Tetrahedron Vol. 47, No. 35, pp. 7329-7342, 1991
Printed in Great Britain

0040-4020/91 $3.00+.00

NEW USES OF THE WESTPHAL CONDENSATION. SYNTHESIS OF PI-DONOR-PI-ACCEPTOR HETEROCYCLES.

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(*Received in UK* 29 *May* 1991)

Abstract: Novel pyrido[1,2-a] and pyridazino[2,3-a]-pyrrolo[2,1-c]pyrazin-7-ium derivatives have been prepared using Westphal condensation, as an example of fused heterocycles with linked π-donor and π-acceptor moieties.

Following our interest in dipolar heterocycles, we are exploring the preparation of polycyclic derivatives, in which π-donor and π-acceptor moieties are covalently bonded in a planar system, allowing a good transfer of electronic density between them.

As one of the more evident examples, we focussed our attention on compounds with a 2,2'-pyrrolylpyrazinium substructure like pyrido[1,2-a]-pyrrolo[2,1-c]pyrazin-7-ium salts **1** (R_1,R_2=H, A-B=-CH=CH-) (Fig. 1), in which the pyrrole moiety would increase the contribution of the resonance form **II** to the electronic distribution of the ground state.

I II

Fig. 1

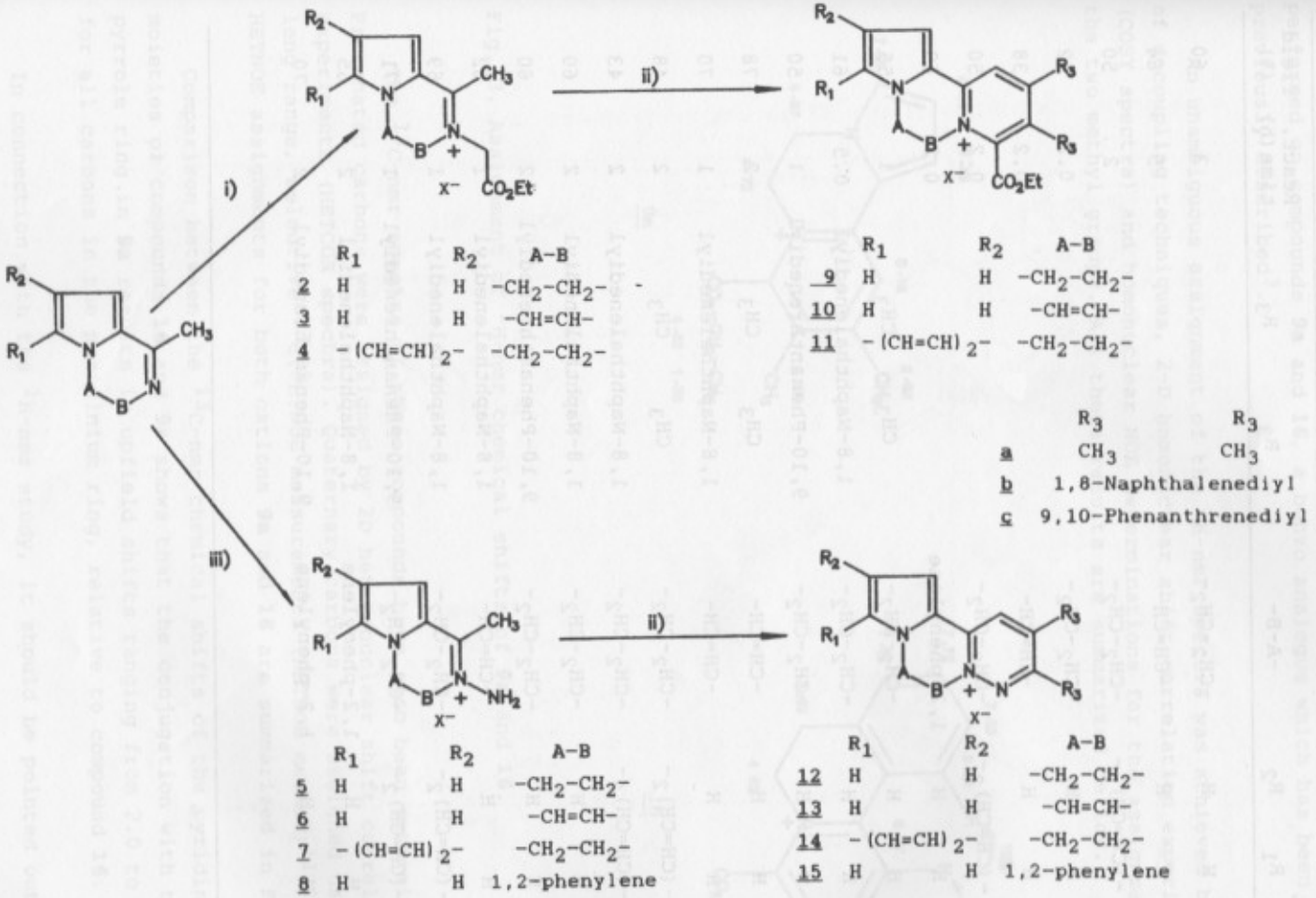
The positive charge of the nucleus would be efficiently delocalized between both nitrogen atoms, producing comparatively stable structures of unusual reactivity and physico-chemical properties. One related example has been described by K. Matoba[1], obtained by a non generalizable process.

