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CONDENSATION OF 2 - SUBSTITUTED - 3(H) - OXONAPHTHO (2, 1 - b) PYRAN WITH KETONES IN THE PRESENCE OF AMMONIUM ACETATE OR AMINES

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ABSTRACT

Several 5 - substituted naphtho (2, 1 - g) 1,3 - oxazocines (IIa - k), 11 - substituted hexahydro - 4a, 9 - alkyliminoethano - 4aH - 7, 8 - benzoxanthenes (IIIa - c) and 5,6 - benzo - 2 - methylimino - 2,3 - trimethylenechroman - 4a - carboxyacetic acid lactam (IV) have been prepared by Michael condensation of 2 - substituted - 3(H) - oxonaphtho (2, 1 - b) pyran (Ia - c) with ketones in the presence of nitrogenous base at room temperature. Preparation of 10 - substituted octahydronaphtho (2,1 - b) pyrano (3,4 - c) quinoline - 8H, 9 - diones (Va - c) was also described.

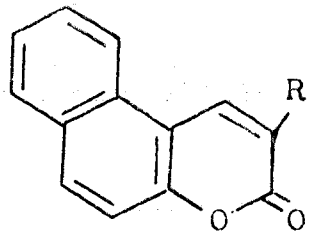
INTRODUCTION

In continuation of our studies on coumarins (Islam, et. al., 1979, 1980; El - Sharied, et. al., 1982), we report in this paper the reactions of 2–substituted–3 (H)–oxonaphtho (2,1–b) pyran with ketones in presence of ammonium acetate or amine at room temperature or at 170°C. Thus, treatment of Ia, b with ketone in the presence of ammonium acetate or methylamine at room temperature yielded 2,3,13–trialkyl / aryl–4–oxo–2, 6–methano–3,4,5,6–tetrahydro–2H–naphtho (2,1–g) 1,3–oxazocine–5–p-tolylcarboxamide / or carboxylic acid (IIa–c) and (IId–h) respectively.

Similarly, reaction of 2–cyano–3 (H)–oxonaphtho–(2,1–b) pyran (Ic) with a ketone as in case of Ia, b gave the corresponding 5–cyano–2, 3,13–trialkyl–4–oxo–2,6–methano–3,4,5,6–tetrahydro–2H–naphtho (2,1 –g) 1,3–oxazocine (IIi–k).

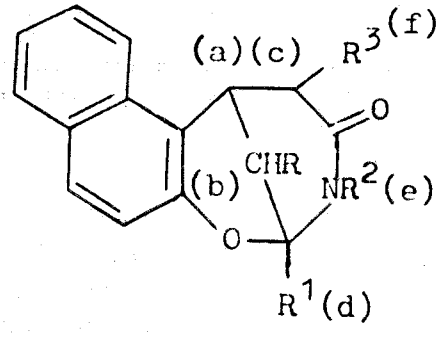
The reaction involves Michael addition of ketone to olefinic $C_1 - C_2$ bond of pyran followed by ammonolysis or aminolysis of the hete-

rocyclic ring and followed by ring closure to give (II), where the p-tolylcarboximide group of (IIa–c) remains intact in contrary to what was reported previously by El-Kady, et. al., 1981.



(I)

I a ; R = $CONHC_6H_4.CH_3$–p
b ; R = COOH
c ; R = CN



(II)

	R	R^1	R^2	R^3
a	H	CH_3	H	$CONHC_6H_4.CH_3$–p
b	H	CH_3	CH_3	$CONHC_6H_4.CH_3$–p
c	CH_3	CH_3	H	$CONHC_6H_4.CH_3$–p
d	H	CH_3	CH_3	COOH
e	CH_3	CH_3	CH_3	COOH
f	CH_3	C_2H_5	CH_3	COOH
g	C_6H_5	CH_3	CH_3	COOH

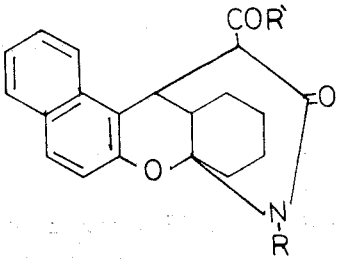
h	H	C_6H_5	CH_3	COOH
i	H	CH_3	H	CN
j	CH_3	CH_3	H	CN
k	CH_3	CH_3	CH_3	CN

The structural assignments of II were based on elemental analyses, IR spectra exhibiting absorption bands attributable to δ-lactam at (1610–1600), ν C=O at 1710 of carboxamide (IIa) and carboxylic group (IId), ν NH (IIa) 3340, ν OH (broad) of COOH group (IId) (2800 –3000) and ν CN (IIi–k) at 2250 cm^{-1}.

