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A GENERAL METHOD FOR THE SYNTHESIS OF 2-ARYLPYRROLES

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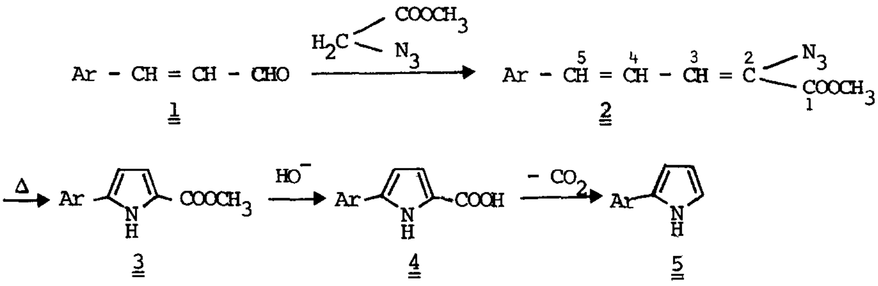
Abstract : Reaction of methyl azidoacetate with β-arylacroleins, followed by cyclisation of the obtained derivatives easily leads to arylpyrroles. N M R and mass spectra data are given and the Vilsmeier formylation of some arylpyrroles is described.

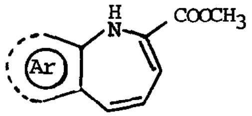
A very large number of bisarylic systems has been described (1 - 4) but few arylarylic compounds are known (5 - 6) : for example when pyrrole is one of the cycles, only 2-phenylpyrrole (7) and more recently 2-(2'-thienyl)pyrrole (8) have been described.

We present in this article a general method for the preparation of 2-arylpyrroles, based on the use of Hemetsberger reaction way (9), which can be schematized as follows :



1a to 5a Ar = phenyl
1b to 5b Ar = 2'-thienyl
1c to 5c Ar = 3'-thienyl
1d to 5d Ar = 2'-furyl
1e to 5e Ar = 3'-furyl

To 50 ml of sodium methanolate (prepared by starting from 50 ml of MeOH and 6.10^{-2} at. g. of Na), a mixture of 10^{-2} M. of β-arylacrolein and 6.10^{-2} M. of methyl azidoacetate was added dropwise. After addition and stirring for an additional 1 h at - 10°C, water was added to the solution and the azide obtained, 2, was extracted with ether (some azides are unstable and spontaneously tend to cyclize to the esters 3). The azide 2 was refluxed in xylene, yielding quantitatively the ester 3. It is worth noting that the cyclisation systematically concerns the carbon atom 5 of the lateral chain but not the carbon in ortho position to the chain, so that the formation of an ester of structure 6 has never been observed.



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Hydrolysis (aqueous solution of KOH 12 %) of the ester 3, followed by decarboxylation of the acid 4 (with baryum promoted copper chromite as catalyst in quinoleine) leads to 2-arylpyrrole 5 with a satisfactory global yield.

The yields of the various reactions so as the melting points of the synthesized products are summarized in table I.

Table I

Ar	Transformations / Starting products	1i → 2i		2i → 3i		3i → 4i		4i → 5i	
		Yd	m.p.	Yd	m.p.	Yd	m.p.	Yd	m.p.
phenyl	1a	75	56	92	146	78	178	65	130*
2'-thienyl	1b	72	62	90	113	75	174	46	72**
3'-thienyl	1c	78	52	87	160	89	192	57	154
2'-furyl	1d	76	44	90	126	79	160	68	44
3'-furyl	1e	52	68	92	140	79	190	43	72

*m.p. Litt (7) : 127 - 132°C ;**m.p. Litt (8) : 62°C. Yd : yield %.

The mass spectra of 2-arylpyrroles have been studied, the main fragments are the following :

5a m/e : 143 $[100, M^{+\cdot}]$, 117 $[14, (M - C_2H_2)^{+\cdot}]$, 116 $[50, (M - HCN)^{+\cdot}$ and $(M - C_2H_3)^{+}]$, 115 $[40, (M - CH_2N)^{+}]$

5b m/e : 149 $[100, M^{+\cdot}]$, 122 $[7, (M - HCN)^{+\cdot}$ and $(M - C_2H_3)^{+}]$, 121 $[15, (M - CH_2N)^{+}]$, 104 $[17, (M - CHS)^{+}]$

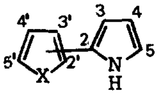
5c m/e : 149 $[100, M^{+\cdot}]$, 122 $[20, (M - HCN)^{+\cdot}$ and $(M - C_2H_3)^{+}]$, 121 $[32, (M - CH_2N)^{+}]$, 104 $[23, (M - CHS)^{+}]$

5d m/e : 133 $[100, M^{+\cdot}]$, 105 $[9, (M - CH_2N)^{+}$ and $(M - CO)^{+\cdot}]$, 104 $[63, (M - CHO)^{+}]$

5e m/e : 133 $[100, M^{+\cdot}]$, 105 $[13, (M - CH_2N)^{+}$ and $(M - CO)^{+\cdot}]$, 104 $[79, (M - CHO)^{+}]$

In all cases, the molecular peak is the base peak and the characteristic fragmentation patterns of the pyrrolic (C_2H_2, HCN, $C_2H_3^{\cdot}$ and $CH_2N^{\cdot}$), thiophenic (C_2H_2, $CHS^{\cdot}$) and furanic ($CHO^{\cdot}$) cycles are observed.