After previous contributions[2-6] to Westphal condensation[7], we have designed a general route for derivatives type **1** by starting with 1-methyl-3,4-dihydropyrrolo[1,2-a]pyrazine[8] (R_1,R_2=H, A-B=-CH_2-CH_2-), 1-methylpyrrolo[1,2-a]pyrazine[9] (R_1,R_2=H, A-B=-CH=CH-), and 1-methyl-3,4-dihydropyrazino[1.2-a]indole (R_1,R_2=-$(CH=CH)_2$-, A-B=-CH_2-CH_2-).

When these heterocycles were treated with ethyl bromoacetate the quaternary salts **2**, **3** and **4** were obtained (Fig. 2). However, quaternization of 1-methyl-6H-pyrrolo[1,2-a]quinoxaline[10] (R_1,R_2=H, A-B= 1,2-phenylene) was unsuccessful.

Basic condensation of bromides **2-3** with 1,2-dicarbonyl derivatives yielded the related pyrido[1,2-a]pyrrolo[2,1-c]pyrazin-7-ium salts **9-10** and the 6,7-dihydropyrido[2',1':3,4]pyrazino[1,2-a]indol-8-ium salt **11** (Fig. 2). As in previous papers[3-5], three representative 1,2-dicarbonyls were used to test the applicability of the method, producing all of them condensation products.

The N-amination of the related heterocyclic precursors produced the derivatives **5-8**, which were used in a modified Westphal process[6], to generate the novel salts **12-14**, aza analogues of the bromides **9-11**, and the pyrrolo[1,2-a]pyridazino[3,2-c]quinoxalin-9-ium mesitylenesulfonates **15** (Fig.2). As it has been previously observed[6], the reaction was produced only with polycyclic *o*-quinones, while benzil and diacetyl were recovered untransformed. All new compounds obtained are listed in Table 1.



	R_1	R_2	A–B
2	H	H	$-CH_2-CH_2-$
3	H	H	$-CH=CH-$
4	$-(CH=CH)_2-$		$-CH_2-CH_2-$

	R_1	R_2	A–B
9	H	H	$-CH_2-CH_2-$
10	H	H	$-CH=CH-$
11	$-(CH=CH)_2-$		$-CH_2-CH_2-$

	R_3	R_3
a	CH_3	CH_3
b	1,8-Naphthalenediyl	
c	9,10-Phenanthrenediyl	

	R_1	R_2	A–B
5	H	H	$-CH_2-CH_2-$
6	H	H	$-CH=CH-$
7	$-(CH=CH)_2-$		$-CH_2-CH_2-$
8	H	H	1,2-phenylene

	R_1	R_2	A–B
12	H	H	$-CH_2-CH_2-$
13	H	H	$-CH=CH-$
14	$-(CH=CH)_2-$		$-CH_2-CH_2-$
15	H	H	1,2-phenylene

Fig 2

i) $BrCH_2CO_2Et$/Acetone, Δ

ii) $R_3COCOR_3/Na^+, CH_3CO_2^-$//Acetone, Δ

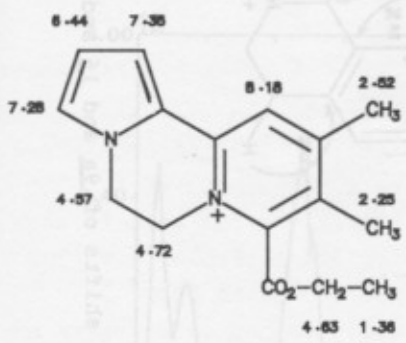
iii) O-Hydroxylaminomesitylenesulfonate/ether, r.t.

