Regioselectivity in the Westphal Condensation

Adolfo Díaz, María P. Matia, José L. García-Navío, Juan J. Vaquero, and Julio Alvarez-Builla*

Departamento de Química Orgánica, Universidad de Alcalá, 28871 Alcalá de Henares, Madrid, Spain

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The Westphal condensation[1] is the basis of convenient easy methodology to build up quaternary aromatic nitrogen bridgehead systems by means of a condensation between α-methylcycloimmonium salts and 1,2-diketones.[2] This procedure has been applied to the synthesis of alkaloids such as sempervirine[3] and flavocorylene[4] which incorporate the zwitterionic indolo[2,3-*a*]quinolizinium ring system. In order to avoid the formation of regioisomers symmetrical 1,2-diketones have always been employed in the condensation.

Recently, we have been testing the method with unsymmetrical 1,2-diketones, and we present here the results obtained from the reaction of 1-aryl-1,2-propanediones (phenyl, 2-thienyl, *p*-tolyl, and 4-pyridyl) with some representative α-methylcycloimmonium substrates (Scheme 2).

Deprotonation of the starting salt **4** should produce the more stable N-ylide intermediate **5**, which should be the attacking nucleophile. In the presence of the diketone **7**, two alternative intermediates are possible. On kinetic grounds, the attack should take place at the more reactive methyl-substituted carbonyl group leading to structure **I** via the intermediate **8**. However, the thermodynamically controlled product **II**, passing through the more conjugated intermediate **9**, is the alternative possibility. The molar ratio **I:II** should be highly dependent on the electronic character of the aryl group in the starting diketone **7** (R = Ar). Thus, diketones bearing π-excessive arenes would increase conjugation in the intermediate **9** with the consequent rise in the proportion of **II**, while conversely, with π-deficient systems, kinetic control should favor the predominance of **I** in the final product.

The results in Table 1[5] show how kinetic control predominates with 1-(4-pyridyl)- and 1-phenyl-1,2-propanediones, producing only 3-methyl derivatives **I**. In contrast, π-excessive aromatic systems such as 1-(2-thienyl)-, and to a lesser extent, 1-(*p*-tolyl)-1,2-propanedione, produced significant amounts of regioisomers **II**, as a consequence of the higher stability of the more conjugated intermediate. Moreover, when 2,3-pentanedione was used (entries **1**, **6**, **18**, and **23**) to demonstrate the behavior of a diketone with no electronic effects differentiating between carbonyls, an approximately 50:50 mixture was formed.

The structures of the isolated products have been established using homonuclear NOE difference spectroscopy,[6] employing a through-space connection between the protons, C1-H and C4-H, of the pyridinium, or C1-H of the pyridazinium moieties, and those of the methyl group directly attached to these fragments.

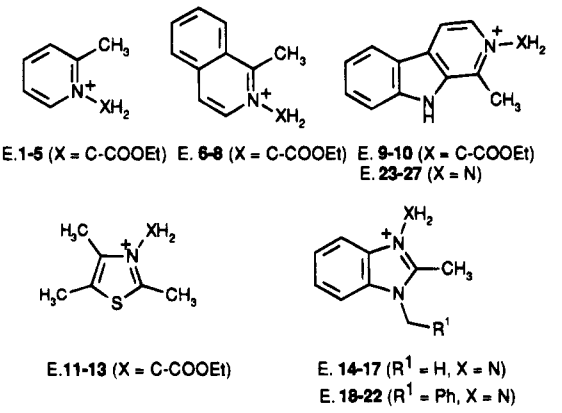
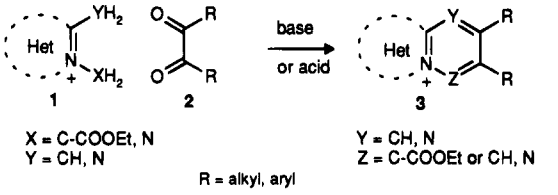
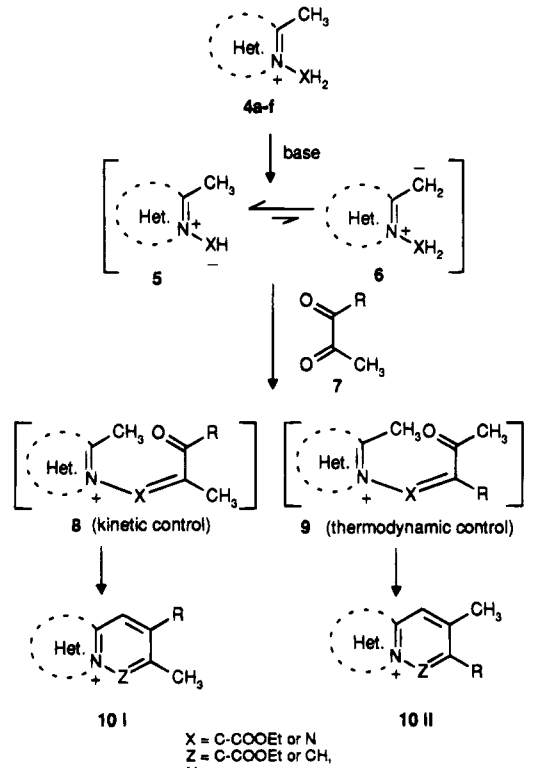


