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SYNTHESIS OF 1*H*-[1]BENZOPYRANO[4,3-*b*]PYRROLE AND 4*H*-THIENO[3,2-*c*][1]BENZOPYRAN DERIVATIVES. FUNCTIONALISATION BY AROMATIC ELECTROPHILIC SUBSTITUTION

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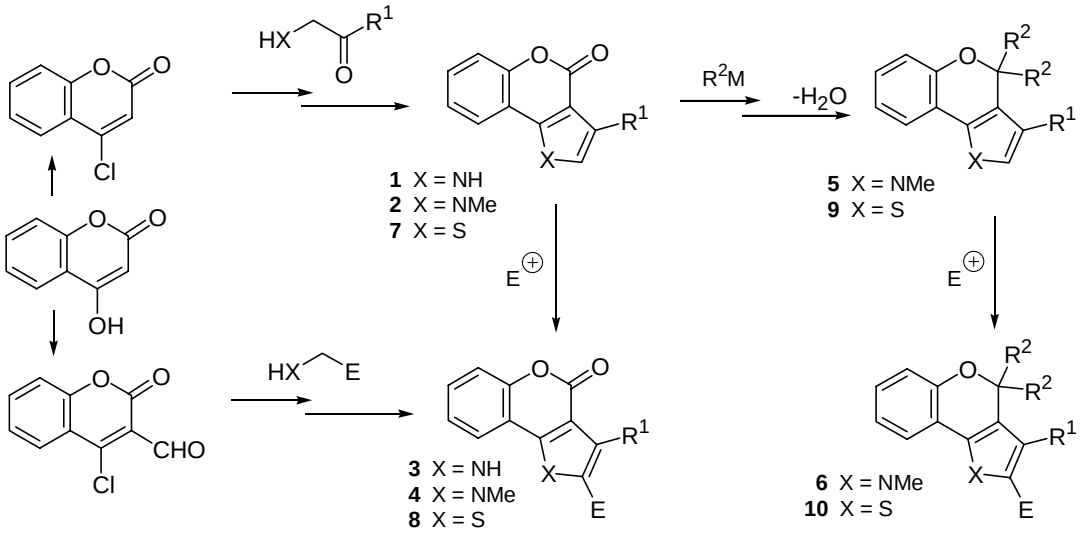
Abstract – 4,4-dialkyl-1*H*-[1]benzopyrano[4,3-*b*]pyrroles were prepared starting from [1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-ones and organometallic reagents. Subsequently, both types of polycyclic compound and their analogous 4*H*-thieno[3,2-*c*][1]benzopyrano derivatives were functionalized at C-2 by aromatic electrophilic substitution (bromination, nitration, acetylation and formylation).

In previous studies[1-3] we have described synthetic methods for preparing [1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-ones (**1-4**) by Knorr or Fischer-Fink type reactions starting from 4-chlorocoumarin or 4-chloro-3-formylcoumarin (Scheme 1).



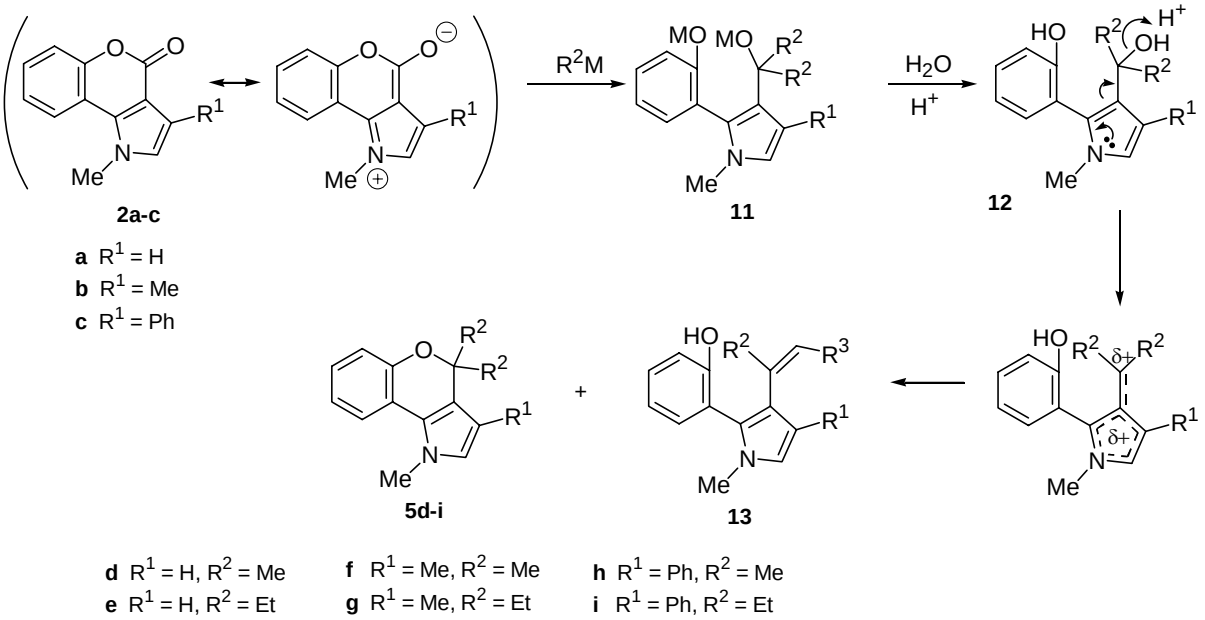
Scheme 1

In this paper, we report the transformation of **2** to 1*H*-[1]benzopyrano[4,3-*b*]pyrroles (**5**) by reaction with organometallic compounds and the incorporation of new functions by aromatic electrophilic substitution in **1**, **2** and **5** to give **3**, **4** and **6**, respectively. We have, thus, completed a comprehensive project regarding different alternative paths for the synthesis of pyrroles fused to coumarins or chromenes starting from 4-hydroxycoumarin as an only remote precursor. Furthermore, due to the pharmacological interest which the thiophenes fused to 1-benzopyrans possess,[4] in this paper we have included and compared aromatic electrophilic substitutions in 4*H*-thieno[3,2-*c*]benzopyrano derivatives (**7**) and (**9**) which present structures referable to **2** and **5**.

REACTION OF [1]BENZOPYRANO[4,3-*b*]PYRROL-4(1*H*)-ONES (2) WITH ORGANO-METALLIC REAGENTS. SYNTHESIS OF 1*H*-[1]BENZOPYRANO[4,3-*b*]PYRROLES (5).

Grignard and organolithium reagents

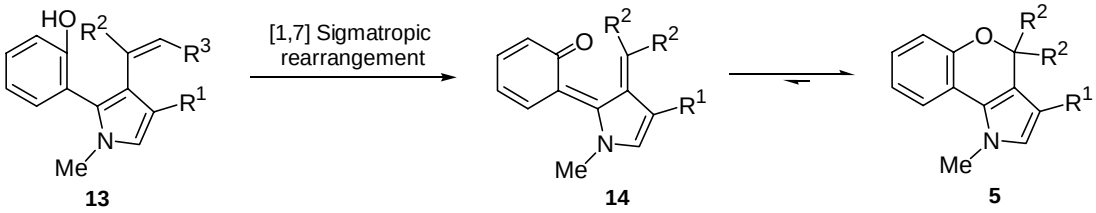
The [1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-ones (**2**) reacted with Grignard and organolithium reagents *via* a 1,2 double addition (Scheme 2) in a similar manner to other coumarins.[5-8] As a differential characteristic, we should point out that the electron-donating character of the fused pyrrole decreased the reactivity of the lactone and, on the other hand, increased the reactivity and instability of the reaction products.