Table 1. New derivatives prepared

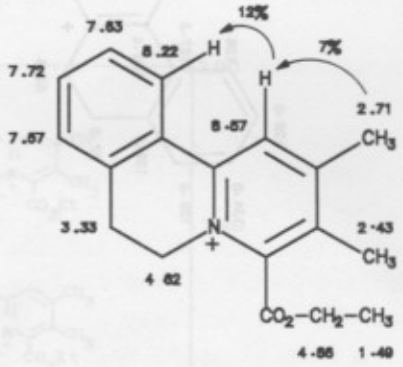
Compd. No.	R_1	R_2	-A-B-	R_3	R_3	React. time (h)	Yield (%)
2	H	H	$-CH_2-CH_2-$			3	60
3	H	H	-CH=CH-			5	64
4	$-(CH=CH)_2-$		$-CH_2-CH_2-$			2	50
5	H	H	$-CH_2-CH_2-$			0.2	52
6	H	H	-CH=CH-			0.2	38
7	$-(CH=CH)_2-$		$-CH_2-CH_2-$			0.2	50
8	H	H	1,2-phenylene			0.2	63
9a	H	H	$-CH_2-CH_2-$	CH_3	CH_3	1	55
9b	H	H	$-CH_2-CH_2-$	1,8-Naphthalenediyl		0.5	61
9c	H	H	$-CH_2-CH_2-$	9,10-Phenanthrenediyl		1	50
10a	H	H	-CH=CH-	CH_3	CH_3	2	78
10b	H	H	-CH=CH-	1,8-Naphthalenediyl		1	70
11a	$-(CH=CH)_2-$		$-CH_2-CH_2-$	CH_3	CH_3	2	48
11b	$-(CH=CH)_2-$		$-CH_2-CH_2-$	1,8-Naphthalenediyl		2	43
12b	H	H	$-CH_2-CH_2-$	1,8-Naphthalenediyl		2	60
12c	H	H	$-CH_2-CH_2-$	9,10-Phenanthrenediyl		2	60
13b	H	H	-CH=CH-	1,8-Naphthalenediyl		1	62
14b	$-(CH=CH)_2-$		$-CH_2-CH_2-$	1,8-Naphthalenediyl		1	69
14c	$-(CH=CH)_2-$		$-CH_2-CH_2-$	9,10-Phenanthrenediyl		1	71
15b	H	H	1,2-phenylene	1,8-Naphthalenediyl		2	65
15c	H	H	1,2-phenylene	9,10-Phenanthrenediyl		2	70

As a way to establish if the contribution of the form **II** was significant to the resonance hybrid, a completely ^{1}H and ^{13}C-nmr study was performed on compounds **9a** and **16**, a benzo analogue which has been previously described[3].

An unambiguous assignment of the ^{1}H-nmr spectra was achieved by means of decoupling techniques, 2-D homonuclear shift correlation experiments (COSY spectra) and homonuclear NOE determinations for the assignment of the two methyl groups. All these results are summarized bellow.



9a



16

Fig. 3. Assignment of ^{1}H-nmr chemical shifts of **9a** and **16**.

The ^{13}C-nmr spectra of these compounds have also been determined. Protonated carbons were assigned by 2D heteronuclear shift correlation experiments (HETCOR spectra). Quaternary carbons were assigned using long range, selective $^{13}C\{^{1}H\}$NOE measurements (HETNOE method)[11,12]. The HETNOE assignments for both cations **9a** and **16** are summarized in Fig. 4.

Comparison between the ^{13}C-nmr chemical shifts of the pyridinium moieties of compounds **16** and **9a** shows that the conjugation with the pyrrole ring in **9a** results in upfield shifts ranging from 2.0 to 5.0 ppm for all carbons in the pyridinium ring, relative to compound **16**.

In connection with the ^{1}H-nmr study, it should be pointed out that

Fig 4. Assignment of ^{13}C-nmr chemical shifts of 9a and 16 and HETNOE measurents.

our results are not in agreement with previous literature assignment[8], where authors described ^{1}H-nmr data for some simple quaternary salts, as 2-methyl and 2-phenethyl 1-methyl-3,4-dihydropyrrolo[1,2-a]pyrazines.

Transfer of electronic density between the pyrrolo and the pyridinium moieties has also been observed in the Uv spectra. As an example, in the 5,6-dihydropyrido[1,2-a]pyrrolo[2,1-c]pyrazin-7-ium bromide **9a**, a bathochromic shift can be observed in comparison with the analogous benzo[a]quinolizinium salt **16** (Fig. 5). A similar effect can be observed from compounds **9** to **15** (see experimental section).

