was added 2.6 mg of $Rh_2(OAc)_4$ (2 mol %), and the resulting solution was stirred vigorously for 60 min. Gas evolution was immediate and continuous at room temperature. NMR analysis after 60 min showed that **3** had been completely converted to a new product which, after chromatographic isolation as a colorless oil from a silica gel column, was identified as **10** (0.069 g, 98% yield): $[\alpha]^{25}_D$ +3.2°; ^{1}H NMR ($CDCl_3$) δ 7.34 (s, Ph), 5.12 (d of d, J = 6.5, 2.8 Hz, PhC*H*OH), 4.46 (inner lines of AB pattern with separation of 0.7 Hz), 4.35 (d of q, J = 6.9, 6.5 Hz, C*H*CH_3), 2.92 (d, J = 2.8 Hz, CHO*H*), 1.52 (d, J = 6.9 Hz, CHC*H*$_3$) [upon addition of D_2O, absorption at δ 2.92 disappears and absorption at δ 5.12 becomes a doublet (J = 6.5 Hz)]; IR (CCl_4) $\tilde{\nu}_{OH}$ 3625 (s), 3502 (br) cm^{-1}, $\tilde{\nu}_{C=O}$ 1823 (m), 1796 (w), 1744 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.04; H, 5.62; N, 5.92.

Decomposition of 3 by Rhodium(II) Acetate in the Presence of Ethanol. The reaction was performed with 0.30 mmol of **3** and 0.30 mmol of ethanol in chloroform according to the previously described procedure for reaction with water. Compound **11** was isolated in 97% yield: ^{1}H NMR ($CDCl_3$) δ 7.50-7.15 (m, Ph), 5.49 (d, J = 7.2 Hz, OC*H*Ph), 4.63 (s, CH_2), 4.22 (quin, J = 7.1 Hz, C*H*CH_3), 3.76 (d of q, J = 7.1, 1.4 Hz, O*CH*$_2$CH$_3$), 1.29 (t, J = 7.1 Hz, OCH$_2$C*H*$_3$), 1.12 (d, J = 7.0 Hz, CHC*H*$_3$); mass spectrum, m/e (relative abundance) 218 (19, M - C_2H_5O), 158 (10), 157 (100), 135 (12), 130 (24), 129 (34), 128 (77), 118 (14), 117 (47), 116 (16), 115 (19), 107 (15), 105 (19), 101 (12), 91 (26), 77 (30), 70 (53). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51. Found: C, 63.76; H, 6.81.

Decomposition of 3 by Boron Trifluoride Etherate in the Presence of Ethanol. Boron trifluoride etherate (1.0 mg) was added to a chloroform solution containing **3** (88 mg, 0.35 mmol) and 1.0 mL of ethanol. The reaction mixture was stirred for 1 h at room temperature after which the solvent was removed under reduced pressure. Spectral analysis showed **10** and at least one other oxazolidone product formed in less than 15% yield.

Acknowledgment. We are grateful to the National Science Foundation for their financial support of this work and to David A. Evans for generous samples of **5** and for helpful discussions concerning the syntheses of these diazo compounds.

Annulation to the Quinazoline Ring Utilizing Mesoionic Ring Systems[1a]

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anhydro-3-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium hydroxides, prepared from the corresponding thioglycolic acid with cyclodehydrating agents and also from 4(3*H*)-quinazolinethiones and α-bromophenylacetyl chloride, were hydrolyzed at the 5-position of the quinazoline ring with hot water. Alkynic and alkenic dipolarophiles cycloadded readily in hot benzene; the former gave pyrido[1,2-*c*]quinazolines and the latter 1:1 cycloadducts which lost H_2S to give the above ring system. These procedures provided convenient annulation of a pyridinone to the *c* side of quinazoline. With ethyl acrylate, in addition to the normal 1:1 cycloadduct, a rearranged pyrrolo[1,2-*c*]quinazoline was obtained depending on the reaction conditions; analogous products were obtained with dimethyl fumarate. *anhydro*-1-Hydroxythiazolo[3,2-*a*]quinazolinium hydroxides, preferably generated in situ from the corresponding thioglycolic acid and dicyclohexylcarbodiimide (DCC), and alkynic dipolarophiles in refluxing benzene readily gave pyrido[1,2-*a*]quinazolines. Alkenic dipolarophiles also gave 1:1 cycloadducts, which lost H_2S to form pyrido[1,2-*a*]quinazolines, resulting in annulation of a pyridinone ring to the *a* side of quinazoline.

Annulation to a heterocyclic ring can often be satisfactorily effected by using the "masked" ylidic system present in mesoionic ring systems,[2,3] and in studies establishing the scope of this approach, we describe the annulation of the pyridinone ring to the *a* and *c* sides of the quinazoline nucleus utilizing appropriate mesoionic precursors.

anhydro-3-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium Hydroxides

The ease of preparation, stability, and reactivity of the *anhydro*-3-hydroxythiazolo[3,2-*c*]quinazolin-4-ium hydroxide system depends markedly on the nature of the 2-substituent and to a lesser degree of the 5-substituent. *anhydro*-3-Hydroxy-5-methylthiazolo[3,2-*c*]quinazolin-4-ium hydroxide (**2a**) reported[4] earlier as an air-sensitive material stable only in suspension in dry ether, can now be conveniently prepared and reacted in situ with dipolarophiles and its cycloaddition products characterized. The 2-phenyl analogue **2b** was readily isolated as air-stable, deep purple needles, but a strongly electron-withdrawing trifluoromethyl group in the 5-position made the quinazoline nucleus more susceptible to hydrolysis, and the corresponding mesoionic system **2c** could not be isolated (see below).