Scheme 2

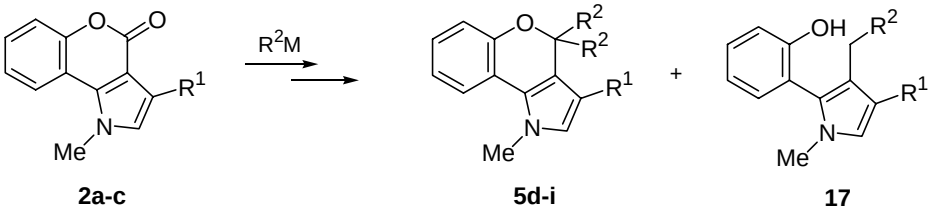
The deactivation of the carboxylate group toward the attack of the organometallic reagents meant that the solvent (tetrahydrofuran, ether or toluene) acquired a greater influence than that expected. In fact, it was the tetrahydrofuran in which **2** was most easily transformed to the intermediate (**11**)**.** Conversely, the high reactivity and instability of the 3-hydroxymethylpyrrole derivatives (**12**), resulting from the hydrolysis of

11, did not allow their isolation and purification.They were easily dehydrated to the olefins (**13**) and the expected 4,4-dialkyl-1*H*-[1]benzopyrano[4,3-*b*]pyrroles (**5**). The formation of the olefins (**13**) was not a synthetic limitation for the preparation of 4,4-dialkyl-1*H*-[1]benzopyrano[4,3-*b*]pyrroles (**5**), given that when **13** was heated to 150 °C, it was transformed to **5,** presumably *via* a [1,7] sigmatropic rearrangement followed by an electrocyclic reaction[9,10] (Scheme 3). In short, the experimental procedure consisted in the reaction of **2** with organometallic reagents, hydrolysis, heating of the reaction concentrates and the final purification of **5**. The optimum yields are shown in Table 1.



Scheme 3

Table 1 Reaction of [1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-ones (**2a-c**) with organometallic reagents

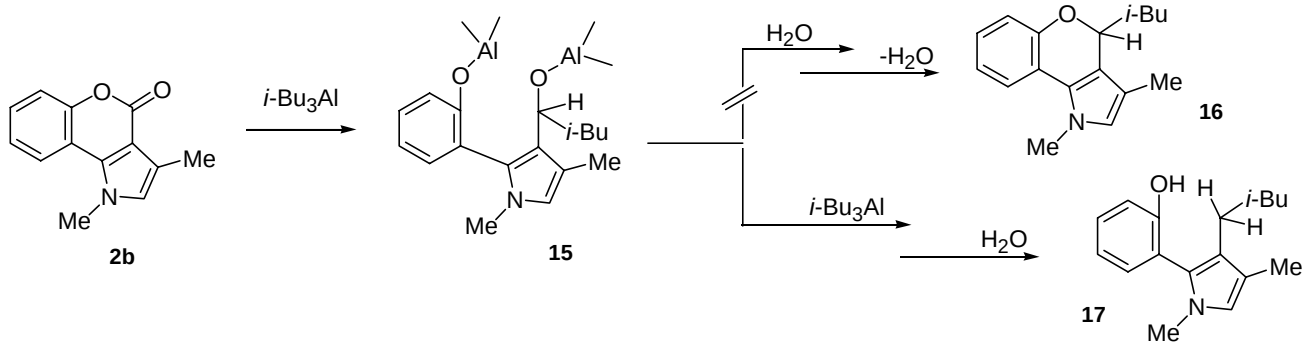


Starting	R^2M	R^1	R^2	Compound	Yield (%)
2a	MeLi	H	Me	**5d**	25
2a	MeMgI	H	Me	**5d**	72
2a	Me_3Al	H	Me	**5d**	40
2a	EtMgBr	H	Et	**5e**	81
2a	Et_3Al	H	Et	**5e**	28
2b	MeMgI	Me	Me	**5f**	73
2b	EtMgBr	Me	Et	**5g**	83
2b	*i*-Bu_3Al	Me	*i*-Bu	**17**	88
2c	MeLi	Ph	Me	**5h**	77
2c	MeMgI	Ph	Me	**5h**	80
2c	Me_3Al	Ph	Me	**5h**	42
2c	EtMgBr	Ph	Et	**5i**	62

Organoaluminum Compounds

The triorganoaluminum compounds, which in their reaction with coumarins[11,12] show a reductive power greater than that of the Grignard reagents, deserve a special mention.

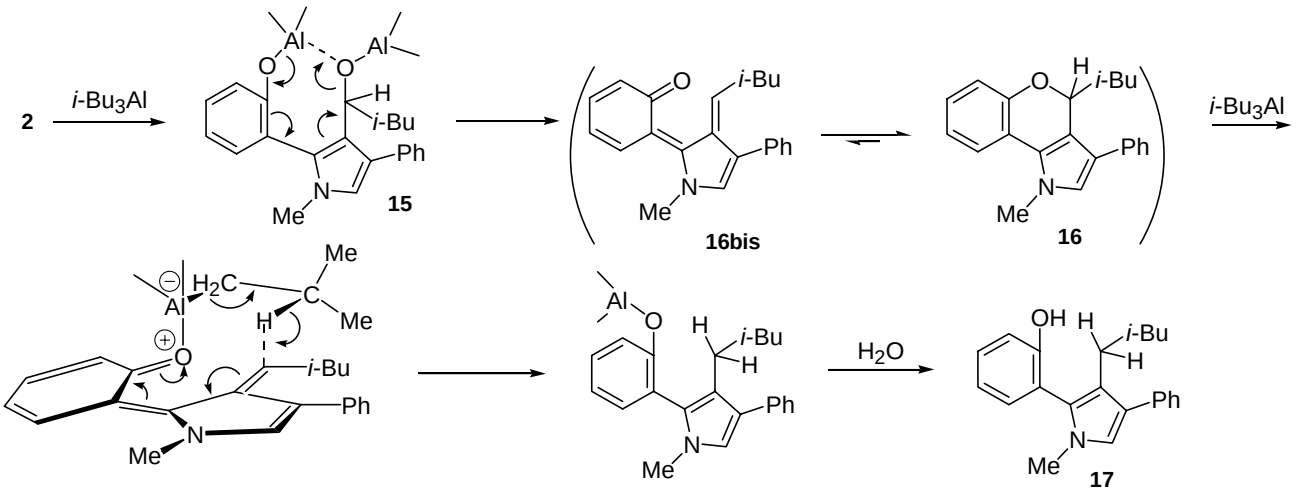
In the first place, we should point out that the reactivity of **2** towards the organoaluminum compounds was very low in electron-donating solvents (tetrahydrofuran or ether), and that the use of toluene at 80-100ºC was necessary in order to obtain the total transformation of the substrate. In the above conditions, the trimethylaluminum, which does not possess a reductive character, only yielded 40-42% of 4,4-dimethylbenzopyran derivatives (**5d** 40%, **5h** 42%). The triethylaluminum, with a greater reductive power, led to complex reaction mixtures in which the yields of 4,4-dialkylbenzopyrans were even lower (28-30%). Starting from triisobutylaluminum, a reagent with greater steric demands and with a strong reductive power, we tried to obtain the corresponding 4-monoalkyl-1-benzopyrano[4,3-*b*]pyrrole (**16**), but the process was not detained at the intermediate (**15**) and evolved toward the compound (**17**) (88%), resulting from one alkylation and two reductions which does not occur with other coumarins (Scheme 4).



Scheme 4

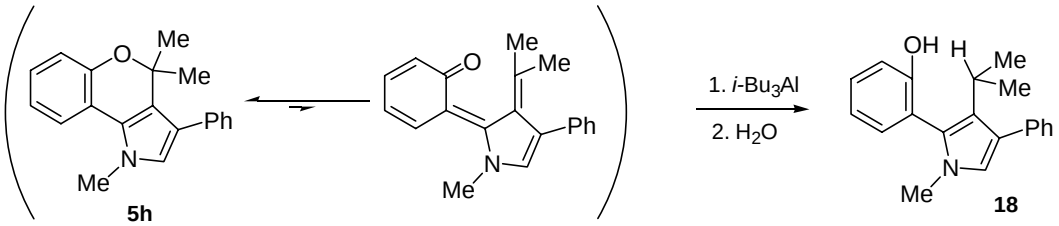
The preparation of alkylpyrroles starting from ethoxycarbonylpyrroles and metal hydrides has been described exclusively for *N*-unsubstituted pyrroles which are capable of *N*-deprotonating and evolving by means of an azafulvene intermediate.[13] This path, consequently, would not be appropriate for our *N*-substituted pyrroles. Among the many possible alternatives for the formation of **17,** in Scheme 5 we describe a hypothetical mechanism which takes into account both the high reactivity of the hydroxymethylpyrroles in the presence of Lewis acids (e.g. R_3Al) as well as the reaction of organometallic compounds with *o*-quinonemethide structures in equilibrium with 2*H*-1-benzopyrans.[14,15]

In our case, the intermediate (**15**) would experience aluminoxane elimination giving the *o*-quinone-methide (**16bis**) (in equilibrium with the benzopyran (**16**)), which would be reduced toward **17** in the presence of triisobutylaluminum.



