ON THE LEUCKART REACTION OF DEOXYBENZOINS. ISOLATION AND CHARACTERIZATION OF 2,3,4,5-TETRAARYLPYRIDINE DERIVATIVES

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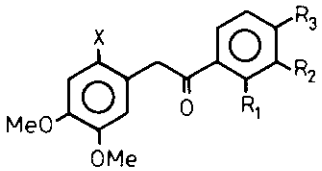
Abstract - The Leuckart reaction of deoxybenzoins has been examined. The deoxybenzoins (1b-c) possessing a phenolic substituent in the ortho position to the carbonyl group react with formamide to afford, besides the known stilbene, pyrimidine and isoflavone derivatives, 2,3,4,5-tetraarylpyridines, whose structures and formation mechanism are discussed. In contrast, the Leuckart reaction of the alkoxy substituted deoxybenzoins (1d-f) leads to the expected formamides in high yields, though always accompanied by the corresponding stilbenes and pyrimidines as by-products.

As a part of a programme of work directed towards the synthesis of 1,2-diarylethylamines and amides (interesting synthetic precursors of 3-arylisoquinolines[1,2]), we have been studying the Leuckart reaction with deoxybenzoins (1). It is known that the Leuckart reaction[3], a classical procedure for reductive amination of carbonyl compounds, suffers from limitations caused by undesirable side reactions when certain aldehydes or ketones are used[4-8]. Thus, we have recently reported[9] that 2-bromo-4,5-dimethoxybenzyl 3,4-methylenedioxyphenyl ketone (1a) gives the expected formamide (6a) with ammonium formate-formic acid, in addition to small amounts of the stilbene (3a) and the pyrimidine (4a). However, the reaction with 2-bromo-4,5-dimethoxybenzyl 2-hydroxy-3,4-dimethoxyphenyl ketone (1b) always fails to yield the anticipated formamide, affording exclusively the corresponding stilbene (3b), pyrimidine (4b) and isoflavone (5b) derivatives in significant yields.

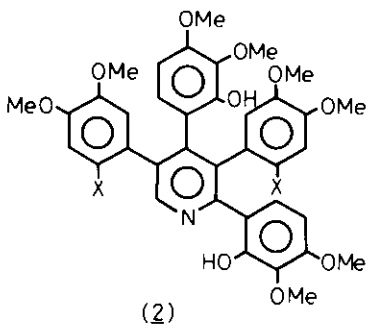
In this paper, we wish to report the extension of the Leuckart reaction to a series of deoxybenzoins (1) with different substituents in the benzenoid rings, in order to examine further the scope of the procedure.

The required deoxybenzoins (1c-f) were prepared *via* the Friedel-Crafts route[10,11] from alkoxylated benzenes and the adequate acyl chloride in dichloromethane as solvent, using $AlCl_3$ as catalyst, except in the synthesis of the ketone (1d), in which case $SnCl_4$ was employed, thus avoiding the cleavage of the methyl ether ortho to the carbonyl group.

It was decided to begin our investigations with the phenolic deoxybenzoin (1c), in order to compare the results with those previously reported[9] for the corresponding brominated ketone (1b). Thus, when (1c) was reacted with formamide under Leuckart reaction conditions and the reaction mixture subjected to flash column chromatography, the expected stilbene (3c), pyrimidine (4c) and isoflavone (5c) derivatives were isolated (Table 3). The structural assignments of these products rest upon spectral evidence and analogy with earlier described data for similar compounds[9]. Surprisingly, an additional product was also eluted from the column (R_f= 0.3, dichloromethane/ethyl acetate 9.5:0.5) in a 24% yield and it was characterized, by spectral studies, as the 3,5-bis(3,4-dimethoxyphenyl)-2,4-bis(2-hydroxy-3,4-dimethoxyphenyl)pyridine (2c).



(1)



(2)

a: X=Br , R_1=H , R_2+R_3=OCH_2O

b: X=Br , R_1=OH , R_2=R_3=OMe

c: X=H , R_1=OH , R_2=R_3=OMe

d: X=Br , R_1=R_2=R_3=OMe

e: X=Br , R_1=H , R_2=R_3=OMe

f X=R_1=H , R_2=R_3=OMe

Since in our preliminary studies we had found no pyridine derivative among the products of the Leuckart reaction of the corresponding brominated deoxybenzoin (1b), we considered it would be interesting to reinvestigate this reaction. Therefore, when (1b) was treated with formamide under the above mentioned conditions, the expected products (3b), (4b) and (5b) were found to be present in the reaction mixture and separated by column chromatography. However, a careful examination of the tarry residue revealed the presence of a small amount of a new component, which could be eluted by increasing the solvent polarity. The so-obtained compound was identified as the 3,5-bis(2-bromo-4,5-dimethoxyphenyl)-2,4-bis(2-hydroxy-3,4-dimethoxyphenyl)pyridine (2b) (ir, uv, pmr, cmr and ms spectral data). In this case, the yield (8%) of the pyridine (2b) has decreased probably due to the steric hindrance of the bromine atom. This low yield, together with the high polarity of this compound (R_f= 0.20, dichloromethane/ethyl acetate 8:2), could be the reason for the previous failure in its isolation.

