Triazole Scission in 5-Amino-1,2,3-triazolo[1,5-*a*]quinazolines. A New Route to 4-Aminoquinazoline Derivatives

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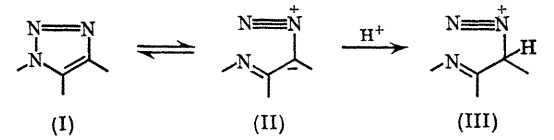
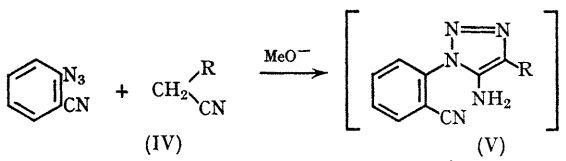
ortho-AZIDOBENZOIC ACID and 2-nitrophenyl azide condense with phenylacetonitrile in the presence of methanolic sodium methoxide yielding derivatives of 1,2,3-triazolo-[1,5-*a*]quinazoline[1] and 1,2,3-triazolo[5,1-*a*]benzo-1,2,4-triazine.[2] The triazole ring (I) in these compounds is readily cleaved by acidic reagents to give products derivable from the corresponding diazonium cation (III).[2] The cation (III) may be formed directly by ring-opening of the protonated triazole or by initial equilibration of the triazole with the diazo-tautomer (II) followed by protonation of the latter. The diazoalkylazomethine–triazole tautomerism [(I) ⇌ (II)] implied by the latter mode of triazole scission would then be analogous to the azidoazomethine–tetrazole equilibria whose existence is now well documented.[3] We have now synthesised 5-amino-1,2,3-triazolo[1,5-*a*]quinazolines (VI). Acid-catalysed triazole scission in these compounds provides

a convenient new route to 4-aminoquinazoline derivatives [*e.g.* (IX)].

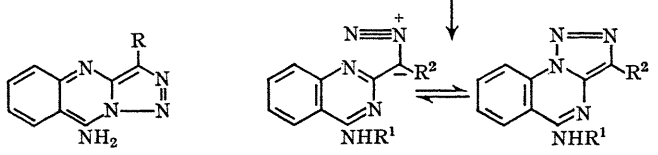
ortho-Azidobenzonitrile[4] when heated with phenylacetonitrile (IV; R = Ph) under reflux in the presence of methanolic sodium methoxide gave (VI; R^1 = H, R^2 = Ph) (90%). The structure of this product is supported by spectral and chemical evidence. Bands due to cyano-group and azide absorption were absent from its i.r. spectrum, but absorption at 3200—3450 cm.$^{-1}$ could be attributed to the presence of a primary amino-group. Hydrolysis of the amino-group occurred when the amine (VI; R^1 = H, R^2 = Ph) was heated under reflux with aqueous alkali to yield the 5-oxo-derivative (X) of known structure.[1]



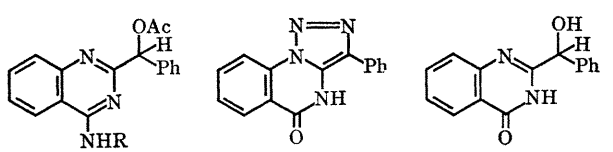
(I) (II) (III)



(IV) (V)



(VIII) (VII) (VI)



(IX) (X) (XI)

In similar reactions *ortho*-azidobenzonitrile smoothly condensed with cyanoacetamide (IV; R = $CONH_2$) or malononitrile (IV; R = CN) to give the triazoloquinazolines (VI; R^1 = H, R^2 = $CONH_2$ or CN) (85—95%). The corresponding 5-amino-(*o*-cyanophenyl)triazole (V) is a probable intermediate in these reactions. No products [*e.g.* (VIII)] formed by Dimroth rearrangement[5] of the intermediates (V) prior to cyclisation could be detected.

The amine (VI; R^1 = H, R^2 = Ph) when warmed with aqueous mineral acid underwent triazole scission[1] and hydrolysis of the amino-group affording the known compound (XI).[1] Under milder conditions acid-catalysed breakdown of the triazole ring occurred without loss of the amino-group to give 4-aminoquinazolines. In typical reactions the amine (VI; R^1 = H, R^2 = Ph) or its acetyl-derivative (VI; R^1 = Ac, R^2 = Ph) were smoothly converted by heating them under reflux with glacial acetic acid into the acetoxy-compounds (IX; R = H or Ac). Despite the ready cleavage of the triazole ring, the absence of diazo-absorption from the i.r. spectra of the triazoloquinazolines (VI; R^1 = H, R^2 = Ph, $CONH_2$, or CN) precludes the presence of the diazo-tautomer (VII) at least in the solid state. However the attainment of a diazoalkylazomethine–triazole equilibrium in solution cannot be excluded.

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