Scheme 5

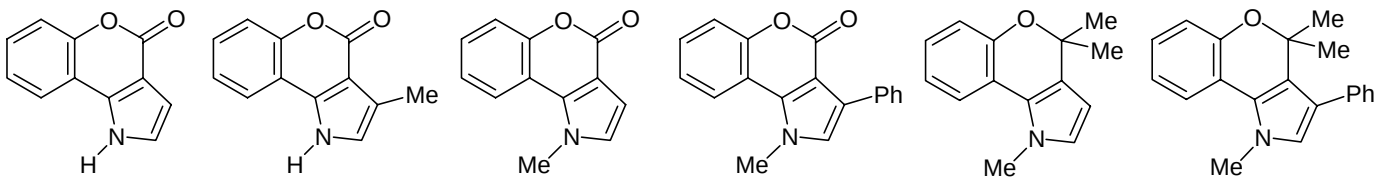
Although this can not be considered as conclusive proof, the previous hypothesis was supported by a complementary experiment in which the 3-phenyl-1,4,4-trimethyl-4*H*-[1]benzopyrano[4,3-*b*]pyrrole (**5h**) was directly transformed to **18** by reaction with triisobutylaluminum in toluene at 100 °C (Scheme 6).



Scheme 6

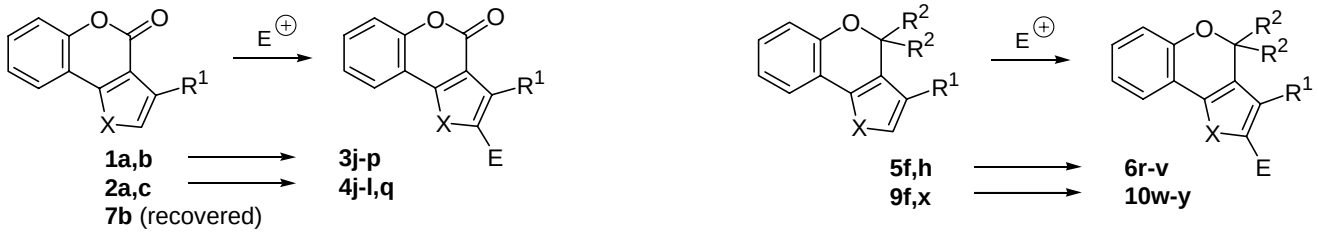
AROMATIC ELECTROPHILIC SUBSTITUTION IN 1*H*-[1]BENZOPYRANO[4,3-*b*]PYRROLES (5) AND [1]BENZOPYRANO[4,3-*b*]PYRROL-4(1*H*)-ONES (1 AND 2).

We selected six different substrates (Scheme 7) which underwent bromination, nitration, acetylation and formylation. The series of experiments provided interesting information regarding the stability of the polyheterocyclic system, the substitution regiochemistry and the scope of the synthetic method.



Scheme 7

Table 2 Aromatic Electrophilic Substitution



Starting	Reactant-Solvent	Temp. °C	Time (h)	X	R^1	R^2	E	Product	Yield (%)
1a	NBS-AcOH	20	4	NH	H	-	Br	**3j**	10[a]
1a	HNO_3-Ac_2O	-5	5	NH	H	-	NO_2	**3k**	65
1a	Ac_2O/$TiCl_4$-Ac_2O	20	24	NH	H	-	Ac	**3l**	10
1a	$POCl_3$/DMF-CH_2Cl_2	20	5	NH	H	-	CHO	**3m**	81
1b	NBS-AcOH	20	2	NH	Me	-	Br	**3n**	52
1b	HNO_3-Ac_2O	-5	4	NH	Me	-	NO_2	**3o**	53
1b	$POCl_3$/DMF-CH_2Cl_2	20	2	NH	Me	-	CHO	**3p**	82
2a	NBS-AcOH	20	10	NMe	H	-	Br	**4j**	78[b]
2a	HNO_3-Ac_2O	-5	4	NMe	H	-	NO_2	**4k**	89
2a	Ac_2O/$TiCl_4$-Ac_2O	20	48	NMe	H	-	Ac	**4l**	72
2c	Ac_2O/$TiCl_4$-Ac_2O	20	12	NMe	Ph	-	Ac	**4q**	75
5d	...[c]			NMe	H	Me	Br	-	0
5d	HNO_3-Ac_2O	-5	1	NMe	H	Me	NO_2	**6r**	18
5d	Ac_2O/$TiCl_4$-Ac_2O	20	1	NMe	H	Me	Ac	**6s**	85[d]
5d	$POCl_3$/DMF-CH_2Cl_2	0	1	NMe	H	Me	CHO	**6t**	62
5h	...[c]			NMe	Ph	Me	Br	-	0
7b	...[e]			S	Me	-	...[e]	-	0
9f	NBS-AcOH	20	1	S	Me	Me	Br	**10u**	71[f]
9f	HNO_3-Ac_2O	-5	2	S	Me	Me	NO_2	**10v**	86[g]
9f	Ac_2O/$TiCl_4$-Ac_2O	20	1	S	Me	Me	Ac	**10w**	41
9f	$POCl_3$/DMF-CH_2Cl_2	20	1	S	Me	Me	CHO	**10x**	85
9y	$POCl_3$/DMF-CH_2Cl_2	20	1	S	H	H	CHO	**10z**	25

[a] 2,3-Dibromo-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (**19**) was isolated (<5%). [b] 2,3-Dibromo-1-methyl-[1]benzopyrano-[4,3-*b*]pyrrol-4(1*H*)-one (**20**) was isolated (<10%). [c] The substrate was degraded in all the conditions employed. [d] 3-Acetyl-1,4,4-trimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (**21**) was isolated (<5%). [e] The substrate was recovered practically untransformed in the bromination, acetylation nitration and formylation reactions. [f] 2,8-Dibromo-3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (**22**) was isolated (<5%). [g] 2,8-Dinitro-3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (**23**) was isolated (<5%).

The bromination (Br_2/AcOH or NBS/AcOH) was without doubt the process in which the substrates showed the greatest instability and in which the results depended decisively on the reaction conditions (temperature and electrophilic equivalents) and on the pyrrole ring substituents. Thus, when starting from pyrroles (**5**), degradation exclusively occurred. But, starting from pyrroles (**1**) and (**2**), with an electron withdrawing group (-COO-), we were able to prepare the corresponding bromo derivatives, obtaining better yields with NBS/AcOH than with Br_2/AcOH. In these last two series, the stability of the substrates and the yield of the processes increased with the presence of additional substituents, above all if they were located at N-1 (e.g.: NH**,** R^1 = H, **3j** 10%; NH, R^1 = Me, **3n** 52%; NMe, R^1 = H, **4j** 78%;). Although with slightly less influence than in the bromination, the stability of the heterocycle and the rigorous control of the reaction conditions were also decisive in the nitrations (-5°C, HNO_3/Ac_2O) and in the acetylations (20°C, $Ac_2O/TiCl_4$). On the other hand, the Vilsmeyer reagent (20°C, $POCl_3$/N,N-DMF) was without doubt the least aggressive of all and with which even the most unstable pyrroles (*N*-unsubstituted pyrroles, series **1**) were formylated with good yields.

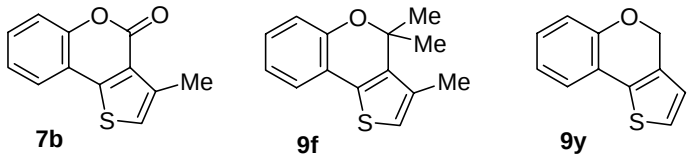
The electrophile always attacked the pyrrole ring and we were unable to confirm that it occurred in the 3-phenyl substituent (in **2c**) or in the fused benzene ring. Starting from the substrates (**1a**, **2a** and **5d**), unsubstituted at the positions C-2 and C-3, we verified that the substitution took place preferentially or exclusively at C-2. In fact, only in the acetylation of **5d** was 3-acetyl-1,4,4-trimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (**21**, <5%) isolated, resulting from the exclusive attack at C-3. In all the cases, the position of the incorporated substituent was confirmed by NOES experiments. As often occurs in pyrroles, polybrominations in **1a** and **2a** were observed to give respectively 2,3-dibromo-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (**19**, <5%) and 2,3-dibromo-1-methyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (**20**, <10%). Nevertheless, the 2-bromo derivatives (**3j**) and (**3n**) were obtained as major products when an equivalent of the bromination reagent was used.

