2-Methylpyridinium Salts as 1,4-Dinucleophiles. II. Westphal Condensation with Substituted Pyridinium Substrates

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Condensation of α-methylpyridinium, quinolinium and isoquinolinium salts with 1,2-dicarbonyls in the presence of base, yielded quinolizinium derivatives. In an analogous process, α-benzyl derivatives produced 2,3-dihydroindolizin-2-ones by intramolecular cyclisation.

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The Westphal condensation [1,2] (Figure 1) is an application of the use in synthesis of 2-methylpyridinium salts and their ability to generate carbanions on two points of the molecule, namely, *N*-methylene and 2-methyl groups. Reactions of a picolinium salt under basic medium with a 1,2-dicarbonyl would produce a quinolizinium salt.

After additions by several authors [3-6] and by our own group [7,8], the method seems to be the simplest one to produce a quinolizinium cation, a poorly studied nitrogen bridgehead heterocycle [9,10]. The present paper describes the use of the Westphal process on different unreactive substrates in a project searching for new antimicrobial agents.

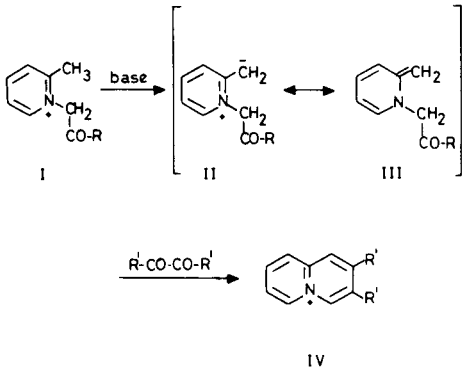


FIG. 1

In pyridinium substrates as I (Figure 1), the 1-methylene reactivity depends on the structure of the stabilizing group R, but 2-methyl reactivity varies with the character of the heterocycle and with the presence or absence of substituents on the same methyl group.

As it is partially represented in Figure 1, for the carbanion generated on that 2-methyl group, two main canonical forms can be drawn, one with charge separation II, another one, with structure of anhydrobase III; the more III predominates in the resonance hybrid, the less reactive the substrate would be to produce IV.

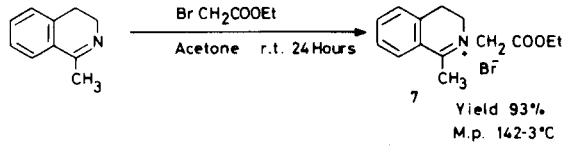


FIG-2

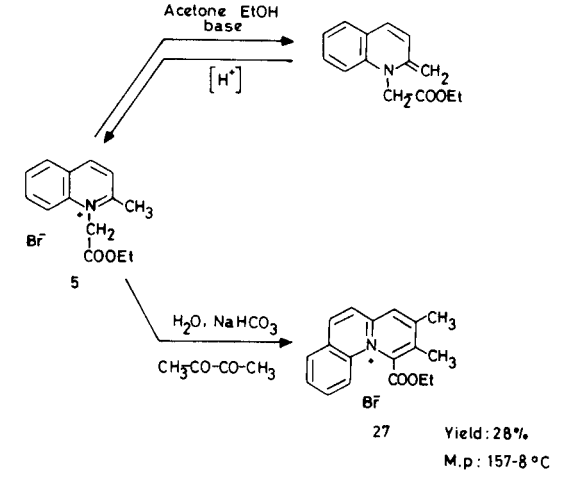


FIG. 3

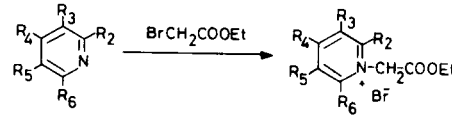
All the substrates prepared are represented in Tables 1 and 2; an example which did not fit into any of them is shown in Figure 2. In some of the substrates, two methyl groups would compete for carbanion formation (compounds **1** and **2**, Table 1), in others, the anhydrobase would be stabilized either by substituents on the 2-methylene group (**3** and **4** Table 1) or by the heterocyclic structure (*i.e.* as in bicyclic systems **5** and **6**, Table 1, and **9-14**, Table 2).

Unexpectedly, two isoquinolines (1-benzyl and 1-(*o*-Cl-benzyl)) suffered debenzylation on quaternisation, perhaps through the cation radical III (Table 2).