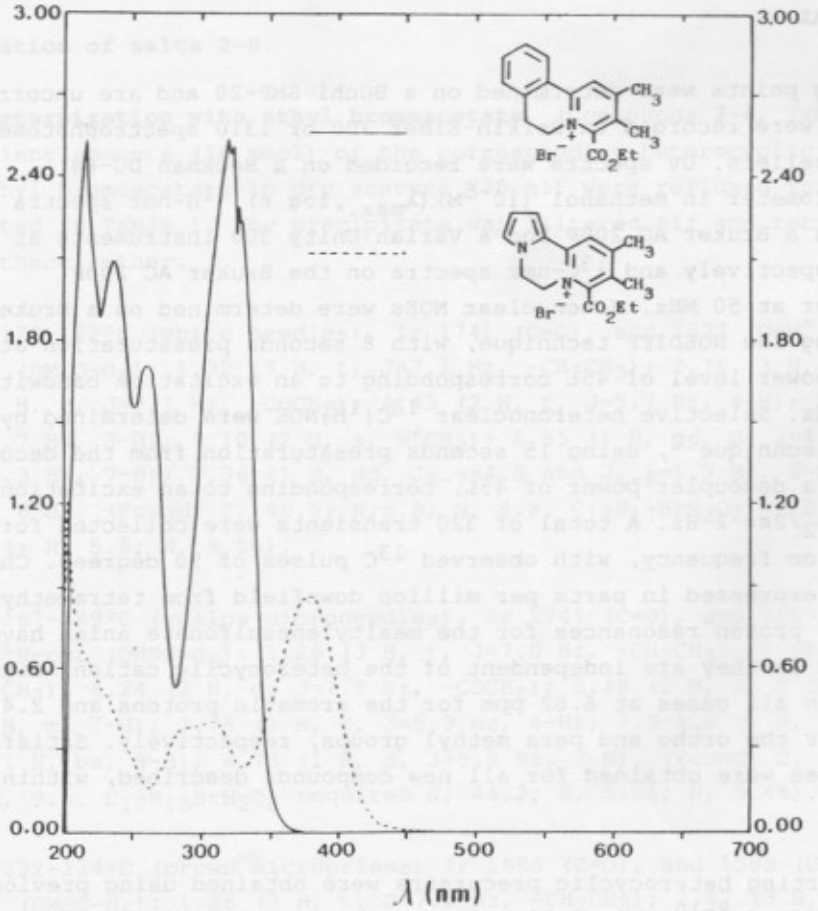


Fig. 5

As a conclusion, in the pyrido[1,2-a]pyrrolo[2,1-c]pyrazin-7-ium derivative **9a** seems to be a clear transfer of electronic density from the pyrrole to the pyridinium ring, favored by coplanarity in the tricyclic system. This effect appears, with small differences, in all related compounds. Further experiments in relation with the electronic structure of all products are in progress and would be published elsewhere.

In relation with the synthesis, the Westphal condensation provides a simple an efficient methodology for the preparation of fused pyridinium and pyridazinium derivatives. However, the N-C condensation[6] seems rather limited to the use of *o*-quinones as dielectrophiles.

EXPERIMENTAL

Melting points were determined on a Büchi SMP-20 and are uncorrected. Ir spectra were recorded on Perkin-Elmer 700 or 1310 spectrophotometers using KBr pellets. Uv spectra were recorded on a Beckman DU-68 spectrophotometer in methanol (10^{-5}M) ($\lambda_{max.}$, log ε). ^{1}H-nmr spectra were obtained on a Bruker AC 200P and a Varian Unity 300 instruments at 200 and 300 MHz respectively and ^{13}C-nmr spectra on the Bruker AC 200P spectrometer at 50 MHz. Homonuclear NOEs were determined on a Bruker AM-400-WB using the NOEDIFF technique, with 8 seconds presaturation at a decoupler power level of 45L corresponding to an excitation bandwith $\gamma B_2/2\pi$= 2 Hz. Selective heteronuclear $^{13}C\{^{1}H\}$NOE were determined by means of HETNOE technique[12], using 15 seconds presaturation from the decoupler channel at a decoupler power of 45L, corresponding to an excitation bandwith $\gamma B_2/2\pi$= 2 Hz. A total of 320 transients were collected for each presaturation frequency, with observed ^{13}C pulses of 90 degrees. Chemical shifts are expressed in parts per million downfield from tetramethylsilane. The proton resonances for the mesitylenesulfonate anion have not been listed as they are independent of the heterocyclic cation, signals appearing in all cases at 6.62 ppm for the aromatic protons and 2.44 and 2.15 ppm for the ortho and para methyl groups, respectively. Satisfactory microanalyses were obtained for all new compounds described, within 0.4% error.

The starting heterocyclic precursors were obtained using previously described methods[8-10], by cyclization of the acetyl derivatives of N-(2-aminoethyl or aminophenyl)pyrrole, and only the indole precursor has not been reported before. The benzo[a]quinolizinium bromide **16** was synthetized[3] by basic condensation between 1-methyl-2-(ethoxycarbonyl-

methyl)-3,4-dihydro-isoquinolinium bromide and diacetyl.