From a synthetic point of view, we can conclude that, with the exception of the bromination of **5f**, **5h** and **1a,** these compounds could be functionalised at C-2 by aromatic electrophilic substitution. In some cases (e.g. **3l** 10% or **6r** 18%) the low yield was due to the insolubility of the substrates and the impurities, which made their isolation and purification difficult.

AROMATIC ELECTROPHILIC SUBSTITUTION IN 4*H*-THIENO[3,2-*c*]BENZOPYRANS (9*)* AND THIENO[3,2-*c*]BENZOPYRAN-4(4*H*)-ONES (7).

In this last section three substrates have been studied: **7b, 9f** and **9y** (Scheme 8). The 3-methylthieno[3,2-*c*][1]benzopyran-4(4*H*)-one (**7b**) was prepared by cyclization of the 4-acetonylmercaptocoumarin in polyphosphoric acid.[16] The compound (**7b**) reacted with methylmagnesium iodide to give 3,4,4-trimethyl-

4*H*-thieno[3,2-*c*][1]benzopyran (**9f**). 4*H*-Thieno[3,2-*c*][1]benzopyran (**9y**) was obtained by decarboxylation of the thieno[3,2-*c*][1]benzopyran-2(4*H*)-carboxylic acid.[17]



Scheme 8

The lower reactivity of the thiophene with respect to the pyrrole, together with the presence of the electron withdrawing group (-COO-), meant that the 3-methylthieno[3,2-*c*][1]benzopyran-4(4*H*)-one (**7b**) remained unaltered towards the electrophiles which did react with the pyrroles (**1**) or (**2**) analogues of **7b**. As for the 4*H*-thieno[3,2-*c*]benzopyrans (**9f**) and (**9y**), aromatic electrophilic substitution did occur at C-2 (bromination, nitration, acetylation and formylation) with moderate to good yields, with the exception of the formylation of **9y** which only reached 25%. From these results we would emphasise: a) that the greater stability of the polycyclic system meant that brominations were possible which in **5** gave rise to degradations; b) although the directing effect continued to appear especially at C-2, additional electrophilic substitutions were observed in low yield at the C-8 position of the fused benzene: 2,8-dibromo-3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (**22**)**,** <5%; 2,8-dinitro-3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (**23**)**,** <5%.

As a final comment we should point out that although our essential aim was synthetic, the different behavior of **1**, **3**, **5** and **7** which was observed in the aromatic electrophilic substitutions make these substrates a group of polycyclic systems in which the differences concerning the stability and reactivity existing between the pyrroles and the thiophenes are clearly shown to stand out.

EXPERIMENTAL

Melting points were measured on a Reichert-Jung Thermo Galen and are uncorrected. Boiling points correspond to the oven temperature in a Kugelrohr GKR-51. IR spectra were obtained on a Perkin Elmer 1720 X spectrophotometer. NMR spectra were recorded on a Bruker AC300 spectrometer, and chemical shifts are given downfield from $SiMe_4$ as an internal standard; ^{13}C-NMR spectra were carried out with complete ^{1}H decoupling and the assignments were made by additional DEPT experiments. MS spectra were measured on a Hewlett-Packard 5988A mass spectrometer.

The starting compounds (**1a**,**b**,[1] **2a-c**,[1] **7b**[16] and **9y**[17]) were synthesized by literature procedures.

Reaction of compounds 2a-c with organomagnesium or organolithium reagents. General procedure for the preparation of compounds (5d-i). To a magnetically stirred solution of [1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-ones (**2a-c**) (5 mmol) in dry THF (40 mL) at 20 ºC under nitrogen was added dropwise (30 min) the organometallic compound (20 mmol). At the end of the reaction, monitored by TLC (2-3 hours, Table 1), the mixture was hydrolized, extracted with CH_2Cl_2 (3 x 50 mL) and the extracts were washed with saturated aqueous $NaHCO_3$, and dried ($MgSO_4$). After removal of the solvent, the concentrate was heated at 150ºC for one hour and the residue was flash chromatographed on silica gel using CH_2Cl_2/pentane (1:3) as eluent. The following compounds were thus prepared.

1,4,4-Trimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5d). Yield 72%, mp 51-52 ºC (from hexane); IR(film) 1505, 1440, 1261, 1228, 1121, 1105, 930, 752, 691 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.56 (6H, s), 3.75 (3H, s), 5.88 (1H, d, *J* 2.7, H-3), 6.47 (1H, d, *J* 2.7, H-2) and 6.78-7.45 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 28.3 ($2CH_3$), 36.4 (CH_3), 77.6 (C), 101.9 (CH), 117.8 (CH), 119.0 (C), 119.8 (CH), 120.8 (CH), 122.3 (C), 124.7 (CH), 125.6 (C), 126.4 (CH) and 151.7 (C); *m/z* 213 (M^+, 16%) and 198 (100). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N 6.57. Found: C, 79.00; H, 6.95; N 6.42.

4,4-Diethyl-1-methyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5e). Yield 81%, mp 73-74 ºC (from hexane); IR(KBr) 1517, 1476, 1445, 1232, 1113, 934, 755, 693 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.93 (6H, t, *J* 7.4), 1.86 (4H, q, *J* 7.4), 3.91 (3H, s), 5.88 (1H, d, *J* 2.5, H-3), 6.59 (1H, d, *J* 2.5, H-2) and 6.87-7.44 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 8.4 ($2CH_3$), 32.0 ($2CH_2$), 36.9 (CH_3), 83.4 (C), 103.4 (CH), 117.3 (CH), 118.7 (C), 119.6 (CH), 120.3 (CH), 122.3 (C), 123.4 (C), 124.7 (CH), 126.4 (CH) and 152.5 (C); *m/z* 241 (M^+, 24%) and 212 (100). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N 5.80. Found: C, 79.48; H, 7.81; N 5.96.

1,3,4,4-Tetramethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5f). Yield 73%, mp 108 ºC (from hexane); IR(nujol mull) 1502, 1438, 1262, 1143, 770, 761 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.56 (6H, s), 2.06 (3H, s,), 3.75 (3H, s), 6.93 (1H, s, H-2) and 6.85-7.45 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 11.5 (CH_3), 28.1 ($2CH_3$), 36.3 (CH_3), 78.6 (C), 112.3 (C), 117.6 (CH), 119.0 (C), 119.8 (CH), 120.7 (CH), 122.7 (C), 123.6 (C), 124.2 (CH), 126.2 (CH) and 151.7 (C); *m/z* 227 (M^+, 29%) and 212 (100). Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54; N 6.16. Found: C, 79.42; H, 7.44; N 6.03.

4,4-Diethyl-1,3-dimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5g). Yield 83%, mp 55 ºC (from hexane); IR(nujol mull)1497, 1439, 1251, 1232, 1112, 940, 745, 732 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.88 (6H, t, *J* 7.2), 1.85 (4H, q, *J* 7.4), 1.99 (3H, s), 3.74 (3H, s), 6.88 (1H, s, H-2) and 6.87-7.42 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 8.3 ($2CH_3$), 11.1 (CH_3), 31.6 ($2CH_2$), 36.4 (CH_3), 83.9 (C), 111.3 (C), 116.4 (CH), 118.3 (C), 119.2 (C), 119.8 (CH), 120.4 (CH), 122.9 (C), 125.0 (CH), 126.0 (CH) and 152.1 (C); *m/z* 255 (M^+, 23%) and 226 (100). Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N 5.49. Found: C, 80.15; H, 8.39; N 5.24.