The molecular formulae of (2b) and (2c), $C_{37}H_{35}Br_2NO_{10}$ and $C_{37}H_{37}NO_{10}$ respectively, were established by elemental analysis and mass spectrometry and were in agreement with dimeric structures. Their ir and uv spectra were similar to those of the polyaryl substituted pyridines[12,13]. Thus, their ir spectra showed the $\nu_{C=C}$ and $\nu_{C=N}$ ring vibrations at 1630-1600 cm^{-1} and 1580-1510 cm^{-1} respectively, and C-H deformations at 900-700 cm^{-1}. Their uv spectra had two maxima approximately at 295 and 315 nm, displaced to longer wavelengths in acidic media[13]. The most characteristic signals in their nmr spectra were those of the atoms at the non-substituted position in the pyridine ring. In fact, their pmr spectra exhibited singlets at δ 7.8 ppm, due to H-6, and confirmed the presence of two phenolic hydroxyl groups (singlets at δ 9.7-10.2 ppm which integrated for a total of two protons and were exchangeable with D_2O). The cmr spectra recorded for both compounds contained a low field singlet at δ 142-145 ppm (doublet under off-resonance decoupled conditions), due to the C-6 (see Table 2 for assignments). In the mass spectrum of (2b) the parent peak appeared at m/z 811(26%) and it could be observed the characteristic $M^+ + 2$ and $M^+ + 4$ pattern of the dibrominated compounds (m/z(%) 813(55) ($M^+ + 2$) and 815(30) ($M^+ + 4$)). The base peak (m/z 732/734) was produced by loss of a bromine atom from the molecular ion. Moreover, it could be noted a peak at m/z 392/394(7%), due to a diarylacetylenic radical-ion, typical of polyarylpyridines[14,15]. On the other hand, the mass spectrum of (2c) gave the parent peak at m/z 655(22%) and the base peak at m/z 184, which could be produced by a variety of processes from the former.

Table 1. The 2,3,4,5-tetraarylpyridines (2).

Product No.	X	Mp (°C) Solvent	Formula	Calcd. (Found) (%) C	H	Br	N
(2b)	Br	162-163 (CH_2Cl_2/EtOH)	$C_{37}H_{35}Br_2NO_{10}$	54.61 (54.62)	4.31 (4.41)	19.68 (19.79)	1.72 (1.79)
(2c)	H	268-270 (CH_2Cl_2/EtOH)	$C_{37}H_{37}NO_{10}$	67.79 (67.86)	5.65 (5.70)	– –	2.14 (2.09)

Previously, polysubstituted pyridines have been prepared by the condensation of 1,5-diketones with formamide-formic acid[16] and by other synthetic procedures including the Chichibabin method[17] and the Leuckart reaction of chalcones with formamide[13]. Although a number of mechanistic pathways are possible to explain the latter procedures[18,19], the most likely proposals involve an aldol or reverse

Table 2. Spectral Data for the 2,3,4,5-Tetraarylpyridines (2)[a]

Product No.	Pmr ($CDCl_3$/TMS)[b] δ (ppm), J (Hz)	Cmr ($CDCl_3$/TMS)[c] δ (ppm)	Ms m/z (%)
(2b)	3.70(s,6H,2 x MeO), 3.85(s,6H,2 x MeO), 3.95(s,12H,4 x MeO), 6.3(d,J=9,2H,2 x H-5"), 6.7(s,2H,2 x H-6'), 6.8(d,J=9,2H, 2 x H-6"), 7.2(s,2H,2 x H-3'), 7.8(s,1H, H-6), 10.2(s,2H,2 x OH,exchangeable with D_2O).	55.5,55.8,55.9 and 60.6(MeO-); 102.6(C-5"); 113.4(C-Br); 113.9 115.3(C-3' and/or C-6'); 116.6 (C-1"); 125.3(C-6"); 131.7,132.4 (C-3 and/or C-5); 145.0(C-6); 148.1,148.8(C-4' and/or C-5'); 150.1,152.2,152.5 and 153.0(C-2, C-4,C-2",C-3" and/or C-4").	815(M^++4)(30),813(M^++2) (55),811(M^+)(26),766(20), 734(95),733(47),732(100).
(2c)	3.70(s,6H,2 x MeO), 3.80(s,6H,2 x MeO), 3.89(s,6H,2 x MeO), 3.91(s,6H,2 x MeO), 6.27(d,J=8.9,2H,2 x H-5"), 6.77(d,J=1.85 2H,2 x H-2'), 6.80(d,J=8.9,2H,2 x H-6"), 6.87(d,J=8.3,2H,2 x H-5'), 6.95(dd,J=8.2 and 1.85,2H,2 x H-6'), 7.81(s,1H,H-6), 9.7(s,2H,2 x OH,exchangeable with D_2O).	55.8,60.7(MeO-); 102.8(C-5"); 111.3,112.2(C-2' and/or C-5'); 117.0(C-1"); 121.2(C-6' and C-6"); 132.7,134.1(C-5 and/or C-3); 136.6(C-1'); 142.1(C-6); 148.5,148.7(C-3' and/or C-4'); 150.3,151.5 and 153.2(C-2,C-4, C-2",C-3" and/or C-4").	655(M^+)(22),608(26),255 (37),211(31),198(72),197 (76),184(100).