4(3*H*)-Quinazolinethiones **1** are convenient precurosrs to **2**. Direct thiation of 4(3*H*)-quinazolinone with P_4S_{10} in boiling pyridine[5] gave **1** (R = H) in good yield, but for **1** (R = CH_3) the conversion of anthranilonitrile into *o*-acetamidothiobenzamide and subsequent thermal cyclization above its melting point to 2-methyl-4(3*H*)-

(1) (a) Abstracted from the MS (R.L.S.) and Ph.D. (K.G.B.) theses, Rensselaer Polytechnic Institute. (b) Undergraduate Research Participant.

(2) For a recent review, see: Potts, K. T. In "1,3-dipolar Cycloaddition Chemistry"; Padwa, A., Ed.; Wiley: New York, 1984; Chapter 8.

(3) Potts, K. T.; Kanemasa, S. *J. Org. Chem.* **1979**, *44*, 3803, 3808 and references listed therein.

(4) Talukdar, P. B.; Sengupta, S. K.; Datta, A. K.; Roy, T. K. *Indian J. Chem., Sect. B* **1977**, *15B*, 41.

(5) Fry, D. J.; Kendall, J. D.; Morgan, A. J. *J. Chem. Soc.* **1960**, 5062.

(6) Bogert, M. T.; Breneman, H. C.; Hand, W. F. *J. Am. Chem. Soc.* **1903**, *25*, 372. See also: Armarego, W. L. F. In "Quinazolines"; Brown, D. J., Ed.; Interscience: New York, 1967; p 277.

(7) Ferry, M.; Robert, A.; Foucand, A. *Synthesis* **1976**, 261.

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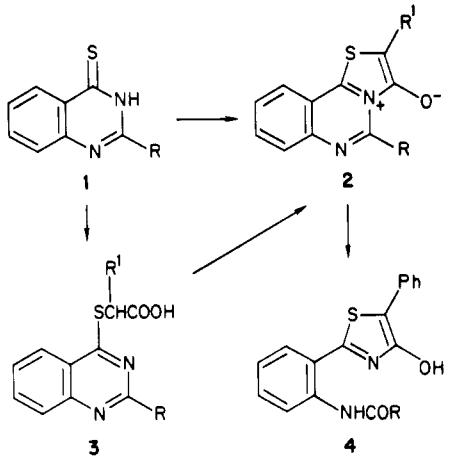


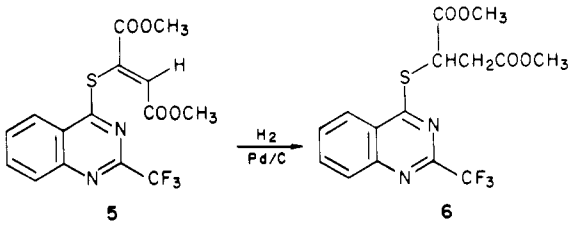
quinazolinethione (1, R = CH_3) were preferable. *o*-Aminothiobenzamide was also a convenient precursor for the introduction of the 2-trifluoromethyl substituent. When the benzamide was treated with $(CF_3CO)_2O$ in boiling, dry $CHCl_3$ in the presence of powdered molecular sieves to remove the water eliminated in the reaction, a 90% yield of 1 (R = CF_3) was obtained. Similarly, a 2-phenyl substituent was also readily introduced by reaction of *o*-aminothiobenzamide with benzoic anhydride.

Two procedures provided convenient access to the mesoionic system 2. Reaction of 4(3*H*)-quinazolinethione (1, R = H) with α-bromophenylacetyl chloride in anhydrous ether/Et_3N (2 mol) gave *anhydro*-3-hydroxy-2-phenylthiazolo[3,2-*c*]quinazolin-4-ium hydroxide (**2b**) in over 90% yield (method A). Spectral and analytical data in Table I established this structure, which was confirmed in two ways. Reaction of the thione (1, R = H) with α-bromophenylacetic acid gave the thioglycolic acid 3 (R = H; R^1 = Ph), which, with a 1:1 mixture of Ac_2O/Et_3N, readily gave **2b** (method B). Hydrolysis of **2b** occurred readily with boiling water to give 4 (R = H), whose structure was evident from the spectral data (Experimental Section).

anhydro-3-Hydroxy-5-methyl-2-phenylthiazolo[3,2-*c*]-quinazolin-4-ium hydroxide (**2d**) was prepared most satisfactorily by the thioglycolic acid route. On hydrolysis with water **2d** gave 4 (R = CH_3), a small amount of an organic cosolvent being necessary to overcome the surface tension. This structural assignment was consistent with an $M^{+\cdot}$ 310 and a CH_3CO^+ ion, *m/e* 43, in the mass spectrum as well as ν_{CO} 1610 and $\nu_{OH,NH}$ 3300–3600 cm^{-1}.