1,4,4-Trimethyl-3-phenyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5h). Yield 80%, mp 95-97 ºC (from hexane); IR(KBr); 1502, 1245, 1102, 745, 702 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.50 (6H, s), 3.90 (3H, s), 6.56 (1H, s, H-2) and 6.92-7.49 (9H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 28.4 ($2CH_3$), 36.6 (CH_3), 78.5 (C), 117.9 (CH), 119.2 (C), 120.4 (CH), 120.5 (C), 121.0 (CH), 123.0 (C), 123.1 (C), 124.2 (CH), 126.4 (CH), 126.8 (CH), 128.0 (2CH), 129.7 (2CH), 136.5 (C) and 151.5 (C); *m/z* 289 (M^+,18%) and 274 (100). Anal. Calcd for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N 4.84. Found: C, 82.85; H, 6.71; N 4.90.

4,4-Dimethyl-1-methyl-3-phenyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (5i). Yield 62%, mp 73-74 ºC (from hexane); IR(KBr) 1478, 1250, 935, 749, 740, 700 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.92 (6H, t, *J* 7.3), 1.84 (4H, q, *J* 7.3), 3.96 (3H, s), 6.59 (1H, s, H-2) and 6.94-7.56 (9H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 8.4 ($2CH_3$), 32.3 ($2CH_2$), 36.9 (CH_3), 84.2 (C), 117.8 (CH), 118.7 (C), 120.0 (CH), 120.1 (C), 120.3 (CH), 120.5 (C), 124.0 (C), 124.4 (CH), 126.5 (CH), 126.6 (CH), 127.8 (2CH), 129.7 (2CH), 136.7 (C) and 152.9 (C); *m/z* 317 (M^+, 6%) and 288 (100). Anal. Calcd for $C_{22}H_{23}NO$: C, 83.24; H, 7.30; N 4.41. Found: C, 83.06; H, 7.28; N 4.62.

3-(1-Ethylpropenyl)-2-(2-hydroxyphenyl)-1-methyl-4-phenylpyrrole (13i).[18] δ_H(300 MHz; DMSO-d_6) 0.72 (3H, t, *J* 7.6), 1.51 (3H, d, *J* 6.6), 1.96 (2H, m), 3.40 (3H, s) 5.21 (1H, q, *J* 6.6), 6.89 (1H,s), 6.72-7.51 (9H, m, Ar) and 9.30 (1H, br, OH).

Reaction of 3-methylthieno[3,2-*c*][1]benzopyran-4(4*H*)-one (7b) with methylmagnesium iodide. Preparation of 3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (9y).

By the previous procedure starting from 0.30 g (1.4 mmol) of 3-methylthieno[3,2-*c*][1]benzopyran-4(4*H*)-one (**7b**) and 5.6 mmol of methylmagnesium iodide, was obtained a reaction mixture which was chromatographed on silica gel using CH_2Cl_2/hexane (1:5) as eluent. 0.26 g (82%) of 3,4,4-trimethyl-4*H*-thieno[3,2-*c*][1]benzopyran (**9y**) was obtained as a pale yellow oil, bp 125 ºC at 1 mmHg. IR(film) 1581, 1488, 1460, 1253, 1132, 750 cm^{-1}. δ_H(300 MHz; DMSO-d_6) 1.58 (6H, s), 2.22 (3H, d, *J* 1.0), 6.88-7.30 (4H, m, Ar) and 7.05 (1H, d, *J* 1.0, H-2); δ_C(75.4 MHz; DMSO-d_6) 16.3 (CH_3), 27.4 ($2CH_3$), 79.4 (C), 116.6 (CH), 119.5 (C), 121.3 (CH), 121.6 (CH), 122.1 (CH), 128.5 (CH), 131.1 (C), 134.4 (C), 137.9 (C) and 150.2 (C); *m/z* 230 (M^+, 16%) and 215 (100). Anal. Calcd for $C_{14}H_{14}OS$: C, 76.01; H, 6.13. Found: C, 75.88; H, 6.27.

Reaction of compound (2b) with triisobuthylaluminum. Preparation of 2-(2-hydroxyphenyl)-1,4-dimethyl-3-(3-methylbutyl)pyrrole (17). A mixture of 1,3-dimethyl[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (**2b**) (1.065 g, 5 mmol) and triisobutylaluminum (12.5 mL, 2M in toluene, 25 mmol) in dry toluene (40 mL) at 100ºC was magnetically stirred for 1 h under nitrogen. It was them hydrolized, extracted with CH_2Cl_2 and the organic layer was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$) and

evaporated under reduced pressure. The residue was flash chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent to yield 1.131 g (88%) of 1,4-dimethyl-2-(2-hydroxyphenyl)-3-(3-methylbutyl)pyrrole (**17**) as a pale yellow oil, bp 150 ºC at 15 mmHg; IR(film) 3234, 1668, 1601, 1456, 1241, 754 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 0.75 (3H, d, *J* 6.5), 0.76 (3H, d, *J* 6.5), 1.26 (2H, m), 1.42 (1H, m), 2.07 (3H, s), 2.27 (2H, m), 3.29 (3H, s), 5.43 (1H, br, OH), 6.48 (1H, s) and 6.89-7.28 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 10.3 (CH_3), 22.2 (CH_3), 22.4 (CH_3), 22.7 (CH_2), 27.7 (CH_2), 33.7 (CH_3), 40.3 (CH_2), 115.0 (CH), 117.3 (C), 119.0 (C), 120.0 (CH), 121.2 (CH), 123.4 (C), 123.6 (C), 129.8 (CH), 131.9 (CH) and 154.5 (C); *m/z* 257 (M^+, 25%) and 200 (100). Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.01; N 5.44. Found: C, 79.15; H, 9.06; N 5.59.

Reaction of 1,4,4-trimethyl-3-phenyl-[1]benzopyrano[4,3-*b*]pyrrole (5h) with triisobutylaluminum. Preparation of 2-(2-hydroxyphenyl)-3-isopropyl-4-phenylpyrrole (18). By the previous procedure, starting from **5h** (0.578 g, 2 mmol) , was obtained 0.436 g (75%) of 2-(2-hydroxyphenyl)-3-isopropyl-4-phenylpyrrole (**18**) as a colorless oil. IR (film) 3369, 1683, 1457, 1388, 1285, 756, 701 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.05 (3H, d, *J* 7.1), 1.12 (3H, d, *J* 7.1), 3.05 (1H, m, *J* 7.1), 3.34 (3H, s), 5.31 (1H, br, OH), 6.77 (1H, s) and 6.99-7.46 (9H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 23.2 (CH_3), 24.2 (CH_3), 25.6 (CH), 33.8 (CH_3), 115.0 (CH), 119.9 (C), 120.1 (CH), 121.3 (CH), 122.8 (C), 124.2 (C), 125.8 (CH), 128.1 (2CH), 128.7 (C), 129.3 (2CH), 130.5 (CH), 132.8 (CH), 136.7 (C) and 154.9 (C); *m/z* 291 (M^+, 34%) and 276 (100).

Bromination of compounds (1, 2, 5, 7 and 9). General procedure. To a solution of **1a**,**1b**, **2a**, **5d**, **5h**, **7b,** or **9f** (2 mmol) in 10 mL of glacial acetic acid was added dropwise with stirring at rt under nitrogen a solution of *N*-bromosuccinimide (0.35 g, 2 mmol) in 8 mL of anhydrous glacial acetic acid. At the end of the reaction (monitored by TLC, see Table 2) the solution was poured into a mixture of ice-water (80 mL) and sodium hydroxide (13 g). The solution was decanted and extracted with ethyl acetate. The organic layer, after drying over $MgSO_4$, was concentrated at rt. The concentrate was chromatographed on silica gel. The following compounds were thus prepared.

2-Bromo-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (3j). Chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent.Yield 10%; mp 251-252 ºC (from acetic acid); IR(KBr) 3195, 1691, 1475, 741 cm^{-1}; δ_H(DMSO-d_6) 6,76 (1H, s, H-3), 7.32-8.0 (4H, m, Ar) and 13.30 (1H, br, NH); δ_C(DMSO-d_6) 106.0 (C), 108.5 (CH), 109.4 (C), 112.9 (C), 116.9 (CH), 121.3 (CH), 124.3 (CH), 129.1 (CH), 136.4 (C), 151.2 (C) and 156.9 (C); *m/z* 265 (M^++2, 100) and 263 (M^+, 90%). Anal. Calcd for $C_{11}H_6NO_2Br$: C, 50.03; H, 2.29; N 5.30. Found: C, 50.12; H, 2.22; N 5.33.

