REACTIVITY OF THE (C₂⁻) BENZYLIC GROUP OF 4–OXOQUINZOLINES TOWARDS CARBONYL COMPOUNDS

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ABSTRACT

As our projected schemes of building tricyclic ring systems required condensations involving the (N₃⁻–NH₂) and the (C₂⁻) benzylic methylene groups, it was necessary to examine the reactivity of the latter towards carbonyl compounds and others.

Key words: Quinazolones, Benzylic methylene, Benzaldehyde, Condensation.

INTRODUCTION

In view of the above considerations, the quinazolone (I) was reacted with 2 mol of benzaldehyde. The product from this reaction was; however, the mono (N₃⁻) benzyldeneamino derivative (II).

\[
\begin{align*}
\text{(I)} & \\
\text{(II)} & 
\end{align*}
\]

The benzylic methylene group at C(2) remained unaffected although heating was continued for a longer time. This reaction was also carried out in ethanolic solution in the presence of piperidine but no further reaction took place after condensation of 1 mol of

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benzaldehyde with the N(3)−NH₂ group. The same product (III) was obtained, when benzaldehyde was replaced by more reactive p-nitrobenzaldehyde in this reaction.

\[
\text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array} \quad \begin{array}{c}
\text{CHO} \\
\text{C} \\
\text{H} \\
\text{C}
\end{array} \quad \text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array}
\]

(I) + 2 \rightarrow (III)

**EXPERIMENTAL**

It was found by some Egyptian workers that condensation occurs at both N(3)−NH₂ and C(2)−CH₂ in the quinazolone (IV), when it was reacted with 2 mol of aromatic aldehyde in the presence of acetic acid-acetic anhydride mixture.

\[
\text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array} \quad \begin{array}{c}
\text{CHO} \\
\text{C} \\
\text{H} \\
\text{C}
\end{array} \quad \text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array}
\]

(IV)

Contrary to expectations, the methylene group in 3-amino-2-benzyl-4-oxoquinazoline (I) and 3-amino-2-p-nitrobenzyl-4-oxoquinazoline (V) failed to condense with aromatic aldehydes.

\[
\text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array} \quad \begin{array}{c}
\text{CHO} \\
\text{C} \\
\text{H} \\
\text{C}
\end{array} \quad \text{O} \quad \begin{array}{c}
\text{N} \\
\text{N} \\
\text{CH} \\
\text{N} \\
\text{N}
\end{array}
\]

(V)
RESULTS AND DISCUSSION

Another approach was made to bring about condensation at the C(2r)-benzylic methylene group under more forcing conditions. For this, the N(3r)-NH$_2$ was protected by acetylation.

The acetamido derivative (VI) was treated with p-nitrobenzaldehyde successively in ethanol, pyridine, acetic acid- acetic anhydride mixture and ethanol containing fused zinc chloride. In each case, the quinazolone (V) was recovered unchanged with the benzylic methylene group remaining unaffected even under rigorous conditions.

\[
\begin{align*}
\text{(VI)}
\end{align*}
\]

Similarly, the following reaction also did not take place.

\[
\begin{align*}
\text{No reaction}
\end{align*}
\]

The non-reactivity of the benzylic methylene in the quinazolones; (I) and (V), at first appeared to be very surprising. The methylene group at C(2r) is activated because of the electron withdrawing influence of the pyrimidine ring, to which it is attached. This reactivity could be enhanced by a phenyl group, and even more by a p-nitrophenyl group attached to it.
CONCLUSION

It was clear that the steric factors must account for the failure of the methylene group to react and a possible explanation may be as follows: The non-reactivity of the benzylic methylene in the quinazolones; (I) and (V) at first appeared to be surprising, and it has already been pointed out that the methylene at C(2) is subject to electron withdrawing influence of the pyrimidine ring to which it is attached. The reactivity of this methylene group can be increased, when p-nitrophenyl group is attached to it. Steric factors, must, therefore be responsible for the lack of reactivity shown by the group. If the C(2)–methylene were to condense with an aromatic aldehyde, the methylene carbon is sp$^2$ hybridized with its three bonds extending at angles of 120° with each other. This would push one of the aryl groups very close to the group attached to N(3)–N. The steric strain caused on account of this would preclude the formation of an arylidene group at C(2)–carbon.

REFERENCES


Accepted: 03.02.2010