Figure 1. Substrates used in entries 1–22 in Table 1.

Scheme 1



Scheme 2



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(5) Hydrolysis and decarboxylation of the ester group were observed in most of the examples, **1–13**, as has been observed before; see ref 2b and references cited therein.

(6) Standard parameters were used, see: Holzer, W. *Tetrahedron* **1991**, *47*, 9783–9792.

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Table 1. Westphal Condensations Performed To Obtain Compounds 10

entry	heterocycle	X	Z	R	react. time (h) solvent, temp	**10 I:II** ratio[a]	yield (%)[b]
1	2-pyridyl	CCOOEt	CH	ethyl	20, Me_2CO, rt	50:50 (**11:12**)	88
2	2-pyridyl	CCOOEt	CH	phenyl	15, Me_2CO, rt	100:0 (**13**)	67[c]
3	2-pyridyl	CCOOEt	CH	*p*-tolyl	24, Me_2CO, rt	75:25 (**14:15**)	92
4	2-pyridyl	CCOOEt	CH	2-thienyl	24, Me_2CO, rt	40:60 (**16:17**)	88
5	2-pyridyl	CCOOEt	CH	4-pyridyl	2, Me_2CO, rflx	100:0 (**18**)	81[c]
6	1-isoquinolyl	CCOOEt	CCOOEt	ethyl	3.5, Me_2CO, rflx	80:20 (**19:20**)[d]	75
7	1-isoquinolyl	CCOOEt	CH	phenyl	5, Me_2CO, rflx	100:0 (**21**)	45[c]
8	1-isoquinolyl	CCOOEt	CH	2-thienyl	3.5, Me_2CO, rflx	50:50 (**22:23**)	85
9	1-(pyrido[3,4-*b*]indol)yl	CCOOEt	CH	phenyl	3, EtOH, rflx	100:0 (**24**)	70[e]
10	1-(pyrido[3,4-*b*]indol)yl	CCOOEt	CH	4-pyridyl	2, EtOH, rflx	100:0 (**25**)	60[c]
11	2-(4,5-dimethylthiazol)yl	CCOOEt	CH	phenyl	2.5, Me_2CO, rflx	100:0 (**26**)	57[c]
12	2-(4,5-dimethylthiazol)yl	CCOOEt	CH	*p*-tolyl	2.5, Me_2CO, rflx	100:0 (**27**)	52[c]
13	2-(4,5-dimethylthiazol)yl	CCOOEt	CH	4-pyridyl	2, EtOH, rflx	100:0 (**28**)	70[e]
14	2-(3-methylbenzimidazol)yl	N	N	phenyl	2.5, EtOH, rflx	100:0 (**29**)	81[e]
15	2-(3-methylbenzimidazol)yl	N	N	*p*-tolyl	2.5, EtOH, rflx	80:20 (**30:31**)	70
16	2-(3-methylbenzimidazol)yl	N	N	2-thienyl	3, EtOH, rflx	25:75 (**32:33**)	42
17	2-(3-methylbenzimidazol)yl	N	N	4-pyridyl	1, EtOH, rflx	100:0 (**34**)	76[e]
18	2-(3-benzylbenzimidazol)yl	N	N	ethyl	3, EtOH, rflx	40:60 (**35:36**)	62
19	2-(3-benzylbenzimidazol)yl	N	N	phenyl	3.5, EtOH, rflx	100:0 (**37**)	60[e]
20	2-(3-benzylbenzimidazol)yl	N	N	*p*-tolyl	5, EtOH, rflx	60:40 (**38:39**)	74
21	2-(3-benzylbenzimidazol)yl	N	N	2-thienyl	2, EtOH, rflx	33:66 (**40:41**)	88[e]
22	2-(3-benzylbenzimidazol)yl	N	N	4-pyridyl	1, EtOH, rflx	100:0 (**42**)	79[e]
23	1-(pyrido[3,4-*b*]indol)yl	N	N	ethyl	2.5, EtOH, rflx	50:50 (**43:44**)	86
24	1-(pyrido[3,4-*b*]indol)yl	N	N	phenyl	3, EtOH, rflx	100:0 (**45**)	37[c]
25	1-(pyrido[3,4-*b*]indol)yl	N	N	*p*-tolyl	2, EtOH, rflx	66:33 (**46:47**)	85[c]
26	1-(pyrido[3,4-*b*]indol)yl	N	N	2-thienyl	3, EtOH, rflx	25:75 (**48:49**)	91[c]
27	1-(pyrido[3,4-*b*]indol)yl	N	N	4-pyridyl	2, EtOH, rflx	100:0 (**50**)	36[c]

