.6 Hz, $CH_2C\underline{H}_2N_3$), 6.22 (s, 1H, H-3), 7.03-7.21 (m, 3H, H-5 + H-6 + H-7), 7.52 (dd, 1H, J= 1.9, 7.6 Hz, H-4), 7.78 (br s, 1H, NH); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 27.77 ($\underline{C}H_2CH_2N_3$), 50.86 ($CH_2\underline{C}H_2N_3$), 100.54 (C-3), 110.66, 119.80, 120.01, 121.49, 128.38(q), 135.71 (q), 135.98 (q); m/z (%) 186 (M^+,12), 130 (100).

2-[2-(Triphenylphosphoranylidene)aminoethyl]indole 3. A solution of triphenylphosphine (0.28 g, 1.1 mmol) in dry diethyl ether (5 ml) was added to a stirred solution of azidoindol **2** (0.2 g, 1.1 mmol) at room temperature under nitrogen. The reaction mixture was stirred at that temperature for 10 h. The white precipitated solid was filtered and recrystallised from dichloromethane/diethyl ether to give **3**: (83%), m. p. 118-120°C (yellow prisms); (Found: C, 80.10; H, 5.84; N, 6.51. $C_{28}H_{25}N_2P$ requires: C, 79.98; H, 5.99; N, 6.66); IR (Nujol) 3200, 3075, 1455, 1438, 1109, 877, 752, 718, 696 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.97 (t, 2H, J= 5.2 Hz, $C\underline{H}_2CH_2N$=PPh_3), 3.46 (dt, 2H, J= 5.2, 14.4 Hz, $CH_2C\underline{H}_2N$=PPh_3), 6.13 (s,1H, H-3), 6.99-7.64 (m, 20H, H_{arom} + NH); ^{13}C-NMR (75MHz, $CDCl_3$) δ 32.38 (d, ^{3}J= 19.3 Hz, $\underline{C}H_2CH_2N$=PPh_3), 45.29 (d, ^{2}J= 5.0 Hz, $CH_2\underline{C}H_2N$=PPh_3), 98.48 (C-3), 110.48, 118.77, 119.40, 120.07, 128.54 (d, ^{3}J= 11.5 Hz, C_m), 131.12 (d, ^{1}J= 95.1 Hz, q, C_i), 131.47 (d, ^{4}J= 2.47 Hz, C_p), 132.37 (d, ^{2}J= 9.0 Hz, C_o), 135.57 (q), 141.59 (q), 146.90 (q); ^{31}P-NMR (125 MHz, $CDCl_3$) δ 12.66; m/z (%) 183 (53), 130 (100).

2-(2-Aminoethyl)indole 4. To a stirred suspension of $LiAlH_4$ (0.22 g, 5.74 mmol) in dry THF (10 ml) was added a solution of azidoindol **2** (0.36 g, 1.91 mmol) in dry THF (5 ml) over for 2 h at room temperature. The resultant mixture was heated under reflux for 3 h and then allowed to cool to room temperature. After water (15 ml) addition, the organic layer was separated, and the aqueous layer was extracted with chloroform (3 x 5 ml); the combined organic fractions were dried over anhydrous $MgSO_4$, filtered and concentrated to dryness. The residue was chromatographed on a silica gel column using ethanol/30% aqueous ammonia solution (9/1) as eluent affording **4**: (80%), m.p. 93-95°C (yellow prisms from dichloromethane/n-hexane); (Found: C, 74.86; H, 7.62; N, 17.60. $C_{10}H_{12}N_2$ requires: C, 74.97; H, 7.55; N, 17.48); IR (Nujol) 3357, 3283, 1580, 732 cm^{-1};^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.47 (br s, 2H, NH_2), 2.80 (t, 2H, J= 6.2 Hz, $C\underline{H}_2CH_2NH_2$), 2.99 (t, 2H, J= 6.2 Hz, $CH_2C\underline{H}_2NH_2$), 6.25 (s, 1H, H-3), 7.02-7.13 (m, 2H, H-5 + H-6), 7.26 (d, 1H, J= 7.3 Hz, H-7), 7.52 (d, 1H, J= 6.1 Hz, H-4), 9.17 (br s, 1H, NH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 31.40 ($\underline{C}H_2CH_2NH_2$), 41.58($CH_2\underline{C}H_2NH_2$), 99.70 (C-3), 110.59, 119.43, 119.70, 120.91, 128.56 (q), 135.96 (q), 138.28 (q); m/z (%) 160 (M^+, 29), 130 (100).