2-Bromo-3-methyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (3n). Chromatographed on silica gel using

CH_2Cl_2/pentane (1:2) as eluent. Yield 52%; mp >300 ºC (from acetic acid); IR(nujol mull) 3205, 1688, 745 cm^{-1}; δ_H(DMSO-d_6) 2.23 (3H, s), 7.34-7.98 (4H, m, Ar) and 13.45 (1H, br, NH); δ_C(DMSO-d_6) 10.2 (CH_3), 105.2 (C), 107.4 (C), 118.2 (C), 116.9 (CH), 117.5 (C), 121.2 (CH), 124.2 (CH), 128.8 (CH), 135.4 (C), 151.1 (C) and 157.6 (C); *m/z* 277 (M^+, 100) and 279 (M^+ +2, 96%). Anal. Calcd for $C_{12}H_8NO_2Br$: C, 51.83; H, 2.90; N 5.04. Found: C, 51.71; H, 2.93; N 5.12.

2-Bromo-1-methyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (4j). Chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent. Yield 78%; mp 203-204 ºC (from MeOH); IR(nujol mull) 1708, 1470, 1162, 1091, 748 cm^{-1}; δ_H(DMSO-d_6) 4.06 (3H, s), 6.83 (1H, s) and 7.32-8.13 (4H, m, Ar); δ_C($CDCl_3$) 35.2 (CH_3), 108.6 (CH), 109.3(C), 111.7 (C), 113.8 (C), 117.2 (CH), 121.5 (CH), 124.0 (CH), 128.6 (CH), 134.9 (C), 151.3 (C) and 156.8 (C); *m/z* 277 (M^+, 100) and 279 (M^+ +2, 97%). Anal. Calcd for $C_{12}H_8NO_2Br$: C, 51.83; H, 2.90; N 5.04. Found: C, 51.92; H, 2.88; N 4.96.

2-Bromo-3,4,4-trimethyl-4*H*-thieno[3,2-*c*]benzopyran (10u). Chromatographed on silica gel using CH_2Cl_2/pentane (1:5) as eluent. Yield 71%; bp 150-152 ºC at 1 mmHg; IR(film) 1490, 1459, 1258, 1141, 752 cm^{-1}; δ_H(DMSO-d_6) 1.57 (6H, s), 2.19 (3H, s) and 6.85-7.24 (4H, m, Ar); δ_C(DMSO-d_6) 15.4 (CH_3), 27.25 ($2CH_3$), 79.36 (C), 109.3 (C), 116.7 (CH), 118.3 (C), 121.7 (CH), 122.3 (CH), 129.3 (CH), 130.6 (C), 134.3 (C), 137.8 (C) and 150.0 (C); *m/z* 309 (M^++1, 100), 311 (M^++3, 97%) and 263 (M^++5, 5%). Anal. Calcd for $C_{14}H_{13}OBrS$: C, 54.38; H, 4.24. Found: C, 54.50; H, 4.25.

2,3-Dibromo-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (19). Chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent. Yield <5%; mp >300 ºC (from acetic acid); IR(KBr) 1699, 753 cm^{-1}; δ_H(DMSO-d_6) 7.34-8.01 (4H, m, Ar), 13.77 (1H, br, NH); δ_C(DMSO-d_6) 96.9 (C), 107.1 (C), 108.8 (C), 112.8 (C), 117.0 (CH), 121.5 (CH), 124.5 (CH), 129.6 (CH), 136.4 (C), 151.2 (C) and 155.5 (C); *m/z* 341 (M^+, 49%), 343 (M^++2, 100) and 345 (M^++4, 50%). Anal. Calcd for $C_{11}H_5NO_2Br_2$: C, 38.52; H, 1.47; N 4.08. Found: C, 38.68; H, 1.29; N 4.19.

2,3-Dibromo-1-methyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (20). Chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent Yield 10%; mp 273-274 ºC (from MeOH); IR(nujol mull) 1719, 1154, 980, 751 cm^{-1}; δ_H(DMSO-d_6) 4.14 (3H, s), 7.25-7.93 (4H, m, Ar); δ_C(DMSO-d_6) 36.7 (CH_3), 97.5 (C), 107.2 (C), 113.1 (C), 114.4 (C), 117.2 (CH), 122.2 (CH), 124.1 (CH), 129.2 (CH), 135.3 (C), 151.1 (C) and 154.7 (C); *m/z* 355 (M^+, 57%), 357 (M^++2, 100) and 359 (M^+ +4, 50%). Anal. Calcd for $C_{12}H_7NO_2Br_2$: C, 40.37; H, 1.98; N 3.92. Found: C, 40.11; H, 2.09; N 3.81.

2,8-Dibromo-3,4,4-trimethyl-4*H*-thieno[3,2-*c*]benzopyran (22). Chromatographed on silica gel using CH_2Cl_2/pentane (1:2) as eluent. Yield <5%; mp 127-129 ºC (from EtOH); IR(nujol mull) 1477, 1269, 1251, 1045, 810 cm^{-1}; δ_H(DMSO-d_6) 1.60 (6H, s), 2.21 (3H, s) and 6.85-7.45 (3H, m, Ar); δ_C(DMSO-d_6) 15.4 (CH_3), 27.24 ($2CH_3$), 80.0 (C), 111.2 (C), 113.0 (C), 119.0 (CH), 120.5 (C), 124.5 (CH), 129.8 (C), 131.6 (CH), 134.4 (C), 138.6 (C) and 149.3 (C); *m/z* 386 (M^+, 9%), 388 (M^++2, 18%), 390 (M^++4, 10%)

and 373 (100). Anal. Calcd for $C_{14}H_{12}OBr_2S$: C, 43.32; H, 3.12. Found: C, 43.19; H, 3.25.

Nitration of compounds (1, 2, 5, 7 and 9). General procedure. The pyrrole (**1a**,**1b**, **2a**, **5d**,) or thiophene (**7b**, **9f**) (1.0 mmol) was dissolved in 8 mL of acetic anhydride and chilled to –5ºC. To this was added under nitrogen a cold mixture of fuming nitric acid (0.124 mL) in 4 mL of acetic anhydride at such a rate as to prevent the temperature from rising above 0ºC. When the reaction, which was monitored by TLC, was completed (Table 2), the mixture was poured into ice-water, neutralized with sodium hydroxide (3.7 g) and extracted with ethyl acetate. The extract was evaporated to dryness at rt and the residue was recrystallized or chromatographed on silica gel. The following compounds were thus prepared.

2-Nitro-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (3k). Recrystallized from toluene/hexane (1:1).Yield 65%, mp >300 ºC; IR(nujol mull) 3140, 1710, 1505, 1320, 972, 760 cm^{-1}; δ_H(DMSO-d_6) 7.61 (1H, s, H-3), 7.35-8.27 (4H, m, Ar) and 14.21 (1H, br, NH); δ_C(DMSO-d_6) 109.0 (C), 109.3 (CH), 113.5 (C), 117.4 (CH), 123.2 (CH), 124.8 (CH), 131.0 (CH), 138.4 (C), 142.4 (C), 152.8 (C) and 157.5 (C);. Anal. Calcd for $C_{11}H_6N_2O_4$: C, 57.40; H, 2.63; N 12.17. Found: C, 57.19; H, 2.50; N 12.30.

3-Methyl-2-nitro-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (3o). Chromatographed on silica gel using CH_2Cl_2/Et_2O (40:1) as eluent.Yield 53%, mp >300 ºC (from acetic acid); IR(nujol mull) 1715, 1453, 1328, 972, 758 cm^{-1}; δ_H(DMSO-d_6) 2.70 (3H, s), 7.39-8.37 (4H, m, Ar) and 14.13 (1H, br, NH); *m/z* 244 (M^+, 82%) and 185 (100). Anal. Calcd for $C_{12}H_8N_2O_4$: C, 59.02; H, 3.30; N 11.47. Found: C, 59.21; H, 3.15; N 11.40.

