

## A systematic study on methyl groups in 3-amino-2-methyl-3,4-dihydro-4-oxoquinazoline towards condensation with aldehydes

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**Abstract:** 3-amino-2-methyl-3,4-dihydro-4-oxoquinazoline was prepared by modified Klosa's method and was condensed with various aliphatic and aromatic aldehydes in two stages (scheme 1-3). The first molecule of aldehyde reacted with the N-3 amino group and the second molecule reacted with the methyl group at C-2. On hydrolysis the benzylidene group at N-3 gets hydrolysed leaving behind the styryl groups at C-2. This preferential reactivity of the two functional groups at N-3 and C-2 positions was investigated.

**(Key Words :** 4-oxoquinazoline, benzaldehyde, p-nitrobenzaldehyde, anisaldehyde, salicylaldehyde)

### Introduction

3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline was first prepared by Bogert and Seil<sup>1</sup>. Most of the method employed commonly for the synthesis of 3-Amino-2-alkyl/aryl-3,4-dihydro-4-oxoquinazoline start with some derivative of anthranilic acid which was cyclised to the corresponding 4-oxoquinazoline on condensing with hydrazine hydrate<sup>2-8</sup>. O-Aminobenzoic acids or their esters have been converted into 4-oxoquinazolines on treatment with hydrazine<sup>9-11</sup>.

In a variation of above method, cyclisation of O-aminobenzoyl hydrazines has been effected by the action of an acylating agent<sup>12</sup>. In all these methods, derivative for its subsequent transformation into 4-oxoquinazolines.

Compared to these methods, Klosa's method<sup>13</sup> of preparing 3-amino-2-methyl-3,4-

dihydro-4-oxoquinazoline from benzoxazinones appeared quite attractive to us, owing to its simplicity and convenience of not isolating the intermediates. Furthermore mechanistic studies of this reaction by Errede *et al*<sup>14-17</sup> prevented any pit falls.

This method with slight modification was used to prepare 3-amino-2-methyl-3,4-dihydro-4-oxoquinazoline. This compound has three reactive centres namely the amino groups at N-3, methyl group at C-2 and the 4-oxo group albit the last group is some that not reactive owing to its being a part of an acid hydrazide chain. Methyl groups at positions 2-and 4-in 3,4-dihydro-4-oxoquinazolines are known to condense with aldehyde<sup>18-21</sup>. Furthermore, methyl group of C-2 position is found to be more reactive<sup>22</sup>. 2,4-DNP derivative of various 4-oxoquinazolines line have been prepared<sup>23</sup>. The amino group at N-3 is also a reactive enough site capable of undergoing condensation with aldehydes. It looked quite worthwhile to examine particularly the comparative reactivity of the N-3 amino and the C-2 methyl groups in compound (III) and hence this endeavour.

### Experimental

Melting points were taken in sulphuric acid bath in open capillary and are uncorrected. IR spectra were recorded on a Parkin-Elmer (577) spectrophotometer.

3-amino-2-methyl-3,4-dihydro-4-

oxoquinazoline (III) : Anthranilic acid (10g) was refluxed with acetic anhydride (30ml) for 3h. Part of acetic anhydride (20ml) was distilled off and hydrazinehydrate (10ml, 90%) was distilled off and hydrazinehydrate (10ml, 90%) in methanol (10ml) was added. The product was isolated by adding excess of ammonium hydroxide solution and recrystallised from distilled water. water crystals, m.p. 148-50°C. (6.8g). [Found : C61.46; H5.33; N23.82%,  $C_9H_9N_3O$  requires : C61.71, H5.14; N24%].  $\nu_{\max}$  (KBr) 1670 $cm^{-1}$  (quinazolone carbonyl Str.), 3330 and 3230 $cm^{-1}$  (N-H bonded hydrazide Str.)

