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PREPARATION OF 1H-2,3,4,5-TETRAARYLPYRROLES BY OXIDATION OF HETEROCYCLIC IMINE-ENAMINES

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Abstract : Heterocyclic imine-enamines **1** were prepared from metalated methyl substituted heterocycles and aromatic nitriles and then oxidized with lead tetracetate to give various tetraarylpyrroles **2**.

The applications of tetraphenylpyrroles are various : electrophotographic products[1-3], sensitizers for organic photoconductors[4], antioxidants[5].

1H-Tetraphenylpyrroles may be prepared in different ways : from ketazines[6-10], from 2,3-diphenyl-2-H-azirine[11], or from 2,3-diphenylaziridine[12,13] by thermal rearrangement. All these processes give only tetraphenylpyrroles. For these reasons we were interested to synthesize tetraarylpyrroles, other than tetraphenyl substituted ones, and now we propose a new route to these compounds from imine-enamines according to Scheme 1.

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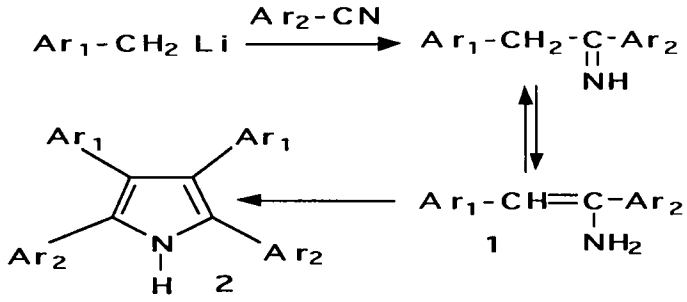
In our laboratory, we had previously used as intermediates some imine-enamines like **1** [14-16]. Thus, when an aralkyllithium was reacted with an aromatic nitrile, imine-enamines **1** were formed but they were very unstable especially in the presence of acids or water. However, if the reaction is performed at - 40°C,



in an anhydrous solvent like THF, under an inert gas, and if the hydrolyse is run with a small amount of water, enamines **1** may be isolated (Table I). When Ar_1 had a nitrogen in the 2 position (2-pyrazinyl, 2-quinoxalinyl), the imines **1a-f** were generally stable enough to be purified by column chromatography and quite easy to obtain. The yields of imine-enamines **1** were lowered when methylpyrazine or methylquinoxaline were used because of the competition with an intramolecular cyclisation of these imines to give pyrrolopyrazines and pyrroloquinoxalines[17].

The addition of lead tetracetate (LTA) to a solution of these imine-enamines gave, after hydrolyse and separation, the 1H-pyrroles **2** with efficient yields. This reaction was run with various aromatic substituents (Table II). We have tested several solvents : in THF, benzene, toluene or xylene LTA was insoluble and no reaction was observed at 20°C ; chloroform or acetic acid gave a mixture with poor yields of pyrroles **2** ; in acetonitrile at 20°C, only a poor yield of tetraarylpyrroles was formed. The best results were obtained within a few minutes in acetonitrile when the solution was cooled down to - 40°C. On the other hand, when the imine-enamines were too difficult to isolate, a solution of the "non

Table I : Purified imines enamines

	Ar1	Ar2	Yields %
1a	2-pyrazinyl	phenyl	25
1b	2-pyrazinyl	2-pyridyl	38
1c	2-pyrazinyl	4-pyridyl	31
1d	2-pyrazinyl	2-furyl	41
1e	2-pyrazinyl	2-thienyl	32
1f	2-quinoxalinyl	phenyl	19

Table II : Tetraarylpyrroles prepared from compound **1**

	Ar1	Ar2	Yields %
2a	2-pyrazinyl	phenyl	90[a]
2b	2-pyrazinyl	2-pyridyl	77[a]
2c	2-pyrazinyl	4-pyridyl	52[a]
2d	2-pyrazinyl	2-furyl	98[a]
2e	2-pyrazinyl	2-thienyl	90[a]
2f	2-quinoxalinyl	phenyl	59[a]
2g	2-pyridyl	phenyl	50[b]
2h	4-pyridyl	phenyl	37[b]

a : based on imine-enamine **1** b : based on aromatic nitrile

purified" imine in acetonitrile was reacted with lead tetracetate under the same conditions (**2g**, **2h**). It was like a "one-pot" reaction.