All the substrates were condensed with different 1,2-dicarbonyls as diacetyl, benzyl, 3,3'-dimethoxybenzyl,

Table 1

1-Substituted-2-alkylpyridinium Salts

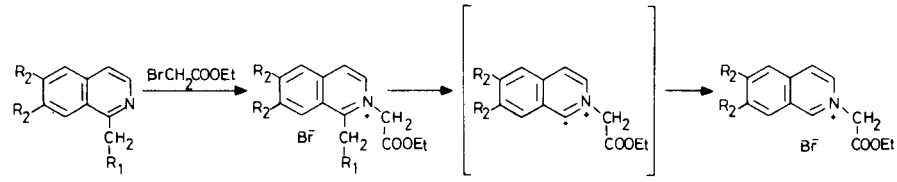


Compound	R_2	R_3	R_4	R_5	R_6	Reaction Time (Hours)	Yield (%) [a]	Mp (°C)	Lit Mp (°C)
1	CH_3	H	CH_3	H	H	72 [b]	89	75-76 [c]	
2	CH_3	H	H	H	CH_3	2	52	201-202 [d]	
3	$C_6H_5CH_2$	H	H	H	H	3	46	183-184 [d]	
4	$-(CH_2)_4-$		H	H	H	2	90	145-146 [d]	
5	CH_3	H	H	$-CH=CH)_2-$		1.5	71	205 [e]	205 [f]
6	CH_3	$-(CH=CH)_2-$		H	H	2	73	212-213 [e]	

[a] In isolated pure product. [b] At room temperature. [c] From acetone. [d] From ethanol. [e] From ethanol-ether. [f] As described in [2].

Table 2

2-Substituted-1-benzylisoquinolinium Salts



I II III IV

Compound	R_1	R_2	Structure	Reaction Time (Hours)	Yield (%) [a]	Mp (°C)	Lit Mp (°C)
8	C_6H_5	H	IV	2	80	199 [b]	199 [c]
8	o-ClC_6H_4	H	IV	2	75	199 [b]	199 [c]
9	p-ClC_6H_4	H	II	2.5	36	201-202 [b]	
10	p-$CH_3C_6H_4$	H	II	2	38	189-190 [d]	
11	p-$CH_3OC_6H_4$	H	II	2	78	188-189 [b]	
12	m,p-$CH_2O_2C_6H_3$	H	II	2	90	198-199 [b]	
13	m,m',p-$CH_3OC_6H_2$	H	II	168	64	219-201 [f]	
14	m,p-$CH_3OC_6H_3$	CH_3O	II	2	67	195-196 [f]	

[a] In isolated pure product. [b] From ethanol. [c] As described in 18. [d] From methanol-ether. [e] At room temperature. [f] From ethanol-ether.

3,3'-dinitrobenzyl, 9,10-phenanthroquinone and 1,2-acenaphthoquinone. Condensation was performed either by acetone/sodium acetate [7] or alternatively, by acetone-ethanol/di-*n*-butylamine [2], always at reflux temperature.

Derivatives are not reported when 1,2-dicarbonyl was recovered unchanged in more than 80% after the process.

Experiments performed with **1** and **2** are reported in Table 3. Better yields were produced as described, using di-*n*-butylamine and acetone-ethanol as solvent.

In one case, a different product **17** was obtained by using sodium acetate and acetone.

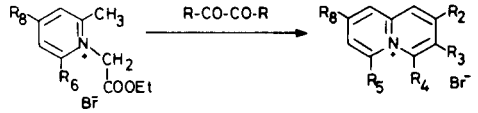
Even the cyclic substrates **4** (Table 4) produced the reaction, as it is shown, although with relatively low yields and only with the more reactive dicarbonyls.

Substrate **5**, derived from the quinoline nucleus was tested with different dicarbonyls, using acetone, acetone-ethanol, ethanol or methanol, and with di-*n*-butylamine as base. In all cases, a deep violet solution was obtained and the dicarbonyl was isolated in more than 80% yield. On acidification, solution decolorized and unreacted **5** was again isolated.

The only condensation reaction with **5** has already been

Table 3

Substituted Quinolizinium Salts from **1** and **2**



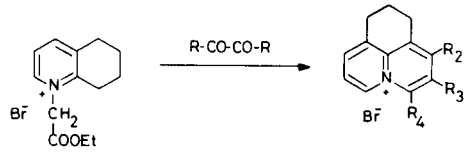
1,2

Compound	R_2	R_3	R_4	R_6	R_8	Reaction Time (Hours)	Yield [a] (%)	Mp (°C) [b]
15	p-ClC_6H_4	p-ClC_6H_4	H	H	CH_3	2	32	310-311
16	m-$O_2NC_6H_4$	m-$O_2NC_6H_4$	H	H	CH_3	2	48	202-203
17	Diphenyl-o,o'-di-yl [c]		COOEt	H	CH_3	2	65	172-173
18	Diphenyl-o,o'-di-yl [c]		H	H	CH_3	2	65	350
19	Naphth-1,8-di-yl [d]		COOEt	H	CH_3	1.5	56	209-210
20	C_6H_5	C_6H_5	H	CH_3	H	2	36	280-281
21	m-$CH_3OC_6H_4$	m-$CH_3OC_6H_4$	H	CH_3	H	5	32	221-222
23	Diphenyl-o,o'-di-yl [c]		H	CH_3	H	1.5	78	350