2-(2-Indolyl)ethylisothiocyanate 5. To a solution of iminophosphorane **3** (0.42 g, 1 mmol) in dry benzene (30 ml) an excess of carbon disulfide (15 ml) was added and the mixture was refluxed for 3 h. After cooling the solvent was removed under reduced pressure and the residue extracted with n-hexane (20 ml). The solvent was evaporated affording the isothiocyanate **5**: (95%), as a colourless oil; (Found: C, 65.49; H, 4.80; N, 13.74. $C_{11}H_{10}N_2S$ requires: C, 65.32; H, 4.98; N, 13.85); IR (film) 3134, 2192, 2107 (NCS), 1455, 793, 753 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.96 (t, 2H, J= 6.6 Hz, $C\underline{H}_2CH_2NCS$), 3.68 (t, 2H, J= 6.6 Hz, $CH_2C\underline{H}_2NCS$), 6.28 (s, 1H, H-3), 7.06-7.19 (m, 2H, H-5 + H-6), 7.28 (d, 1H, J= 7.6 Hz, H-7), 7.54 (d, 1H, J= 7.0 Hz, H-4), 7.86 (br s, 1H,); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 29.17 ($\underline{C}H_2CH_2NCS$), 44.95 ($CH_2\underline{C}H_2NCS$), 101.19 (C-3), 110.77, 120.04, 120.22, 121.88, 128.48 (q), 132.14 (q), 134.24 (q), 136.10 (q); m/z (%) 203 (M^++1, 11), 202 (M^+, 75), 130 (100).

Cyclization of Isothiocyanate 5 with $SnCl_4$. To a solution of isothiocyanate **5** (0.2 g, 1 mmol) in dry carbon tetrachloride (10 ml) at -15 °C was added a solution of $SnCl_4$ (0.25 g, 1 mmol) in dry carbon tetrachloride (10 ml). The reaction mixture was stirred at that temperature for 2 h, then was quenched with an aqueous saturated solution of sodium bicarbonate (20 ml). The precipitated solid was filtered, washed with diethyl ether and dried under vacuum, affording compound **6** : (45%), m.p. 166-169°C (yellow needles from chloroform/diethyl ether); (Found: C, 65.10; H, 4.81; N, 13.73. $C_{11}H_{10}N_2S$ requires: C, 65.32; H, 4.98; N, 13.85); IR (Nujol) 3318, 1552, 1484, 1456, 748 cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d^6) δ 3.01 (t, 2H, J= 7.3 Hz, H-4), 3.49 (dt, 2H, J= 2.5, 7.3 Hz, H-3), 7.08-7.15 (m, 2H, H-7 + H-8), 7.37 (m, 1H, H-6), 8.52 (m, 1H, H-9), 9.09 (br s, 1H, NH), 11.91 (br s, 1H, NH); ^{13}C-NMR (50MHz, DMSO-d^6) δ 21.68 (C-4), 41.39 (C-3), 111.15 (q), 111.57, 120.94, 121.00, 121.99, 126.42 (q), 136.17 (q), 140.36 (q), 188.67 (q, C-1); m/z (%) 203 (M^++1, 10), 202 (M^+, 64), 173 (100).

Cyclization of Isothiocyanate 5 with KHMDS. To a solution of the isothiocyanate **5** (0.2 g, 1 mmol) in dry toluene (30 ml) at -78 °C was added KHMDS (1 mmol, 0.5 M in toluene). The resultant solution was allowed to warm to room temperature and water (20 ml) was added. The reaction mixture was extracted with ethyl acetate (3 x 10 ml) and the combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to dryness. The residue was treated with n-hexane affording the compound **7**, which was recrystallised from chloroform/diethyl ether: (50%), m.p. 154-155°C (yellow prisms); (Found: C, 65.20; H, 4.90; N, 13.97. $C_{11}H_{10}N_2S$ requires: C, 65.32; H, 4.98; N, 13.85); IR (Nujol) 3217, 1557, 1454 cm-1; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.08 (t, 2H, J= 6.2 Hz, H-4), 3.45 (dt, 2H, J= 3.3, 6.2 Hz, H-3), 6.34 (s, 1H, H-5), 7.24-7.3 (m, 2H, H-7 + H-8), 7.47 (dd, 1H, J= 1.3, 6.9 Hz, H-6), 8.27 (br s, 1H, NH), 9.20 (dd, 1H, J= 0.9, 8.1 Hz, H-9); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.99 (C-4), 39.93 (C-3), 104.75 (C-5), 117.08, 120.15, 123.68, 123.85, 130.10 (q), 133.21 (q), 136.94 (q), 176.84 (q, C-1); m/z (%) 202 (M^+, 21), 130 (100).

General Procedure for the Preparation of Ureas 8. To a solution of amine **4** (0.19 g, 1.2 mmol) in dry benzene (5 ml) at room temperature was added, dropwise, a solution of the corresponding isocyanate (1.2 mmol) in dry benzene (5 ml). The mixture was stirred at room temperature under nitrogen for 15 h. The separated solid was filtered, washed with diethyl ether and dried under vacuum, affording the corresponding urea **8**.