3-(Benzylideneamino)-2-methyl-3,4-dihydro-4-oxoquinazoline (IV); 3-amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III) (0.01 mole) has been heated under reflux with benzaldehyde (0.01 mole) in glacial acetic acid (10mL) for 1h. The product was isolated by adding excess of ammonium hydroxide solution and recrystallised from aqueous alcohol (1:1) using activated charcoal for decolorisation. White flakes m.p. 186-187°C (yield 85%) [Found : C73.22, H5.60; N15.82%,  $C_{16}H_{13}N_3O$  requires C73.00, H4.94; N15.97%]  $\nu_{\max}$  (KBr) 1660 $cm^{-1}$  (quinazolone carboxyl str.) 3-(Benzylideneamino)-2-styryl-3,4-dihydro-4-oxoquinazoline (v) : 3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III) (0.01mole) was heated under reflux with benzaldehyde (0.2 mole) in glacial acetic acid (20mL) for 1.5h. The product was isolated by cooling and adding excess of ammonium hydroxide solution. Crystallisation from rectified spirit gave yellow solid, m.p. 170-171°C (yield 78%) [Found : C 78.02; H 5.61; N12.00%,  $C_{23}H_{17}N_3O$  required: C78.63; H 4.84; N 11.97p]  $\nu_{\max}$  (KBr) 1670 $cm^{-1}$  (quinazolone carboxyl Str.) and 1605 $cm^{-1}$  (C=C conjugated with aromatic ring Str.)

**3-Amino-2-Styryl-3,4-dihydro-4-oxoquinazoline (VIII) :** This compound was synthesised by two different methods.

#### Method-A

3-(Benzylideneaminol)-2-Styryl-3,4-

dihydro-4-oxoquinazoline (1.75g) was heated under reflux with concentrated hydrochloric acid (10ml) for 1h. Product was isolated by chilling and adding excess of ammonium hydroxide solution. Recrystallisation from rectified spirit gave yellow solid, m.p. 160-61°C (0.8g) [Found : C72.91; H5.10; N15.91%,  $C_{16}H_{13}N_3O$  requires : C 73.00, H.50; N 15.91%,  $C_{16}H_{13}N_3O$  requires : C73.00, H4.94; N 15.97%]  $\nu_{\max}$  (KBr) 1660, 1550 $cm^{-1}$  (quinazolone carbonyl Str.) 1620 $cm^{-1}$  (C = C conjugated with aromatic ring Str.) and 3210  $cm^{-1}$  (N-H bonded hydrazide Str.)

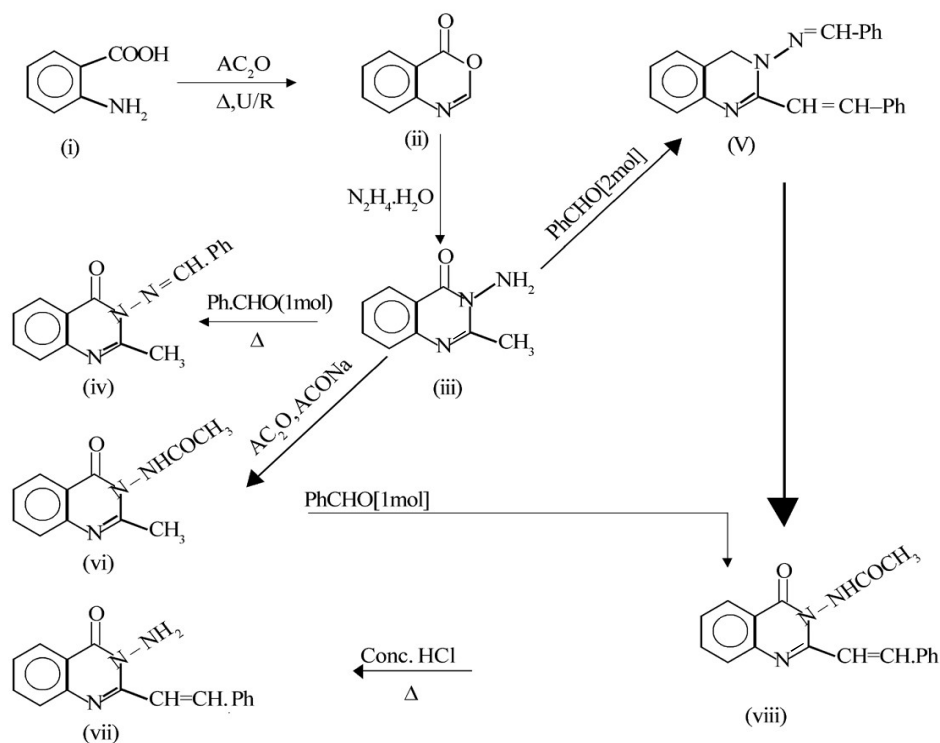
#### Method-B

3-(Acethylamino)-2-methyl-3,4-dihydro-4-oxoquinazoline (VI); 3-Amino-2-methyl-3,4-dihydro-4-oxo-quinazoline (5g) was heated under reflux with acetic anhydride (10ml) and freshly fused sodium acetate (2.5g) for 1.5h and product (VI) was isolated by pouring in crushed ice (300g). Recrystallised from distilled water, m.p. 174-175°C (yield 4.8g 75%)

