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Reactivity of Amino and Methyl Groups in 3-Amino-2-methyl-3,4-dihydro-4-oxo-quinazoline towards Condensation with Aldehydes

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3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline was prepared (Scheme I–III) and was found to condense with benzaldehyde in two stages. The first molecule of benzaldehyde reacted with the amino group at $\underline{N}_{(\bar{3})}$ and the second molecule reacted with the methyl group at $\underline{C}_{(\bar{2})}$. This preferential reactivity of the two groups was studied.

INTRODUCTION

3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline was prepared by Bogert and Seil[1] and also by Josef Klosa.[2] The later prepared it by a much simpler process. This compound has two reactive centres, namely the amino group at $\underline{N}_{(\bar{3})}$ and the methyl group at $\underline{C}_{(\bar{2})}$. Methyl groups at position 2- and 4-in 3,4-dihydro-4-oxoquinazoline are known to condense with aldehydes.[3–6] Further, methyl group at position 2 is found to be more reactive.[7] The amino group at $\underline{N}_{(\bar{3})}$ is also a reactive site capable of undergoing condensation reaction with aldehydes. It looked interesting to examine particularly the comparative reactivity of the amino and the methyl groups in compound (III) and hence the work was taken up.

EXPERIMENTAL

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

3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III): Anthranilic acid (10 g) was refluxed with acetic anhydride (30 mL) for 3 h. Part of acetic anhydride (20 mL) was distilled off and hydrazine hydrate (10 mL, 90%) in methanol (10 mL) was added. The product was isolated by adding excess of ammonium hydroxide solution and recrystallised from water. White crystals, m.p. 148–50°C (6.8 g). [Found: C, 61.46; H, 5.33; N, 23.82%. $C_9H_9N_3O$ requires: C, 61.71; H, 5.14; N, 24.00%]. ν_{max} (KBr) 1670 cm^{-1} (quinazolone carbonyl str.), 3330 and 3230 cm^{-1} (N—H bonded hydrazide str.).

3 - (Benzylidene amino) - 2-methyl - 3, 4 - dihydro - 4 - oxoquinazoline (IV):

3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III) (0.01 mole) was heated under reflux with benzaldehyde (0.01 mol) in glacial acetic acid (10 mL) for 1 h. The product was isolated by adding excess of ammonium hydroxide solution and recrystallised from aqueous alcohol (1 : 1). White flakes mp 186–87°C (yield 85%). [Found: C, 73.22; H, 5.60; N, 15.82%. $C_{16}H_{13}N_3O$ requires: C, 73.00; H, 4.94; N, 15.97%]. ν_{max} (KBr) 1660 cm^{-1} (quinazolone carbonyl str.).

3-(Benzylidene amino)-2-styryl-3, 4-dihydro-4-oxoquinazoline (V): 3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III) (0.01 mol) was heated under reflux with benzaldehyde (0.02 mol) in glacial acetic acid (20 mol) for 1.5 h. The product was isolated by cooling and adding excess of ammonium hydroxide solution. Crystallisation from rectified spirit gave yellow solid, mp 170–71°C (yield 78%). [Found: C, 78.02; H, 5.61; N, 12.00% $C_{23}H_{17}N_30$ requires: C, 78.63; H, 4.84; N, 11.97%]. ν_{max} (KBr) 1670 cm^{-1} (quinazolone carbonyl 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 prepared by two different methods.

Method-A

3-(Benzylidine amino)-2-styryl-3,4-dihydro-4-oxoquinazoline (1.75 g) was heated under reflux with concentrated hydrochloric acid (10 mL) for 1 h. Product was isolated by cooling and adding excess of ammonium hydroxide. Recrystallisation from rectified spirit gave yellow solid, mp 160–61°C (0.8 g). [Found: C, 72.91; H, 5.10; N, 15.91%. $C_{16}H_{13}N_3O$ requires: C, 73.00; H, 4.94; N, 15.97%]. ν_{max} 1660, 1550 cm^{-1} (quinazolone carbonyl str.), 1620 cm^{-1} (C═C conjugated with aromatic ring) and 3210 cm^{-1} (N—H bonded hydrazide str.).