8a (Ar= C_6H_5): (83%), m.p. 160-163°C (white needles from ethanol/n-hexane); (Found: C, 73.21; H, 6.19; N, 15.18. $C_{17}H_{17}N_3O$ requires: C, 73.10; H, 6.13; N, 15.04); IR (Nujol) 3389, 3333, 1638, 1570 (vs) cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d^6) δ 2.89 (t, 2H, J= 6.0 Hz, $C\underline{H}_2CH_2NH$), 3.47 (q, 2H, J= 6.0 Hz, $CH_2C\underline{H}_2NH$), 6.16 (t, 1H, J= 6.0 Hz, NH), 6.21 (s, 1H, H-3), 6.83-7.03 (m, 3H, H_{arom}), 7.16-7.44 (m, 6H, H_{arom}), 8.48 (s, 1H, NH), 10.98 (s, 1H, NH); ^{13}C-NMR (75MHz, DMSO-d^6) δ 28.75 ($\underline{C}H_2CH_2NH$), 38.76 ($CH_2\underline{C}H_2NH$), 98.96 (C-3), 110.73, 117.61, 118.67, 119.20, 120.19, 121.01, 128.42 (q), 128.67, 136.12 (q), 137.64 (q), 140.57 (q), 155.19 (q); m/z (%) 279 (M^+, 3), 143 (100).

8b (Ar= 4-$CH_3C_6H_4$): (77%), m.p. 178-180°C (white prisms from ethanol/n-hexane); (Found: C, 73.79; H, 6.55; N, 14.41. $C_{18}H_{19}N_3O$ requires: C, 73.70; H, 6.53; N, 14.32); IR (Nujol) 3383, 3336, 1639, 1597 cm^{-1};^{1}H-NMR (300 MHz, DMSO-d^6) δ 2.20 (s, 3H, CH_3), 2.88 (t, 2H, J= 6.7 Hz, $C\underline{H}_2CH_2NH$), 3.46 (q, 2H, J= 6.7 Hz, $CH_2C\underline{H}_2NH$), 6.13 (t, 1H, J= 6.7 Hz, NH), 6.21 (s, 1H, H-3), 6.9-7.02 (m, 4H, H-5 + H-6 + H_{arom}), 7.25 (d, 2H, J= 10.4 Hz, H_{arom}), 7.29 (d, 1H, J= 8.1 Hz, H-7), 7.42 (d, 1H, J= 7.6 Hz, H-4), 8.39 (s, 1H, NH), 10.98 (s, 1H, NH); ^{13}C-NMR (75MHz, DMSO-d^6) δ 20.42 CH_3), 28.86 ($\underline{C}H_2CH_2NH$),

38.82 ($CH_2\underline{C}H_2NH$), 99.02, (C-3) 110.81, 117.78, 118.76, 119.27, 120.27, 129.15, 128.47 (q), 129.79 (q), 136.16 (q), 137.73 (q), 138.04 (q), 155.35 (q); m/z (%) 293 (M^+, 4), 130 (100).

8c (Ar= 4-$CH_3OC_6H_4$): (83%), m.p. 163-165°C (white needles from ethanol/n-hexane); (Found: C, 69.80; H, 6.30; N, 13.43. $C_{18}H_{19}N_3O_2$ requires: C, 69.88; H, 6.19; N, 13.58); IR (Nujol) 3340, 1621, 1599 cm^{-1}; ^{1}H-NMR (200 MHz, DMSO-d^6) δ 2.88 (t, 2H, J= 6.6 Hz, $C\underline{H}_2CH_2NH$), 3.36 (s, 3H, OCH_3), 3.45 (q, 2H, J= 6.6 Hz, $CH_2C\underline{H}_2NH$), 6.06 (t, 1H, J= 6.6 Hz, NH), 6.20 (s, 1H, H-3), 6.79 (d, 2H, J= 8.8 Hz, H_{arom}), 6.92-7.00 (m, 2H, H-5 + H-6), 7.27 (d, 2H, J= 8.8 Hz, H_{arom}), 7.33 (d, 1H, J= 7.4 Hz, H-7), 7.42 (d, 1H, J= 7.4 Hz, H-4), 8.29 (s, 1H, NH), 10.97 (s, 1H, NH); ^{13}C-NMR (50MHz, DMSO-d^6) δ 28.82 ($\underline{C}H_2CH_2NH$), 38.76 ($CH_2\underline{C}H_2NH$), 55.18 (OCH_3), 98.93 (C-3), 110.73, 113.93, 118.66, 119.19, 119.36, 120.18, 128.42 (q), 133.70 (q), 136.10 (q), 137.68 (q), 153.93 (q), 155.42 (q); m/z (%) 309 (M^+, 5), 143 (100).