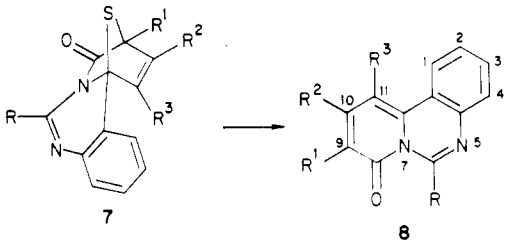
anhydro-2,5-Diphenyl-3-hydroxythiazolo[3,2-*c*]-quinazolin-4-ium hydroxide (**2e**) was obtained as deep purple needles by Ac_2O ring closure of the corresponding thioglycolic acid 3 (R = R^1 = Ph), but it always tenaciously retained trace amounts of solvent ($CHCl_3$). Although the isolated system underwent cycloadditions (see below), the in situ technique in which **2e** was generated by DCC cyclization of the thioglycolic acid 3 (R = R^1 = Ph) in the presence of the dipolarophile (method C) was a satisfactory alternative.

A 2-trifluoromethyl substituent as in **2c** resulted in the mesoionic system being extremely susceptible to hydrolysis. The characteristic purple color of the thiocarbonyl ylide system could be generated in solution with cyclodehydration agents, but minute traces of moisture present resulted in rapid bleaching of the solution color. However, generation of the mesoionic system from the thioglycolic acid in the presence of dipolarophiles with DCC provided a satisfactory method for obtaining the corresponding cycloaddition products. An alternative approach, reaction of the 4(3*H*)-quinazolinethione with α-bromophenylacetyl chloride, was unsuccessful. The product isolated from this last reaction carried out in the presence of dimethyl acetylenedicarboxylate (DMAD) was methyl 3-(2-(trifluoromethyl)quinazolin-4-ylthio)-3-(methoxycarbonyl)-acrylate (**5**). This underwent ready reduction with H_2/



10% Pd C to give the corresponding propionate **6**, and the analytical and spectral data consistent with these assignments are described in the Experimental Section. Compound **5** was not obtained from 1 (R = CF_3) and DMAD/Et_3N. The α-bromophenylacetyl chloride was essential for this addition to occur, implicating **2c** in the reaction.

Cycloadditions with Alkynic Dipolarophiles. The *anhydro*-3-hydroxy[3,2-*c*]quinazolin-4-ium hydroxide system **2** underwent ready cycloaddition with a variety of dipolarophiles, the reaction conditions chosen depending on the 2- and 5-substituents. With a hydrogen atom in the 2-position of **2**, the in situ procedure (method C) was utilized. The glycolic acid **3** (R = CH_3; R^1 = H), DMAD, and DCC were refluxed together in dry benzene, giving dimethyl 6-methyl-8-oxo-8*H*-pyrido[1,2-*c*]quinazoline-10,11-dicarboxylate (**8a**) (Table II). The thiocarbonyl

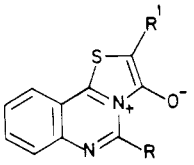


ylide present in **2a** underwent ready reaction to give the postulated intermediate **7** (R = CH_3; R^1 = H; R^2 = R^3 = $COOCH_3$) from which sulfur was extruded under the reaction conditions.

With a 2-phenyl substituent, it was more convenient to use the isolated mesoionic system itself (method D). Thus, **2d** and DMAD in boiling toluene gave **8b** in 65% yield (Table II). A similar facile reaction of **2b** and DMAD also occurred in boiling toluene, giving **8c**. However, with a 2,5-diphenyl substitution pattern in **2**, trapping of the intermediate mesoionic system was the preferred procedure. Reaction of the thioglycolic acid **3** (R = R^1 = Ph) with DCC in the presence of DMAD gave **8d** in 80% yield. Generation of the mesoionic system **2c** by DCC ring closure and its subsequent trapping with DMAD also gave the corresponding pyridinone **8e** but in only 17% yield.

Ethyl propiolate underwent reaction with **2d**. Two regioisomers are possible from this reaction, either **8f** or its 10-ethoxycarbonyl isomer. Assignment of structure **8f** to this product was made on the basis of the following data. In the ^1H NMR spectrum, the protons on the 9-phenyl substituent of **8f** appeared as a broad multiplet in contrast to the corresponding phenyl protons in **8b**. In the latter these protons appeared as a broad singlet due to the adjacent 2-carbomethoxy group forcing the 9-phenyl substituent out of the plane of the pyridinone ring. A similar regiospecific cycloaddition occurred with the 2,5-diphenyl-substituted mesoionic system **2e**. In this instance the mesoionic system was generated and reacted in situ

Table I. *anhydro*-1-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium Hydroxides 2[a]