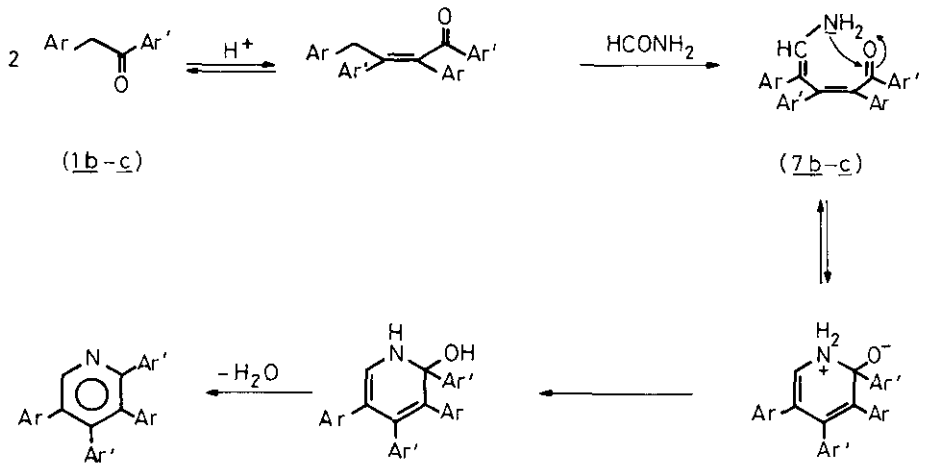
a) The uv and ir spectra of both compounds are virtually identical. Uv($CHCl_3$): λ max(log ε): 238 (4.66), 293 (4.46) and 315 (4.40) nm. Ir(KBr): ν max: 1620, 1590 and 1520 (C=C and C=N) cm^{-1}.

b) s, singlet; d, doublet; dd, doublet of doublets.

c) Assignments made using "off-resonance" experiments.