[a]Determined by ^1H NMR analysis of the crude reaction mixture. Compound identification is shown in brackets. [b]Total yield in **10 I:II** mixture. [c]Experimental procedure. Method A. [d]Overlapped signals. [e]Experimental procedure. Method B. Abbreviations: rt, room temperature; rflx, reflux.

In conclusion, the Westphal condensation, when performed using 1-aryl-1,2-propanediones, shows a typical kinetic *vs* thermodynamic control pattern, showing preference for the kinetically-controlled regioisomers. Mixtures of varying composition were obtained when π-excessive aryl groups were present in the 1,2-dicarbonyl fragment.

Experimental Section

Melting points are uncorrected. Mesitylenesulfonate anion signals are independent of the heterocyclic cations and appear at fixed values: 2.2 ppm for the *p*-methyl group, 2.4 ppm for the two *o*-methyl groups, and 6.7 ppm for the aromatic protons, and are not listed.

Starting heterocycles and 1,2-dicarbonyls were commercially available or obtained by previously described methods.[7] The (ethoxycarbonyl)methyl salts **4a–d** (Scheme 2) were obtained as described for pyridine,[8a] isoquinoline,[9] β-carboline,[4] and thiazole[8b] derivatives, respectively. The *N*-amino salts **4e,g** were obtained as described for 1-methylbenzimidazole[2d] and β-carboline[3] derivatives. Only experiments allowing the isolation of single isomers are described.

1-Amino-3-benzyl-2-methylbenzimidazolium Mesitylenesulfonate (4f). To a stirred solution of amino mesitylenesulfonate (MSH) (0.97 g, 4.5 mmol) in CH_2Cl_2 (10 mL) was added 1-benzyl-2-methylbenzimidazole (1 g, 4.5 mmol) in CH_2Cl_2 (5 mL) dropwise. After 10 min of stirring at room temperature, Et_2O was added to precipitate the *N*-aminobenzimidazolium salt, which was filtered and recrystallized from EtOH–Et_2O to give 1.48 g of **4f**, 75%: mp 195–198 °C; IR (KBr) 1654 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.89 (s, 3H); 5.77 (s, 2H); 6.65 (bs, 2H); 7.3–7.4 (m, 5H); 7.57 (t, 1H, J = 7.6 Hz); 7.63 (t, 1H, J = 7.6 Hz); 7.86 (d, 1H, J = 7.6 Hz); 7.90 (d, 1H, J = 7.6 Hz). Anal. Calcd for $C_{24}H_{27}N_3O_3S$: C, 65.87; H, 6.21; N, 9.60. Found: C, 65.52; H, 5.95; N, 9.28.

