

Reaction of 2-benzoyl-1,2-dihydroisoquinoline-1-carbonitrile tetrafluoroborate salt with 2-arylmethylene-1,3-indanediones. Regio- and stereochemistry of the reaction. Formation of spiro compounds[†]

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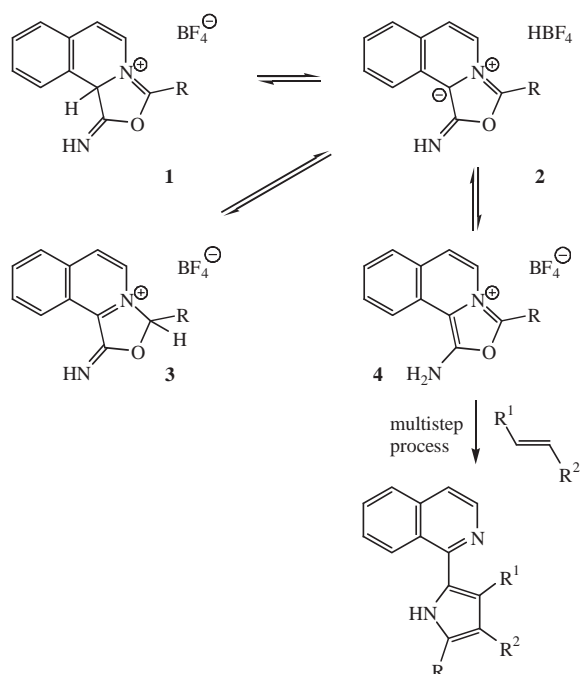
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The regio- and stereochemistry of spiro-adducts derived from [4+2] cycloaddition between the title compounds were deduced by ¹H NMR data and the elucidated structure of the tetrasubstituted pyrroles obtained by acidic hydrolysis.

Keywords: isoquinolines, Reissert compounds, pyrroles, spiro compounds

Previous studies^{1,2} have established that solutions of tetrafluoroborate salts of 2-acyl-1,2-dihydroisoquinoline-1-carbonitriles (Reissert compounds) exist as equilibrium mixtures of **1-4**, with **4** being the major component (Scheme 1). According to McEwen and coworkers², acid-catalysed condensation-rearrangement of these salts with alkenes afford substituted 2-(1-isoquinolinyl)pyrroles **5** (Scheme 1). The initial step of this process is a Diels-Alder reaction involving **4** as the heterodiene.²⁻⁴

As a part of the research of our group on the reactivity of the tetrafluoroborate salts of Reissert compounds,³⁻⁵ we report

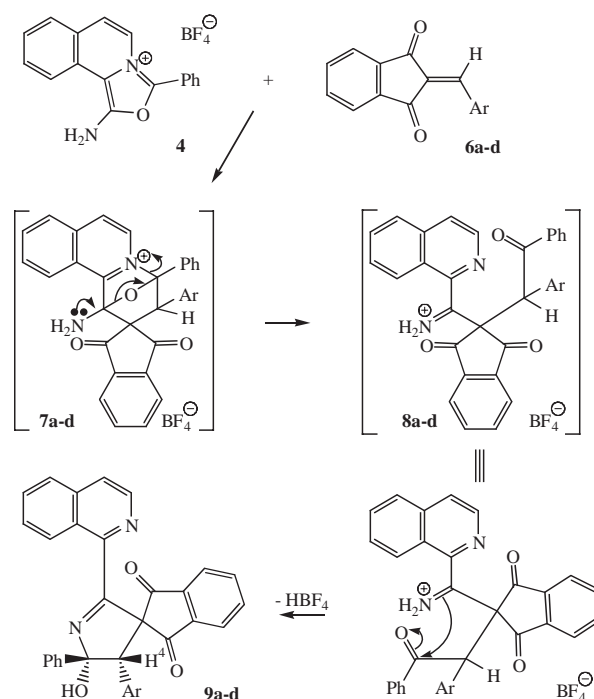


Scheme 1 Cycloaddition to Reissert compound tetrafluoroborates

here the reaction of a tetrafluoroborate salt **1-4** (R = Ph) with some 2-arylmethylene-1,3-indanediones **6a-d**. To our knowledge, the only published study of the dienophilic reactivity of enones with a Reissert salt was our own previous report.⁴

According to the results of McEwen *et al.*² and to previous work of our group,³⁻⁵ spiro[4-aryl-5-hydroxy-2-(1-isoquinolinyl)-5-phenyl-4,5-dihydro-3*H*-pyrrole-3:2'-1',3'-indanediones] **9** result from the initial Diels-Alder reaction of the heterodiene **4** (R = Ph), followed by a rearrangement sequence involving the intermediate species **7** and **8** (Scheme 2).