1-Methyl-3,4-dihydropyrazino[1,2-a]indole. N-(2-acetamidoethyl)indole[13] (16.5 mmol) was refluxed for 1 h in phosphorus oxychloride (15 ml). Then, the mixture was concentrated in vacuo, and the residue was dissolved in dichloromethane (20 ml), washed with NaOH 10% solution (2x10 ml), and with water (10 ml). Finally, the organic layer was dried (Mg_2SO_4), concentrated and the residue triturated with hydrobromic acid to obtain the cited compound as hydrobromide (2 g, 50%), mp >260ºC (white microprisms, from ethanol); ^{1}H-nmr (DMSO-d_6): 2.78 (3 H, s, 1-CH_3); 4.0-4.2 (2 H, m, 4-H); 4.4-4.6 (2 H, m, 3-H); 7.2-7.9 (5 H, m). (Found: C, 50.7; H, 4.75; N, 9.7. $C_{12}H_{13}BrN_2.H_2O$ requires C, 50.9; H, 4.6; N, 9.9%).

Preparation of salts 2-8.

A.- Quaternization with ethyl bromoacetate. (Compounds **2-4**, Table 1). Equivalent amounts (10 mmol) of the corresponding heterocyclic precursor and ethyl bromoacetate in dry acetone (30 ml) were refluxed for the time indicated in Table 1. The precipitate was filtered off and recrystallized from ethanol-ether.

2: mp 120-122ºC (white needles). Ir 1741 (C=O), and 1632 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.32 (3 H, t, J=7.1 Hz, -CH_2CH_3); 2,76 (3 H, s, 1-CH_3); 4.28(2 H, q, J=7.1 Hz, -$COCH_2$); 4.43 (2 H, t, J=5.7 Hz, 4-H); 4.70 (2 H, t, J=5.7 Hz, 3-H); 5.10 (2 H, s, N^+CH_2); 6.55 (1 H, dd, J_{7-6}=4.5 and J_{7-8}=2.3 Hz, 7-H); 7.36 (1 H, dd, J_{6-7}=4.5 and J_{6-8}=1.3 Hz, 6-H); 7.66 (1 H, bs, 8-H). (Found: C, 46.0; H,5.8; N, 8.8. $C_{12}H_{17}BrN_2O_2$. 1/2H_2O requires C, 46.4; H, 5.5; N, 9.0%).

3: mp 187-189ºC (yellow microneedles). Ir 1741 (C=O), and 1647 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.26 (3 H, t, J=7.0 Hz, -CH_2CH_3), 2.96 (3 H, s, 3H, 1-CH_3); 4.24 (2 H, q, J=7.0 Hz, -$COCH_2$); 5.48 (2 H, s, N^+CH_2); 7.35-7.4 (1H, m, 7-H); 7.75 (1 H, d, J=5.9 Hz, 4-H); 7.9-8.0 (1 H, m, 6-H); 8.43 (1 H, bs, 8-H); 8.73 (1 H, d, J=5.9 Hz, 3-H). (Found: C, 43.9; H, 5.2; N, 9.1. $C_{12}H_{15}BrN_2O_2$ requires C, 44.2; H, 5.05; N, 9.4%).

4: mp 232-234ºC (brown microprisms) Ir 1690 (C=O), and 1599 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.28 (3 H, t, J=7.0 Hz, -CH_2CH_3); 2,87 (3 H, s, 1-CH_3); 4.27 (2 H, q, J=7.0 Hz, -$COCH_2$); 4.3-4.4 (2 H, m, 4-H); 4.5-4.6 (2 H, t, J=6.9 Hz, 3-H) 5.13 (2 H, s, N^+CH_2); 7.25-7.3 (1 H, m, 8-H); 7.55-7.6 (1 H, m, 7-H); 7.69 (1 H, d, J_{6-7}=8.6 Hz, 6-H); 7.85 (1 H, d, J_{9-8}=7.6 Hz,

9-H); 8.13 (1 H, s, 10-H). (Found: C, 54.45; H,5.7; N, 7.75. $C_{16}H_{19}BrN_2O_2$ requires C, 54.7; H, 5.45; N, 8.0%).

B.- Amination with MSH. (Compounds **5-8**, Table 1).
To a stirred solution of O-hydroxylaminomesitylenesulfonate (MSH) (2.15 g, 10 mmol) in dichloromethane (20 ml), the corresponding azine (10 mmol) in the same solvent (20 ml) was dropwise added. The mixture was stirred at room temperature for 10 min. Diethyl ether (30 ml) was then added to precipitate the N-aminoazinium salts **5-8** which were triturated with ether (3x5 ml) and recrystallized from the suitable solvent.

5: mp 145-147ºC (white prisms, from ethanol-ether). Ir 1620 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 2.85 (3 H, s, 1-CH_3); 4.4-4.7 (4 H, m, 3-H and 4-H); 6.65-6.7 (1 H, m, 7-H); 7.2-7.25 (1 H, m, 8-H); 7.6-7.65 (1 H, m, 6-H). (Found: C, 56.5; H,6.6; N, 12.0. $C_{17}H_{23}N_3O_3S$. $1/2H_2O$ requires C, 56.9; H, 6.5 N, 11.7%).