Westphal Condensation. General Procedure. Equimolar amounts of the corresponding azinium or azolium salt **4** (10 mmol), the dicarbonyl compound, and anhydrous sodium acetate were refluxed in the dry solvent indicated (10 mL), for the time described (Table 1). **Method A.** When a precipitate formed, the warm mixture was filtered and crystallization of the residue yielded the condensation product, which was analytically pure. **Method B.** Alternatively, when no precipitate was observed, the reaction mixture was concentrated to dryness, the residue triturated with acetone, and the mixture filtered. Recrystallization of the solid afforded the condensation product.

3-Methyl-2-phenylquinolizinium Bromide (13). Obtained by method A, 67%: mp 227–229 °C (from EtOH–Et_2O); IR (KBr) 1631 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.49 (s, 3H); 7.5–7.6 (m, 5H); 8.07 (t, 1H, J = 7.2 Hz); 8.33 (t, 1H, J = 7.2 Hz); 8.5–8.6 (m, 2H); 9.31 (d, 1H, J = 7.2 Hz); 9.50 (s, 1H). Anal. Calcd for $C_{16}H_{14}BrN{\cdot}1/_2H_2O$: C, 62.15; H, 4.89; N, 4.53. Found: C, 62.10; H, 4.92; N, 4.55.

3-Methyl-2-pyridylquinolizinium Bromide (18). Obtained by method A, 81%: mp 251–253 °C (from EtOH–Et_2O); IR (KBr) 1638 cm^{-1}; ^1H NMR (CD_3OD) δ 2.46 (s, 3H); 7.65 (d, 2H, J = 5.1 Hz); 8.12 (t, 1H, J = 6.6 Hz); 8.37 (t, 1H, J = 8.0 Hz); 8.53 (d, 1H, J = 8.4 Hz); 8.61 (s, 1H); 8.81 (d, 2H, J = 5.1 Hz); 9.32 (d, 1H, J = 6.3 Hz); 9.50 (s, 1H). Anal. Calcd for $C_{15}H_{13}BrN_2{\cdot}H_2O$: C, 56.44; H, 4.74; N, 8.78. Found: C, 56,25; H, 4.89; N, 8.61.

3-Methyl-2-phenylbenzo[*a*]quinolizinium Bromide (21). Obtained by method A, 45%: mp 337–339 °C (from EtOH–Et_2O); IR (KBr) 1639 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.54 (s, 3H); 7.6–7.7 (m, 5H); 8.00 (t, 1H, J = 8.3 Hz); 8.10 (t, 1H, J = 7.3 Hz); 8.25 (d, 1H, J = 8.0 Hz); 8.33 (d, 1H, J = 7.1 Hz); 8.91 (d, 1H, J = 7.3 Hz); 9.27 (d, 1H, J = 8.6 Hz); 9.33 (s, 1H); 9.55 (s, 1H). Anal. Calcd for $C_{20}H_{16}NBr{\cdot}2H_2O$: C, 62.19; H, 5.22; N, 3.63. Found: C, 62.12; H, 5.51; N, 3.32.

3-Methyl-2-phenyl-12*H*-indolo[2,3-*a*]quinolizinium Bromide (24). Obtained by method B, 70%: mp >360 °C (from CH_3CO_2H); IR (KBr) 1633 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.51 (s,

(7) Both 2,3-pentanedione and 1-phenyl-1,2-propanedione are commercially available, 1-(2-thienyl)- and 1-(*p*-tolyl)-1,2-propanediones were prepared by nitrosation of the corresponding 1-substituted 1-propanones with isoamyl nitrite and final acid hydrolysis of the formed α-oximino ketones as described by Gianturco, M. A. et al. *Tetrahedron*, **1964**, 2951–2961. Finally, the 4-pyridyl derivative was obtained, as described by Knaus, E. E. *Can. J. Chem.*, 1980, *58*, 130–133, starting with 4-pyridinecarboxaldehyde.

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3H); 7.44 (t, 1H, J = 7.8 Hz); 7.6–7.7 (m, 6H); 7.80 (d, 1H, J = 7.8 Hz); 8.41 (d, 1H, J = 7.8 Hz); 8.78 (d, 1H, J = 6.6 Hz); 8.90 (s, 1H); 8.94 (d, 1H, J = 6.6 Hz); 9.43 (s, 1H); 13.35 (bs, 1H). Anal. Calcd for $C_{22}H_{17}N_2Br·H_2O$: C, 64.87; H, 4.70; N, 6.88. Found: C, 64.52; H, 4.97; N, 6.56.