Determination of the structure of compounds **9** has enabled us to establish the regio- and stereochemistry of the reaction. The regiochemistry of the reaction corresponds to that which is usually observed²⁻⁵ in the case of a dienophilic alkene activated by an electron-withdrawing group: this group is always



Scheme 2 Formation of the spiro-pyrrolines **9**. a, Ar = Ph; b, Ar = *p*-C₆H₄CH₃; c, Ar = *p*-C₆H₄OCH₃; d, Ar = *p*-C₆H₄NO₂.

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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

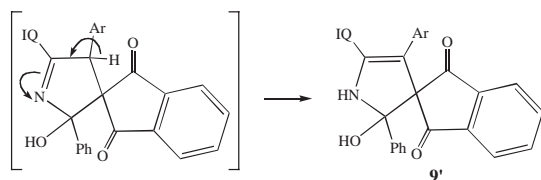
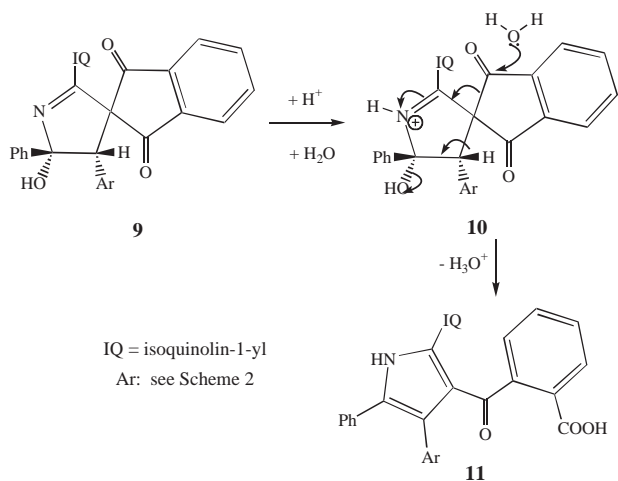


Fig. 1 Hypothetical formation of **9'** from, reverse cycloaddition mode.



Scheme 3 Formation of the pyrroles **11**.

found at the 3-position of the resulting pyrrole. In the case of the reverse regiochemistry, the product from the initial cycloadduct would be a 4,5-dihydropyrrole **9'** (Fig. 1) and the presence of the pyrroline NH should be easily characterised by IR and ^1H NMR spectroscopy.

Moreover, the observation of a long range coupling $^4J = 0.90 - 1.45$ Hz between OH and H^4 allows us to propose a

trans-pseudoaxial conformation for OH and H^4 in order to attain the W disposition.⁴⁻⁶ This proposition was confirmed on the one hand by a decoupling double-irradiation experiment, and on the other hand by the disappearance of the signal of the OH proton after addition of D_2O , whereupon the signal of the H^4 proton became a singlet. It is in good agreement with the more thermodynamically stable *trans*-disubstitution for the two 4- and 5-aryl groups.

Refluxing compounds **9** in an AcOH : HCl 12N (10:1) mixture yields quantitatively products **11** (Scheme 3). Acid-promoted dehydration is followed by the attack of a water molecule on the ring of the indanedione. The acid-catalysed isomerisation of the strained spiro compounds **9** thus gives the more stable pyrroles **11** in good yield. Elemental analysis, IR, ^1H , ^{13}C NMR data are in good agreement with the proposed structures.