1-Methyl-2-nitro-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (4k). Chromatographed on silica gel using CH_2Cl_2 as eluent.Yield 89%, mp 235-236 ºC (from MeOH); IR(nujol mull)1733, 1505, 1453, 1350, 1303, 1285, 970 cm^{-1}; δ_H(DMSO-d_6) 4.35 (3H, s), 7.70 (1H, s, H-3) and 7.38-8.26 (4H, m, Ar); δ_C(DMSO-d_6) 36.2 (CH_3), 107.6 (C), 110.9 (CH), 112.3 (C), 117.7 (CH), 123.1 (CH), 124.3 (CH), 130.8 (CH), 137.5 (C), 141.3 (C), 152.7 (C) and 156.4 (C); *m/z* 244 (M^+, 100). Anal. Calcd for $C_{12}H_8N_2O_4$: C, 59.02; H, 3.30; N 11.47. Found: C, 59.25; H, 3.40; N 11.22.

1,4,4-Trimethyl-2-nitro-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (6r). Recrystallized from toluene/hexane. Yield 18%, mp 145-146 ºC; IR(KBr) 1440, 1392, 1297, 1271, 1200 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.57 (6H, s), 4.20 (3H, s), 7.10 (1H, s, H-3) and 7.02-7.60 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 27.5 ($2CH_3$), 36.3 (CH_3), 77.2 (C), 109.2 (CH), 115.8 (C), 119.2 (CH), 121.7 (CH), 122.9 (CH), 125.6 (C), 130.5 (CH), 131.2 (C), 139.3 (C) and 154.6 (C); *m/z* 258 (M^+,17%) and 243 (100). Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N 10.85. Found: C, 65.30; H, 5.28; N 10.97.

3,4,4-Trimethyl-2-nitro-4*H*-thieno[3,2-*c*]benzopyran (10v). Chromatographed on silica gel using CH_2Cl_2/Et_2O (40:1) as eluent.Yield 86%, mp 126-127 ºC (from EtOH); IR(KBr) 1486, 1457, 1308, 1296,

1240, 745 cm^{-1}; δ_H(DMSO-d_6) 1.67 (6H, s), 2.65 (3H, s) and 6.95-7.58 (4H, m, Ar); δ_C(DMSO-d_6) 15.1 (CH_3), 27.3 ($2CH_3$), 79.1 (C), 116.5 (C), 117.4 (CH), 122.2 (CH), 124.0 (CH), 132.5 (CH), 136.6 (C), 138.8 (C), 139.9 (CH), 145.1 (CH) and 151.6 (C); *m/z* 275 (M^+, 19%), 277 (M^++2, 1%) and 260 (100). Anal. Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N 5.09. Found: C, 60.91; H, 4.82; N 5.22.

3,4,4-Trimethyl-2,8-dinitro-4*H*-thieno[3,2-*c*]benzopyran (23). Chromatographed on silica gel using CH_2Cl_2 as eluent.Yield <5%, mp 233-235 ºC (from EtOH); IR(KBr) 1510, 1341, 1312, 1283 cm^{-1}; δ_H(DMSO-d_6) 1.74 (6H, s), 2.66 (3H, s) and 7.17-8.40 (4H, m, Ar); δ_C(DMSO-d_6) 15.1 (CH_3), 27.8 ($2CH_3$), 81.6 (C), 116.5 (C), 118.2 (CH), 119.6 (C), 127.4 (CH), 128.7 (C), 131.5 (C), 133.6 (C), 139.4 (CH), 141.8 (C) and 156.7 (C); *m/z* 320 (M^+, 16%), 322 (M^++2, 1%) and 305 (100). Anal. Calcd for $C_{14}H_{12}N_2O_5S$: C, 52.49; H, 3.78; N 8.75. Found: C, 52.28; H, 3.90; N 8.91.

Acetylation of compounds (1, 2, 5, 7 and 9). General procedure. A solution of **1a**, **2a**, **2c**, **5d**, **7b,** or **9f** (0.5 mmol) in 2 mL of Ac_2O was added to a solution of 0.17 mL (1.5 mmol) of $TiCl_4$ in 4 mL of Ac_2O and the mixture was stirred at rt under nitrogen. When the reaction was completed, monitored by TLC, the mixture was hydrolized and neutralized with NaOH/ice/water, and then extracted with ethyl acetate. The extract, after drying (Na_2SO_4), was evaporated and chromatographed on silica gel . The following compounds were thus prepared.

2-Acetyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (3l). Chromatographed on silica gel using CH_2Cl_2/Et_2O (10:1) as eluent.Yield 10%, mp 292-294 ºC (from MeOH) (lit.,[3] mp 292-294 ºC), IR(KBr) 3286, 3020, 1735, 1640, 1461, 753; δ_H(300 MHz; DMSO-d_6) 2.51 (3H, s), 7.31-8.39 (4H, m, Ar), 7.64 (1H, d, *J* 1.6, H-3), 13.27 (1H, br, NH); δ_C(75.4 MHz; DMSO-d_6) 26.0 (CH_3), 109.2 (C), 113.0 (C), 115.5 (CH), 117.1 (CH), 123.1 (CH), 124.4 (CH), 130.5 (CH), 135.4 (C), 138.6 (C), 152.3 (C), 157.8 (C) and 188.8 (C); *m/z* 227 (M^+, 90%), 212 (100).

2-Acetyl-1-methyl-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (4l). Chromatographed on silica gel using CH_2Cl_2/Et_2O (30:1) as eluent. Yield 72%,. mp 202-204 ºC (from MeOH) (lit.,[3] mp 202-204 ºC), IR(KBr) 1724, 1652, 750; δ_H(300 MHz; $CDCl_3$) 2.55 (3H, s), 4.39 (3H, s), 7.32-8.04 (4H, m, Ar), 7.54 (1H, s, H-3); δ_C(75.4 MHz; $CDCl_3$) 27.9 (CH_3), 35.8 (CH_3), 108.9 (C), 113.4 (C), 117.7 (CH), 118.1 (CH), 122.2 (CH), 124.1 (CH), 130.0 (CH), 134.0 (C), 139.0 (C), 152.7 (C), 157.9 (C) and 189.6 (C); *m/z* 241 (M^+, 82%), 226 (100).

2-Acetyl-1-methyl-3-phenyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrol-4(1*H*)-one (4q). Chromatographed on silica gel using CH_2Cl_2/Et_2O (30:1) as eluent. Yield 75%, mp 198-200 ºC (from MeOH); IR(KBr) 1780, 1638, 1366, 1195, 1090, 758 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.96 (3H, s), 4.28 (3H, s) and 7.26-8.10 (9H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 31.0 (CH_3), 36.6 (CH_3), 108.1 (C), 113.7 (C), 118.3 (CH), 122.6 (CH), 124.0 (CH), 128.2 (2CH), 128.3 (CH), 128.4 (CH), 130.0 (2CH), 132.3 (C), 133.2 (C), 134.1 (C), 138.0 (C),

153.1 (C), 157.4 (C) and 192.7 (C); *m/z* 317 (M^+, 100%). Anal. Calcd for $C_{20}H_{15}NO_3$: C, 75.70; H, 4.76; N 4.41. Found: C, 75.52; H, 4.80; N 4.20.

2-Acetyl-1,4,4-trimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (6s). Chromatographed on silica gel using CH_2Cl_2 as eluent. Yield 85%, mp 150-152 ºC (from EtOH); IR(KBr) 1639, 1455, 1365, 1228, 112, 930 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.58 (6H, s), 2.46 (3H, s), 4.20 (3H, s), 6.75 (1H, s, H-3) and 6.96-7.61 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 27.6 (CH_3), 27.8 ($2CH_3$), 35.7 (CH_3), 77.0 (C), 113.6 (CH), 117.2 (C), 118.6 (CH), 121.3 (CH), 122.5 (CH), 125.4 (C), 129.0 (CH), 131.1 (C), 132.0 (C), 153.7 (C) and 188.1 (C); *m/z* 255 (M^+, 19%) and 240 (100). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N 5.49. Found: C,75.40 ; H, 6.83; N 5.56.