3-Methyl-2-pyridyl-12*H*-indolo[2,3-*a*]quinolizinium Bromide (25). Obtained by method A, 60%: mp >360 °C (from CH_3CO_2H); IR (KBr) 1633 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.53 (s, 3H); 7.48 (t, 1H, J = 7.4 Hz); 7.73 (t, 1H, J = 7.4 Hz); 7.86 (d, 1H, J = 7.5 Hz); 8.01 (d, 2H, J = 4.8 Hz); 8.46 (d, 1H, J = 7.7 Hz); 8.90 (d, 1H, J = 7.5 Hz); 9.0–9.1 (m, 4H); 9.53 (s, 1H); 13.48 (s, 1H). Anal. Calcd for $C_{21}H_{16}N_3Br·^1/_2H_2O$: C, 63.17; H, 4.29; N, 10.52. Found: C, 62.93; H, 4.61; N, 10.73.

1,2,6-Trimethyl-5-phenylthiazolo[3,2-*a*]pyridinium Bromide (26). Obtained by method A, 57%: mp 273–275 °C (from EtOH–Et_2O); IR (KBr) 1636 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.53 (s, 3H); 2.69 (s, 3H); 2.72 (s, 3H); 7.5–7.6 (m, 5H); 8.46 (s, 1H); 9.04 (s, 1H). Anal. Calcd for $C_{16}H_{16}NSBr·H_2O$: C, 54.55; H, 5.15; N, 3.97. Found: C, 54.53; H, 5.35; N, 3.69.

1,2,6-Trimethyl-5-*p*-tolylthiazolo[3,2-*a*]pyridinium Bromide (27). Obtained by method A, 52%: mp 251–253 °C (from EtOH–Et_2O); IR (KBr) 1633 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.44 (s, 3H); 2.54 (s, 3H); 2.69 (s, 3H); 2.71 (s, 3H); 7.39 (d, 1H, J = 8.1 Hz); 7.47 (d, 2H, J = 8.1 Hz); 8.44 (s, 1H); 9.02 (s, 1H). Anal. Calcd for $C_{17}H_{18}NSBr$: C, 58.62; H, 5.21; N, 4.02. Found: C, 58.37; H, 5.11; N, 4.42.

1,2,6-Trimethyl-5-pyridylthiazolo[3,2-*a*]pyridinium Bromide (28). Obtained by method B, 70%, mp 285–287 °C (from EtOH–Et_2O); IR(KBr) 1627 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.58 (s, 3H); 2.74 (s, 3H); 2.77 (s, 3H); 8.19 (d, 2H, J = 6.6 Hz); 8.71 (s, 1H); 9.03 (d, 2H, J = 6.6 Hz); 9.19 (s, 1H). Anal. Calcd for $C_{15}H_{15}N_2SBry·H_2O$: C, 51.00; H, 4.85; N, 7.93. Found: C, 50.78; H, 5.00; N, 7.78.

2,5-Dimethyl-3-phenylpyridazino[1,6-*a*]benzimidazolium Mesitylenesulfonate (29). Obtained by method B, 81%: mp 235–238 °C (from EtOH–Et_2O); IR (KBr) 1636 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.70 (s, 3H); 4.24 (s, 3H); 7.6–7.7 (m, 5H); 7.81 (t, 1H, J = 7.7 Hz); 7.94 (t, 1H, J = 7.7 Hz); 8.21 (d, 1H, J = 8.3 Hz); 8.44 (d, 1H, J = 8.3 Hz); 8.90 (s, 1H). Anal. Calcd for $C_{27}H_{27}O_3N_3S$: C, 68.47; H, 5.75; N, 8.87. Found: C, 68.38; H, 5.55; N, 8.76.

