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AN EFFICIENT SYNTHESIS OF 1,2-OXAZINO[4,5-*b*]QUINOLIN-1-ONE

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Abstract:
2-Formyl-3-carbethoxy quinolines **1** on treatment with hydroxylamine hydrochloride in the presence of an acid quencher triethyl amine resulted in 1,2-oxazino[4,5-*b*]quinolin-1-ones **2** in quantitative yield.

Introduction:

Oxazines are a class of six-membered heterocycles containing one oxygen and a single nitrogen atom. A number of isomeric structures are possible depending upon the relative positions of the two heteroatoms and the degree of oxidation of the ring system. Interest in their derivatives dates back well into the early part of the last century largely because many derivatives exhibit colour (1), *e.g.,* rhodommatin is found in the wings of the small tortoise shell butterfly *Agla's urticae*.

Oxazinoquinolines possess varied pharmaceutical properties such as cytotoxic activity (2) and antibacterial (3,4) properties. They are tough compounds and only a few methods (5,6,7) are available for their synthesis. In the present work here with we report a facile and simple route towards the synthesis of oxazinoquinolines.

Results and Discussion:

2-Formyl-3-carbethoxy quinoline (8) **1a** on treatment with hydroxylamine hydrochloride was expected to give 1,2-oxazino[4,5-*b*]quinolin-1-one **2b** through-*β*-annelation on the 2-formyl-3-carbethoxy side. Subsequently when equal moles of the reactants in the presence of catalytic amount of the acid quencher Et_3N were refluxed in ethanol medium, TLC revealed a new spot after 36 hours with the complete disappearance of the starting compound. After work up, the mixture was chromatographed over silica gel using petroleum ether: ethyl acetate (60:40) to yield a dirty yellow compound.

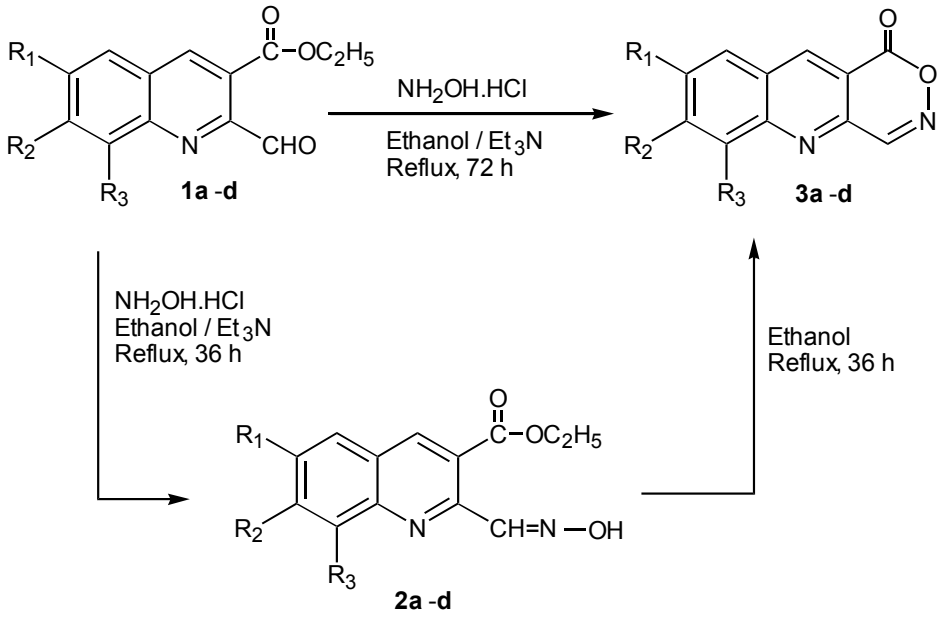
The IR data revealed a sharp band at 1620 cm^{-1} (C=N), a band at 1730 cm^{-1} (C=O ester carbonyl), 3400 cm^{-1} (-OH). The ^1H NMR of the compound showed the following peaks, δ 1.3 (t,

J = 7.12 Hz, 3H, C_3-$OCH_2C\underline{H}_3$), δ 4.4 (q, J = 7.1 Hz, 2H, C_3-$OC\underline{H}_2CH_3$), δ 5.72 (bs, 1H, N-OH), δ 7.64 (s, 1H, CH=N azo methine), δ 7.72 (t, J = 7.12 Hz, 1H, C_6-H), δ 7.94 (t, J = 7.16 Hz, 1H, C_7-H), δ 7.9 (d, J = 8.12 Hz, 1H, C_5-H), δ 8.30 (d, J = 8.4 Hz, 1H, C_8-H), δ 8.6 (s, 1H, C_4-H). The data inferred the compound to be 2-hydroxyimino-3-carbethoxy quinoline **2a**.

Further when the heating time was increased to 72 hours a new spot was obtained in the TLC. The compound was worked up and column chromatography on silica gel yielded a white colour compound at (90:10) chloroform: methanol.

