Synthesis of Pyridinium Heterocyclic Ylides. Degradation of the Pyridinium Group

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The synthesis of pyridinium-quinolone chlorides and ylides, a pyridinium-methylquinazolone ylide, 9-pyridinium acridine chloride, and their behaviour by treatment with boiling aniline are described.

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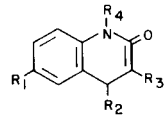
In a previous short communication we have reported the synthesis of a 3-pyridinium-quinolon-2-one ylide (1) obtained in the course of our investigations concerning acetylpyridinium as an amino-protecting group (2). The present work completes that investigation and reports the degradation of the pyridinium ring by aniline.

The pyridinium chlorides (I) were obtained in high yields from the interaction of an excess of boiling pyridine and the corresponding 2-chloroacetamidophenones (3). The cyclisation proceeds by a Knoevenagel reaction of the non-isolable intermediate acylpyridinium (II) (4) and is similar to that observed when 2-acetamido-2-'-acetanilidobenzophenone is boiled with a mixture of piperidine and pyridine (5). The structures of these compounds were first established by analysis, uv, ir (Table I) and protonic resonance.

By the action of one equivalent of alkali on aqueous solution of the pyridinium chlorides (I), the pyridinium ylides (III) precipitate as yellow amorphous solids. These compounds possess an indeterminate degree of hydration; on heating *in vacuo* over 120°, orange anhydrous substances are obtained. Comparatively, the uv spectra of

Table I



Compound No.	R_1	R_2	R_3	H	Yield %	M.p. °C	Ir (cm^{-1}) C=O	Ir (cm^{-1}) NH (a)	Recrystallization Solvent	Formula	Analyses: Calcd. / Found C%	H%	N%
Ia	Cl	C_6H_5	$C_5H_5\overset{+}{N}\cdot Cl^-$	H	90	375	1660	3000	ethanol-benzene	$C_{20}H_{14}Cl_2N_2O$	65.04	3.79	7.59
											65.06	3.85	7.58
Ib	NO_2	C_6H_5	$C_5H_5\overset{+}{N}\cdot Cl^-$	H	93	320 dec.	1670	3050	ethanol-benzene	$C_{20}H_{14}ClN_3O_3$	63.24	3.69	11.05
											63.20	3.73	11.02
Ic	H	CH_3	$C_5H_5\overset{+}{N}\cdot Cl^-$	H	85	300 dec.	1660	3390	ethanol	$C_{15}H_{13}ClN_2O$	66.05	4.77	10.27
											66.02	4.80	10.23
IIIa	Cl	C_6H_5	$C_5H_5\overset{+}{N}\cdot Cl^-$	-	92	307	(b)	—	methanol-xylene	$C_{20}H_{13}ClN_2O$	72.18	3.91	8.42
											72.15	3.96	8.43
IIIb	NO_2	C_6H_5	$C_5H_5\overset{+}{N}\cdot Cl^-$	-	95	310 dec.	(b)	—	methanol-water	$C_{20}H_{13}N_3O_3$	69.97	3.79	12.24
											69.93	3.75	12.20
IIIc	H	CH_3	$C_5H_5\overset{+}{N}\cdot Cl^-$	-	90	150 dec.	(b)	—	isopropanol-benzene	$C_{15}H_{12}N_2O$	76.27	5.08	11.86
											76.25	5.12	11.84
IVa (c)	Cl	C_6H_5	NH_2	H	87	239	1660	3350 35000	methanol-dioxane	$C_{15}H_{11}ClN_2O$	66.54	4.06	10.35
											66.57	4.09	10.31
IVb (d)	NO_2	C_6H_5	NH_2	H	91	330 dec.	1660	3350 3500	DMF-water	$C_{15}H_{11}N_3O_3$	64.06	3.91	14.94
											64.03	3.95	14.90
IVc	H	CH_3	NH_2	H	82	225	1660	3390 3500	isopropanol	$C_{10}H_{10}N_2O$	68.96	5.74	16.09
											68.92	5.78	16.11
V	Cl	C_6H_5	$C_5H_5\overset{+}{N}\cdot Cl^-$	CH_3	94	265	1660	—	DMF-benzene	$C_{21}H_{16}Cl_2N_2O$	65.79	4.18	7.31
											65.74	4.22	7.28

(a) Ir: in potassium bromide. (b) No typical C=O bands. (c) Compound previously described in reference 8. (d) Compound previously described in reference 5.