2,5-Dimethyl-3-pyridylpyridazino[1,6-*a*]benzimidazolium Bromide (34). After complexion of the refluxing time (Table 1), the solution was acidified with HBr drops (48%), and then the standard workup (method B) was carried out, 76%: mp 260–262 °C (from EtOH–Et_2O); IR (KBr) 1636 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.73 (S, 3H); 4.29 (s, 3H); 7.8–7.9 (m, 3H); 8.00 (t, 1H, J = 7.9 Hz); 8.26 (d, 1H, J = 8.40 Hz); 8.50 (d, 1H, J = 8.4 Hz); 8.94 (d, 2H, J = 5.1 Hz); 9.09 (s, 1H). Anal. Calcd for $C_{17}H_{15}N_4Br·H_2O$: C, 54.70; H, 4.59; N, 15.01. Found: C, 54.38; H, 4.76; N, 14.89.

5-Benzyl-2-methyl-3-phenylpyridazino[1,6-*a*]benzimidazolium Mesitylenesulfonate (37). Obtained by method B, 60%: mp 192–194 °C (from EtOH–Et_2O); IR (KBr) 1626 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.57 (s, 3H); 6.10 (s, 2H); 7.3–7.5 (m, 5H); 7.6–7.7 (m, 5H); 7.81 (t, 1H, J = 8.1 Hz); 7.89 (t, 1H, J = 8.3 Hz); 8.06 (d, 1H, J = 8.3 Hz); 8.50 (d, 1H, J = 8.1 Hz); 9.13 (s, 1H). Anal. Calcd for $C_{33}H_{31}N_3O_3S·H_2O$: C, 69.81; H, 5.86; N, 7.40. Found: C, 69.81; H, 5.54; N, 7.29.

5-Benzyl-3-methyl-2-(2-thienyl)pyridazino[1,2-*a*]benzimidazolium Mesitylenesulfonate (40). Obtained by method B, 60%: mp 218–220 °C (from CH_3CN); IR (KBr) 1636 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.88 (s, 3H); 6.07 (s, 2H); 7.3–7.4 (m, 4H); 7.5–7.6 (m, 2H); 7.79 (t, 1H, J = 7.3 Hz); 7.88 (t, 1H, J = 7.6 Hz); 7.9–8.0 (m, 2H); 8.09 (d, 1H, J = 8.3 Hz); 8.45 (d, 1H, J = 8.0 Hz); 9.26 (s, 1H). Anal. Calcd for $C_{31}H_{29}N_3O_3S_2·^1/_2H_2O$: C, 65.93; H, 5.35; N, 7.44. Found: C, 65.76; H, 5.18; N, 7.60.

5-Benzyl-2-methyl-3-(2-thienyl)pyridazino[1,2-*a*]benzimidazolium Bromide (41). This compound was isolated from the mother liquor of **39** by acidification of the acetone solution with HBr (48%), 28%: mp 285–287 °C (from EtOH); IR (KBr) 1600 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.98 (s, 3H); 6.12 (s, 2H); 7.3–7.5 (m, 6H); 7.79 (t, 1H, J = 7.1 Hz); 7.87 (t, 1H, J = 7.1 Hz); 7.96 (dd, 1H, J = 3.8 Hz, J = 1.0 Hz); 8.04 (d, 1H, J = 8.3 Hz); 8.09 (dd, 1H, J = 2.6 Hz, J = 1.0 Hz); 8.47 (d, 1H, J = 8.1 Hz); 9.16 (s, 1H). Anal. Calcd for $C_{22}H_{18}N_3SBr·^1/_2H_2O$: C, 59.32; H, 4.30; N, 9.44. Found: C, 59.46; H, 4.17; N, 9.28.

5-Benzyl-2-methyl-3-pyridylpyridazino[1,6-*a*]benzimidazolium Mesitylenesulfonate (42). Obtained by method B, 79%: mp 185–187 °C (from EtOH–Et_2O); IR (KBr) 1633 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.75 (s, 3H); 6.01 (s, 2H); 7.3–7.4 (m, 3H); 7.46 (d, 2H, J = 8.5 Hz); 7.78 (d, 2H, J = 6.0 Hz); 7.85 (t, 1H, J = 7.5 Hz); 7.92 (t, 1H, J = 7.5 Hz); 8.09 (d, 1H, J = 8.5 Hz); 8.53 (d, 1H, J = 8.5 Hz); 8.91 (d, 2H, J = 6.0 Hz); 9.24 (s, 1H). Anal. Calcd for $C_{32}H_{30}N_4O_3S$: C, 69.79; H, 5.49; N, 10.17. Found: C, 69.43; H, 5.68; N, 10.22.