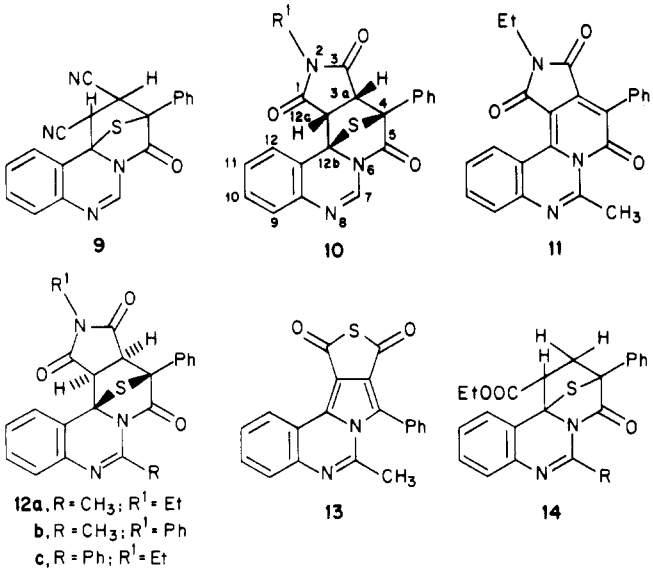
compd	R	R^1	method[b]	mp °C	yield %	crystal habit	mol form.	$M^{+\cdot}$[c]	ν_{CO}, cm^{-1}	NMR data ($CDCl_3$), δ
2a	CH_3	H	C							
2b	H	Ph[d]	A, B	242–244	95, 64	dark red needles ($CHCl_3$, cyclohexane)	$C_{16}H_{10}N_2OS$	278	1630	6.7–8.3 (m, 9, arom), 9.41 (s, 1, C_5-H)
2c	CF_3	Ph	C							
2d	CH_3	Ph	B	199–200	89	fluffy purple needles (EtOAc)	$C_{17}H_{12}N_2OS$	292	1645	3.38 (s, 3, CH_3), 7.98–6.85 (m, 9, arom)
2e	Ph	Ph	B, C	209–211	90	red needles (Ac_2O)	$C_{22}H_{14}N_2OS$	354	1645	7.10–8.22 (m, arom)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all compounds in the table. [b] A = α-Bromophenylacetyl chloride route; B = Thioglycolic acid route; C = Generated and reacted in situ from the thioglycolic acid (Experimental Section). [c] All 100% relative intensity except **2b** (70%). [d] UV data: λ_{max} (dioxane) 549 nm (log ε 4.07), 4.15 (3.69), 324 sh (3.83), 310 sh (3.86), 277 (4.13), 224 (4.43).

with ethyl propiolate, giving **8g**.

Cycloadditions with Alkenic Dipolarophiles. Fumaronitrile and **2b** underwent reaction in refluxing toluene (24 h) to give **8h** (Table II). The C_1 proton was found as a low-field doublet at δ 9.2–9.4, attributed to deshielding by the C_{11} cyano group. The corresponding proton in the analogous **8c** was not shifted downfield from the other aromatic protons, reflecting a poor deshielding exerted by the C_{11}–$COOCH_3$ group due to steric considerations. Similar effects were observed in the phthalazine series.[8]

The intermediate cycloadduct **9** from which H_2S was eliminated to give **8h** was not isolated. However, the analogous adducts **10** (R^1 = Et and Ph) formed from **2b**



9 **10** **11**

12a, R = CH_3; R^1 = Et
b, R = CH_3; R^1 = Ph
c, R = Ph; R^1 = Et

13 **14**

and *N*-ethyl- and *N*-phenylmaleimide (refluxing toluene, 2 h) were stable, analytical and spectral data establishing the retention of the sulfur bridge. In the cycloadduct **12a** from **2d** and *N*-ethylmaleimide, elimination of H_2S occurred readily when the cycloadduct was heated with potassium *tert*-butoxide in dry toluene (or on prolonged heating in toluene), giving the corresponding pyridinone **11**. The NMR chemical shift changes of the quinazoline methyl protons and the disappearance of the ring junction hydrogen atoms 3a and 12c provide a convenient method for monitoring this conversion. The in situ procedure may also be used, as in the reaction of the thioglycolic acid **3** (R = R^1 = Ph), *N*-ethylmaleimide, and DCC, which yielded **12c** in 87% yield.

Reaction of **2d** with *N*-phenylmaleimide (6 h, refluxing toluene) gave the anticipated cycloadduct **12b** whose spectral data were consistent with the assigned structure. It was not possible to obtain satisfactory analytical data due to the ease of decomposition of the 1:1 cycloadduct when recrystallized. This decomposition also occurred with the 1:1 cycloadduct of *N*-phenylmaleimide and *anhydro*-1-hydroxy-5-methyl-6-oxo-2-phenylthiazolo[3,2-*a*]-quinazolinium hydroxide (**24b**) (see below).

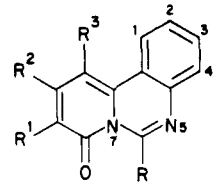
The ^1H NMR spectra of the above cycloadducts from *N*-phenyl- and *N*-ethylmaleimide showed doublets for the C_{3a} and C_{12c} protons at δ 3.79 and 3.85, J = 6.0 Hz. Only one isomer, confirmed by both TLC and NMR data, was obtained in these cycloadditions. The configuration of the C_{3a} and C_{12c} protons cannot be determined directly, and configurational assignments were made by comparison of their chemical shifts with those of model systems. The chemical shifts for the endo isomer appear at lower field due to the deshielding effects of the sulfur bridge. Therefore, the protons α to the imide carbonyl groups for the exo and endo isomers are expected to be near δ 3.4 and 4.1, respectively. The *N*-ethylmaleimide adduct from **2b** had the C_{3a} and C_{12c} bridgehead protons as a singlet at δ 4.27. Since the analogous adducts in the phthalazine series[8] had these bridgehead protons as a singlet at δ 4.20 (the maleic anhydride adducts' protons were a singlet at δ 4.64) and these systems were assigned the endo configuration, the endo configuration **10** was assigned to this cycloadduct. Thus, the cycloadducts derived from **2** with 5-substituents were assigned the exo configuration **12**.

In contrast to the above facile cycloadditions, reaction of **2** with maleic anhydride resulted in largely unidentified products. In one instance **2d** finally gave a product with m/e 344 (100%). Loss of CO and S was observed in its mass spectrum, and in view of the rearrangements described below, a structure such as **13** is not too unlikely.