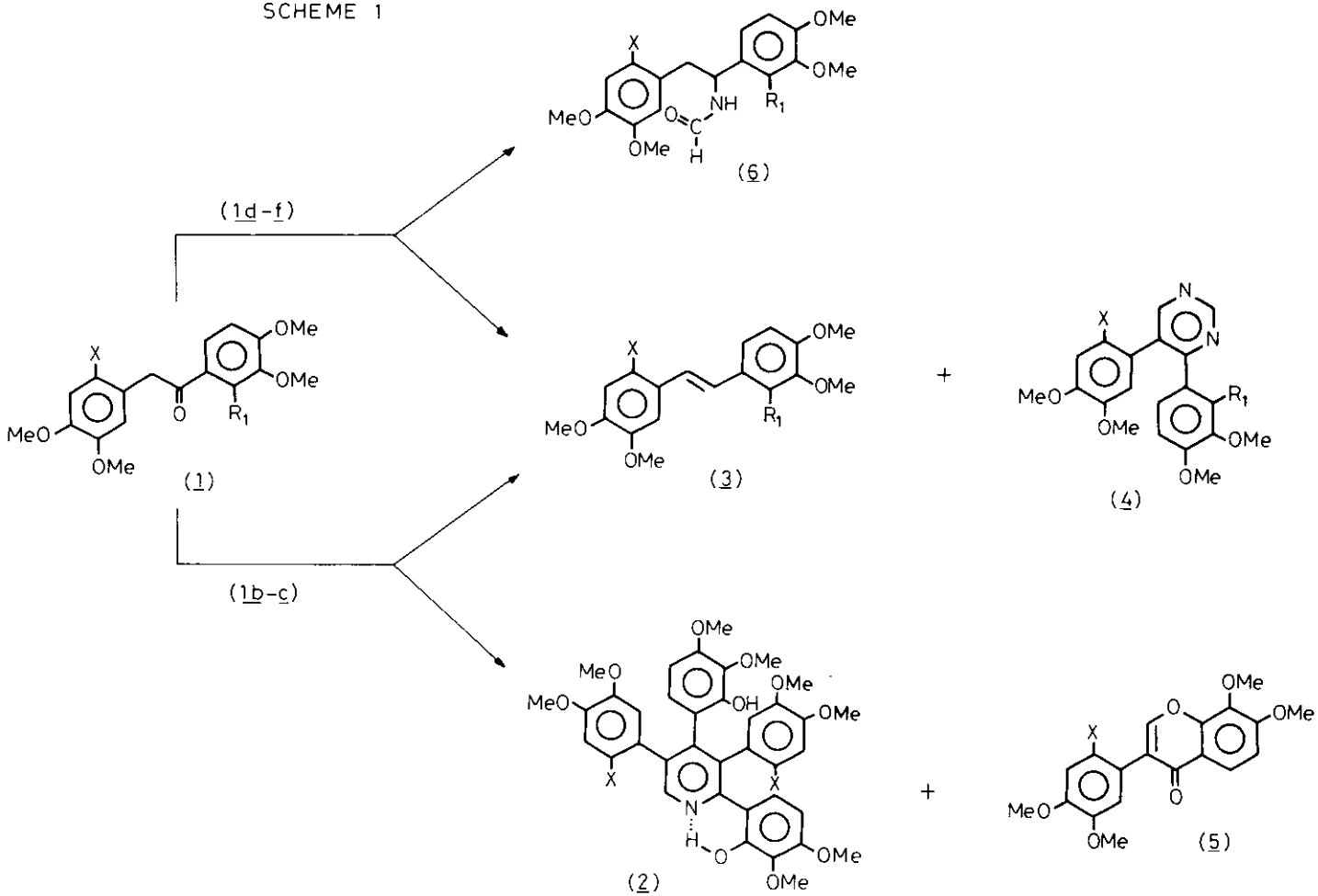
aldol reaction, followed by a Michael-type reaction and condensation with ammonia (or certain of its derivatives) to yield the dihydropyridines, which in turn would be dehydrogenated to a pyridine[13,20,21]. Therefore, we propose that, in our case, the formation of the pyridines (2) could be rationalized by assuming that an aldolic reaction takes place between two molecules of the corresponding deoxybenzoins (1). Subsequent condensation with formamide and cyclodehydration of the intermediate enamine (7) should lead to the pyridines (2), as illustrated in the following Scheme.

SCHEME 2



In order to complete our study, we undertook the Leuckart reaction of the alkoxylated deoxybenzoins (1d-f), using formamide - formic acid - ammonium formate as reagent. The corresponding 1,2-diarylethylformamides (6d-f) were always obtained as the major products, though accompanied by lesser quantities of certain by-products. The mother liquors from the crystallization of the formamides (6) were column chromatographed, affording stilbene (3) and pyrimidine (4) derivatives (see Table 3), whereas no tetraarylpyridines (2) could be found. On the other hand, when the Leuckart reaction was applied to the ketone (1d), possessing a methoxyl group in the β-position to the carbonyl group, the isoflavone (5b) could also be isolated.

SCHEME 1



b: X=Br, R_1=OH ; c: X=H, R_1=OH ; d: X=Br, R_1=OMe ; e: X=Br, R_1=H ; f: X=R_1=H

Table 3. Leuckart Reaction of the Deoxybenzoins (1).

Substrate No.	X	R_1	Pyridine (2)	Stilbene (3)	Pyrimidine (4)	Isoflavone (5)	Formamide (6)
(1b)[a]	Br	OH	8	12	25	24	–
(1c)[a]	H	OH	24	11	16	19	–
(1d)[b]	Br	OMe	–	3	3	5	83
(1e)[b]	Br	H	–	4	6	–	85
(1f)[b]	H	H	–	4	4	–	80

a) Amounts used: formamide (0.5 ml) per 1 mmol of ketone.
b) Amounts used: formamide (0.1 ml)/ ammonium formate (10 mmole)/ formic acid (0.1 ml) per 1 mmol of ketone.

EXPERIMENTAL

Melting points were determined on either Electrothermal 1A 6304 or Büchi apparatus and are uncorrected. Microanalyses were performed by the "Colegio Universitario de Alava". Mass spectra were measured with a Hewlett-Packard 5830 B mass spectrometer. Ir spectra were recorded in potassium bromide on a Perkin-Elmer 1430 spectrophotometer. Uv spectra were determined in chloroform solution on a Beckmann 5260 spectrophotometer. Pmr and cmr spectra were run on a Varian XL-200 or a Bruker WM-250 apparatus, in deuteriochloroform solution with tetramethylsilane as internal standard. For thin-layer chromatography Merck Kieselgel GF 254 plates (0.2 mm thick) were used. Visualization was accomplished by uv light or by spraying with Dragendorff's reagent. The flash column chromatography was carried out on Merck Kieselgel 60 (0.040-0.063 nm, 230-400 mesh).