8d (Ar= CH=CH-C_6H_5): (74%), m.p. 188-190°C (white prisms from ethanol); (Found: C, 74.60; H, 6.39; N, 13.89. $C_{19}H_{19}N_3O$ requires: C, 74.73; H, 6.27; N, 13.76); IR (Nujol) 3381, 3349, 1668, 1632, 1577 cm-1; ^{1}H-NMR (300 MHz, DMSO-d^6) δ 2.89 (t, 2H, J= 6.6 Hz, $C\underline{H}_2CH_2NH$), 3.47 (q, 2H, J= 6.6 Hz, $CH_2C\underline{H}_2NH$), 5.86 (d, 1H, J= 14.7 Hz, CH=C<u>H</u>Ph), 6.20 (s, 1H, H-3), 6.36 (t, 1H, J= 6.6 Hz, NH), 6.96 (dd, 1H, J= 10.8, 14.7 Hz, C<u>H</u>=CHPh), 7.02-7.08 (m, 2H, H-5 + H-6), 7.22-7.38 (m, 6H, H-7 + H_{arom}), 7.44 (d, 1H, J= 7.5 Hz, H-4), 8.69 (d, 1H, J= 10.8 Hz, NH), 10.98 (s, 1H, NH); ^{13}C-NMR (75 MHz, DMSO-d^6) δ 28.56 ($\underline{C}H_2CH_2NH$), 38.87 ($CH_2\underline{C}H_2NH$), 98.80 (C-3), 105.88, 110.59, 118.52, 119.04, 120.04, 124.73, 124.87, 125.69, 128.23 (q), 128.40, 135.93 (q), 137.38 (q), 137.49 (q), 154.33 (q); m/z (%) 305 (M^+, 13), 143 (100).

General Procedure for the Generation of Carbodiimides 9. A mixture of the corresponding urea **8** (1 mmol), triphenylphosphine (0.52 g, 2 mmol), triethylamine (0.3 g, 3 mmol) and carbon tetrachloride (0.45 g, 3 mmol) in dry dichloromethane (20 ml) was heated under reflux for 5 h. After cooling the solvent was removed under reduced pressure and residue was extracted with dry toluene (3 x 10 ml). The toluene solution of the corresponding carbodiimide **9** was used for the next reaction without further purification.

General Procedure for the Cyclization of Carbodiimides 9.

Method A (with $SnCl_4$). The toluene solution of carbodiimide **9** was evaporated to dryness and dry carbon tetrachloride (10 ml) was added. A solution of $SnCl_4$ (0.25 g, 1 mmol) in dry carbon tetrachloride (10 ml) was added dropwise at -15 °C. The reaction mixture was allowed to warm to room temperature and stirred for 15 h. Then the reaction mixture was quenched with a saturated aqueous solution of sodium bicarbonate (20 ml). The organic layer was separated and the aqueous layer was extracted with ethyl acetate (3 x 5 ml), the combined organic layers were dried over anhydrous $MgSO_4$, filtered and evaporated to dryness. The residue was purified by chromatography on silica gel column with ethyl acetate as eluent, affording the corresponding compound **10**.

Method B (with KHMDS). The same as described for the preparation of compound **7** from **5**.

Method C (thermal treatment). A toluene solution containing the corresponding carbodiimide **9** was heated at 160 °C in a sealed tube for 15 h. After cooling, the solution was concentrated to dryness and the residue was purified by chromatography on a silica gel column with ethyl acetate as eluent, affording the corresponding compound **10**.

10a (Ar= C_6H_5): (Method A: 32%; Method B: 80%; Method C: 43%), m.p. 98-100 °C (white needles from ethyl acetate/n-hexane) (Found: C, 78.26; H, 5.61; N, 16.00. $C_{17}H_{15}N_3$ requires: C, 78.13; H, 5.79; N, 16.08); IR (Nujol) 3412, 1657, 1596, 1480, 1460 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.09 (t, 2H, J= 5.9 Hz, H-4), 3.37 (t, 2H, J= 5.9 Hz, H-3), 4.81 (br s, 1H, NH), 6.35 (s, 1H, H-5), 6.99-7.42 (m, 7H, H_{arom}), 7.51 (d, 1H, J= 7.2 Hz, H-6), 8.70 (d, 1H, J= 8.1 Hz, H-9); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 24.32 (C-4), 39.28 (C-3), 102.15 (C-5), 116.40, 119.73 (q), 122.18, 122.66, 122.85, 123.13, 129.38 (q), 129.63, 134.58 (q), 135.21 (q), 144.82 (q, C-1), 148.03 (q); m/z (%) 262 (M^++1, 13), 261 (M^+, 70), 130 (100).