2-Acetyl-3,4,4-trimethyl-4*H*-thieno[3,2-*c*]benzopyran (10w). Chromatographed on silica gel using CH_2Cl_2/pentane (1:1) as eluent. Yield 41%, mp 84-85 ºC (from EtOH); IR(KBr) 1646, 1405, 1293, 1238, 750 cm^{-1}; δ_H(DMSO-d_6) 1.64 (6H, s), 2.50 (3H, s), 2.53 (3H, s) and 6.92-7.48 (4H, m, Ar); δ_C(DMSO-d_6) 15.6 (CH_3), 27.5 ($2CH_3$), 30.2 (CH_3), 79.5 (C), 117.0 (CH), 117.9 (C), 121.9 (CH), 123.3 (CH), 131.0 (CH), 135.2 (C), 135.4 (C), 140.4 (C), 141.1 (C), 151.0 (C) and 190.8 (C); *m/z* 272 (M^+, 18%), 272 (M^++2, 1%) and 257 (100). Anal. Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92. Found: C, 70.72; H, 5.81.

3-Acetyl-1,4,4-trimethyl-1*H*-[1]benzopyrano[4,3-*b*]pyrrole (21). Chromatographed on silica gel using CH_2Cl_2 as eluent. Yield <5%, mp 140-142 ºC (from toluene); IR(KBr) 1648, 1360, 1251, 1102, 751 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.73 (6H, s), 2.40 (3H, s), 3.91 (3H, s), 7.22 (1H, s, H-2) and 6.87-7.44 (4H, m, Ar); δ_C(75.4 MHz; $CDCl_3$) 27.7 ($2CH_3$), 27.9 (CH_3), 38.7 (CH_3), 79.5 (C), 116.8 (C), 116.9 (CH), 119.1 (C), 120.7 (CH), 120.8 (CH), 123.2 (C), 124.2 (C), 127.5 (CH), 134.6 (CH), 151.3 (C) and 192.0 (C); *m/z* 255 (M^+, 14%) and 240 (100). Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N 5.49. Found: C, 75.40; H, 6.59; N 5.32.

Formylation of compounds (1, 5, ,7 and 9). General procedure. To 0.34 mL (0.32 g, 4.4 mmol) of *N*,*N*-dimethylformamide cooled in an ice bath was added dropwise 0.41 mL (0.676 g, 4.4.mol) of phosphorous oxychloride at such a rate as to maintain the internal temperature at 10-15ºC. The ice bath was removed, and the mixture was stirred for 15 min at rt. The ice bath was replaced, and 8 mL of ethylene dichloride were added to the mixture. When the internal temperature dropped to 10-15ºC, a solution of 4 mmol of pyrrole (**1a**, **b**, **5d**) or thiophene (**7b**, **9f, 9y**) in 8 mL of ethylene dichloride was added. After the addition was completed, the mixture was stirred at rt until the reaction was complete (monitored by TLC, Table 2). To this was added 3 g (22 mmol) of sodium acetate trihydrate in 30 mL of water and the reaction mixture was again refluxed for 15 min.

The cooled mixture was decanted and extracted with ethyl acetate. The organic layer, was washed with saturated aqueous sodium carbonate solution, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was

recrystallized or chromatographed on silica gel. The following compounds were thus prepared.

4-Oxo-[1]benzopyrano[4,3-*b*]pyrrole-2(1*H*)-carboxaldehyde (3m). Recrystallized from acetone. Yield 81%, mp >300 ºC; (lit.,[3] mp >300 ºC), IR(KBr) 3260, 1729, 1643, 1163, 753 cm^{-1}; δ_H(300 MHz; DMSO-d_6) 7.35-8.33 (4H, m, Ar), 7.63 (1H, s, H-3), 9.76 (1H, s, CHO)and 13.52 (1H, br, NH); δ_C(75.4 MHz; DMSO-d_6) 109.5 (C), 112.8 (C), 117.1 (CH), 119.5 (CH), 123.0 (CH), 124.4 (CH), 130.8 (CH), 135.8 (C), 139.4 (C), 152.4 (C) 157.5 (C) and 181.3 (CH); *m/z* 213 (M^+, 100%).

3-Methyl-4-oxo-[1]benzopyrano[4,3-*b*]pyrrole-2(1*H*)-carboxaldehyde (3p). Recrystallized from THF. Yield 82%, mp >300 ºC; IR(KBr) 3230, 1722, 1639, 1611, 1455, 760 cm^{-1}; δ_H(300 MHz; DMSO-d_6) 2.63 (3H, s), 7.27-8.31 (4H, m, Ar), 9.86 (1H, s, CHO) and 12.97 (1H, br, NH); δ_C(75.4 MHz; DMSO-d_6) 8.8 (CH_3), 108.1 (C), 112.6 (C), 116.4 (CH), 122.7 (CH), 123.7 (CH), 130.1 (CH), 131.3 (C), 131.6 (C), 138.3 (C), 152.2 (C) 157.3 (C) and 178.9 (CH); *m/z* 227 (M^+, 100%). Anal. Calcd for $C_{13}H_9NO_3$: C, 68.72; H 3.99; N 6.16. Found: C, 68.56; H, 4.12N 6.22.

1,4,4-Trimethyl-[1]benzopyrano[4,3-*b*]pyrrole-2(1*H*)-carboxaldehyde (6t). Recrystallized from toluene/hexane (1:1). Yield 62%, mp 139-141 ºC; IR(KBr) 1749, 1450, 1367, 1255, 1150, 747 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.58 (6H, s), 4.24 (3H, s), 6.68 (1H, s, H-3), 6.97-7.63 (4H, m, Ar) and 9.49 (1H, s, CHO); δ_C(75.4 MHz; $CDCl_3$) 27.8 ($2CH_3$), 34.8 (CH_3), 77.0 (C), 116.7 (C), 118.1 (CH), 118.6 (CH), 121.3 (CH), 122.6 (CH), 126.6 (C), 129.6 (CH), 132.5 (C), 132.8 (C), 153.9 (C) and 178.9 (CH); *m/z* 241 (M^+, 13%), 226 (100). Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H 6.27; N 5.81. Found: C, 74.51; H, 6.38; N 5.91.

3,4,4-Trimethylthieno[3,2-*c*]benzopyran-2(4*H*)-carboxaldehyde (10x). Chromatographed on silica gel using CH_2Cl_2/pentane (1:1) as eluent. Yield 85%, mp 120-122 ºC (from EtOH); IR(KBr) 1635, 1466, 1384, 1298, 1233, 1193, 751 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 1.69 (6H, s), 2.59 (3H, s), 6.89-7.41 (4H, m, Ar) and 10.04 (1H, s, CHO); δ_C(75.4 MHz; $CDCl_3$) 14.3 (CH_3), 27.8 ($2CH_3$), 79.2 (C), 117.3 (CH), 118.3 (C), 121.6 (CH), 123.7 (CH), 131.2 (CH), 137.1 (C), 139.8 (C), 141.3 (C), 143.5 (C), 151.6 (C) and 181.8 (CH); *m/z* 258 (M^+, 17%), 260 (M^++2, 1%), 243 (100). Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H 5.46. Found: C, 69.91; H, 5.30.

Thieno[3,2-*c*]benzopyran-2(4*H*)-carboxaldehyde (10z). Chromatographed on silica gel using CH_2Cl_2/pentane (1:1) as eluent. Yield 25%, mp 116-117 ºC (from EtOH); IR(KBr) 1652, 1451, 1433, 1230, 1146, 1108, 748 cm^{-1}; δ_H(300 MHz; $CDCl_3$) 5.30 (2H, s), 6.96-7.4 (4H, m, Ar) 7.50 (1H, s, H-3) and 9.87 (1H, s, CHO); δ_C(75.4 MHz; $CDCl_3$) 65.6 (CH_2), 117.2 (CH), 119.1 (C), 122.4 (CH), 124.2 (CH), 131.3 (CH), 132.1 (C), 132.9 (C), 141.9 (C), 142.5 (C), 153.1 (C) and 182.3 (CH); *m/z* 216 (M^+, 74%), 218 (M^++2, 4%), 215 (100). Anal. Calcd for $C_{12}H_8O_2S$: C, 66.65; H 3.73. Found: C, 66.82; H, 3.61.

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18 Compounds (**13**) were not isolated. We have selected the ^{1}H-NMR of the compound (**13i**), precursor of the pyrrole (**5i**), as a representative example of these intermediates.