

Cycloaddition of Anhydro-3-hydroxy-2-phenylthiazolo[3,2-c]quinazolin-4-ium Hydroxide with Olefinic Dipolarophiles

Kevin T. Potts,* Kirk Bordeaux, William Kuehning, and Ronald Salsbury

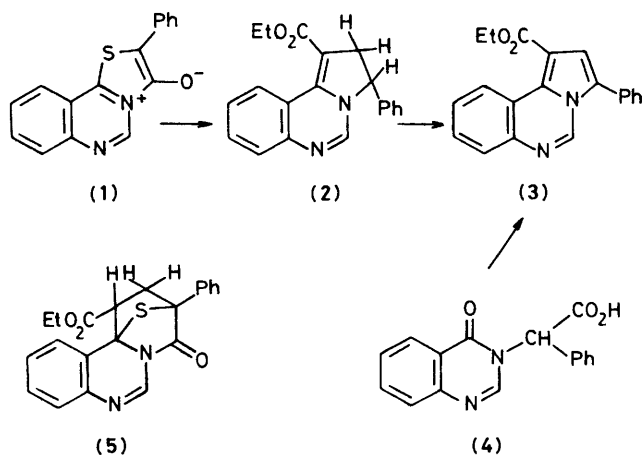
Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12181, U.S.A.

Anhydro-3-hydroxy-2-phenylthiazolo[3,2-c]quinazolin-4-ium hydroxide (1) underwent cycloaddition with ethyl acrylate and dimethyl fumarate to give pyrroloquinazoline derivatives [(3) and (7)] and COS, whereas with acetylenic dipolarophiles the anticipated ring-fused pyridinones *e.g.* (8) were obtained with extrusion of sulphur from the initial 1:1-cycloadducts; these represent the first rearrangements observed with olefinic dipolarophiles and mesoionic systems of this type.

Anhydro-3-hydroxy-2-phenylthiazolo[3,2-c]quinazolin-4-ium hydroxide (1) was obtained¹ as deep purple needles from chloroform-cyclohexane, (m.p. 242–244 °C) by reaction of 3*H*-quinazoline-4-thione with α -bromophenacyl chloride or by reaction of the thione with (α -bromophenyl)acetic acid and subsequent ring closure of the resultant thioglycolic acid with Ac_2O . Compound (1) reacted with ethyl acrylate (10% excess) overnight in boiling dry xylene (*ca.* 140 °C) and gave (2) which crystallized from ethanol as bright yellow prisms [m.p. 148–149 °C, 54%, ν_{CO} 1670, 1620 cm^{-1} , M^+ 318 (75%)]. Carbonyl sulphide was identified as the effluent gas of the reaction by condensation with piperidine in ethanol.² The structure of (2) was established by the following spectral data and chemical transformations. The ¹H n.m.r. spectrum (200 MHz, CDCl_3)

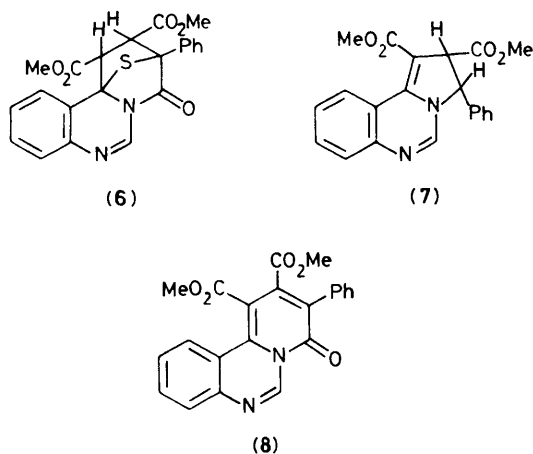
showed an ABX pattern[†] and a ¹³C attached proton test³ confirmed the presence of 9 \times CH, 1 \times CH₃, 5 \times C, 1 \times CO, and 2 \times CH₂ carbon atoms. On oxidation with 2,3,5,6-dichlorodicyanobenzoquinone in boiling dioxane, (2) formed ethyl 3-phenylpyrrolo[2,1-c]quinazoline-1-carboxylate (3)[‡] obtained as fawn microprisms from ethanol [m.p. 124–125 °C, 66%, ν_{CO} 1690 cm^{-1} , M^+ 316 (100%)]. The pyrroloquinazoline (3) was synthesized in an unambiguous fashion from the acid (4), using an excess of ethyl propiolate and acetic anhydride (reflux, dry xylene, N₂, 18 h). An intermediate anhydro-2-hydroxy-3-phenyl-1,3-oxazolo[3,2-c]quinazolinium hydroxide was undoubtedly involved in this last reaction, undergoing *in situ* cycloaddition with the ethyl propiolate with the elimination of CO₂ from the primary 1:1-cycloadduct.