6: mp 147-148ºC (white prisms, from ethanol-ether). Ir 1635 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 2.95 (3 H, 1-CH_3); 7.26 (1 H, dd, J_{7-6}=4.5 and J_{7-8}=2.3 Hz, 7-H); 7.54 (1H, d, J=5.9 Hz, 4-H); 7.64-7.66 (1 H, m, 6-H); 8.11 (1H, dd, J_{8-7}=2.3 and J_{8-6}=1.2 Hz, 8-H); 8.44 (1 H, d, J=5.8 Hz, 3-H). (Found: C, 55.5; H,6.5; N, 11.6. $C_{17}H_{21}N_3O_3S$ requires C, 55.9; H, 6.3; N, 11.5%).

7: mp 142-144ºC (white microprisms, from ethanol-ether). Ir 1643 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 2.70 (3 H, s, 1-CH_3); 4.24 (2 H, q, J=6.0 Hz, 4-H); 4.47 (2 H, q, J=6.1 Hz, 3-H); 7.3-7.9 (5 H, m). (Found: C, 63.35; H,6.5; N, 10.2. $C_{21}H_{25}N_3O_3S$ requires C, 63.1; H, 6.3; N, 10.5%).

8: mp 224-226ºC (white prisms, from methanol-ether). Ir 1633 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 3.13 (3 H, s, 4-CH_3); 7.35 (1 H, dd, J_{2-1}=4.4 Hz and J_{2-3}=2.6 Hz, 2-H), 7.6-8.0 (3 H, m), 8.4-8.7 (2 H, m), 9.04 (1 H, dd, J_{3-2}=2.6 and J_{3-1}=1.2 Hz, 3-H). (Found: C, 60.2; H, 6.2; N, 10.2. $C_{21}H_{25}N_3O_3S$. H_2O requires C, 60.4; H, 6.0; N, 10.0%).

Westphal Condensation. General Procedure. Equivalent amounts (10 mmol) of the azinium salts **2-8**, the dicarbonyl derivative, and anhydrous sodium acetate (0.82 g, 10 mmol) were suspended in dry acetone (10 ml). The mixture was refluxed for the time described (Table 1). The precipitate was filtered. Crystallization from the suitable solvent yielded the compounds **9-15** in analytical grade.

9a: mp 190-192°C (yellow needles, from ethanol).Ir 1734 (C=O), 1618 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.36 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 2.25 (3 H, s, 9-CH_3); 2.52 (3 H, s, 10-CH_3); 4.5-4.7 (6 H, s, 3 CH_2); 6.45 (1 H, dd, J_{2-3}=4.0 and J_{2-1}=2.4 Hz, 2-H); 7.38 (1 H, dd, J_{1-2}=4.0 and J_{1-3}=1.4 Hz, 1-H); 7.42-7.43 (1 H, m, 3-H); 8.35 (1H, s, 11-H). ^{13}C-nmr (DMSO-d_6). Uv (378, 3.93), (308, 3.60), (293, 3.58), (202.5, 4.08) (Found: C, 51.1; H,5.15; N, 7.1. $C_{16}H_{19}BrN_2O_2$. 1/2H_2O requires C, 50.8; H, 5.1; N, 7.4%).

9b: mp 197-200°C (brown prisms, from ethanol). Ir 1741 (C=O), 1632 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.57 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 4.6-4.7 (2 H, m, 5-H); 4.8-5.0 (4 H, m, $COCH_2$ and 6-H); 6.57 (1 H, dd, J_{2-3}=4.1 and J_{2-1}= 2.1 Hz, 2-H); 7.39 (1 H, bs, 1-H); 7.57 (1 H, dd, J_{3-2}=4.0 and J_{3-1}=1.2 Hz, 3-H); 7.8-8.2 (4 H, m); 8.31 (1 H, d, J=8.2 Hz); 8.55 (1 H, d, J=7.1 Hz); 8.87 (1 H, s, 11-H). Uv (470, 4.43), (455.5, 4.43), (343, 4.43), (298, 4.42), (243, 4.42), (218, 4.40). (Found: C, 59.8; H, 4.4; N, 5.8. $C_{24}H_{19}BrN_2O_2$. H_2O: requires C, 61.9; H, 4.2; N, 6.0%).