Method-B

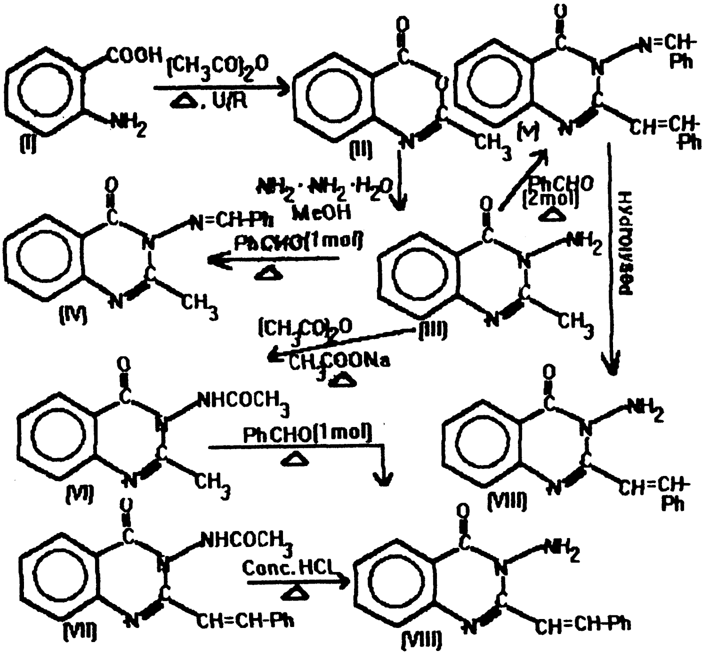
3-(Acetylamino)-2-methyl-3,4-dihydro-4-oxoquinazoline (VI): 3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (5 g) was heated under reflux with acetic anhydride (10 mL) and freshly fused sodium acetate (2.5 g) for and product (VI) was isolated by pouring in crushed ice (250 g). Recrystallised from water, mp 174–75°C (4.8 g. Lit[8]; mp 176.5°C).

3-(Acetylamino)-2-styryl-3,4-dihydro-4-oxoquinazoline (VII): 3-(Acetylamino)-2-methyl-3,4-dihydro-4-oxoquinazoline (2 g) was refluxed with benzaldehyde (1 mL) in glacial acetic acid (10 mL) for 1.5 h. The product was isolated by isolated by pouring in crushed ice (100 g). Recrystallised from rectified spirit, mp 262–64°C (2.3 g). [Found: C, 71.1; H, 5.07; 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-(Acetylamino)-2-styryl-3,4-dihydro-4-oxoquinazoline (1.5 g) was refluxed with concentrated hydrochloric acid (10 mL) for 1 h. The product was isolated by adding excess of ammonium hydroxide solution and recrystallised from rectified spirit. Yellow solid, mp 160–61°C. Mixed mp of the compound with (VIII) prepared by Method A was undepressed.

RESULTS AND DISCUSSION

The full scheme of preparative work is shown below:



3-Amino-2-methyl-3,4-dihydro-4-oxoquinazoline (III) was prepared by the method available in literature[2] with slight modification. The compound gave correct m.p. (148–49°C) and analysed correctly. It showed characteristic absorptions ν_{max} (KBr) 1670 cm^{-1} (quinazolone carbonyl str.), 3330 and 3230 cm^{-1} (N—H hydrazide bounded str.). It (III) reacted with benzaldehyde (1 mol) and a monobenzylidene derivative (IV) was obtained. It analysed correctly for $C_{16}H_{13}N_3O$. Infrared spectra revealed that the bounded N—H (hydrazide) str. originally present in (III) was completely absent. Absorption at 1670 cm^{-1} (quinazolone carbonyl str.) was intact. This initially indicated that first mol. of benzaldehyde has condensed with the amino group at $\underline{C}_{(3)}$. 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 (1 mol) to give (VII) and finally hydrolysed to give (VIII). This compound (VIII) is an isomer of (IV). It analysed correctly for $C_{16}H_{13}N_3O$. Its infrared spectra showed characteristic absorption ν_{max} (KBr) 1660, 1550 cm^{-1} (quinazolone carbonyl str.); 1620 cm^{-1} (C=C conjugated with aromatic ring) and 3210 cm^{-1} (N—H hydrazide bonded str.). This product (VIII) was thus the monobenzylidene derivative of (III) in which benzaldehde condensed with the methyl group at $\underline{C}_{(\bar{2})}$.

The identity of (VIII) was further established by preparing it by different route. (III) was condensed with benzaldehyde (2 mol) to give 3-(benzylidene amino)-

2-styryl-3,4-dihydro-4-oxoquinazoline (V). This on hydrolysis gave (VIII) and analysed correctly. Mixed mps of (VIII) prepared by two different routes were undepressed.

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

TABLE-1
MELTING POINTS OF VARIOUS COMPOUNDS (°C)

Aldehydes	Mono condensation at $\underline{N}_{(\bar{3})}$	Bis-condensation product	Mono condensation at $\underline{C}_{(\bar{2})}$
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	215–16
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
Acetaldehyde	188–89	161–62	202–03

In all cases the $\underline{C}_{(\bar{3})}$ amino group was found to react preferentially.

The greater reactivity of the amino group in comparison to the methyl group in (III) is thus established.

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