Experimental

Melting points were determined on a Kofler bank. IR spectra were recorded from KBr pellets (5% dispersion) with a Vector 22 spectrometer; only structurally important peaks (ν) are reported. NMR spectra were recorded with a Bruker-Spectrospin AC 250 spectrometer operating at 250 MHz for ^1H and 62.9 MHz for ^{13}C . The NMR solvents were CDCl_3 for the compounds **6**, $\text{DMSO}-d_6$ for the spiro-compounds **9**, and $\text{C}_5\text{D}_5\text{N}$ for the pyrroles **11**. Elemental analyses were performed by the Microanalysis Center of Claude Bernard University (Lyon I Vernaison). The tetrafluoroborate **4** ($\text{R} = \text{Ph}$) was prepared according to the literature.²⁻⁵

2-Benzylidene-1,3-indanediones 6: These compounds were obtained by an adaptation of a published procedure.⁷ *General procedure:* 1,3-Indanedione (20 mmoles) and the arylaldehyde (20 mmol) in toluene (50 ml) were refluxed 24 hrs with a catalytic amount of *p*-toluenesulfonic acid, removing water using a Dean-Stark apparatus. The reaction mixture was poured into water (100 ml) and extracted with ether (3×50 ml). The organic phase was washed with water (3×50 ml) and dried over anhydrous Na_2SO_4 . The solvents were evaporated off and the residue dissolved into and crystallised from 50 ml of an ethanol : toluene (50 : 50) mixture. The products (**6a-d**) agreed in melting-points and IR and NMR spectra with data previously published.^{7,8}

Table 1 Physical and spectroscopic data of the spiro[4-aryl-5-hydroxy-2-(1-isoquinolinyl)-5-phenyl-4,5-dihydro-3H-pyrrole-3:2'-1',3'-indanediones] **9**

Compound	Ar	M.p./ °C	yield /%	IR/ cm^{-1}			^1H NMR / ^{13}C NMR/ δ ppm	
				$\nu_{\text{C=O}}$	$\nu_{\text{C=N}}$	ν_{OH}		
9a	C_6H_5	228	65	1739, 1692	1611	3381	3.94 (d, 1H, $^4J = 0.90$, H4); 6.49 (br.s., 1H, OH); 7.05–9.81 (m, 20 arom. H) 63.3 (C^4); 77.85 ($\text{C}^{3,2}$); 103.9 (C^5); 122.65–173.5 (23 sigs, C^2 and 27 ar. C); 197.75, 198.15 (2 C=O)	
9b	<i>p</i> - $\text{C}_6\text{H}_4\text{CH}_3$	238	60	1735, 1694	1611	3380	2.21 (s, 3H, CH_3); 3.93 (d, 1H, $^4J = 1.15$, H4); 6.44 (br.s., 1H, OH); 6.86–9.82 (m, 19 arom. H) 20.25 (CH_3); 63.0 (C^4); 77.7 ($\text{C}^{3,2}$); 103.85 (C^5); 122.6–173.45 (21 sig., C^2 , 27 ar. C); 196.9, 198.3 (2 C=O)	
9c	<i>p</i> - $\text{C}_6\text{H}_4\text{OCH}_3$	223	70	1733, 1686	1610	3402	3.58 (s, 3H, OCH_3); 3.93 (d, 1H, $^4J = 1.45$, H4); 6.47 (br.s., 1H, OH); 6.62–9.85 (m, 19 arom. H) 54.65 (OCH_3); 62.65 (C^4); 77.75 ($\text{C}^{3,2}$); 103.75 (C^5); 122.6–173.5 (21 sigs, C^2 , 27 ar. C); 196.9, 198.3 (2 C=O)	
9d	<i>p</i> - $\text{C}_6\text{H}_4\text{NO}_2$	226	58	1738, 1706	1600	3413	4.10 (d, 1H, $^4J = 1.05$, H4); 7.70 (br.s., 1H, OH); 7.31–9.87 (m, 19 arom. H) 62.7 (C^4); 78.65 ($\text{C}^{3,2}$); 104.15 (C^5); 122.35–173.15 (21 sig C^2 , 27 ar. C); 195.90, 197.80 (C=O)	

Table 2 Physical and spectroscopic data of the 2-[[4-aryl-2-(1-isoquinolinyl)-5-phenylpyrrol-3-yl]carbonyl]benzoic acids **9**