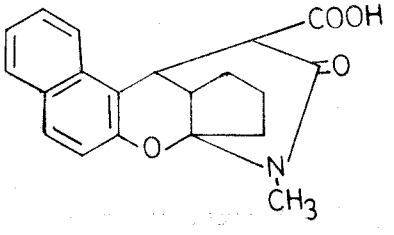
The PMR spectrum of compound (IIa) showed a signals at 1.77, 2.3 [s, 3H, CH_3(d) and CH_3(f) of p-tolyl group]; 6.97 and 9.25 [s, 1H, NH (e), (CONH)]; (1.95, 2.25) [d, 2H, bridged methylene protons (b) Jgem = 18Hz]; (3.70, 3.75) [d, 1H, C–H-(c) Jac = 6Hz]; 4.66 [m, 1H, C–H (a)]; (7.35–8.0) [m, 10H, Ar–H] ppm.

Also, the structure of IIb was further supported by alkaline hydrolysis with KOH alc. where IId was obtained (m.p. and m.m.p.).

On similar lines, condensation of Ia, b with alicyclic ketones at room temperature in the presence of nitrogenous base afforded 12–oxo–1, 2, 3, 4, 9, 9a–hexahydro–4a, 9–alkyliminoethano–4a H–7,8–benzoxanthene–11–p–tolylcarboxamide (IIIa, b) or–11–carboxylic acid (IIIc) and 5,6–benzo–2–methylimino–2,3– trimethylene–chroman–4a–carboxyacetic acid lactam (IV) respectively.



(III)

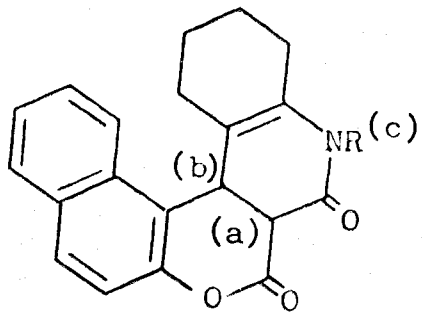


(IV)

	R	R′
III a ;	H	p–toluidino
b ;	CH_3	p–toluidino
c ;	CH_3	OH

The assigned structures III and IV were supported by IR spectra which showed bands at (1640–1660) of δ–lactam, ν C = O imide (1680); ν NH 3310 (IIIa), ν CH aliphatic (2860–2880) and ν OH broad (IIIc) at 2460–2760 cm^{-1}.

However, when Ia was reacted with cyclohexanone and ammonium acetate or primary amine at 170°C, 10–alkyl / aryl–8a, 9, 10, 11, 12, 13, 14,14b–octahydro [1] naphtho (2, 1-b) pyrano (3,4–c) quinoline 8 (H), 9–diones (Va–c) produced.



(V)

V a ; R = H
b ; R = C_2H_5
c ; R = C_5H_5

The assigned structure (V) was supported by the IR spectrum of (Va) exhibiting bands at 1660 (saturated δ–lactone), 1610 (δ–lactam), 2895 (cyclic aliphatic, CH) and 3265 (broad, NH) and the PMR spectrum of (Va) showing a signals at δ 1.8 [m, 8H, cyclohexene (broad)]; (1.70, 1.85) [d, 1H, C–H (b)]; 3.6 [d, 1H, C–H (a)]; 6.5 [s, 1H, NH (c)] and (7.0 – 9.0) [m, 6H, Ar–H] ppm. It is obvious that H_a is shifted downfield in comparing with H_b, this is due to the magneting anisotropic effect of the two neighbouring carbonyl groups.

Table I. Characterization data of various compounds prepared.