In contrast, reaction of (1) with an excess of boiling ethyl acrylate (99 °C) in the absence of solvent (5 h) gave the anticipated 1:1-cycloadduct (5), obtained as colourless prisms from ethanol [m.p. 178–180 °C (decomp.), 15%, ν_{CO} 1730 cm^{-1} , M^+ 378 (11%)]. The simple relationship between (1) and (5) was shown by the appearance of the M^+ of (1) as the most intense ion in the mass spectrum of (5). The ¹H n.m.r. spectrum of (5) was of the ABX type,[†] further complicated by a 16 line ABX₃ spectrum for the methylene protons of the 1-carboxylate substituent. The cycloadduct (5)



[†] Refinement of chemical shifts and coupling constants, and spectral simulations (ABX and ABX₃ patterns) were carried out using a LAME program on a Varian XL-200 n.m.r. spectrometer.

[‡] N.m.r. data for other compounds cited were consistent with the assigned structures. All compounds gave satisfactory analytical data (\pm 0.04% C, H, N).



did not form the rearranged product (2) on prolonged heating in xylene.

Reaction of the mesoionic system (1) with dimethyl fumarate in boiling xylene overnight gave a mixture of two products, separated by h.p.l.c. (Prep. 500, hexane-ethyl acetate). These were the normal cycloadduct (6) obtained as colourless microprisms from methanol [m.p. 170–174°C (decomp.), 40%, ν_{CO} 1730 cm^{-1} , M^+ 422 (100%)] and the rearranged product (7) which crystallized from methanol as fine, pale yellow needles [m.p. 210–212°C (decomp.), 12%, ν_{CO} 1730, 1690 cm^{-1} , M^+ 362 (30%)]. The ^1H n.m.r. spectra of both these products‡ were consistent with the assigned structures.

In contrast to the above cycloadditions, reaction of (1) with dimethyl acetylenedicarboxylate in boiling toluene (110°C) gave the pyridinone (8) obtained as yellow needles from

methanol [m.p. 231–232°C, 67%, M^+ 388 (100%), ν_{CO} 1750, 1760 cm^{-1}] further verifying the structure of the mesoionic system (1).

Anhydro-3-hydroxy-2-phenylthiazolo[2,3-*a*]phthalazin-2-ium hydroxide also gave analogous products to those described above with ethyl acrylate and dimethyl fumarate and, with acetylenic dipolarophiles, ring-fused pyridin-2-ones were also formed.

Several speculative mechanisms may be advanced to account for the formation of the rearranged cycloadduct, especially the loss of COS. These rearrangements represent the first observed in the cycloadditions of anhydro-hydroxythiazolium hydroxide mesoionic systems with olefinic dipolarophiles although reaction of acetylenic dipolarophiles with anhydro-1-hydroxythiazolo[3,2-*a*]quinolinium hydroxide resulted⁴ in the formation of a substituted pyrrolo[1,2-*a*]quinoline and carbonyl sulphide.

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References

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