[a] In isolated pure product. [b] From ethanol-ether. [c] Obtained from sodium acetate in acetone. [c] Produces phenantrene ring. [d] Produces acenaphthylene ring.

Table 4

Substituted Quinolizinium Salts from **4**

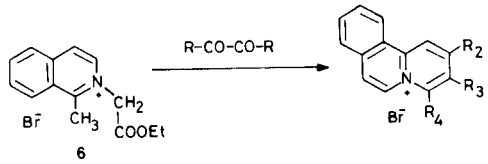


Compound	R_2	R_3	R_4	Reaction Time (Hours)	Yield [a] (%)	Mp (°C) [b]	Lit Mp (°C)
23	CH_3	CH_3	H	2	15	285-286	285-286 [c]
24	M-$O_2NC_6H_4$	m-$O_2NC_6H_4$	H	2	57	277-278	—
25	Diphenil-o,o'-di-yl [d]		H	2	44	253-254	—
26	Naphth-1,8-di-yl [e]		COOEt	2	31	177-179	—

[a] In isolated pure product. [b] From methanol-ether. [c] As described in 2. [d] Produces phenanthrene ring. [e] Produces acenaphthylene ring.

Table 5

Benzo[a]quinolizinium Salts from **6**



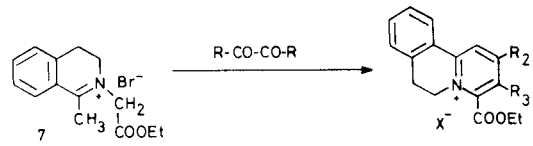
6

Compound	R_2	R_3	R_4	Reaction Time (Hours)	Yield [c] (%)	Mp (°C)
28	CH_3	CH_3	COOEt	2	47	212-213 [b]
29	m-$O_2NC_6H_4$	m-$O_2NC_6H_4$	COOEt	2	60	159-160 [c]
30	Diphenyl-o,o'-di-yl [d]		H	2	85	350 [e]
31	Naphth-1,8-di-yl [f]		COOEt	2	44	288-290 [g]

[a] In isolated pure product. [b] From ethanol. [c] From ethanol-ether. [d] Produces phenanthrene ring. [e] From methanol-ether. [f] Produces acenaphthylene ring. [g] From methanol.

Table 6

Benzo a quinolizinium Salts Derived from **7**

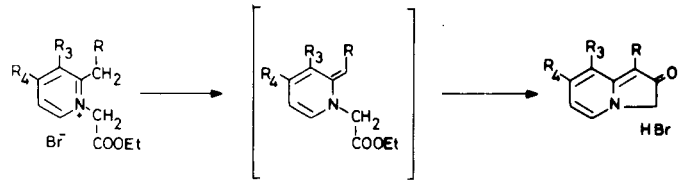


Compound	R_2	R_3	X^-	Reaction Time (Hours)	Yield (%) [a]	Mp (°C)
32	CH_3	CH_3	Br	2	52	232-233 [b]
33	Diphenyl-*o,o'*-di-yl [c]		BF_4	2	97	155-156 [d]
34	Naphth-1,8-di-yl [e]		Br	2	61	179-180 [d]

[a] In isolated pure product. [b] From ethanol-ether. [c] Produces phenanthrene ring. [d] From methanol-ether. [e] Produces acenaphthylene ring.

Table 7

1-Aryl-2-indolizin-2-ones

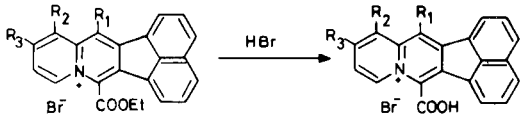


Compound	R	R_3	R_4	Reaction Time (Hours)	Yield [a] (%)	Mp (°) [b]	Lit Mp (°)
35	C_6H_5	H	H	4	62	272-273	74 [c]
36	*p*-Cl-C_6H_4	-(CH=CH)$_2$-		3	80	253-255	—
	p-$CH_3C_6H_4$	-(CH=CH)$_2$-		No Reaction After 6 Hours [d]			
37	*p*-$CH_3OC_6H_4$	-(CH=CH)$_2$-		2	78	244-245	—
38	*m,p*-$CH_2O_2C_6H_3$	-(CH=CH)$_2$-		3	69	234-235	—
39	*m,m',p*-$CH_3OC_6H_2$	-(CH=CH)$_2$-		3	52	224-225	—
	m,p-$CH_3OC_6H_3$	-CH=C(OCH_3)-C(OCH_3)=CH-		No Reaction After 6 Hours [d]			