Compd*	m.p. °C	Mol. formula	Found (%) (Calc.)		
			C	H	N
IIa	240	$C_{24}H_{22}O_3N_2$	74.15 (74.61)	5.30 (5.70)	7.10 (7.25)
IIb	156	$C_{23}H_{24}O_3N_2$	74.65 (75.00)	5.70 (6.00)	6.65 (7.00)
IIc	235	$C_{23}H_{24}O_3N_2$	74.50 (75.00)	6.40 (6.00)	6.55 (7.00)
IId	240	$C_{18}H_{17}O_4N$	69.50 (69.95)	5.40 (5.47)	4.30 (4.50)
IIe	195	$C_{19}H_{19}O_4N$	70.00 (70.15)	5.25 (5.85)	4.10 (4.31)
IIf	200	$C_{20}H_{21}O_4N$	70.20 (70.80)	6.50 (6.19)	4.40 (4.13)
IIg	230	$C_{23}H_{21}O_4N$	73.80 (73.60)	5.70 (5.60)	4.00 (3.73)
IIh	241	$C_{23}H_{19}O_4N$	74.10 (73.99)	5.10 (5.09)	4.00 (3.75)
IIi	235	$C_{17}H_{14}O_2N_2$	73.00 (73.38)	5.00 (5.04)	10.20 (10.07)
IIj	215	$C_{18}H_{16}O_2N_2$	74.10 (73.97)	5.60 (5.48)	10.00 (9.59)
IIk	250	$C_{19}H_{18}O_2N_2$	74.00 (74.51)	6.10 (5.88)	9.50 (9.15)
IIIa	254	$C_{27}H_{20}O_3N_2$	75.80 (76.06)	5.95 (6.10)	6.36 (6.57)
IIIb	230	$C_{28}H_{28}O_3N_2$	76.80 (76.36)	6.20 (6.36)	6.10 (6.36)
IIIc	210	$C_{21}H_{21}O_4N$	72.00 (71.79)	5.80 (5.98)	4.20 (3.99)
IV	192	$C_{20}H_{19}O_4N$	74.50 (71.22)	5.80 (5.64)	4.40 (4.15)
Va	245	$C_{20}H_{17}O_3N$	75.10 (75.24)	5.20 (5.33)	3.15 (3.39)
Vb	230	$C_{22}H_{21}O_3N$	75.90 (76.08)	5.80 (6.05)	4.00 (4.03)
Vc	257	$C_{26}H_{21}O_3N$	79.10 (78.99)	3.40 (3.32)	3.25 (3.54)

* Solvents used for crystallization were: EtOH for IIa - d, IIi - k, Va,c; Benzene for IIe - h, IIIc, Vb, IV.

EXPERIMENTAL PROCEDURE

Melting points reported are uncorrected. IR specta were recorded on a Pye – Unicam Sp. 1200 and Sp. 1000 and PMR spectra in $CDCl_3$ were measured at BM 360 n.m.r. instrument using TMS as internal standard (chemical shifts in δ ppm).

Condensation of 2-Substituted -3(H) - oxonaphtho (2,1 - b) pyran (I) with ketones:

(i) At room temperature–A solution of (I) (0.01 mole), ketone (0.01 mole) and ammonium acetate or amine (0.025 mole) in ethanol was kept at room temperature for 3 days or boiled on a water-bath for 10 hr., evaporated to syrup, stirred with conc. HCl (20 ml), then with water (50 ml) and finally allowed to stand for several hr. The products were crystallized from suitable solvents to give IIa–k, IIIa–c and IV (Table 1), yield 50–80 %.

(ii) At 170°C–A mixture of Ia (0.01 mole), cyclohexanone (0.01 mole) and ammonium acetate or amine (ethylamine or aniline) (0.025 mole) in a sealed tube was heated at 170°–190°C for 6 hrs. The residue was stirred with conc. HCl (20 ml), washed with water and crystallized from a suitable solvent to give (Va–c) (yield 30–70 %) respectively (Table 1).

Hydrolysis of IIb to IId:

A mixture of IIb (1g) and ethanolic KOH (10 ml, 5 %) was heated for 3 hr., cooled and poured into water (50 ml) acidified with HCl. The solid separated recrystallized from suitable solvent to give IId (m.p. and m.m.p.) (Table 1).

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