3,4-Dimethoxybenzyl 2-Hydroxy-3,4-dimethoxyphenyl Ketone (1c)

To a solution of 1,2,3-trimethoxybenzene (3.5 g, 0.020 mole) and 3,4-dimethoxyphenylacetyl chloride (4 g, 0.020 mole), freshly prepared[11], in dry dichloromethane (20 ml), anhydrous $AlCl_3$ (3.5 g, 0.026 mole) was added. The mixture was heated under reflux for 2.5 h and then cooled to room temperature. The reaction mixture was poured into water (7 ml), 12M HCl (15 ml) and ice (20 g) and extracted with dichloromethane. The dried extract (Na_2SO_4 anh.) was concentrated and the residue crystallized from ethanol to afford the ketone (1c) as white prismatic crystals (4.6 g), mp 139-140°C, yield 70%. Anal. calcd. for $C_{18}H_{20}O_6$: C, 65.06; H, 6.02.

Found: C, 64.81; H, 6.12%. Ir: ν max 1645 (C=O) cm^{-1}. Pmr: δ 3.88 (s, 6H, 2 × MeO), 3.94 (s, 6H, 2 × MeO), 4.20 (s, 2H, $-CH_2-CO-$), 6.56 (d, J= 9 Hz, 1H, H-5'), 6.90 (m, (m, 3H, H-2, H-5 and H-6), 7.70 (d, J= 9 Hz, 1H, H-6'), 12.40 (s, 1H, OH, exchang. with D_2O) ppm.

2-Bromo-3,4-dimethoxybenzyl 2,3,4-Trimethoxyphenyl Ketone (1d)

To a cooled solution of 1,2,3-trimethoxybenzene (9.3 g, 0.055 mole) and $SnCl_4$ (15.3 g, 0.060 mole) in dry dichloromethane (50 ml) kept around -10°C under nitrogen, a solution of 2-bromo-4,5-dimethoxyphenylacetyl chloride (14.7 g, 0.050 mole), freshly prepared[11], in dry dichloromethane (50 ml) was added. The mixture was stirred at room temperature for 3 h and then poured into 6M HCl (100 ml) and stirred for further 16 h. Usual work-up gave a solid residue, which was purified by crystallization from ethanol to afford white crystals (16.6 g), mp 107-109°C, yield 78%. Anal. calcd. for $C_{19}H_{21}BrO_6$: C, 53.65; H, 4.94; Br, 18.82. Found: C, 53.21; H, 5.04; Br, 18.44%. Ir: ν max 1675 (C=O) cm^{-1}. Pmr: δ 3.85 (s, 6H, 2 × MeO), 3.90 (s, 6H, 2 × MeO), 4.05 (s, 3H, MeO), 4.40 (s, 2H, $-CH_2-CO-$), 6.70 (d, J= 8.6 Hz, 1H, H-5'), 6.80 (s, 1H, H-6), 7.00 (s, 1H, H-3), 7.50 (d, J= 8,6 Hz,1H, H-6') ppm.

Reaction of the Phenolic Deoxybenzoins (1b-c) under Leuckart Conditions. General Procedure.

A mixture of the deoxybenzoin(1 mmol) and formamide (0.5 ml) was heated at 185-190°C until the disappearance of the starting material (tlc monitoring, silica gel, dichloromethane/ethyl acetate 9.5:0.5). After cooling to room temperature, the reaction mixture was poured into water and an abundant precipitate was produced, which was collected and washed. In this manner, the following reactions were carried out (Table 3).

Deoxybenzoin (1c) (4.6 g, 0.014 mole) with formamide (7 ml) yielded a residue, which showed four spots by tlc. The four components were isolated by column chromatography on silica gel with dichloromethane/ethyl acetate 9.5:0.5 as eluent and identified as:

(E)-1-(3,4-Dimethoxyphenyl)-2-(2-hydroxy-3,4-dimethoxyphenyl)ethylene (3c): R_f= 0.59, 490 mg (yield 11%), mp 132-134°C (chloroform/methanol). Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.35; H, 6.33. Found: C, 68.22; H, 6.39%. Ir: ν max 3500 (OH) cm^{-1}. Uv:λ max(log ε) 251(4.23), 299(4.24), 340(4.26) nm. Pmr: δ 3.85 (s, 3H, MeO), 3.87 (s, 3H, MeO), 3.89 (s, 3H, MeO), 3.92 (s, 3H, MeO), 6.30 (s, 1H, OH, exchang. with D_2O), 6.50 (d, J= 9.0 Hz, 1H, H-5''), 7.00 (d, J= 9.0 Hz, 1H, H-5'), 7.10-7.30 (m, 5H, H-2', H-6', H-6'' and -CH=CH-) ppm.