9c: mp >250°C (brown microprisms, from ethanol). Ir 1731 (C=O), 1612 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.41 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 4.5-4.7 (6 H, m, 3 CH_2); 6.54 (1 H, dd, J_{2-3}= 4.1 and J_{2-1}=2.5 Hz, 2-H); 7.33 (1 H, dd, J_{3-2}=2.5 and J_{3-1}=1.3 Hz, 3-H); 7.6-7.9 (5 H, m); 8.1-8.2 (1 H, m); 8.6-8.8 (2 H, m); 9.08 (1 H, s, 11-H). (Found: C, 63.5; H, 4.7; N, 5.4. $C_{26}H_{21}BrN_2O_2$. H_2O requires C, 63.55; H, 4.3; N, 5.2

10a: mp >250°C (yellow needles, from ethanol). Ir 1733 (C=O), 1628 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.49 (3 H, t, J=7.0 Hz, $-CH_2CH_3$); 2.44 (3 H, s, 9-CH_3); 2.68 (3 H, s, 1-CH_3); 4.73 (2 H, q, J=7.0 Hz, $-CH_2CH_3$); 7.1-7.2 (1 H, m, 2-H); 7.77 (1 H, d, J=6.1 Hz, 5-H); 7.87 (1 H, d, J_{3-2}=4.1 Hz, 3-H); 8.0-8.05(1 H, bs, 1-H); 8.50 (1 H, d, J=6.1 Hz, 6-H); 8.63 (1 H, s, 11-H). (Found: C, 52.3; H,4.8; N, 8.0. $C_{16}H_{17}BrN_2O_2$. H_2O requires C, 52.3; H, 4.7; N, 7.6%).

10b: mp 223-225°C (brown prisms, from ethanol-ether). Ir 1731 (C=O), 1645 ($C=N^+$) cm^{-1}; ^{1}H-nmr (DMSO-d_6): 1.58 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 4.90 (2 H, q, J=7.1 Hz, $-CH_2CH_3$); 7.24 (1 H, dd, J_{2-3}=4.5 and J_{2-1}=2.5 Hz, 2-H); 7.5-8.6 (10 H, m); 9.29 (1H, s, 11-H). Uv (450, 4.13), (412.5, 4.16), (348, 4.31), (341, 4.29), (305, 4.31), (243, 4.46), (225, 4.44). (Found: C, 62.3; H, 3.4; N, 5.8. $C_{24}H_{17}BrN_2O_2$. H_2O requires C, 62.2; H, 3.7; N, 6.05%).

11a: mp >250°C (yellow needles, from ethanol). Ir 1733 (C=O), 1638 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 1.50 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 2.41 (3 H, s, 11-CH_3); 2.66 (3 H, s, 12-CH_3); 4.6-4.7 (4 H, m, 7-H and $-CH_2CH_3$); 4.8-4.9 (2 H, m, 8-H); 7.2-7.25 (1 H, m, 3-H); 7.4-7.45 (1 H, m, 4-H); 7.69 (1 H, d, J_{5-4}=8.6 Hz, 5-H); 7.85 (1 H, d, J_{2-3}=7.6 Hz, 2-H); 8.49 (1 H, s, 13-H). Uv (389.5, 4.32), (235, 4.15), (219.5, 4.33). (Found: C, 61.3; H, 5.0; N, 6.7. $C_{20}H_{21}BrN_2O_2$ requires C, 61.0; H, 5.1; N, 6.8%).

11b: mp >250°C (brown needles, ethanol-ether). Ir 1737 (C=O), 1616 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 1.58 (3 H, t, J=7.1 Hz, $-CH_2CH_3$); 4.7-4.9 (4 H, m, 7-H and $-CH_2CH_3$); 5.1-5.2 (2 H, m, 8-H); 7.2-7.3 (1 H, m, 3-H); 7.4-7.5 (1 H, m, 4-H); 7.62 (1 H, d, J_{5-4}=8.1 Hz, 5-H); 7.82 (1 H, d, J_{2-3}=7.7 Hz, 2-H); 7.9-8.2 (4 H, m); 8.3-8.5 (2 H, m); 8.7-8.8 (1 H, m); 9.37 (1 H, s, 13-H). Uv (469, 4.08), (318, 3.96), (251.5, 4.13), (212, 4.41). (Found: C, 67.35; H, 4.3; N, 5.8. $C_{28}H_{21}BrN_2O_2$ requires C, 67.6; H, 4.3; N, 5.6%).

12b: mp >250°C (brown prisms, from ethanol-ether). Ir 1627 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 4.75 (2 H, t, J=7.3 Hz, 5-H); 5.16 (2 H, t, J=7.3 Hz, 6-H); 6.62 (1 H, dd, J_{2-3}=4.1 Hz and J_{2-1}=2.3 Hz, 2-H); 7.47 (1 H, bs, 1-H); 7.6-7.7(1 H, m, 3-H); 8.0-8.1 (2 H, m); 8.4-8.7 (4 H, m); 9.15 (1 H, s, 11 H). Uv (450, 4.40), (439, 4.40), (346, 4.27), (298, 4.405), (275, 4.375), (233.5, 4.43) (Found: C, 68.8; H, 5.4; N, 8.5. $C_{29}H_{25}N_3O_3S$. $1/2H_2O$ requires C, 69.0; H, 5.0; N, 8.3%).