10b (Ar= 4-$CH_3C_6H_4$): (Method A: 38%; Method B: 72%; Method C: 67%), m.p. 101-102 °C (white prisms from ethyl acetate/n-hexane) (Found: C, 78.40; H, 6.39; N, 15.39. $C_{18}H_{17}N_3$ requires: C, 78.52; H, 6.22; N, 15.26); IR (Nujol) 3416, 1662, 1594, 1478, 1453 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.26 (s, 3H, CH_3), 3.01 (t, 3H, J= 5.9 Hz, H-4), 3.28 (t, 2H, J= 5.9 Hz, H-3),

4.77 (br s, 1H, NH), 6.25 (s, 1H, H-5), 6.86 (d, 2H, J= 7.7 Hz, H_{arom}), 7.09 (d, 2H, J= 7.7 Hz, H_{arom}), 7.13-7.20 (m, 2H, H-7 + H-8), 7.43 (d, 1H, J= 7.6 Hz, H-6), 8.62 (d, 1H, J= 7.8 Hz, H-9); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 20.90 (CH_3), 24.37 (C-4), 39.31 (C-3), 102.09 (C-5), 116.46, 119.71, 122.14, 122.44, 123.11, 129.42 (q), 130.27, 132.18 (q), 134.62 (q), 135.29 (q), 144.97 (q, C-1), 145.36 (q); m/z (%) 275 (M^+, 21), 145 (100).

10c (Ar= 4-$CH_3OC_6H_4$): (Method A: 30%; Method B: 66%; Method C: 51%), m.p. 182-183°C (colourless prisms from chloroform); (Found: C, 74.05; H, 5.93; N, 14.40. $C_{18}H_{17}N_3O$ requires: C, 74.21; H, 5.88; N, 14.42); IR (Nujol) 3367, 1657, 1505, 1462 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.09 (t, 2H, J= 5.7 Hz, H-4), 3.37 (t, 2H, J= 5.7 Hz, H-3), 3.80 (s, 3H, OCH_3), 4.87 (br s, 1H, NH), 6.34 (s, 1H, H-5), 6.88-6.96 (m, 4H, H_{arom}), 7.17-7.25 (m, 2H, H_{arom}), 7.51 (d, 1H, J= 6.8 Hz, H-6), 8.69 (d, 1 H, J= 7.9 Hz, H-9); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 24 .39 (C-4), 39.33 (C-3), 55.66 (OCH_3), 102.11 (C-5), 115.09, 116.45, 119.73, 122.18, 123.13, 123.41, 129.42 (q), 134.62 (q), 135.26 (q), 141.06 (q), 145.38 (q, C-1), 155.61 (q); m/z (%) 292 (M^++1, 18), 291 (M^+, 100).

Generation of Ketenimine 11. To a cooled 0 °C suspension of iminophosphorane **3** (0.4 g, 1 mmol) in dry toluene (20 ml) was added dropwise a solution of diphenylketene (0.19 g, 1 mmol) in dry toluene (5 ml). The reaction mixture was stirred 15 min at 0 °C and allowed to warm at room temperature. This solution was used for the next step without further purification.

Cyclization of Ketenimine 11 to 12.

Method A (with $SnCl_4$): As described for the cyclization of carbodiimide **9**.

Method C (thermal treatment). The toluene solution containig the ketenimine **11** was heated under reflux for 6 h. After cooling the precipitate was filtered and recrystallised from chloroform/n-hexane.

12: (Method A: 20%; Method C: 25%), m.p. 83-85°C (colourless prisms); (Found: C, 85.79; H, 5.83; N, 8.42. $C_{24}H_{20}N_2$ requires: C, 85.68; H, 5.99; N, 8.33); IR (Nujol) 3137, 1602, 1532, 1497 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d^6) δ 3.33 (t, 2H, J= 8.5 Hz, H-4), 3.93 (t, 2H, J= 8.5 Hz, H-3), 6.44 (s, 1H, C<u>H</u>Ph_2), 7.16 (t, 1H, J= 7.8 Hz, H-7 or H-8), 7.22 (t, 1H, J= 7.8 Hz, H-7 or H-8), 7.28-7.45 (m, 10H, H_{arom}), 7.52 (d, 1H, J= 7.8 Hz, H-6), 7.64 (d, 1H, J= 7.8 Hz, H-9), 10.55 (br s, 1H, NH); ^{13}C-NMR (75 MHz, DMSO-d^6) δ 20.98 (C-4), 41.74 (C-3), 53.58 (<u>C</u>HPh_2), 106.16 (q), 113.35, 120.30 , 123.27, 123.53 (q), 123.94, 128.07, 129.17, 129.58, 136.99 (q), 137.50 (q), 150.75 (q), 172.72 (q); m/z (%) 336 (M^+, 37), 165 (100).

Cyclization of Ketenimine 11 to 13.

Method B (with KHMDS): The same method as described for the cyclization of carbodiimide **9**.