0022-152X/81/051061-03$02.25

Scheme I

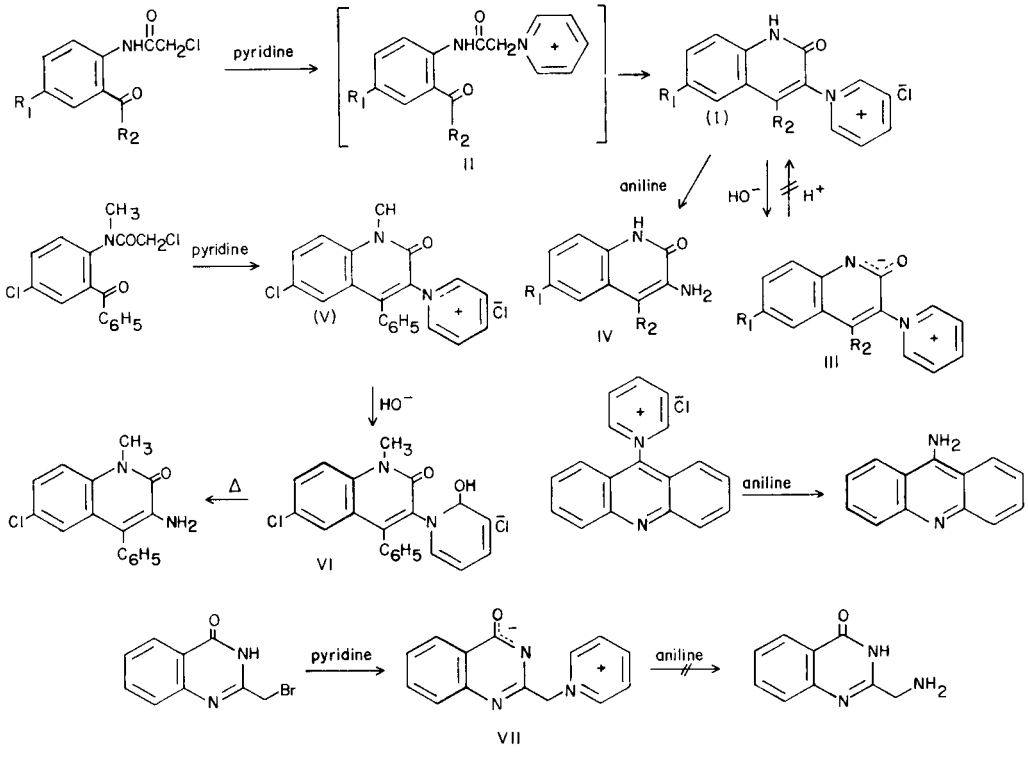
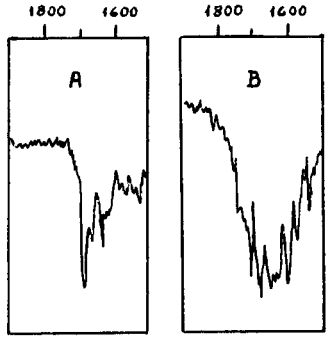


Figure 1



Ir spectra:
A: compound Ib (C=O band)
B: compound IIb

the compounds I and III show no difference between each other, but the ir spectra of the compounds III do not show the typical C=O and NH bands (Figure 1).

