SYNTHESIS AND PROPERTIES OF PYRROLO[3,2,1-ij]- AND PYRAZOLO[4,3,2-ij]-QUINOLINONES, AZA-ANALOGUES OF PHENALENONES

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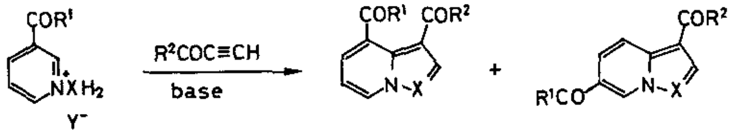
Abstract —— Pyrrolo[3,2,1-ij]- and pyrazolo[4,3,2-ij]-quinolinones were synthesized by the intramolecular aldol condensation of 1,8-diacylindolizines and 3,4-diacylpyrazolo[1,5-a]pyridines, respectively. These compounds showed properties analogous to those of 1H-phenalen-1-ones.

The chemistry of 1H-phenalen-1-one (1a) is of particular interest because of its unusual properties (high bacisity, high dipole moment, low frequency shift of the ir carbonyl absorption, and so on). These properties have been attributed to an important contribution of ionic structure (1b) to the resonance hybrid.[1] A similar behavior would be expected for the pyrrolo[3,2,1-ij]- and pyrazolo[4,3,2-ij]-quinolinones and it was of interest to investigate their synthesis and properties.


(1a) (1b)

Synthesis —— The synthetic route is outlined in the next page. The 1,3-dipolar cycloaddition of N-ethoxycarbonylmethyl-3-acetylpyridinium salt (2a) with ethynyl phenyl ketone in tetrahydrofuran in the presence of base gave the isomeric indolizines (3a) and (4a)[2] in 33 and 26% yields, respectively. The structural differentiation between the two isomers was readily made on the basis of the spectroscopic evidence.[3] Intramolecular condensation of the indolizine (3a) was achieved by passing a solution of (3a) in benzene through an alumina column to give the pyrrolo[3,2,1-*ij*]quinolinone (5a), mp 216-219°C, in 82% yield. The 1,3-dipolar cycloaddition of the 3-benzoyl congener (2b) with ethylnyl methyl ketone again gave two indolizines (3b)(31%) and (4b)(5%). Intramolecular aldol condensation of (3b) gave (7a), mp 182-184°C, in 78% yield. Similar reactions starting from the *N*-amine salts (2c) and (2d) gave the corresponding pyrazolo[1,5-*a*]pyridines (3c,d) and (4c,d),[3,5] the former two of which were converted into the pyrazolo[4,3,2-*ij*]quinolinones (5b), mp 222-224°C, and (7b), mp 174-175°C, in 59 and 71% yields, respectively.

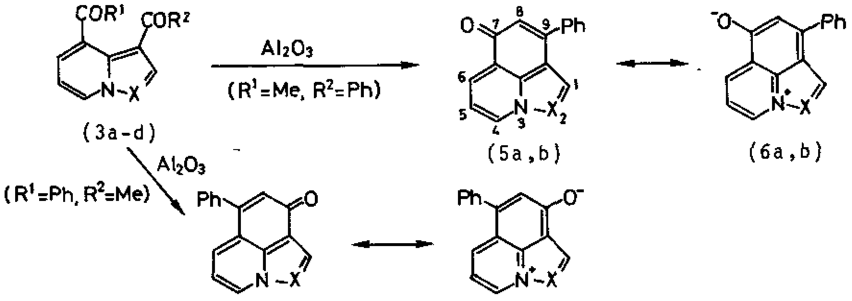


(2a-d) (3a-d) (4a-d)

a; R^1=Me, X=CCO_2Et, Y=Br
b; R^1=Ph, X=CCO_2Et, Y=Br
c; R^1=Me, X=N, Y=OMes
d; R^1=Ph, X=N, Y=OMes

Table 1. 1,3-Dipolar cycloaddition of (2a-d)

	R^1	R^2	X	Conditions	Yields (%) (3)[4]	(4)[4]
a	Me	Ph	CCO_2Et	Et_3N in THF	33	26
b	Ph	Me	CCO_2Et	K_2CO_3 in MeCN	31	5
c	Me	Ph	N	Et_3N in MeCN	30	21
d	Ph	Me	N	Et_3N in MeCN	32	23



(7a,b) (8a,b)

a; X=CCO_2Et
b; X=N

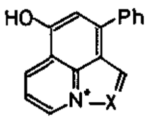
Physical Properties —— The uv absorption maxima of (5) and (7) are listed in Table 2. The 7-oxo derivatives (5a) and (5b) are red crystals and have longer wave-length absorption bands than the 9-oxo derivatives (7a) and (7b) which are yellow crystals.