13: (34%) , unstable oil; (Found: C, 85.80; H, 5.83; N, 8.44. $C_{24}H_{20}N_2$ requires: C, 85.68; H, 5.99; N, 8.33); IR (film) 3069, 1642 cm-1; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.89 (dt, 2H, J= 0.9, 6.6 Hz, H-4), 3.70 (t, 2H, J= 6.6 Hz, H-3), 6.01 (s, 1H, C<u>H</u>Ph_2), 6.33 (d, 1H, J= 0.9 Hz, H-5), 7.04-7.14 (m, 2H, H_{arom}), 7.22-7.36 (m, 10H, H_{arom}), 7.48-7.51 (m, 2H, H_{arom}); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 22.68 (C-4), 44.31 (C-3), 55.23 (<u>C</u>HPh_2), 101.70 (C-5), 113.17, 120.59, 121.84, 122.62, 127.05, 128.63, 129.49, 129.53 (q), 132.69 (q), 137.33 (q), 140.98 (q), 154.67 (q); m/z (%) 336 (M^+, 36), 167 (100).

General Procedure for the Preparation of Aldimines 14. A mixture of iminophosphorane **3** (0.3 g, 0.71 mmol), the corresponding aldehyde (0.71 mmol) and dry toluene (15 ml) was heated under reflux for 5 h under nitrogen. The toluene solution of aldimine **14** was used for the next step.

General Procedure for the Cyclization of Aldimines 14.

Method A (with $SnCl_4$): As described for the cyclization of carbodiimide **9**.

Method B (with KHMDS). As described for the preparation of compound **7** from **5**.

15a (R= C_6H_5): (Method A: 20%; Method B: 56%), m.p. 196-199°C (white prisms from chloroform); (Found: C, 82.30; H, 6.59; N, 11.22. $C_{17}H_{16}N_2$ requires: C, 82.21; H, 6.50; N, 11.29); IR (Nujol) 3136, 3063, 1455, 700 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d^6) δ 2.7-3.17 (m, 4H, H-3 + H-4), 4.13 (br s, 1H, NH), 5.10 (s, 1H, H-1), 6.58 (d, 1H, J= 7.5 Hz, H-9), 6.69 (t, 1H, J= 7.5 Hz, H-7), 6.91 (t, 1H, J= 7.5 Hz, H-8), 7.25-7.3 (m, 6H, H_{arom}), 10.94 (s, 1H, NH); ^{13}C-NMR (75 MHz, DMSO-d^6) δ 23.97

(C-4), 41.30 (C-3), 56.81 (C-1), 110.04 (q), 110.82, 117.91, 118.15, 119.98, 125.77 (q), 127.05, 127.96, 128.62, 134.33 (q), 135.68 (q), 144.10 (q); m/z (%) 248 (M^+, 19), 171 (100).

15b (R= 4-$CH_3C_6H_4$): (Method A: 35%, Method B: 49%) , m.p. 235-236°C (yellow prisms from chloroform); (Found: C, 81.90; H, 7.74; N, 10.51. $C_{18}H_{20}N_2$ requires: C, 81.78; H, 7.63; N, 10.60); IR (Nujol) 3235, 1465 cm-1; ^{1}H-NMR (300 MHz, DMSO-d^6) δ 2.27 (s, 3H, CH_3), 2.82-3.24 (m, 4H, H-3 + H-4), 4.97 (br s, 1H, NH), 5.37 (s, 1H, H-1), 6.54 (d, 1H, J= 7.8 Hz, H-9), 6.71 (t, 1H, J= 7.8 Hz, H_{arom}), 6.94 (t, 1H, J= 7.8 Hz, H_{arom}), 7.09 (d, 2H, J= 7.6 Hz, H_{arom}), 7.24 (d, 2H, J= 7.6 Hz, H_{arom}), 7.29 (d, 1H, J= 7.8 Hz, H-6), 11.08 (s, 1H, NH); ^{13}C-NMR (75 MHz, DMSO-d^6) δ 20.75 (CH_3), 22.39 (C-4), 40.45 (C-3), 56.08 (C-1), 107.80 (q), 110.90, 117.87, 118.33, 120.32, 125.37 (q), 128.69, 128.97, 133.39 (q), 135.81 (q), 137.01 (q), 137.75 (q); m/z (%) 264 (M^+, 2), 261 (100).