Compound	Ar	M.p./ °C	yield /%	IR/ cm^{-1}			^1H NMR / ^{13}C NMR/ δ ppm	
				$\nu_{\text{C=O}}$	ν_{NH}	ν_{COOH}		
11a	C_6H_5	248	93	1688, 1651	3208	2750–3700	6.57–8.67 (m, 20 arom. H and OH); 13.22 (s, 1H, NH) 120.75–154.45 (27 signals for 31 arom. C); 169.2 (C=O) _{acid} ; 192.4 (C=O)	
11b	<i>p</i> - $\text{C}_6\text{H}_4\text{CH}_3$	252	94	1701, 1654	3200	2600–3650	2.17 (s, 3H, CH_3); 6.83–8.66 (m, 19 arom. H and OH); 13.15 (s, 1H, NH) 21.1 (CH_3); 120.70–154.75 (27 signals for 31 arom. C); 169.15 (C=O) _{acid} ; 192.45 (C=O)	
11c	<i>p</i> - $\text{C}_6\text{H}_4\text{OCH}_3$	245	94	1700, 1640	3223	2500–3700	3.60 (s, 3H, OCH_3); 6.60–8.66 (m, 19 arom. H and OH); 13.15 (s, 1H, NH) 55.1 (OCH_3); 113.90–158.85 (27 signals for 31 arom. C); 169.2 (C=O) _{acid} ; 192.55 (C=O)	
11d	<i>p</i> - $\text{C}_6\text{H}_4\text{NO}_2$	261	96	1690, 1640	3300	2400–3600	7.17–8.66 (m, 19 arom. H and OH); 13.47 (s, 1H, NH) 121.0–153.75 (27 signals for 31 arom. C); 169.05 (C=O) _{acid} ; 192.5 (C=O)	

Table 3 Analytical data of compounds **9a-d** and **11a-d**

Compound	Molecular formula	Found/calc. (%)		
		C	H	N
9a	C ₃₃ H ₂₂ N ₂ O ₃	80.16	4.45	5.67
		80.04	4.53	5.42
9b	C ₃₄ H ₂₄ N ₂ O ₃	80.31	4.72	5.51
		80.54	4.73	5.42
9c	C ₃₄ H ₂₄ N ₂ O ₄	77.86	4.58	5.34
		78.04	4.63	5.12
9d	C ₃₃ H ₂₁ N ₃ O ₅	73.33	4.07	7.77
		73.15	4.13	7.82
11a	C ₃₃ H ₂₂ N ₂ O ₃	80.16	4.45	5.67
		80.34	4.33	5.57
11b	C ₃₄ H ₂₄ N ₂ O ₃	80.31	4.72	5.51
		80.71	4.63	5.48
11c	C ₃₄ H ₂₄ N ₂ O ₄	77.86	4.58	5.34
		77.84	4.73	5.42
11d	C ₃₃ H ₂₁ N ₃ O ₅	73.33	4.07	7.77
		73.25	4.13	7.92

Spiro[4-aryl-5-hydroxy-2-(1-isoquinolinyl)-5-phenyl-4,5-dihydro-3H-pyrrole-3:2'-1',3'-indanediones] 9: *General procedure*: Each enone **6** (0.5 g) was dissolved in DMF (20 ml) in a 100 ml Erlenmeyer flask. The tetrafluoroborate **4** (R = Ph) (0.6 g) was added and the mixture was magnetically stirred at 50°C. When all the salt **4** was dissolved, the reaction mixture was poured onto crushed ice. After filtration, the solid was washed with water. The obtained products **9** were crystallised from an ethanol : toluene (95 : 5) mixture (Table 1). Analytical data are listed in Table 3.

4-Aryl-2-(1-isoquinolinyl)-3-o-carboxybenzoyl-4-phenylpyrroles 11: *General procedure*: Each spiro-compound **9** (0.5 g) was dissolved in acetic acid (15 ml) and 12N HCl (three drops) were added. The mixture was refluxed 4 hrs and then poured into iced water. The obtained solid pyrrole **11** was crystallised from an ethanol : toluene (95 : 5) mixture (Table 2). Analytical data are listed in Table 3.

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