Ethyl acrylate and the mesoionic system **2e** underwent reaction in boiling xylene overnight, giving a 1:1 cycloadduct assigned structure **14** (R = Ph) on the basis of $M^{+\cdot}$ 454 (6%), with the major fragment resulting from the loss of ethyl acrylate to give the radical cation of **2e**, m/e 354 (100%). The ^1H NMR spectrum showed the normal ABX pattern for the CH_2CH moiety but was further complicated by a 16-peak pattern due to the prochiral nature of the methylene protons of the ethyl ester. The proton spectrum was simplified considerably by using the *J*-resolved 2-di-

(8) Potts, K. T.; Bordeaux, K. G.; Kuehnling, W. R.; Salsbury, R. L. *J. Org. Chem.*, following paper in this issue.

Table II. Cycloadducts 8 of *anhydro*-1-Hydroxythiazolo[3,2-*c*]quinazolin-4-ium Hydroxides 2 and Alkynic/Alkenic Dipolarophiles[a]



compd	R	R^1	R^2	R^3	mp, °C	yield, %	method	crystal habit	ν_{CO}, cm^{-1}	mol form	$M^{+,b}$	NMR data ($CDCl_3$), δ
8a	CH_3	H	CO_2CH_3	CO_2CH_3	205–206	51	C	yellow needles ($EtAc/CHCl_3$)	1730, 1720, 1685	$C_{17}H_{14}N_2O_5$	326	2.90 (s, 3, C_6-CH_3), 3.91, 3.93 (s, 3, $COOCH_3$), 7.05 (s, 1, C_9-H)
8b	CH_3	Ph	CO_2CH_3	CO_2CH_3	228–230	65	D	small yellow needles (MeOH)	1740, 1730, 1670	$C_{23}H_{18}N_2O_5$	402	2.82 (s, 3, C_6-CH_3), 3.53, 3.80 (s, 3, $COOCH_3$), 8.00–7.33 (m, 9, arom)
8c	H	Ph	CO_2CH_3	CO_2CH_3	231–232	67	D	yellow needles (MeOH)	1750, 1660	$C_{22}H_{16}N_2O_5$	388	3.55, 3.86 (s, 3, $COOCH_3$), 7.28–8.3 (m, 9, arom), 9.54 (s, 1, C_6-H)
8d	Ph	Ph	CO_2CH_3	CO_2CH_3	222–223	80	C	yellow needles	1730, 1685	$C_{28}H_{20}N_2O_5$	464	3.60, 3.92 (s, 3, $COOCH_3$), 7.81–7.35 (m, 14, arom)
8e	CF_3	Ph	CO_2CH_3	CO_2CH_3	203–210 dec	17	C	yellow needles (ethyl acetate)	1700	$C_{23}H_{15}F_3N_2O_5$	394	3.59, 3.89 (s, 3, $COOCH_3$), 7.4–9.9 (m, 9, arom)
8f	CH_3	Ph	H	CO_2Et	123–124	52	D	fluffy yellow needles (EtAc)	1715, 1675	$C_{22}H_{18}N_2O_3$	358	1.30 (t, 3, J = 7.0 Hz, OCH_2CH_3), 2.97 (s, 3, CH_3), 4.38 (q, 2, J = 7.0 Hz, OCH_2CH_3), 8.03–7.2 (m, 9, arom), 7.97 (s, 1, C_{10}-H)
8g	Ph	Ph	H	CO_2Et	182–184	40	C	yellow-orange needles (EtOH)	1660	$C_{27}H_{20}N_2O_3$	420	1.38 (t, 3, J = 7.20 Hz, OCH_2CH_3), 4.45 (q, 2, J = 7.20 Hz, OCH_2CH_3), 7.27–8.13 (m, 14, arom)
8h	H	Ph	CN	CN	229–230	80	D	golden prisms (MeOH)	1680, 2210, (ν_{CN})	$C_{20}H_{10}N_4O$	322	7.3–8.2 (m, 8, arom), 9.2–9.4 (d, 1, C_1-H), 9.5 (s, 1, C_6-H)[c]
8i	H	Ph	H	$COCH_3$	200–211	20	D	yellow prisms (MeOH)	1650	$C_{20}H_{14}N_2O_2$	314	1.95 (s, 3, CH_3), 7.20–8.4 (m, 9, arom), 9.64 (s, 1, C_6-H)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all compounds in the table. [b] Relative intensity 100% except **8h**. [c] Me_2SO-d_6.

mensional NMR technique,[9] and by use of a broad-band homonuclear decoupled spectrum and the chemical shifts of the readily observable signals, the ^1H NMR spectrum was simulated,[10] which led to the chemical shifts of the protons of the CH_2CH moiety. The triplet observed for the methyl protons is actually an unresolvable overlapping double doublet due to the slight difference in the coupling constants of the diastereotopic methylene protons.[11]