15c (R= 4-$CH_3OC_6H_4$): (Method B: 61%), m.p. 164-167°C (white prisms from chloroform); (Found: C, 77.01; H, 7.23; N, 9.90. $C_{18}H_{20}N_2O$ requires: C, 77.11; H, 7.19; N, 9.99); IR (Nujol) 3404, 1612, 1517 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d^6) δ 2.49-3.13 (m, 4H, H-3 + H-4), 3.70 (s, 3H, OCH_3), 4.18 (br s, 1H, NH), 5.07 (s, 1H, H-1), 6.59 (d, 1H, J= 6.6 Hz, H-9), 6.70 (dd, 1H, J= 6.6, 8.1 Hz, H-7), 6.81 (d, 2H, J= 7.5 Hz, H_{arom}), 6.91 (t, 1H, J= 6.6 Hz, H-8), 7.21 (d, 2H, J= 7.5 Hz, H_{arom}), 7.27 (d, 1H, J= 8.1 Hz, H-6), 10.92 (s, 1H, NH); ^{13}C-NMR (75 MHz, DMSO-d^6) δ 23.92 (C-4), 41.30 (C-3), 54.97 (OCH_3), 56.19 (C-1), 110.24 (q), 110.78, 113.28, 118.02, 118.12, 119.95, 125.81 (q), 129.64, 134.23 (q), 135.69 (q), 135.97 (q), 158.34 (q); m/z (%) 280 (M^+, 10), 171 (100).

15d (R= 2-$N_3C_6H_4$): (Method B: 39%), m.p. 167-168°C (white needles from diethyl ether); (Found: C, 70.69; H, 5.31; N, 24.01. $C_{17}H_{15}N_5$ requires: C, 70.57; H, 5.23; N, 24.20); IR (Nujol) 3154, 2126, 1454 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.71-3.13 (m 5H, H-3 + H-4 + NH), 5.57 (s, 1H, H-1), 6.79-7.28 (m, 8H, H_{arom}), 8.35 (s, 1H, NH); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 24.28 (C-4), 40.69 (C-3), 51.03 (C-1), 109.14 (q), 110.66, 118.19, 118.68, 119.31, 121.21, 124.61, 125.99 (q), 128.80, 130.34, 133.64 (q), 134.32 (q), 135.79 (q), 138.11 (q); m/z (%) 261 (M^+-28, 86), 219 (100).

15e (R= C_6H_5-CH=CH): (Method B: 52%), m.p. 169-170°C (brown prisms from chloroform); (Found: C, 83.31; H, 6.54; N, 10.19. $C_{19}H_{18}N_2$ requires: C, 83.17; H, 6.62; N, 10.22); IR (Nujol) 3140, 3062, 1500, 1425 cm-1; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 2.37 (br s, 1H, NH), 2.57-2.74 (m, 2H, H-4), 3.07 (dt, 1H, J= 6.0, 11.8 Hz, H_A-3), 3.28 (dt ,1H, J= 5.5, 11.8 Hz, H_B-3), 4.81 (d, 1H, J= 7.5 Hz, H-1), 6.42 (dd, 1H, J= 7.5, 15.7 Hz, C<u>H</u>=CHPh), 6.66 (d, 1H, J= 15.7 Hz, CH=C<u>H</u>Ph), 6.97 (t, 1H, J= 7.5 Hz, H_{arom}), 7.06 (dd, 1H, J= 7.2, 7.8 Hz, H_{arom}), 7.18-7.35 (m, 6H, H_{arom}), 7.43 (d, 1H, J= 7.5 Hz, H-6), 8.50 (s, 1H, NH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 24.13 (C-4), 40.82 (C-3), 55.02 (C-1), 110.18 (q), 110.58, 118.61, 119.21, 120.98, 126.12 (q), 126.93, 127.37, 128.42, 131.54, 131.61, 132.86 (q), 135.59 (q), 136.92 (q); m/z (%) 275 (M^++1, 15), 274 (M^+, 58), 171 (100).

15f (R= Et) (Method B: 42%), m.p. 142-144°C (white prisms from chloroform); (Found: C, 77.83; H, 8.14; N, 14.07. $C_{13}H_{16}N_2$ requires: C, 77.96; H, 8.05; N, 13.99); IR (Nujol) 3285, 3138, 1456 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.04 (t, 3H, J= 7.4 Hz, $CH_AH_BC\underline{H}_3$), 1.68-1.83 (m, 1H, $C\underline{H}_AH_BCH_3$), 2.10-2.23 (m, 1H, $CH_A\underline{H}_BCH_3$), 2.62-2.82 (m, 2H, H-4), 3.02-3.10 (m, 1H, H_A-3), 3.31-3.38 (m, 1H, H_B-3), 4.10-4.14 (m, 1H, H-1), 7.06 (dt, 1H, J= 1.5, 7.2 Hz, H_{arom}), 7.11 (dt, 1H, J= 1.5, 7.2 Hz, H_{arom}), 7.27 (dd, 1H, J= 1.5, 7.2 Hz, H-6), 7.5 (dt, 1H, J= 1.5, 7.2 Hz, H-9), 8.0 (s, 1H, NH); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 10.40 ($CH_2\underline{C}H_3$), 24.76 (C-4), 27.92 ($\underline{C}H_2CH_3$), 41.09 (C-3), 53.87 (C-1), 110.59, 113.06 (q), 118.70, 119.20, 120.93, 125.93 (q), 132.79 (q), 135.60 (q); m/z (%) 200 (M^+, 8), 171 (100).