The structure of compound **2a** was established unambiguously by X ray cristallography[18]. A possible reaction path to pyrroles **2** was considered by S. K. Khetan[19] : the first step was an oxidation with C-C coupling in the presence of LTA, then an amine was eliminated to give a regiospecific cyclisation to pyrroles **2**.

EXPERIMENTAL SECTION

Melting points were measured by using a Köffler apparatus and are uncorrected. The ^1H NMR spectra were recorded on a Varian EM 360 and a Bruker 200 A C spectrometers. ^{13}C NMR spectra were realized on a Bruker 200 A C spectrometer. Mass spectral data were obtained on a VG 70-70F spectrometer. Elemental analyses were performed on a Perkin Elmer 240 apparatus.

Acetonitrile was dried over Na_2SO_4. THF was dried and prior to use distilled over benzophenone and sodium. Diisopropylamine was dried over BaO and distilled. Used butyllithium was Merck 1,6 molar solution in hexane.

General procedure for the preparation of imine-enamines 1a-1f :

To a stirred, 0°C nitrogen atmosphere solution of diisopropylamine (8.9 g, 88 mmol) in 100ml of dry THF, via syringe, n-butyllithium (88 mmol, 55 ml of a solution 1.6 M in hexane) was added. After 20 min at O°C the solution was cooled to - 40°C and a solution of 2-methylpyrazine (7.52 g, 80 mmol) in 15 ml of THF was added slowly. After complete addition, the solution was stirred 45 min at - 40°C and a solution of aromatic nitrile (80 mM) in 15 ml of THF was added. Then the mixture was stirred for 1h and was allowed to warm to room temperature, 2 ml of water was added, stirred during a few minutes and dried on anhydrous sodium sulfate. The solvent was evaporated and the residue was purified by chromatography.

-1-Amino-1-phenyl-2-(2'-pyrazinyl)ethylene 1a :

Yellow powder (3.94 g, 25%) ; mp 125°C ; ^{1}H NMR ($CDCl_3$) δ ; 8.30 (2H,m) ; 8.05 (1H, m) ; 7.7-7.3 (5H, m) ; 6.8 (2H, s, NH_2) ; 5.5 (1H,s) ; ms m/z (%) : 197 (M, 67) ; 196 (M-1, 100) ; 94 ; 77 ; ir (ν cm-^{1}) (KBr) ; 3350, 3150, 1600. Anal. Calcd for $C_{12}H_{11}N_3$: C, 73.07 ; H, 5.62 ; N, 21.31. Found : C, 73.0 ; H, 5.54 ; N, 21.37.

-1-Amino-1-(2'-pyridyl)-2-(2'-pyrazinyl)ethylene 1b :

Yellow powder (6.03 g, 38%) ; mp 123°C ; ^{1}H NMR ($CDCl_3$) δ: 8.7 (1H, m) ; 8.4 (2H, m) ; 8.1-7.2 (6H, m) ; 6.0 (1H,s) ; ms m/z (%) : 198 (M, 100) ; 197 (M-1, 82) ; 170 (27) ; 144 (77) ; 120 (30) ; 78 (57) ; ir (ν cm-1) (KBr) : 3500, 3325, 1620, 1150, 760. Anal. Calcd for $C_{11}H_{10}N_4$: C, 66.65 ; H, 5.08 ; N, 28.26 ; Found : C, 66.58 ; H, 5.06 ; N, 28.20.