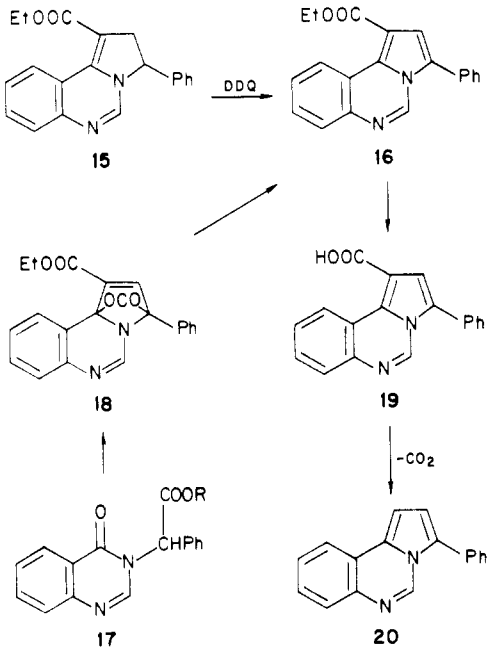
The reaction of **2b** with ethyl acrylate in refluxing xylene was more complex. In addition to very small quantities of the expected 1:1 cycloadduct **14** (R = H) and its H_2S

(9) A contour plot of the above ABX pattern was created with four acquisitions being used, and this contour plot showed the positions of the largest peaks of the two ABX patterns. Although a contour plot that contains all of the peaks can be obtained, it was found that as the vertical scale (VS) increases, the amount of noise also increases as well as the length of time needed for plotting.

(10) ^1H NMR simulations were accomplished with the program available for the Varian XL-200 NMR spectrometer. This utilizes the program LAME, which is LAOCOON with magnetic equivalence added. See also: "XL-200 NMR Spectrometer System Operator's Manual", Varian Publication No. 87-146-000 Rev. B780 and references.

(11) The best fit was obtained for the ABX_3 spin system with chemical shifts (Hz) of A = 822.58, B = 791.80, and X = 201.84 and coupling constants J_{AB} = −10.72 Hz, J_{AX} = 6.65 Hz, and J_{BX} = 6.64 Hz. The best fit was obtained for the ABX spin system with chemical shift (Hz) of A = 576.27, B = 684.88, and X = 799.83, coupling constants J_{AB} = 13.15 Hz, J_{AX} = 8.11 Hz, and J_{BX} = 4.47 Hz, and a peak width of 1.0 Hz at half-height.

elimination product (both characterized spectroscopically), a third, major product was obtained (54%) with molecular formula $C_{20}H_{18}N_2O_2$ [M^+· 318 (75%)]. Structure **15** was



assigned to this product as its ^1H NMR spectrum (200 MHz, $CDCl_3$) showed an ABX pattern (Experimental Section), and the combination of the ^{13}C and a ^{13}C APT experiment showed the presence of 9 × CH, 1 × CH, 5 × C, 1 × CO, and 2 × CH carbon atoms. On oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in boiling dioxane, **15** formed ethyl 3-phenylpyrrolo[1,2-*c*]-quinazoline-1-carboxylate (**16**).

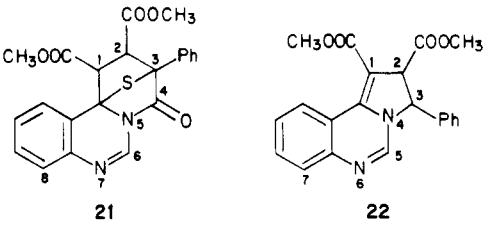
The pyrroloquinazoline **16** was synthesized in an unambiguous fashion from the acetic acid **17**, excess ethyl propiolate, and Ac_2O on refluxing in dry xylene under dry nitrogen for 18 h. An intermediate *anhydro*-2-hydroxy-3-phenyloxazolo[2,3-*a*]quinazolin-4-ium hydroxide was undoubtedly involved in this last reaction, undergoing in situ cycloaddition with the ethyl propiolate and elimination of CO_2 from the primary 1:1 cycloadduct **18**. Hydrolysis of **16** to the corresponding acid **19** and decarboxylation of this acid resulted in **20** in which the chemical shift of the C_{10} proton had shifted from the downfield position to the normal aromatic region.

Carbonyl sulfide was eliminated from the reaction in which compound **15** was formed, the COS being identified as its piperidine derivative by passage of the effluent gas through an alcohol solution of piperidine.

The initial mesoionic compound **2b** was stable to prolonged reflux in xylene, and the 1:1 cycloadduct **14** (R = H) was also not converted into **15** on prolonged reflux in xylene. It has been shown[12] that the *anhydro*-1-hydroxy-2-phenylthiazolo[3,2-*a*]quinolinium hydroxide underwent cycloaddition with DMAD with rearrangement and elimination of COS during the course of the reaction, a pyrrolo[1,2-*a*]quinoline being obtained. The mechanism proposed to account for this rearrangement can, with slight modification, rationalize the loss of COS from cycloadducts of thiocarbonyl ylides and olefinic as well as acetylenic dipolarophiles, but such rationalization are purely speculative at this time.

Reaction of **2b** with ethyl acrylate in the absence of solvent gave a 15% yield of **14** (R = H). This cycloadduct also showed a complex NMR pattern due to the prochiral nature of the methylene protons of the C_1 ethyl ester group. With the NMR procedures described above, it was found that the triplet observed for the methyl protons is actually an unresolvable overlapping double doublet due to the slight difference in the coupling constants of the diastereotopic methylene protons.[13]

The reaction of **2b** with dimethyl fumarate in refluxing xylene overnight gave two isolable products. After separation by HPLC (Waters Prep 500-A) one fraction crystallized from methanol as colorless microprisms in 40% yield. Spectral and analytical data were consistent with the assigned structure **21**, especially M^+· 422 (100%) and



two doublets at δ 3.94 and 4.51 corresponding to the two protons on C_1 and C_2. The second product isolated (12%) corresponded to a rearranged product whose structure was assigned as **22**. Spectral and analytical data were consistent with this structure, especially M^+· 362 (30%) and two doublets at δ 4.48 and 5.61 corresponding to the two protons on C_2 and C_3.