[a] In isolated pure product. [b] From ethanol ether. [c] Described in [16] as base. [d] Starting material was recovered unchanged in more than 80 %.

Table 8

Hydrolysis of Compounds **26** and **31**



Compound	R_1	R_2	R_3	Reaction Time (Hours)	Yield (%) [a]	mp (°C) [b]
40	-(CH$_2$)$_3$-		H	18	29	350
41	H	-(CH=CH)-		24	56	350

[a] In isolated pure product. [b] From methanol-ether.

described [2]. It was produced with water as solvent and sodium bicarbonate as base and performed at 0°. In that way, **5** reacts with the dicarbonyl provided it would be water soluble. We were able to produce **27**, as it is represented in Figure 3. Other water soluble dicarbonyls were tested against **5**, as 1,2-cyclohexanedione and glyoxal, but the former is stabilised as a hydrogen bonded monoenol form [8] and even in water did not react, and the latter did form a non reactive hydrate [6]. The final conclusion should be that the anhydrobase seems to be too stable to be used in moderately polar solvents, and only in water the betain canonical form predominates enough to permit the condensation process.

In contrast isoquinoline substrates **6** and **7** from which a similar behaviour was expected, reacted producing

Table 9

Analytical and Spectroscopic Data for Compounds **1-41**

Compound	M.p (°C)	Molecular Formulae	Found (%) C	Found (%) H	Found (%) N	Required (%) [a] C	Required (%) [a] H	Required (%) [a] N	C=N	Others	^{1}H NMR Data (δ)
1 [b,c]	75-76	$C_{11}H_{16}BrNO_2$	48.03	5.56	4.87	(48.19)	(5.58)	(5.10)	1645	1750	9.2 (d, 1H, 6 Hz), 8.2 (s, 1H), 8.0 (d, 1H, J ^{5} 6 Hz), 5.9 (s, 2H), 4.3 (c, 2H), 2.8 (s, 3H), 2.65 (s, 3H), 1.3 (t, 3H)
2 [b,c]	201-202	$C_{11}H_{16}BrNO_2$	48.01	5.66	4.97	(48.19)	(5.88)	(5.10)	1630	1750	8.0-8.75 (m, 3H), 5.75 (s, 2H), 4.35 (c, 2H), 2.9 (s, 6H), 1.3 (t, 3H)
3 [b,c]	183-184	$C_{16}H_{18}BrNO_2$	59.71	5.55	4.36	(59.81)	(5.60)	(4.36)	1630	1755	9.3 (d, 1H, J ^{5} 6 Hz), 8.75 (d, 1H, J ^{5} 6 Hz), 8.2 (t, 2H), 7.4 (s, 5H), 5.95 (s, 2H), 4.7 (s, 2H), 4.0 (c, 2H), 1.15 (t, 3H)
4 [b,c]	145-146	$C_{13}H_{18}BrNO_2$	52.39	6.44	4.85	(52.01)	(6.04)	(4.66)	1640	1755	9.1 (d, 1H, J ^{5} 6 Hz), 8.55 (d, 1H, J ^{5} 6 Hz), 8.1 (t, 1H, J ^{5} 6 Hz), 5.9 (s, 2H), 4.3 (c, 2H), 3.1 (m, 4H), 2.9 (m, 4H), 1.3 (t, 3H)
5 [b,c]	205 [d]	$C_{14}H_{16}BrNO_2$	—	—	—				1610	1740	9.4 (d, 1H, J ^{5} 10 Hz), 7.9-8.65 (m, 5H), 6.2 (s, 2H), 4.3 (c, 2H), 3.18 (s, 3H), 1.25 (t, 3H)
6[b,c]	212-213	$C_{14}H_{16}BrNO_2$	54.43	5.23	4.47	(54.20)	(5.19)	(4.51)	1630	1740	7.9-8.9 (m, 6H), 6.0 (s, 2H), 4.25 (c, 2H), 3.25 (s, 3H), 1.28 (t, 3H)
7 [b,c]	142-143	$C_{14}H_{18}BrNO_2{\cdot}\frac{1}{2}H_2O$	52.05	5.53	4.81	(52.34)	(5.96)	(4.36)	1640	1750	7.4-8.4 (m, 4H), 5.4 (s, 2H), 4.24 (c, 2H), 3.6-4.0 (m, 2H), 3.0 (s, 3H), 3.1-3.5 (m, 2H), 1.3 (t, 3H)