-1-Amino-1-(4'-pyridyl)-2-(2'-pyrazinyl)ethylene 1c :

Yellow powder (4.92 g, 31%) ; mp 142°C ; ^{1}H NMR ($CDCl_3$) δ: 8.75 (2H, m) ; 8.45 (2H, s) ; 8.15 (1H, m) ; 7.5 (2H, m) ; 6.9 (2H, s, NH_2) ; 5.6 (1H, s) ; ms m/z (%) : 198 (M, 76) ; 197 (M-1, 100) ; 170 (31) ; 120 (11) ; 105 (13) ; 94 (21) ; ir (ν cm-1) (KBr) : 3470, 3320, 1640, 1570. Anal. Calcd for $C_{11}H_{10}N_4$: C, 66.65 ; H,5.08 ; N, 28.26 ; Found : C, 66.59 ; H, 5.18 ; N, 28.10.

-1-Amino-1-(2'-furyl)-2-(2'-pyrazinyl)ethylene 1d :

Yellow powder (6.14 g, 41%) ; mp 102°C ; ^{1}H NMR ($CDCl_3$) δ: 8.35 (2H, m) ; 8.10 (1H, m) ; 7.5 (1H, m) ; 6.8-6.4 (4H, m, NH_2) ; 5.8 (1H, s) ; ir (ν cm^{-1}) (KBr) : 3550, 3200, 1630. Anal. Calcd for $C_{10}H_9N_30$: C, 64.16 ; H, 4.85 ; N, 22.45 ; Found : C, 64.08 ; H, 4.91 ; N, 22.32.

-1-Amino-1-(2'-thienyl)-2-(2'-pyrazinyl)ethylene 1e :

Yellow powder (5.20 g, 32%) ; mp 126-127°C ; ^{1}H NMR ($CDCl_3$) δ : 8.3 (2H, m) ; 8.05 (1H, m) ; 7.4-7 (3H, m) ; 6.7 (2H, s NH_2) ; 5.65 (1H, s) ; ir (ν cm^{-1}) (KBr)

3400, 3200, 1630, 1590, . Anal. Calcd for $C_{10}H_9N_3S$: C, 59.09 ; H, 4.46 ; N, 20.67 ; Found : C, 59.22 ; H, 4.56 ; N, 20.49.

-1-Amino-1-(2'-quinoxalinyl)-2-(2'-pyrazinyl)ethylene 1f :

Yellow powder (3.76 g, 19%) ; mp 137°C ; ^{1}H NMR ($CDCl_3$) δ : 8.5 (1H, s) ; 8.0-7.4 (11H, m, NH_2) ; 5.7 (1H,s) ; ms m/z (%) : 247 (M), 246 (M-1, 100), 219, 77 ; ir (ν cm^{-1}) (KBr) : 3400, 3200, 1640. Anal. Calcd for $C_{16}H_{13}N_3$: C,77.71 ; H, 5.30 ; N, 16.99 ; Found : C, 77.62 ; H, 5.42 ; N, 16.83.

General procedure for compounds 2a-2h :

Method A compounds 2a-2f : Compound **1a** (1.97g, 10 mmol) in 75 ml of acetonitrile was cooled down to - 40°C and then powdered lead tetracetate (2.22g, 5 mmol) was added. The mixture was stirred for 15 min and 12 ml of a solution of aqueous saturated sodium carbonate was added. The precipitate was washed out with acetonitrile and chloroform. The organic phase was dried over anhydrous sodium sulfate, evaporated and purified by chromatography on silica gel column, elution with ethyl acetate.

Method B compounds 2g-2h : The imines are prepared according to the general procedure for **1a-1f** but the residue of the reaction was dissolved in dry acetonitrile, the solution was cooled down to - 40°C and lead tetracetate (17.6 g, 40 mmol) was added. The workup of the procedure was the same as for method A.