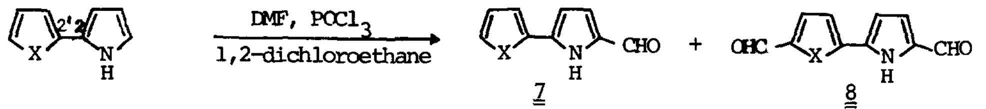
The NMR characteristics of the 2-arylpyrroles obtained are listed in table II :

Table II : NMR data of the 2-arylpyrroles, 5  (solvent $(CD_3)_2SO$).

X	Carbon aton of Ar bounded to pyrrole	Compounds	PROTONS																	
			THIOPHFNIC OR FURANIC										PYRROLIC							
			$H_{2'}$		$H_{3'}$		$H_{4'}$		H_5'		Spectrum	J(Hz)	H_3		H_4		H_5		Spectrum	J(Hz)
			m/i	δ	m/i	δ	m/i	δ	m/i	δ			m/i	δ	m/i	δ	m/i	δ		
S	2'	5b			2d/1	7 16	2d/1	7.02	2d/1	7 27	A M X	$J_{3'4'}$= 3.6 $J_{3'5'}$= 1.3 $J_{4'5'}$= 5 0	2d/1	6.28	2d/1	6.09	2d/1	6.79	A M X	J_{34}= 3.5 J_{35}= 1.5 J_{45}= 2 7
S	3'	5c		7 44				7 35		7 48	A B C	$J_{2'4'}$= 1.3 $J_{2'5'}$= 2 8 $J_{4'5'}$= 4 8	2d/1	6.35	2d/1	6 06	2d/1	6 75	A M X	J_{34}= 3 4 J_{35}= 1 5 J_{45}= 2.7
O	2'	5d				6.50		6 47		7.52	A B X	$J_{3'4'}$= 3 3 $J_{3'5'}$= 0 7 $J_{4'5'}$= 1 8	2d/1	6.31	2d/1	6 08	2d/1	6 79	A M X	J_{34}= 3 4 J_{35}= 1 5 J_{45}= 2 6
O	3'	5e	2d/1	7.86			2d/1	6.76	2d/1	7.64	A M X	$J_{2'4'}$= 0.8 $J_{2'5'}$= 1 6 $J_{4'5'}$= 1.8	2d/1	6 26	2d/1	6 07	2d/	6 76	A M X	J_{34}= 3 3 [illegible] J_{45}= [illegible]

The NMR data of 2-phenylpyrrole are in good agreement with those of the litterature (10) and - for all the compounds - the pyrrolic protons give an A M X system. The A B X and A B C systems due to the thiophenic and furanic protons observed for 5d and 5c have been interpreted by a comparison with the calculated spectra (11).

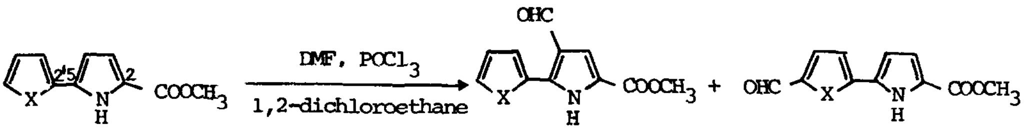
The Vilsmeier formylation of the 2-(2'-thienyl and 2'-furyl) pyrroles and of the methyl 5-(2'-thienyl and 2'-furyl) pyrrole-2-carboxylates has been studied. The results can be schematized as shown below :



7 8

X = S, O

X = O : m.p.(°C)=106 ; Yd=62% m.p.(°C)=218–220; Yd=14%
X = S : m.p.(°C)=166–168; Yd=85%



9 10

X = S, O

X = O : m.p.(°C)=192 ; Yd=88%
X = S : m.p.(°C)=176 ; Yd=85% m.p.(°C)=234–236; Yd= 5%

5-[2'-(5'-formyl)furyl] pyrrole-2-carbaldehyde will be made to react with a series of pyrromethane-5,5' dicarboxylic acids, in order to obtain "isocorrins", for which we plan to test the possibilities of coordination to metals.

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