However, when **2b** was heated with methyl vinyl ketone in the absence of solvent, the product obtained was found to be **8i**. Spectral data consistent with this assignment are reported in Table II.

anhydro-1-Hydroxythiazolo[3,2-*a*]quinazolinium Hydroxides

Several representatives of this mesoionic system have been described previously,[4,15,16] and our studies with this ring system complement this earlier work in extending the synthetic procedures as well as describing the cycloaddition reactions that the mesoionic system undergoes.

3,4-Dihydro-3-methyl-4-oxo-2(1*H*)-quinazolinethione, prepared from anthranilic acid and methyl isothiocyanate,[4,14,16] underwent ready reaction with α-bromocarboxylic acids to give the corresponding thioglycolic acids **23** in good yields. Cyclodehydration of the thioglycolic acid **23** with Ac_2O gave the *anhydro*-1-hydroxythiazolo[3,2-*a*]quinazolinium hydroxide system **24**, and in contrast to the representatives of this system reported earlier,[4,15,16] the products prepared in this study were stable to ethanol. Analytical and spectral data established the assigned structures, and the cycloadditions described below provide confirmatory evidence. We have found the cyclodehydration of the thioglycolic acid **23** to **24** to be preferable to reaction of 3,4-dihydro-3-methyl-4-oxo-2(1*H*)-quinazolinethione and an appropriate α-haloacid halide such as α-bromophenylacetyl chloride. With the latter procedure, difficulty in purification of the mesoionic sys-

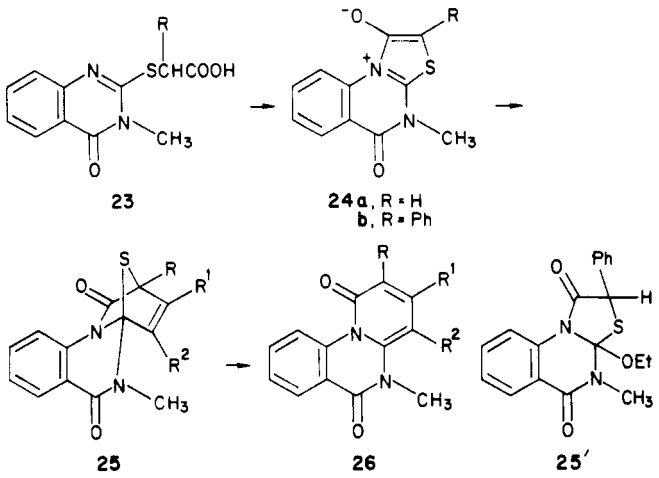
(12) Potts, K. T.; Choudhury, D. R. *J. Org. Chem.* **1978**, *43*, 2700.

(13) The best fit was obtained for the ABX_3 spin system with chemical shifts (Hz) of A = 813.64, B = 783.55, and X = 197.60 and coupling constants J_{AB} = −10.86 Hz, J_{AX} = 6.73 Hz, and J_{BX} = 7.65 Hz. The best fit was obtained for the ABX spin system with chemical shifts (Hz) of A = 538.11, B = 658.95, and X = 740.11 and coupling constants J_{AB} = −12.87 Hz, J_{AX} = 7.87 Hz, and J_{BX} = 4.97 Hz.

(14) Ghosh, T. N. *J. Indian Chem.* **1930**, *7*, 981.

(15) Talukdar, P. B.; Sengupta, S. K.; Datta, A. K. *Indian J. Chem., Sect. B* **1978**, *16B*, 678.

(16) Talukdar, P. B.; Sengupta, S. K.; Datta, A. K. *Indian J. Chem., Sect. B* **1979**, *18B*, 39; **1980**, *19B*, 638.



23 24a, R = H; b, R = Ph

25 26 25′

tem caused reductions in yield.

The mesoionic system **24** readily underwent cycloaddition with alkynic and alkenic dipolarophiles, refluxing benzene giving a sufficiently high reaction temperature with reactive dipolarophiles. Dibenzoylacetylene and ethyl acrylate, however, required refluxing toluene and xylene, respectively, for the cycloaddition to go to completion. The mesoionic system may also be generated in situ from the thioglycolic acid precursor **23** and DCC in the presence of the dipolarophile. The latter procedure is preferred to the use of Ac_2O, and from the thioglycolic acid **23** (R = H) and DMAD/DCC in refluxing benzene overnight dimethyl 1,6-dioxo-5-methyl-5*H*,11*H*-pyrido[1,2-*a*]quinazoline-3,4-dicarboxylate (**26a**) was obtained in 50% yield. The intermediate **25** is postulated as the initial 1:1 cycloadduct from which sulfur is extruded under these reaction conditions. The structure of **26a** was evident from its analytical and spectral data in Table III. No pure product could be isolated from the reaction of the mesoionic compound **24a** with ethyl propiolate.