-1H-2,5-diphenyl-3,4-dipyrazinylpyrrole 2a :

Yellow powder (1.68 g, 90%) from silicagel chromatography (ethyl acetate) and ethanol recrystallisation ; mp 218°C ; ^{1}H NMR (DMSO-d6) δ : 12 (1H, s, NH) ; 7.3 (10H, m) ; 8..25-8.50 (6H, m) ; ^{13}C NMR (DMSO-d6) δ : 150.8 (s) ; 146.1 (d) ; 143.9 (d) ; 141.5 (d) ; 132.0 (s) ; 131.7 (s) ; 128.5 (d) ; 128.3 (d) ; 127.4 (d) ; 119.5 (s) ; ms m/z (%) : 377 (M+2, 2) ; 376 (M+1, 18) ; 375 (M, 74) ; 374 (M-1, 100) ; 347 (9) ; 320 (10) ; 319 (4) ; 295 (4). ir (ν cm^{-1}) (KBr) : 3300-3100, 1580,

1545-1480,. Anal. Calcd for $C_{24}H_{17}N_5$: C, 76.78 ;H, 4.56 ; N, 18.65. Found : C, 76.85 ; H, 4.63 ; N, 18.54.

-1H-2,5-di-(2-pyridyl)-3,4-dipyrazinylpyrrole 2b :

Brown powder (1.45 g, 77%) ; mp 260°C ; ^{1}H NMR ($CDCl_3$) δ : 11 (1H, s, NH) ; 8.7-8.4 (8H, m); 7.65-7.35 (2H, m) ; 7.2-6.95 (4H, m) ; ^{13}C NMR ($CDCl_3$) δ : 150.4 (s) ; 149.3 (d) ; 148.8 (s) ; 146.7 (d) ; 143.8 (d) ; 142.1 (d) ; 136.1 (d) ; 130.3 (s) ; 121.8 (d) ; 121.1 (s) ; 120.2 (d) ; ms m/z (%) : 379 (M+2, 3); 378 (M+1, 24) ; 377 (M, 100) ; 376 (M-1, 90) ; 350 (15) ; 349 (18) ; 323 (41) ; 322 (46) ; 299 (28) ; 298 (13) ; ir (ν cm^{-1}) (KBr) : 3500 ; 3350 ; 3100 ; 1625 ; 1550. Anal. Calcd for $C_{22}H_{15}N_7$: C, 70.01 ; H, 4.01 ; N 25.98 ; Found : C, 69.88 ; H, 3.96 ; N, 25.91.

-1H-2,5-di-(4-pyridyl)-3,4-dipyrazinylpyrrole 2c :

White powder (0.98 g, 52%) ; mp 260°C ; ^{1}H NMR (DMSO-d6) δ : 12.5 (1H, s, NH) ; 8.7-8.3 (10H, m) ; 7.4 (4H, m) ; ^{13}C NMR (CD_3OD) δ : 150.1 (s) ; 149.9 (d) ; 146.2 (d) ; 144.5 (d) ; 142.6 (d) ; 139.3 (s) ; 131.2 (s) ; 122.4 (d) ; 121.9 (s) ; ms m/z (%) : 378 (9) ; 377 (M, 46) ; 376 (100) ; 349 (15) ; 323 (13) ; 322 (16) ; ir (ν cm^{-1}) (KBr) : 3470 ; 3100 ; 1640 ; 1585. Anal. Calcd for $C_{22}H_{15}N_7$: C, 70.01 ; H, 4.01 ; N, 25.98 ; Found : C, 69.82 ; H, 4,19 ; N, 25.80.

-1H-2,5-di-(2-furyl)-3,4-dipyrazinylpyrrole 2d :

Brown powder (1.74 g, 98%) ; mp 132°C ; ^{1}H NMR ($CDCl_3$) δ : 9.6 (1H, s, NH) ; 8.7-8.45 (6H, m); 7.45 (2H, m) ; 6.45 (4H, s) ; ^{13}C NMR (CD_3OD) δ : 149.9 (s) ; 146.1 (d) ; 146.0 (s) ; 143.7 (d) ; 142.6 (d) ; 141.9 (d) ; 123.1 (s) ; 119.5 (s) ; 111.6 (d) ; 107.7 (d) ; ms m/z (%) : 357 (4) ; 356 (35) ; 355 (M, 100) ; 354 (31) ; 327 (16) ; 326 (15) ; 301 (14) ; 177 (11) ; 164 (10) ; 163 (8) ; 149 (10) ; 123 (8) ; 122 (11) ; 110 (8); 109 (15). ir (ν cm^{-1}) (KBr) : 3500 ; 3180 ; 1470. Anal. Calcd for $C_{20}H_{13}N_5O_2$: C, 67.60 ; H, 3.69 ; N, 19.71 ; Found : C, 67.44 ; H, 3.97 ; N, 19.48.