3-(3,4-Dimethoxyphenyl)-7,8-dimethoxyisoflavone (5c): R_f= 0.40, 870 mg (yield 19%), mp 168-170°C (ethanol). Anal. calcd. for $C_{19}H_{18}O_6$: C, 66.67; H, 5.26. Found: C, 66.29; H, 5.47%. Ir: ν max 1645 (C=O)cm^{-1}. Uv: λ(log ε) 256(4.49), 290(4.17) nm. Pmr: δ 3.85 (s, 3H, MeO), 3.90 (s, 3H, MeO), 4.00 (s, 6H, 2 × MeO), 6.90 (d, J= 8 Hz, 1H, H-5'), 7.03 (dd, J= 8 and 2 Hz, 1H, H-6'), 7.05 (d, J= 9 Hz, 1H, H-6), 7.20 (d, J= 2 Hz, 1H, H-2'), 8.00 (m, 2H, H-2 and H-5) ppm. Cmr: δ 55.8, 56.3 and 61.4 (4 × MeO), 110.2 (C-6), 111.4,112.7 (C-2' and/or C-5'), 120.9, 121.5 (C-5 and/

or C-6'), 124.3, 124.5 (C-10 and/or C-3), 136.5 (C-1'), 148.7, 149.1 (C-7, C-8, C-3' and/or C-4'), 152.2 (C-2), 156.2 (C-9), 175.8 (C=O) ppm. Ms: m/z(%) 342(100) (M^+), 327(20), 171 (10).

3,5-Bis(3,4-dimethoxyphenyl)-2,4-bis(2-hydroxy-3,4-dimethoxyphenyl)pyridine (2c): R_f= 0.30, 2.23 g (yield 24%) (Tables 1 and 2).

5-(3,4-Dimethoxyphenyl)-4-(2-hydroxy-3,4-dimethoxyphenyl)pyrimidine (4c): R_f= 0.14, 800 mg (yield 16%), mp 140-141°C (ethanol). Anal. calcd. for $C_{20}H_{20}N_2O_5$: C, 65.22; H, 5.43; N, 7.61. Found: C, 64.89; H, 5.59; N, 7.71%. Ir: ν max 1620, 1570 and 1520 (C=C and C=N) cm^{-1}. *Uv λ max(log ε) 240(4.22), 307(4.13), 335 (4.08) nm.* Pmr: δ 3.63 (s, 3H, MeO), 3.70 (s, 3H, MeO), 3.75 (s, 3H, MeO), 3.80 (s, 3H, MeO), 6.05 (d, J= 9.2 Hz, 1H, H-5"), 6.65 (d, J= 1.8 Hz, 1H, H-2'), 6.70 (d, J= 9.2 Hz, 1H, H-6"), 6.80 (dd, J= 8.2 and 1.8 Hz, 1H, H-6'), 6.85 (d, J= 8.2 Hz, 1H, H-5'), 8.50 (s, 1H, H-6), 8.90 (s, 1H, H-2), 12.40 (s, 1H, OH, exchang. with D_2O) ppm. Cmr: δ 55.4, 55.5, 55.6 and 60.1 (4 × MeO), 102.1 (C-5"), 111.5,111.8 (C-2' and/or C-5'), 120.8 (C-6'), 126.4 (C-6"), 129.0, 131.7 (C-1" and/or C-5), 136.8 (C-1'), 148.9, 149.0 (C-3' and/or C-4'), 153.6 (C-6), 154.2, 155.0 (C-2", C-3" and/or C-4"), 158.8 (C-2), 161.2 (C-4) ppm. Ms: m/z(%) 368(100) (M^+), 367(25), 353(34), 291(21).

Deoxybenzoin (1b) (7.8 g, 0.019 mole) with formamide (9.5 ml) afforded a residue which was submitted to flash column chromatography on silica gel with dichloromethane/ethyl acetate 9:1 as eluent, thus giving the following compounds:

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-2-(2-hydroxy-3,4-dimethoxyphenyl)ethylene (3b): R_f= 0.61, 345 mg (yield 12%), mp 176-177°C (chloroform/ethanol) (Lit.[9] mp 176-177°C).

3-(2-Bromo-4,5-dimethoxyphenyl)-7,8-dimethoxyisoflavone (5b): R_f= 0.38, 705 mg (yield 24%), mp 213-215°C (ethyl acetate/dichloromethane) (Lit.[9] mp 213-215°C).