Unfortunately, the nmr spectra gives little information about chlorides (I) and ylides (III); for instance, Ia only shows three complex multiplets between δ 7.0-9.3 and is similar to IIIa, δ 5.4-7.1 (DMSO-d_6, TMS).

Significant evidence of the stability of these ylides is that by boiling with concentrated hydrochloric acid, neither regenerated the pyridinium chloride, nor decomposed.

In 1903, Zincke (6) reported the transformation of 2,4-dinitrophenylpyridinium chloride into 2,4-dinitroaniline by treatment with boiling aniline or with other primary amines. When we assayed the same procedure on the pyridinium chlorides (I), the corresponding 3-amino-quinolones were easily obtained with excellent yield and purity. They were identical in mixed mp and ir spectra with authentical samples obtained by Fryer's method (5).

In order to explore the scope of this practical transformation in heterocyclic compounds, two other pyridinium heterocycles were synthesized from the corresponding halogenated derivatives. Boiling 9-pyridiniumacridine chloride with aniline afforded 9-aminoacridine in 46% yield, but the pyridinium-quinazolone ylide (VII) only produced a non-identified product by the same treatment.

To complete the quinolone series, the 1-methyl derivative of Ia (V) was also obtained by the same general procedure from 5-chloro-2-methylaminobenzophenone. When V was treated with base, it yielded a deep red amorphous solid the structure of which, on basis of analysis, uv and ir, was that of a pyridinium pseudo-base (VI). When V was treated with boiling aniline only, an unstable and non-identified material was isolated. However, by heating VI at 220° under vacuum, the desired 1-methyl-3-amino-quinolone was generated as a sublimated product, which was identical in mp, mixed mp and ir spectra to an authentic sample (5).

Lepke (7) has reported that *N*-substituted 3-nitro-4-aminophenylpyridinium salts are also difficult to cleave by the method of Zinke (6). However, we have observed that 2,4-dinitrophenylpyridinium chloride reacted quickly with dilute aniline below 0° giving 2,4-dinitroaniline. Therefore, the Zinke's cleavage appears limited to pyridinium salts conjugated to π-deficient structures.

EXPERIMENTAL

All melting points were taken on a Büchi-Tottoli capillary melting point apparatus and are uncorrected. The ir spectra were recorded with a Perkin-Elmer 700 Spectrophotometer; nmr with a 60-Mc Perkin Elmer R-12 Spectrometer and uv spectra with a Perkin Elmer Model 202.

2-Chloroacetanilidephenones.

These compounds were synthesized by the method of Sternbach (3).

3-Pyridinio-2-(1*H*)quinolone Chlorides (Ia, Ib, Ic and IV). General Procedure.

A mixture of 0.01 mole of the corresponding 2-chloroacetanilidephenone and 20 ml of anhydrous, freshly distilled pyridine, was gently refluxed for 15 minutes. After cooling, the solid was filtered, washed with benzene and recrystallized from the proper solvent (see Table I).

2-Amino-2-(1*H*)quinolones (IVa, IVb, IVc). General Procedure.

A mixture of 0.01 mole of Ia, Ib or Ic and 60 ml of freshly distilled aniline were gently refluxed for 2 hours. The excess of aniline was removed by distillation *in vacuo* at 100° and the dark solid residue was crystallized from the proper solvent (see Table I).

3-Pyridinio-2-(1*H*)quinolone Ylides (IIIa, IIIb and IIIc). General Procedure.

To a 10% solution in water of compound Ia or Ib was added dropwise a solution of 40% sodium hydroxide until no more insoluble product was formed. The solid was filtered, dried *in vacuo* at 120° and recrystallized from the proper solvent (see Table I). In the case of compound IIIc, the aqueous solution of Ic was passed through basic Amberlite ion exchange resin IR 400 and the effluent was collected and evaporated *in vacuo* at 80°. The yellow solid residue was recrystallized from the proper solvent (see Table I).