8 [b,c]	199 [e]	$C_{13}H_{14}BrNO_2$	—	—	—				1640	1750	8.0-9.0 (m, 7H), 5.9 (s, 2H), 4.3 (c, 2H), 1.3 (t, 3H)
9 [b,c]	201-202	$C_{20}H_{19}BrClNO_2$	57.33	4.47	3.45	(57.09)	(4.55)	(3.33)	1640	1750	8.0-9.1 (m, 6H), 7.45 (d, 2H, J ^{5} 6 Hz), 7.15 (d, 2H, J ^{5} 6 Hz), 6.05 (s, 2H), 5.88 (c, 2H), 4.0 (c, 2H), 3.15 (t, 3H)
10 [b,c]	189-190	$C_{21}H_{22}BrNO_3$	62.87	5.36	3.25	(63.00)	(5.53)	(3.49)	1635	1650	7.9-8.9 (m, 6H), 7.0 (s, 4H), 5.9 (s, 2H), 5.2 (s, 2H), 3.9 (c, 2H), 2.2 (s, 3H), 1.1 (t, 3H)
11 [b,c]	188-189	$C_{21}H_{22}BrNO_3$	60.35	5.55	3.36	(60.58)	(5.32)	(3.36)	1635	1750	8.0-9.1 (m, 6H), 7.15 (d, 2H, J ^{5} 9 Hz), 6.9 (d, 2H, J ^{5} 9 Hz), 6.0 (s, 2H), 5.3 (s, 2H), 4.0 (c, 2H), 3.7 (s, 3H), 1.15 (t, 3H)
12 [b,c]	198-199	$C_{21}H_{20}BrNO_4$	58.61	4.78	3.35	(58.61)	(4.68)	(3.25)	1640	1760	8.1-9.1 (m, 6H), 6.9 (d, 1H, J ^{5} 9 Hz), 6.85 (s, 1H), 6.6 (d, 1H, J ^{5} 9 Hz), 6.0 (s, 2H), 5.2 (s, 2H), 4.0 (c, 2H), 1.15 (t, 3H)
13 [b,f,g]	219-220	$C_{23}H_{26}BrNO_5$	58.26	5.73	2.72	(57.99)	(5.50)	(2.49)	1640	1745	8.0-8.9 (m, 6H), 5.8 (s, 2H), 5.2 (s, 2H), 4.2 (c, 2H), 3.95 (s, 3H), 3.8 (s, 6H), 1.2 (t, 3H)
14 [b,h]	195-196	$C_{24}H_{28}BrNO_6{\cdot}\frac{1}{2}H_2O$	56.02	5.51	2.57	(55.92)	(5.67)	(2.71)	1610	1750	9.0 (d, 1H, 6 Hz), 8.95 (d, 1H, 6 Hz), 7.9 (s, 1H), 7.6 (s, 1H), 7.1 (s, 1H), 6.85 (d, 1H, J ^{5} 6 Hz), 6.4 (d, 1H, J ^{5} 6 Hz), 6.1 (s, 2H), 5.1 (s, 2H), 4.2 (s, 6H), 4.05 (c, 2H), 3.8 (s, 6H), 1.2 (t, 3H)
15 [b,f]	310-311	$C_{22}H_{16}BrNCl_2$	59.66	3.67	2.88	(59.35)	(3.62)	(3.14)	1655		9.0-9.45 (m, 2H), 7.5-8.9 (m, 11H), 2.8 (s, 3H)
16 [b,f]	202-203	$C_{22}H_{16}BrN_3O_4{\cdot}H_2O$	54.25	3.88	8.25	(54.56)	(3.74)	(8.67)	1650		9.1-9.5 (m, 2H), 7.5-8.7 (m, 11H), 2.9 (s, 3H)
17 [b,f]	171-173	$C_{23}H_{20}BrNO_2$	66.98	4.86	2.91	(67.27)	(4.51)	(3.13)	1650	1760	8.3 (d, 1H, J ^{5} 6 Hz), 7.2-8.1 (m, 11H), 4.45 (c, 2H), 2.7 (s, 3H), 1.3 (t, 3H)
18 [b,f]	350	$C_{22}H_{16}BrN$	70.42	4.54	4.08	(70.56)	(4.30)	(3.74)	1660		9.25 (s, 1H), 8.7 (d, 1H, J ^{5} 6 Hz), 7.0-8.35 (m, 11H), 2.75 (s, 3H)
19 [b,f]	209-210	$C_{23}H_{18}BrNO_2$	65.38	4.45	3.42	(65.72)	(4.31)	(3.33)	1650	1740	8.85 (d, 1H, J ^{5} 6 Hz), 8.5 (s, 1H), 7.6-8.3 (m, 8H), 5.0 (c, 2H), 2.85 (s, 3H), 1.7 (t, 3H)
20 [b,c]	280-281	$C_{22}H_{18}BrN$	70.42	4.69	3.63	(70.22)	(4.82)	(3.72)	1645		9.1 (s, 1H), 8.85 (s, 1H), 8.1-8.7 (m, 3H), 7.4 (s, 12H), 3.15 (s, 3H)
21 [b,f]	221-222	$C_{24}H_{22}BrNO_2$	65.80	5.29	3.36	(66.06)	(5.08)	(3.21	1630		9.1 (s, 1H), 8.9 (s, 1H), 8.1-8.8 (m, 3H), 7.0-7.5 (m, 8H), 3.3 (s, 6H), 3.2 (s, 3H)
22 [b,f]	350	$C_{22}H_{16}BrN$	70.77	4.25	3.67	(70.59)	(4.30)	(3.74)	1630		9.2 (s, 1H), 8.65 (s, 1H), 7.2-8.3 (m, 11H), 3.0 (s, 3H)
23 [b,f]	285-286[i]	$C_{14}H_{16}BrN$	—	—	—				1635		9.9 (bs, 2H), 7.6-8.1 (m, 2H), 3.3 (t, 4H), 2.65 (s, 6H), 2.0-2.4 (m, 2H)