The IR spectra of the compound showed the following peaks 1710 cm^{-1} (-C(O)=O) 1-carbonyl, 1610 cm^{-1} (C=N). The ^1H NMR of the compound showed the following peaks, δ 7.6-8.8 (m, 4H, C_6-H, C_7-H, C_8-H, C_9-H), δ 8.9 (s, 1H, C_{10}-H), δ 9.2 (s, 1H, C_4-H). The compound was confirmed as 1,2-oxazino[4,5-*b*]quinolin-1-one (**3a**), as mass spectra also supported the conclusion with a base peak at (m/z)(%) 198 M^+. The reaction was very well generalised and was extended to the derivatives **3b-d. Scheme: 1, Table: 1.**

Scheme: 1



a. $R_1 = R_2 = R_3 = H$
b. $R_1 = CH_3$, $R_2 = R_3 = H$
c. $R_1 = R_2 = H$, $R_3 = CH_3$
d. $R_1 = CH_3$, $R_2 = H$, $R_3 = CH_3$
e. $R_1 = H$, R_2 = -CH=CH-CH=CH- = R_3

Table: 1 Spectral and Physical data's of compounds 2a, 2d and 3a-d.

Cpd	m.p (yield)	IR ν_{max} cm^{-1}	^{1}H NMR δ ppm
2a	135-37 ^oC (65 %)	1620 (C=N) 1730 (C=O ester) 3400 (N-OH)	1.3 (t, J = 7.12 Hz, 3H, -$OCH_2C\underline{H}_3$), 4.4 (q, J = 7.1 Hz, 2H, -$OC\underline{H}_2CH_3$), 5.72 (bs, 1H, N-OH), 7.64 (s, 1H, CH=N azo methine), 7.72 (t, J = 7.12 Hz, 1H, C_6-H), 7.94 (t, J = 7.16 Hz, 1H, C_7-H), 7.9 (d, J = 8.12 Hz, 1H, C_5-H), 8.30 (d, J = 8.4 Hz, 1H, C_8-H), 8.6 (s, 1H, C_4-H).
2d	165 ^oC (74 %)	1623 (C=N) 1735 (C=O ester) 3390 (N-OH)	1.4 (t, 3H, J = 7.16 Hz, -OCH_2-$C\underline{H}_3$), 2.5 (s, 3H, C_6-CH_3), 2.7 (s, 3H, C_8-CH_3), 4.5 (q, J = 7.12 Hz, 2H, -$OC\underline{H}_2$-CH_3), 5.7 (bs, 1H, N-OH), 7.5 (s, 1H, C_5-H), 7.8 (s, 1H, CH=N azo methine), 8.2 (s, 1H, C_7-H), 8.5 (s, 1H, C_4-H).
3a	>300 ^oC (51 %)	1710 (-C(O)=O) 1610 (C=N)	7.6-8.8 (m, 4H, C_6-H, C_7-H, C_8-H, C_9-H), 8.9 (s, 1H, C_{10}-H), 9.2 (s, 1H, C_4-H).
3b	>300 ^oC (54 %)	1708 (-C(O)=O) 1615 (C=N)	2.8 (s, 3H, C_8-CH_3), 7.5-8.2 (m, 2H, C_6-H, C_7-H), 8.7 (s, 1H, C_9-H), 9.0 (s, 1H, C_{10}-H), 9.4 (s, 1H, C_4-H).
3c	>300 ^oC (65 %)	1715 (-C(O)=O) 1620 (C=N)	2.7 (s, 3H, C_6-CH_3), 7.7-8.4 (m, 3H ,C_7-H, C_8-H C_9-H), 8.6 (s, 1H, C_{10}-H), 9.4 (s, 1H, C_4-H).
3d	>300 ^oC (68 %)	1705 (-C(O)=O) 1612 (C=N)	2.5 (s, 3H, C_6-CH_3), 2.8 (s, 3H, C_8-CH_3), 7.9 (s, 1H, C_7-H), 8.1 (s, 1H, C_9-H), 8.7 (s, 1H, C_{10}-H), 9.1 (s, 1H, C_4-H).
3e	>300 ^oC (59 %)	1710 (-C(O)=O) 1625 (C=N)	7.73-9.65 (m, 8H, C_1-H, C_2-H, C_3-H, C_4-H, C_5-H, C_6-H, C_7-H, C_{11}-H).

Experimental:

Melting points were determined on a Boetius microheating table and are uncorrected. Thin layer chromatography [TLC] was performed using glass plates coated with silicagel G containing $CaSO_4$ (13%) as binder.

IR spectra were recorded on Shimadzu FT IR PC (S) 8201spectrometer and Nicolet FT IR (Avatar model) spectrometer, using KBr discs and the frequencies are quoted in reciprocal centimeters.

NMR spectra were taken on AMX-300 [300 MHz] and AMX-400 [400 MHz] spectrometer using trimethyl silane (TMS) as internal reference and the chemical shifts are quoted in δ ppm. Mass spectra were recorded on an Auto Tuning-EI mass spectrometer.

The solvents and reagents used for synthesis were of analytical grades and gravimetrical grades, purified by standard methods.

1,2-oxazino[4,5-*b*]quinolin-1-one:

2-Formyl-3-carbethoxy quinoline and hydroxylamine 1 milli moles respectively was taken in a round bottom flask and dissolved in 20 mL of ethanol to which 2-3 drops of triethylamine was added. It was heated over a water bath for 72 hours. The mixture was poured

into a petridish and ethanol was evaporated. The dirty white substance was activated using silica gel and was column chromatographed using (90:10) chloroform: methanol, a white colour solid was obtained.

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