3-(acetyl amino)-2-styryl-3,4-dihydro-4-oxoquinazoline (VII) : 3-(acetyl amino)-2-methyl-3,4-dihydro-4-oxoquinazoline (2g) was refluxed with benzaldehyde (1ml) in glacial acetic acid (10ml) for 1.5h. The product was isolated by pouring in crushed ice (250g). Recrystallised from rectified Spirit, m.p. 262-64°C (2.3g 75%) [Found : C71.1, H5.07; N 13.79%,  $C_{18}H_{15}N_3O_2$  requires C 70.81; H 4.92; N 13.77%] 3-Amino-2-Styryl-3,4-dihydro-4-oxoquinazoline (VIII) : 3-(Acetyl amino)-2-styryl-3,4-dihydro-4-oxoquinazoline (1.5g) was refluxed with concentrated hydrochloric acid (10ml) for 1h. The product was isolated by adding excess of ammonium hydroxide solution and pouring on ice (300 g). Recrystallised from rectified spirit. Yellow solid, m.p. 160-61°C. Mixed m.p. of the compound (VIII) prepared by method A was undepressed.

#### Results and Discussion

The full scheme of preparative work is given below :



3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline was prepared by Klosa's method with slight modification. The compound gave correct m.p. (148-149°C) and analysis correctly. It showed characteristic absorption peaks  $\nu_{\text{max}}$  (KBr) 1670 $\text{cm}^{-1}$  (N-H bonded hydrazide Str.) It (III) reacted with benzaldehyde (1mol) and a monobenzylidene derivative (IV) was obtained. It analysed correctly for  $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}$ . Infrared spectra revealed that the bonded N-H (hydrazide) Str. originally present in (III) was completely absent. Absorption at 1670 $\text{cm}^{-1}$  (quinazolone carbonyl Str.) was intact. This initially indicated that first mol. of benzaldehyde has condensed with the N-3 amino group. The isomeric benzylidene derivative namely, 3-amino-2-styryl-3,4-dihydro-4-oxoquinazoline (VIII) was also prepared. (III) was acetylated to (VI), condensed with benzaldehyde (1mol.) to give (VII) and finally hydrolysed to give (VIII). This compound (VIII) is an isomer of (IV). It is analysed correctly for  $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}$ . Its IR

spectra showed characteristic absorption  $\nu_{\text{max}}$  (KBr) 1660, 1550 $\text{cm}^{-1}$  (quinazolone carbonyl Str.); 1620 $\text{cm}^{-1}$  (C=C conjugated aromatic ring) and 3210 $\text{cm}^{-1}$  (N-H bonded hydrazide Str.) This product (VIII) was thus the monobenzylidene derivative of (III) in which benzaldehyde had condensed with the C-2-methyl group.

The identity of (VIII) was further established by preparing it by a different route. (III) was condensed with benzaldehyde (2mol) to give 3-(benzylideneamino)-2-styryl-3,4-dihydro-4-oxoquinazoline (V). This on partial hydrolysis gave (VIII) and also analysed correctly. Mixed melting prints of (VIII) prepared by two different routes were undepressed.

Following the pathway above (III) was condensed with eight different aldehydes. The two isomeric mono condensation products and the bis-condensation products were synthesised.

**Table- 1**  
**Melting points of various synthesised compound °C**

| Aldehydes             | Mono-Condensation<br>at M-3 | Bis-condensation<br>product | Monocondensation<br>at C-2 |
|-----------------------|-----------------------------|-----------------------------|----------------------------|
| Benzaldehyde          | 186-87                      | 170-71                      | 211-12                     |
| p-Nitrobenzaldehyde   | 214-15                      | 245-46                      | 198-99                     |
| p-Hydroxybenzaldehyde | 236-37                      | 212                         | 200-01                     |
| Salicylaldehyde       | 165-66                      | 198-200                     | 215-216                    |
| Anisaldehyde          | 164-65                      | 152-53                      | 182-83                     |
| p-chlorobenzaldehyde  | 204-05                      | 185-86                      | 220-21                     |
| Cinnamaldehyde        | 234-35                      | 202-03                      | 192-94                     |
| Formaldehyde          | 203-04                      | 228-30                      | 190-91                     |
| Actualdehyde          | 188-89                      | 161-62                      | 202-03                     |

In all cases the N-3 amino group was found to react preferentially.

groups toward condensation with aldehydes in comparison to C-2 methyl group in (III) is thus clearly established.

The greater reactivity of the amino

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