-1H-2,5-di-(2-thienyl)-3,4-dipyrazinylpyrrole 2e :

White powder (1.76 g, 91%) ; mp 221°C ; ^{1}H NMR (DMSO-d6) δ : 12.1 (1H, s, NH) ; 8.5 (6H, m); 7.5 (4H, m) ; 7.1 (2H, m) ; ^{13}C NMR (DMSO-d6) δ : 149.9 (s) ; 146.2 (d) ; 144.0 (d) ; 142.1 (d) ; 132.6 (s) ; 127.3 (d) ; 126.5 (d) ; 126.3 (d) ; 125.8 (s) ; 119.8 (s) ; ms m/z (%) : 389 (13) ; 388 (40); 387 (M,100) ; 386 (68) ; 327 (11) ; 194 (8) ; 193 (13) ; 52 (6) ; 39 (8). ir (ν cm^{-1}) (KBr) : 3200 ; 3100 ; 1580. Anal. Calcd for $C_{20}H_{13}N_5S_2$: C, 61.99 ; H, 3.38 ; N, 18.07 ; Found : C, 62.05 ; H, 3.54 ; N, 17.92.

-1H-2,5-diphenyl-3,4-di-(2-quinoxalinyl)pyrrole 2f :

Yellow powder (1.40 g, 59%) ; mp 237°C ; ^{1}H NMR ($CDCl_3$) δ : 9.0 (1H, s, NH) ; 8.75 (2H, s) ; 8.1-7.8 (4H, m) ; 7.7-7.2 (14H, m) ; ^{13}C NMR ($CDCl_3$) δ : 150.3 (s) ; 147.3 (d) ; 141.9 (s) ; 140.1 (s) ; 133.8 (s) ; 131.4 (s) ; 129.5 (d) ; 128.8 (d) ; 128.7 (d) ; 128,0 (d) ; 120.0 (s). ms m/z (%) : 477 (4.5) ; 476 (27) ; 475 (M, 93) ; 474 (100) ;371 (4) ; 346 (4) ; 345 (4) ; 344 (3) ; 238 (5) ; 237 (8) ; ir (ν cm^{-1}) (KBr): 3470 ; 3250 ; 3100 ; 1615. Anal.Calcd for $C_{32}H_{21}N_5$: C, 80.22 ; H, 4.45 ; N, 14.73 ; Found : C, 80.59 ; H, 4.67 ; N, 14.58.

-1H-2,5-diphenyl-3,4-di-(2-pyridyl)pyrrole 2g :

White powder (7.46 g, 50%) ; mp 201°C ; ^{1}H NMR ($CDCl_3$) δ : 8.5 (1H, s, NH) ; 8.3-8.1 (2H, m) ; 7.3-6.7 (16H, m) ; ir (ν cm^{-1}) (KBr) : 3500-3100, 1600, 1510. Anal. Calcd for $C_{26}H_{19}N_3$: C, 83.62 ; H, 5.13 ; N, 11.25 ; Found : C, 83.56 ; H, 5.15 ; N, 11.22.

-1H-2,5-diphenyl-3,4-di-(4-pyridyl)pyrrole 2h :

White powder (5.5 g, 37%) ; mp 260°C ; ^{1}H NMR ($CDCl_3$) δ : 8.5-8.4 (1H, s, NH) ; 8.1 (4H, m), 7.0-6.9 (10H, m), 6.6 (4H, m) ; ir (ν cm^{-1}) (KBr) : 3200, 1610, 840. Anal. Calcd for $C_{26}H_{19}N_3$: C, 83.62 ; H, 5.13 ; N, 11.25 ; Found : C, 83.44 ; H, 5.30 ; N, 11.11.

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