Table 9 (CONT)

Compound	M.p (°C)	Molecular Formulae	Found (%) C	Found (%) H	Found (%) N	Required (%) [a] C	Required (%) [a] H	Required (%) [a] N	C=N ⟨	Others	^{1}H NMR Data (δ)
24 [b,f]	277-278	$C_{24}H_{18}BrNO_4 \cdot H_2O$	56.16	3.64	8.23	(56.48)	(3.95)	(8.23)	1635		9.0-9.3 (m, 2H), 8.0-8.5 (m, 6H), 7.5-7.9 (m, 4H), 3.0-3.7 (m, 4H), 2.0-2.5 (m, 2H)
25 [b,f]	253-254	$C_{24}H_{18}BrN \cdot 5H_2O$	67.33	4.65	3.14	(67.45)	(4.95)	(3.27)	1630		9.45 (s, 1H), 8.7-8.9 (m, 1H), 8.0-8.4 (m, 4H), 7.4-7.9 (m, 6H), 3.7 (t, 2H), 3.3 (t, 2H), 1.8-2.2 (m, 2H)
26 [b,f]	177-179	$C_{25}H_{20}BrNO_2 \cdot H_2O$	62.52	4.98	2.99	(62.24)	(5.01)	(2.90)	1630	1745	8.9 (d, 1H, J [s] 6 Hz), 8.45 (d, 1H, J [s] 9 Hz), 7.5-8.2 (m, 7H), 3.8 (c, 2H), 2.7-3.9 (m, 4H), 2.0-2.6 (m, 2H), 1.1 (t, 3H)
27 [b,c]	157-158	$C_{18}H_{18}BrNO_3 \cdot H_2O$	51.98	5.76	3.15	(52.18)	(5.83)	(3.38)	1625	1750	9.25 (d, 1H, J [s] 6 Hz), 7.8-8.7 (m, 6H), 4.1 (c, 2H), 1.8 (s, 3H), 1.4 (s, 3H), 1.1 (t, 3H)
28 [k,c]	212-214	$C_{18}H_{18}BrNO_2 \cdot H_2O$	54.34	5.98	3.37	(54.55)	(5.59)	(3.53)	1630	1730	9.35 (s, 1H), 9.13-9.2 (m, 1H), 8.68 (d, 1H, J [s] 7 Hz), 8.02-8.32 (m, 4H), 4.29 (c, 2H), 2.77 (s, 3H), 2.80 (s, 3H), 1.43 (t, 3H)
29 [b,f]	159-160	$C_{28}H_{20}BrN_3O_6 \cdot H_2O$	56.90	3.86	7.28	(56.76)	(3.74)	(7.09)	1640	1745	7.1-9.0 (m, 15H), 4.35 (c, 2H), 1.0 (t, 3H)
30 [b,l]	350	$C_{25}H_{16}BrN \cdot 5H_2O$	68.27	3.98	3.29	(68.65)	(4.37)	(3.20)	1630		9.15 (s, 1H), 8.4 (s, 1H), 8.15 (d, 1H, J [s] 6 Hz), 6.9-7.9 (m, 13H)
31 [b,c]	288-290	$C_{26}H_{18}BrNO_3 \cdot H_2O$	61.67	4.64	2.53	(61.18)	(4.73)	(2.74)	1630	1740	7.7-9.4 (m, 13H), 5.05 (c, 2H), 1.55 (t, 3H)
32 [b,l]	232-233	$C_{18}H_{20}BrNO_2$	59.32	5.61	4.20	(59.67)	(5.56)	(3.86)	1625	1740	8.7 (s, 1H), 8.2 (d, 1H, J [s] 5 Hz), 7.3-7.8 (m, 3H), 4.4-4.8 (m, 4H), 3.1-3.5 (m, 2H), 2.65 (s, 3H), 2.35 (s, 3H), 1.9 (t, 3H)