Table 2. The uv spectra for (5) and (7)

Compd.	λ_{max} nm (log ε) in EtOH
(5a)	220 (3.48), 297 (4.65), 323 (4.29), 335sh (4.23), 510 (3.84), 536sh (3.77)
(5b)	251 (4.29), 330 (4.11), 452sh (3.37), 478 (3.76), 514sh (3.29)
(7a)	223 (4.42), 254 (4.44), 278 (4.25), 288 (4.26), 304sh (3.81), 372sh (3.85) 409 (4.03), 428sh (3.92)
(7b)	236 (4.42), 244 (4.39), 304 (3.61), 368sh (3.77), 385 (4.11), 400sh (3.66)

The ir carbonyl absorption band (in $CHCl_3$) of (5a)(1645 cm^{-1}) and (5b)(1660 cm^{-1}) is shifted to a lower frequency (*ca*. 40-45 cm^{-1}) than the acetyl carbonyl absorption of (3a)(1690 cm^{-1}) and (3c)(1700 cm^{-1}). The carbonyl absorption band of (7a)(1645 cm^{-1}) and (7b)(1650 cm^{-1}) is again shifted to the lower frequency but the shift is small (*ca*. 15 cm^{-1}) if compared to the acetyl carbonyl absorption of (3b)(1660 cm^{-1}) and (3d)(1665 cm^{-1}) which have the vinylogous amide structures with highly polarized carbonyl group. These results demonstrate that the contributions of the ionic structures (6 and 8) are important to the resonance hybrids of (5) and (7) as in the case of 1*H*-phenalen-1-one.

In the ^{1}H-nmr spectra (Table 3) of (5) and (7), the signals of the ring protons are shifted 0.28-0.95 ppm for (5a) and (5b) and 0.36-0.94 ppm for (7a) and (7b) to lower magnetic field by addition of a few drops of CF_3CO_2D to the $CDCl_3$ solution, indicating that protonation takes place at the carbonyl group at the 7- and 9-positions to give (9) and (10), respectively. This behavior is also similar to that of 1*H*-phenalen-1-one (1) and its related compounds.[6]



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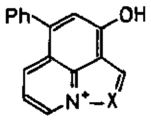

(10)

Table 3. The ^{1}H-nmr spectra for (5) and (7) (200 MHz)

Compd.	Solvent	Chemical shifts (δ) H-1	H-4	H-5	H-6	H-8	Coupling constants (Hz) $J_{4,5}$	$J_{4,6}$	$J_{5,6}$
(5a)	$CDCl_3$	7.70 (s)	9.62 (dd)	7.33 (dd)	8.36 (dd)	6.59 (s)	7.5	1	6.5
	$+CF_3CO_2D$[a]	8.20 (s)	10.20 (dd)	8.04 (dd)	9.30 (dd)	7.54 (s)	8	1	6.5
the difference		-0.50	-0.58	-0.71	-0.94	-0.95			
(5b)	$CDCl_3$	8.38 (s)	8.90 (dd)	7.41 (t)	8.50 (dd)	6.71 (s)	7	1	7
	$+CF_3CO_2D$	8.66 (s)	9.26 (br d)	b	8.99 (br d)	7.26 (s)	7	~1	7
the difference		-0.28	-0.36		-0.49	-0.55			
(7a)	$CDCl_3$	8.16 (s)	9.55 (dd)	7.20 (dd)	7.74 (dd)	6.83 (s)	9	1	7
	$+CF_3CO_2D$	8.54 (s)	10.07 (br d)	7.88 (dd)	8.68 (br d)	7.52 (s)	6.5	~1	8
the difference		-0.38	-0.52	-0.68	-0.94	-0.69			
(7b)	$CDCl_3$	8.70 (s)	8.75 (d)	7.24 (t)	7.86 (d)	6.86 (s)	7	~0	7
	$+CF_3CO_2D$	9.06 (s)	9.18 (d)	7.69 (t)	8.44 (d)	7.33 (s)	7	~0	7
the difference		-0.36	-0.43	-0.45	-0.58	-0.47			

[a] A few drops of CF_3CO_2D was added to the $CDCl_3$ solution. [b] Overlapped with signals of the phenyl group.

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