5-(2-Bromo-4,5-dimethoxyphenyl)-4-(2-hydroxy-3,4-dimethoxyphenyl)pyrimidine (4b): R_f= 0.25, 790 mg (yield 25%), mp 162-163°C (ethanol) (Lit.[9] mp 162-163°C).

Successive elution with dichloromethane/ethyl acetate (8:2) gave a new component: 3,5-bis(2-bromo-4,5-dimethoxyphenyl)-2,4-bis(2-hydroxy-3,4-dimethoxyphenyl)pyridine (2b): R_f= 0.20 (dichloromethane/ ethyl acetate 8:2), 80 mg (yield 8%) (Tables 1 and 2).

Reaction of the Alkoxylated Deoxybenzoins (1d-f) under Leuckart Conditions. General Procedure.

The alkoxylated deoxybenzoin (1 mmol) was reacted with formamide (0.1 ml), ammonium formate (10 mmole) and formic acid (0.1 ml) at 185-190°C for the required period of time. The reaction was followed by tlc on silica gel using dichloromethane / ethyl acetate (9:1) and stopped when the starting material was consumed. After work-up as described above, the crude product was crystallized to give the corresponding formamides (6) as the major products. The mother liquors from the filtration were evaporated to dryness and the residue was column chromatographed on silica gel, in order to isolate the additional by-products. In this manner, the Leuckart reaction was applied to the following deoxybenzoins (Table 3):

Deoxybenzoin (1d) (4.25 g, 10 mmole), which afforded the N-2-(2-bromo-4,5-dimethoxyphenyl)-1-(2,3,4-trimethoxyphenyl)ethylformamide (6d) as the major product, 3.8 g (yield 83%), mp 138-139°C (ethanol). Anal. calcd. for $C_{20}H_{24}BrNO_6$: C, 52.86; H, 5.29; Br, 17.62; N, 3.08. Found: C, 52.59; H, 5.25; Br, 17.78; N, 3.01%. Ir: ν max 3300 (N-H) and 1660 (C=O) cm^{-1}. Pmr: δ 2.75 (d, J= 7.2 Hz, 2H, $-CH_2-$), 3.45 (s, 3H, MeO), 3.50 (s, 12H, 4 × MeO), 5.30 (m, 1H, -CH-), 6.40-7.00 (m, 4H, aromatic protons), 7.75 (s, 1H, -CHO), 8.20 (broad d, 1H, -NH-) ppm.

The flash column chromatography (eluent: dichloromethane/ ethyl acetate 9:1) of the mother liquors furnished:

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-2-(2,3,4-trimethoxyphenyl)ethylene (3d): R_f= 0.80, 123 mg (yield 3%), mp 150-152°C (ethanol). Anal. calcd. for $C_{19}H_{21}BrO_5$: C, 55.75; H, 5.13; Br, 19.56. Found: C, 55.44; H, 4.97; Br, 19.80%. Uv: λ(log ε) 298(4.25), 322(4.26) nm. Pmr: δ 3.65 (s, 6H, 2 × MeO), 3.68 (s, 3H, MeO), 3.72 (s, 3H, MeO), 3.75 (s, 3H, MeO), 6.50 (d, J= 9 Hz, 1H, H-5"), 6.80 (s, 1H, H-6'), 6.90-7.20 (m, 4H, H-3', H-6" and -CH=CH-) ppm.

3-(2-Bromo-4,5-dimethoxyphenyl)-7,8-dimethoxyisoflavone (5b): R_f= 0.38, 210 mg (yield 5%), mp 213-215°C (dichloromethane/ethyl acetate) (Lit.[9] 213-215°C).

5-(2-Bromo-4,5-dimethoxyphenyl)-4-(2,3,4-trimethoxyphenyl)pyrimidine (4d): R_f= 0.30, 140 mg (yield 3%), mp 165-167°C (ethanol). Anal. calcd. for $C_{21}H_{21}BrN_2O_5$: C, 54.66; H, 4.56; Br, 17.35; N, 6.07. Found: C, 54.57; H, 4.55; Br, 17.28; N, 6.04%. Ir: ν max 1610, 1570 and 1520 (C=C and C=N) cm^{-1}. Uv: λ(log ε) 243(4.25), 275 (4.30), 292(4.29) nm. Pmr: δ 3.80 (s, 3H, MeO), 3.85 (s, 3H, MeO), 3.90 (s, 6H, 2 × MeO), 3.95 (s, 3H, MeO), 6.20 (d, J= 9.3 Hz, 1H, H-5"), 6.70 (s, 1H, H-6'), 6.75 (d, J= J= 9.3 Hz, 1H, H-6"), 7.15 (s, 1H, H-3'), 8.60 (s, 1H, H-6), 9.10 (s, 1H, H-2) ppm. Ms: m/z(%) 462(3) (M^++ 2), 460(3) (M^+), 448(36), 446(36), 368(25), 367(100), 349 (25), 336(22), 281(33).