33 [b,l]	155-156	$C_{28}H_{22}BF_4NO_2$	68.35	4.23	2.72	(68.45)	(4.51)	(2.85)	1620	1740	9.4 (s, 1H), 8.9 (d, 1H, J [s] 6 Hz), 8.3-8.7 (m, 3H), 7.4-8.25 (m, 3H), 4.5-5.0 (m, 4H), 3.2-3.6 (m, 2H), 1.45 (t, 3H)
34 [b,f]	179-180	$C_{26}H_{20}BrNO_2 0.5 \cdot H_2O$	66.81	4.39	2.72	(66.81)	(4.52)	(2.99)	1625	1750	9.5 (s, 1H), 8.85 (d, 1H, J [s] 6 Hz),. 7.5-8.6 (m, 9H), 4.7-5.1 (m, 4H), 3.4-3.7 (m, 2H), 1.6 (t, 3H)
35 [b,f]	272-273	$C_{14}H_{12}BrNO$	57.70	4.25	4.70	(57.95)	(3.82)	(4.82)		1630	8.75 (d, 1H, J [s] 6 Hz), 8.28 (t, 1H), 7.45-7.85 (m, 7H), 5.6 (s, 2H)
36 [b,f]	253-255	$C_{15}H_{13}BrClN$	57.64	3.54	3.71	(57.70)	(3.49)	(3.73)		1635	7.4-8.4 (m, 10H), 5.7 (s, 2H)
37 [b,f]	244-245	$C_{19}H_{16}BrNO$	61.94	4.68	3.68	(61.63)	(3.45)	(3.78)		1630	7.2-8.4 (m, 10H), 5.65 (s, 2H), 4.1 (s, 3H)
38 [b,f]	234-235	$C_{19}H_{14}BrNO_3 0.5 \cdot H_2O$	57.69	3.91	3.34	(58.03)	(3.58)	(3.56)		1640	8.3 (d, 1H, J [s] 6 Hz), 7.7-8.2 (m, 6H), 7.1 (s, 1H), 7.1 (d, 1H, J [s] 3 Hz [m]), 6.1 (s, 2H), 5.6 (s, 2H)
39 [b,f,g]	244-245	$C_{21}H_{20}BrNO_4$	58.27	4.41	3.38	(58.61)	(4.68)	(3.25)		1640	7.5-8.4 (m, 6H), 5.65 (s, 2H), 4.1 (s, 3H), 3.95 (s, 6H)
40 [b,f]	350	$C_{23}H_{16}BrNO_2$	65.96	4.30	2.95	(66.04)	(3.85)	(3.34)	1470	1740	9.0 (d, 1H, J [s] 6 Hz), 7.6-8.3 (m, 8H), 3.3-3.9 (m, 4H), 2.1-2.7 (m, 2H)
41 [b,f]	350	$C_{24}H_{14}BrNO_2$	69.98	3.04	2.95	(67.30)	(3.29)	(3.27)	1640	1745	9.0 (s, 1H), 7.3-8.8 (m, 12H)

[a] Analysis is described for new compounds. [b] Perkin Elmer R 24 B 60 MHz. [c] ^{1}H nmr in DMSO, TMS as internal reference. [d] 205° in [2]. [e] 199° in [18]. [f] ^{1}H nmr in TFA, TMS as internal reference. [g] Two Protons of the phenyl group are interchange by deuterium. [h] ^{1}H nmr in deuteriochloroform, TMS as internal reference. [i] 285-286° in [2]. [j] 170° in [2] is described with $1 \cdot H_2O$. [k] Variant FT 80 A 80 MHz. [l] ^{1}H nmr in DMSO-TFA, TMS as internal reference. [m] Overlapped signal with a singlet.

quinolizinium salts with good yields in acetone, as it is shown in Tables 5 and 6.