3-Pyridinio-6-chloro-1-methyl-4-phenyl-2-(1*H*)quinolone Pseudo Base (VI).

This compound was obtained by the same procedure as that used in the preparation of IIIa. It was purified by column chromatography over neutral alumina using benzene-chloroform (2:1) as the solvent. The effluent was evaporated *in vacuo* to give a deep-red microcrystalline solid, mp 143° dec.; uv: δ max 255 mμ; ir: 1680 (C=O).

Anal. Calcd. for $C_{21}H_{16}ClN_2O_2$: C, 69.32; H, 4.40; N, 7.70. Found: C, 69.38; H, 4.45; N, 7.73.

9-Pyridinioacridine Chloride.

A mixture of 9-chloroacridine (1.0 g) and 10 ml of pyridine was heated with stirring at 100° for 15 minutes and then 10 ml of benzene was added. On standing, a solid separated, which was filtered, dried and recrystallized from benzene-ethanol to yield 0.95 g (74%) of product, mp 152-154°; ir (potassium bromide): 3400, 3050, 1640, 1480, 1420 and 780 cm^{-1}.

Anal. Calcd. for $C_{18}H_{13}ClN_2$: C, 73.84; H, 4.44; N, 9.97. Found: C, 73.79; H, 4.48; N, 9.55.

9-Aminoacridine from 9-Pyridinioacridine.

A mixture of 9-pyridinioacridine chloride (1.0 g) and 20 ml of freshly distilled aniline was refluxed for 2 hours and then distilled *in vacuo* (2 mm/100°). The dark solid residue was dissolved in 20 ml of chloroform and allowed to stand at 0° overnight; the crude 9-aminoacridine crystallized. The product was purified of acridone by dissolving in 30% hydrochloric acid. The solution was filtered and the 9-aminoacridine precipitated by neutralization with dilute sodium hydroxide solution to yield 0.26 g (46%) of 9-aminoacridine mp 220° dec. A small sample was recrystallized from acetone, which was identical in mixed mp and ir spectra with an authentic sample.

2-Pyridiniomethyl-4-(3*H*)quinazolinone Ylide (VII).

A mixture of 2-bromomethyl-4-(3*H*)quinazolinone (1.0 g) obtained according to the literature (10) and 6 ml of pyridine was heated under reflux for 30 minutes and cooled. The solid was filtered, washed with benzene and recrystallized from benzene-pyridine, giving 0.8 g (81%) of the pure product, mp 229-230°; ir (potassium bromide): 2700, 2850, 1690 (C=O), 1600 (aromatic C=C), 1470 and 790.

Anal. Calcd. for $C_{14}H_{11}N_3O$: C, 70.88; H, 4.64; N, 17.72. Found: C, 70.93; H, 4.68; N, 17.69.

3-Amino-6-chloro-1-methyl-4-phenyl-2-(1*H*)quinolone.

Compound VI (0.5 g) was heated in a vacuum sublimator at 220°/0.5 mm to yield 0.15 g (38%) of a yellow solid, mp 133-134°, that crystallized from acetone-petroleum ether giving a white sample identical in mixed mp and ir spectra to an authentic sample obtained as in the literature (5).

2,4-Dinitroaniline from 2,4-Dinitrophenylpyridinium Chloride.

To a stirring solution of 2,4-dinitrophenylpyridinium chloride (2.8 g, 0.01 mole) in DMF (150 ml) at 0°, was added dropwise a solution of aniline (0.9 g, 0.01 mole) in 50 ml of DMF during 1 hour. The solvent was removed under reduced pressure at 60° and the solid residue was extracted with ethanol and filtered. The ethanol was removed *in vacuo* and the solid residue crystallized from acetone-water giving 41 g (44%) of 2,4]dinitroaniline, mp 188°, identical in mixed mp and ir to an authentic sample.

Acknowledgement.

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