General Procedure for the Preparation of 16. To a suspension of iminophosphorane **3** (0.31 g, 0.73 mmol) in dry toluene (15 ml) at -78 °C was added a solution of KHMDS (1.47 mmol, 0.5 M in toluene). After stirring the mixture 15 min at -78 °C the corresponding acid chloride was added (1.47 mmol). The mixture was allowed to warm to room temperature and stirred over 12 h. Water was added (15 ml) and the organic layer was separated, the aqueous layer was extracted with ethyl acetate (3 x 5 ml). The resultant organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated to dryness. The resultant residue was purified by chromatography on a silica gel column with ethyl acetate/n-hexane (9/1) as eluent, affording compound **16**.

16a (Ar= C_6H_5): (25%), m.p. 69-70 °C (white prisms from diethyl ether/n-hexane); (Found: C, 82.12; H, 5.24; N, 8.09. $C_{24}H_{18}N_2O$ requires: C, 82.25; H, 5.18; N, 8.00); IR (Nujol) 1631, 1599, 1555 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 2.98 (t, 2H, J= 6.3 Hz, H-4), 3.72 (t, 2H, J= 6.3 Hz, H-3), 6.38 (d, 1H, J= 7.7 Hz, H-9), 6.96 (t, 1H, J= 7.7 Hz, H-8), 7.15 (t, 1H, J= 7.7 Hz, H-7), 7.41-7.68 (m, 8H, H_{arom}), 7.73 (d, 2H, J= 7.9 Hz, H_{arom}), 7.74 (d, 2H, J= 7.7 Hz, H-6); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 23.11 (C-4), 44.18 (C-3), 113.75, 114.73 (q), 121.49, 123.06, 123.16, 127.70 (q), 128.58, 128.73, 128.77, 129.12, 131.03, 132.37, 134.01 (q), 134.59 (q), 140.54 (q), 143.73 (q), 152.10 (q), 191.45 (q); m/z (%) 350 (M^+, 15), 77 (100).

16b (Ar= 4-$CH_3OC_6H_4$): (21%), m.p. 69-70°C (white needles from diethyl ether/n-hexane); (Found: C, 76.15; H, 5.56; N, 6.80. $C_{26}H_{22}N_2O_3$ requires: C, 76.07; H, 5.41; N, 6.83); IR (Nujol) 1630, 1600, 1570 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 3.01 (t, 2H, J= 6.5 Hz, H-4), 3.70 (t, 2H, J= 6.5 Hz, H-3), 3.89 (s, 6H, 2 OCH_3), 6.49 (d, 1H, J= 8.2 Hz, H-9), 6.95-7.01 (m, 5H, H_{arom}), 7.14 (t, 1H, J= 7.8 Hz, H-7), 7.55 (d, 2H, J= 8.7 Hz, H_{arom}), 7.78 (d, 1H, J= 7.8 Hz, H-6), 7.86 (d, 2H, J= 8.0 Hz, H_{arom}); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 23.17 (C-4), 43.97 (C-3), 55.45 (OCH_3), 55.49 (OCH_3), 113.71, 113.83, 114.00, 114.85 (q), 121.33, 122.79, 122.93, 126.74 (q), 127.84 (q), 130.39, 131.62, 132.90 (q), 134.02 (q), 142.86 (q), 153.49 (q), 161.80 (q), 163.23 (q), 191.00 (q); m/z (%) 411 (M^++1, 15), 410 (M^+, 50), 277 (100).

16c (Ar= 4-ClC_6H_4): (26%), m.p. 175-176°C (yellow prisms from diethyl ether/n-hexane); (Found: C, 68.94; H, 3.75; N, 6.76. $C_{24}H_{16}N_2OCl_2$ requires: C, 68.89; H, 3.86; N, 6.70); IR (Nujol) 1638, 1587, 1565 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 3.02 (t, 2H, J= 6.6 Hz, H-4), 3.74 (t, 2H, J= 6.6 Hz, H-3), 6.45 (d, 1H, J= 7.8 Hz, H-9), 7.02 (t, 1H, J= 7.8 Hz, H-8), 7.17 (t, 1H, J= 7.8 Hz, H-7), 7.49-7.57 (m, 6H, H_{arom}), 7.66 (d, 1H, J= 7.8 Hz, H-6), 7.78 (d, 2H, J= 8.1 Hz, H_{arom}); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 23.03 (C-4), 44.19 (C-3), 113.71, 114.53 (q), 121.50, 123.32, 123.46, 127.52 (q), 128.96, 129.12, 130.17, 130.65, 132.89 (q), 133.82 (q), 137.38 (q), 138.65 (q), 138.89 (q), 143.74 (q), 151.06 (q), 190.95 (q); m/z (%) 421 (M^++2, 8), 420 (M^++1, 32), 419 (M^+, 13), 281 (100).

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