Benzyl derivatives **3** and **9-14**, did not produce Westphal condensation with any usual dicarbonyl. Instead of it, 2,3-dihydroindolizin-2-one derivatives were isolated even in the presence of the most reactive dicarbonyls. Results of intramolecular cyclisation are presented in Table 7. Yields in the presence of dicarbonyls were 10-25% smaller, but no traces of quinolizinium salts were detected in any example.

The process is a little-known modification of the Tschitschibabin synthesis of indolizines **15** and related products have been described as useful intermediates [16] and antifungal agents [17].

As described in [8], hydrolysis of quinolizinium esters was performed by treatment with concentrated hydrobromic acid at reflux temperatue. Surprisingly enough the acids were isolated without decarboxylation as it is shown in Table 8.

Microanalytical and spectroscopic data of the products are presented in Table 9.

EXPERIMENTAL

The melting points were determined in open capillary tubes and are uncorrected. Spectra were recorded with a Perkin Elmer 577 grating ir spectrophotometer and with a Perkin-Elmer R 24B (60 MHz) 1H nmr spectrometer. The 1,2-dicarbonyls were either from commercial sources or prepared from previously described methods.

General Procedure for Preparation of 1-Substituted-α-alkylcycloimmonium Salts (Tables 1 and 2, Figure 2, Compounds **1-14**).

To a stirred solution of the substituted pyridine (0.11 mole) in acetone (25 ml), ethyl bromoacetate (0.1 mole) was added dropwise. The mixture was maintained at room temperature (compounds **1**, **7** and **13**) or refluxed as indicated in Tables 1 and 2. The salt was filtered off as a white powder which was crystallized from ethanol-ether.

General Procedure for the Preparaton of Quinolizinium Salts **15-22** (Table 3).

N-Ethoxycarbonylmethylpyridinium salts **1** to **3** (5 mmoles) and the corresponding dicarbonyl (5 mmoles) were suspended in a 2:1 acetone/-ethanol mixture (30 ml). Di-*n*-butylamine (0.85 ml) was added and the solution was refluxed as described in Table 3. The mixture was concentrated to dryness, the residue was boiled with 10 ml of acetone, the mixture was filtered and the solid crystallised in ethanol/ether.

General Procedure for Preparaton of Quinolizinium Salts **23-26** (Table 4).

1-Ethoxycarbonylmethyl-5,6,7,8-tetrahydroquinolinium bromide **4** (0.6 g, 2 mmoles) and the corresponding dicarbonyl (2 mmoles) were suspended in 5 ml of acetone. Anhydrous sodium acetate (0.164 g, 2 mmoles) was added, and the mixture was refluxed for two hours, acidified with hydrobromic acid and concentrated to dryness. The residue was triturated with 5 ml of acetone, and crystallized in methanol/ether.

2,3-Dimethyl-4-ethoxycarbonylbenzo[*c*]quinolizinium Bromide (**27**).

It was obtained as described by Westphal [2] being isolated in 28% yield.

General Procedure for Preparation of Benzo[*a*]quinolizinium Salts **28-34** (Tables 5 and 6).

1-Ethoxycarbonylmethylisoquinolinium salts **6** or **7** (2.5 mmoles) and the corresponding dicarbonyl (3 mmoles) were suspended in 6 ml of acetone, anhydrous sodium acetate was added (0.21 g, 2.5 mmoles) and the mixture was refluxed for 2 hours, then acidified with hydrobromic acid and concentrated to dryness. The residue was triturated with 5 ml of acetone, and crystallized as described in Tables 5 and 6.

General Procedure for Preparation of 1-Aryl-2-indolizin-2-ones **35-39** (Table 7).

The corresponding *N*-ethoxycarbonylmethylbenzylpyridinium **3** or isoquinolinium salts **9-14** (5 mmoles) were suspended in 12 ml of acetone and 0.42 g (5 mmoles) of anhydrous sodium acetate was added. The mixture was refluxed for the time described in Table 7, then acidified with hydrobromic acid and concentrated to dryness. The residue was triturated with 5 ml of acetone, filtered and crystallized with ethanol/ether.

Hydrolysis of Compounds **26** and **31** (Table 8).

It was performed as described in [8]. The isolated products were crystallised from methanol-ether.

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