3-Methyl-2-phenyl-12*H*-pyridazino[1′,6′:1,2]pyrido[3,4-*b*]-indol-5-ium Mesitylenesulfonate (45). Obtained by method A, 37%: mp 294–296 °C (from CH_3CO_2H); IR (KBr) 1635 cm^{-1}; ^{1}H NMR (CF_3CO_2D) δ 2.75 (s, 3H); 7.4–7.5 (m, 6H); 7.6–7.7 (m, 2H); 8.24 (d, 1H, J = 8.1 Hz); 8.52 (d, 1H, J = 6.8 Hz); 8.78 (s, 1H); 8.98 (d, 1H, J = 7.1 Hz). Anal. Calcd for $C_{30}H_{27}N_3O_3S·^1/_2H_2O$ C, 69.47; H, 5.44; N, 8.10. Found: C, 69.15; H, 5.19; N, 8.42.

3-Methyl-2-*p*-tolyl-12*H*-pyridazino[1′,6′:1,2]pyrido[3,4-*b*]-indol-5-ium Mesitylenesulfonate (46). Obtained by method A, 46%: mp 307–309 °C (from CH_3CO_2H); IR (KBr) 1638 cm^{-1}; ^{1}H NMR (CD_3OD) δ 2.49 (s, 3H); 2.83 (s, 3H); 7.47 (d, 2H, J = 7.9 Hz); 7.53 (t, 1H, J = 8.1 Hz); 7.62 (d, 1H, J = 7.9 Hz); 7.81 (d, 1H, J = 9.0 Hz); 7.83 (t, 1H, J = 9.9 Hz); 8.46 (d, 1H, J = 8.0 Hz); 8.84 (d, 1H, J = 7.1 Hz); 8.84 (d, 1H, J = 7.1 Hz); 8.98 (s, 1H); 9.18 (d, 1H, J = 7.1 Hz). Anal. Calcd for $C_{31}H_{29}N_3O_3S·H_2O$: C, 68.74; H, 5.77; N, 7.76. Found: C, 68.46; H, 6.01; N, 7.42.

2-Methyl-3-(2-thienyl)-12*H*-pyridazino[1′,6′:1,2]pyrido-[3,4-*b*]indol-5-ium Mesitylenesulfonate (49). Obtained by method A, 49%: mp >360 °C (from CH_3CO_2H); IR (KBr) 1638 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.83 (s, 3H); 7.16 (t, 1H, J = 7.5 Hz); 7.33 (t, 1H, J = 4.4 Hz); 7.47 (t, 1H, J = 7.3 Hz); 7.81 (d, 1H, J = 8.5 Hz); 7.9–8.0 (m, 2H); 8.32 (d, 1H, J = 7.8 Hz); 8.62 (d, 1H, J = 6.8 Hz); 8.73 (d, 1H, J = 7.1 Hz); 9.30 (s, 1H). Anal. Calcd for $C_{28}H_{25}N_3O_3S_2·H_2O$: C, 63.01; H, 5.10; N, 7.87. Found: C, 63.34; H, 4.99; N, 8.12.

3-Methyl-2-pyridyl-12*H*-pyridazino[1′,6′:1,2]pyrido[3,4-*b*]indol-5-ium Mesitylenesulfonate (50). Obtained by method A, 36%: mp 308–310 °C (from CH_3CO_2H); IR (KBr) 1622 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.79 (s, 3H); 7.54 (t, 1H, J = 7.0 Hz); 7.78 (d, 2H, J = 5.5 Hz); 7.81 (t, 1H, J = 7.0 Hz); 7.94 (d, 1H, J = 7.9 Hz); 8.88 (d, 2H, J = 5.5 Hz); 9.07 (d, 1H, J = 7.0 Hz); 9.30 (s, 1H); 9.40 (d, 1H, J = 7.0 Hz). Anal. Calcd for $C_{29}H_{26}N_4O_3S$: C, 68.22; H, 5.13; N, 10.97. Found: C, 68.03; H, 5.42; N, 10.85.

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