Deoxybenzoin (1e)[11] (3.95 g, 10 mmole), which gave the N-2-(2-bromo-4,5-dimethoxyphenyl)-1-(3,4-dimethoxyphenyl)ethylformamide (6e) as the major product, 3.6 g (yield 85%), mp 181-182°C (methanol/chloroform) (Lit.[11] mp 181-183°C).

The filtrates from crystallization were eluted with chloroform/ethyl acetate (9:1) and provided the following compounds:

(E)-1-(2-Bromo-4,5-dimethoxyphenyl)-2-(3,4-dimethoxyphenyl)ethylene (3e): R_f= 0.83, 150 mg (yield 4%), mp 131-132°C (methanol) (Lit.[22] 131-132°C).

5-(2-Bromo-4,5-dimethoxyphenyl)-4-(3,4-dimethoxyphenyl)pyrimidine (4e): R_f= 0.32, 260 mg (yield 6%), mp 93-95°C (ethanol). Anal. calcd. for $C_{20}H_{19}BrN_2O_4$: C, 55.68; H, 4.41; Br, 18.56; N, 6.50. Found: C, 55.53; H, 4.39; Br, 18.36; N, 6.40%. Ir: ν max 1620, 1580 and 1515 (C=C and C=N) cm^{-1}. UV: λ(log ε) 240(4.27), 292(4.11), 310(4.07) nm. Pmr: δ 3.68 (s, 3H, MeO), 3.70 (s, 3H, MeO), 3.85 (s, 3H, MeO), 3.90 (s, 3H, MeO), 6.65 (s, 1H, H-6'), 6.75 (d, J= 8.9 Hz, 1H, H-5"), 7.09 (dd, J= 8.9 and 2.2 Hz, 1H, H-6"), 7.10 (d, J= 2.2 Hz, 1H, H-2"), 7.12 (s, 1H, H-3'), 8.60 (s, 1H, H-6), 9.20 (s, 1H, H-2) ppm. Cmr: δ 55.3, 55.5, 55.7 and 56.0 (4 × MeO), 113.7 (C-Br), 110.4, 112.0, 113.6 and 115.5 (C-2", C-5", C-6' and/or C-3'), 122.4 (C-6"), 129.3, 131.6 (C-1", C-1' and/or C-5), 148.2, 148.6, 149.5 and 150.2 (C-3", C-4", C-4' and/or C-5'), 157.4, 158.6 (C-6 and/or C-2), 162.5 (C-4) ppm. Ms: m/z(%) 432(9) (M^++ 2), 430(9) (M^+), 352(21), 351(100), 336(14), 335(38), 307(10).

Deoxybenzoin (1f)[10] (3.16 g, 10 mmole), which yielded the N-1,2-bis(3,4-dimethoxyphenyl)ethylformamide (6f) as the main product, 2.7 g (yield 80%), mp 127-129°C (methanol) (Lit.[2] mp 127-128°C).

The following by-products were isolated by column chromatography of the mother liquors using dichloromethane/ethyl acetate (9.5:0.5) as eluent:

(E)-1,2-Bis(3,4-dimethoxyphenyl)ethylene (3f): R_f= 0.83, 120 mg (yield 4%), mp 151-152°C (ethanol) (Lit.[2] mp 151-152°C).

4,5-Bis(3,4-dimethoxyphenyl)pyrimidine (4f): R_f= 0.31, 140 mg (yield 4%), mp 125-127°C (ethanol). Anal. calcd. for $C_{20}H_{20}N_2O_4$: C, 68.18; H, 5.68; N, 7.95. Found: C, 68.35; H, 5.71; N, 7.82%. Ir: ν max 1610, 1580 and 1520 (C=C and C=N) cm^{-1}. Uv: λ(log ε) 240(4.40), 292(4.16), 310(4.07) nm. Pmr: δ 3.7 (s, 6H, 2 × MeO), 3.80 (s, 6H, 2 × MeO), 6.68 (d, J= 1.8 Hz, 1H, H-2'), 6.75 (d, J= 8.6 Hz, 1H, H-5''), 6.80 (d, J= 9.5 Hz, 1H, H-5'), 6.85 (d, J= 2.0 Hz, H-2''), 7.05-7.15 (m, 2H, H-6' and H-6''), 8.60 (s, 1H, H-6), 9.41 (s, 1H, H-2) ppm. Ms: m/z(%) 352(100) (M^+), 351(47), 337(19), 321(15).

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