12c: mp >250°C (brown prisms, from ethanol-ether). Ir 1615 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 4.82 (2 H, t, J=6.7 Hz, 5-H): 5.29 (2 H, t, J=6.7 Hz, 6-H); 6.59 (1 H, dd, J_{2-3}=4.1 and J_{2-1}=2.3 Hz, 2-H); 7.42 (1 H, bs, 1-H); 7.7-8.0 (5 H, m); 8.6-8.7 (2 H, m); 8.9-9.0 (2 H, m); 9.50 (1 H, s, 11H). Uv (439, 3.855), (362.5, 4.35), (340, 4.50), (253.5, 4.35), (223.5, 4.47) (Found: C, 68.2; H, 5.3; N, 7.5. $C_{31}H_{27}N_3O_3S$. $1/2H_2O$ requires C, 67.9; H, 5.0; N, 7.7%).

13b: mp >250°C (brown prisms, from ethanol). Ir 1627 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 7.35 (1 H, dd, J_{2-3}=4.0 and J_{2-1}=2.6 Hz); 7.9-8.0 (2 H, m); 8.0-8.1 (1 H, m, 3-H); 8.19-8.21 (1 H, m, 1-H); 8.3-8.7 (6 H, m); 9.48 (1 H, s, 11-H). Uv (412.5, 4.39), (380, 4.39), (353.5, 4.51), (300, 4.405), (242.5, 4.51). (Found: C, 67.2; H, 4.8; N, 8.3. $C_{29}H_{23}N_3O_3S$. $1/2H_2O$: requires C, 66.9; H, 4.45; N, 8.1%).

14b: mp >250°C (brown prisms, from ethanol). Ir 1624 ($C=N^+$) cm^{-1}; ^{1}H-nmr

(CD_3OD): 4.8-4.9 (2 H, m, 7-H); 5.3-5.4 (2 H, m, 8-H); 7.2-7.3 (1 H, m, 3-H); 7.4-7.5 (1 H, m, 4-H); 7.66 (1 H, d, J_{5-4}=8.3 Hz, 5-H); 7.83 (1 H, d, J_{2-3}=7.9 Hz, 2-H); 8.0-8.15 (2 H, m); 8.5-8.7 (4 H, m); 9.50 (1 H, s, 13-H). Uv (452, 4.14), (309, 4.01), (273, 3.92), (246, 4.03), (215.5, 4.44). (Found: C, 71.3; H, 5.0; N, 7.4. $C_{33}H_{27}N_3O_3S$. 1/2H_2O requires C, 71.5; H, 4.9; N, 7.6%)

14c: mp >250ºC (brown needles, from ethanol). Ir 1624 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 4.9-5.0 (2 H, m, 7-H); 5.5-5.6 (2 H, m, 8-H); 7.2-7.3 (1 H, m, 3-H); 7.45-7.55 (1 H, m, 4-H); 7.66 (1 H, d, J_{2-3}=7.7 Hz, 2-H); 7.8-8.1 (6 H, m); 8.8-8.9 (2 H, m); 9.1-9.2 (2 H, m); 9.93 (1 H, s, 13-H). Uv (371, 4.37), (353, 4.47), (257, 4.40), (232.5, 4.51). (Found: C, 71.5; H, 5.1; N, 7.3. $C_{35}H_{29}N_3O_3S$. H_2O requires C, 71.3; H, 5.0; N, 7.1%).

15b: mp >250ºC (brown prisms, from ethanol). Ir 1631 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 7.24 (1 H, dd, J_{2-3}=4.3 and J_{2-1}=2.7 Hz); 7.7-7.9 (4 H, m); 8.04 (1 H, bd, 3-H); 8.1-8.5 (5 H, m); 8.65 (1 H, bd, 1-H); 8.9-9.0 (1 H, m); 9.40 (1 H, s, 11-H) (Found: C, 70.3; H, 5.0; N, 7.3. $C_{33}H_{27}N_3O_3S$. H_2O requires C, 70.3; H, 4.8; N, 7.5%).

15c: mp >250ºC (brown prisms, from ethanol-ether). Ir 1639 ($C=N^+$) cm^{-1}; ^{1}H-nmr (CD_3OD): 7.20-7.25 (1 H, m, 2-H); 7.5-7.7 (5 H, m); 7.85-7.95 (1 H, m); 8.10 (1 H, bd , 3-H); 8.2-8.3 (3 H, m); 8.4-8.6 (3 H, m); 8.69 (1 H, bd, 1-H); 9.47 (1H, s, 11-H) (Found: C, 72.7; H, 5.2; N, 7.0. $C_{35}H_{29}N_3O_3S$. 1/2H_2O requires C, 72.4; H, 5.0; N, 7.2%)

ACKNOWLEDGEMENTS

Authors wish to acknowledge the assistance provided by LILLY S.A. in Nmr analysis, and to the Comisión Interministerial de Ciencia y Tecnología (CICYT) for financial support (Project PB87-0755).

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