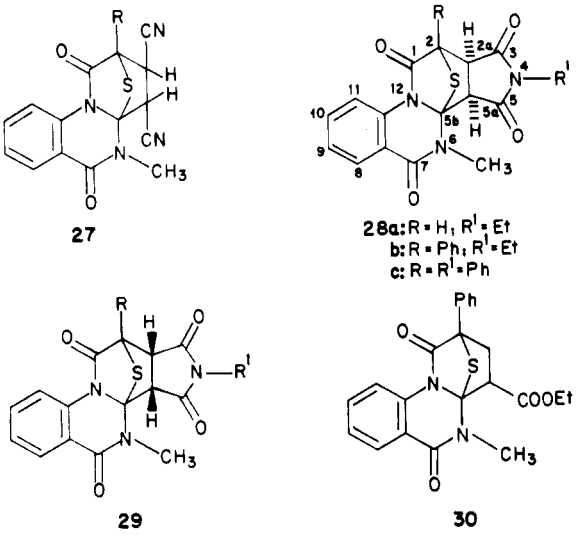
The corresponding 2-phenyl-substituted mesoionic system **24b** was readily prepared from the thioglycolic acid **23** (R = Ph) and Ac_2O. The orange mesoionic product crystallized from $CHCl_3$, to which a few drops of Ac_2O had been added, as bright, orange needles. In absolute ethanol the mesoionic compound decomposed slowly, probably by hydrolysis. It has been reported[17] that **24b** reacted with ethanol to yield a 1:1 adduct; however, we were not able to verify structure **25′**.

Cycloaddition reactions with **24b** were carried out either by direct cycloaddition with the isolated mesoionic compound (method D) or by generating it in situ from the thioglycolic acid **23** (R = Ph) with either Ac_2O or DCC in the presence of the dipolarophile (method C). The use of the isolated mesoionic compound **24b** was the preferred method, resulting in higher yields of the cycloadduct.

DMAD reacted readily with **24b** in refluxing benzene overnight, and dimethyl 1,6-dioxo-5-methyl-2-phenyl-5*H*,11*H*-pyrido[1,2-*a*]quinazoline-3,4-dicarboxylate (**26b**) was obtained in 56% yield (Table III). Dibenzoylacetylene and **24b** underwent reaction in boiling dry toluene overnight, giving **26c** (Table III).

In contrast to **24a** the 2-phenyl-substituted system underwent ready reaction with ethyl propiolate. Assignment of structure **26d** in this product was made on the basis of the data in Table III.

Fumaronitrile reacted readily with both **24a** and **24b** in refluxing benzene overnight. The primary cycloadduct **27**



27 28a: R = H, R′ = Et; b: R = Ph, R′ = Et; c: R = R′ = Ph

29 30

(R = H; R = Ph) was obtained initially, identified by ν_{CN} 2330 (R = H) and 2210 cm^{-1} (R = Ph), respectively, and the ^1H NMR spectra were characterized by the presence of a doublet at δ 4.0 (R = Ph). Purification of the 1:1 cycloadduct **27** (R = H) led only to decomposition via both the reverse Diels–Alder reaction and the loss of H_2S. The fully aromatized product for R = H could not be isolated, but for R = Ph purification of the 1:1 cycloadduct gave 3,4-dicyano-5-methyl-2-phenyl-1(11*H*),6(5*H*)-pyrido[1,2-*a*]-quinazolinedione (**26e**) (Table III).

N-Ethylmaleimide reacted readily with **24a** and **24b** and gave excellent yields of the 1:1 cycloadducts. Both adducts gave low-intensity molecular ions [*m/e* 357 (4%), R = H; *m/e* 433 (11%), R = Ph], with the major fragment resulting from the loss of *N*-ethylmaleimide to give the radical cations of the initial systems **24a** and **24b**. These adducts were obtained as a mixture of stereoisomers which can be readily distinguished by ^1H NMR data on the basis of the observed spectra for the *N*-phenylmaleimide cycloadducts derived from benzo[*c*]thiophene[18] and *anhydro*-3-hydroxythiazolo[2,3-*b*]benzothiazolium hydroxide.[19] The ^1H NMR spectrum of the cycloadduct showed it to be a 2:1 mixture of *exo*-**28a** and *endo*-**29a** isomers. The C_{2a}-H and C_{5a}-H for both the exo and endo isomers appeared as singlets, whereas for the corresponding protons in the cycloadduct derived from the mesoionic system **2e** described above, two doublets at δ 3.91 and 4.18, J = 6.6 Hz, were observed.

The C_{2a}-H and C_{5a}-H appear as singlets at δ 4.52 for the endo isomer, and the exact chemical shifts of the exo isomer's protons cannot be determined due to the complexity of the NMR spectrum. However, it may tentatively be assigned at δ 3.57. Similarly, reaction of the mesoionic compound **24b** with *N*-ethylmaleimide gave a 1:1 cycloadduct whose ^1H NMR spectrum was also characterized by the two singlet corresponding to the C_{2a}-H and C_{5a}-H of the *endo*-**29b** and *exo*-**28b** isomers being δ 4.39 and 3.77, respectively. The two isomers were separated by HPLC (Waters Prep 500A; ethyl acetate/hexane), and spectral and analytical data verified the structural assignments for both isomers. This mesoionic system **24b** and *N*-phenylmaleimide gave cycloadducts in a 2:1 ratio which were separated by HPLC (Waters Prep 500A; ethyl acetate/hexane). The C_{2a}H and C_{5a}H were also singlets at δ

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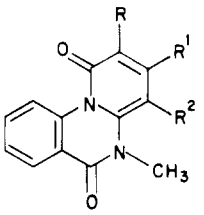
Table III. Cycloadducts 26 of *anhydro*-1-Hydroxy-4-methyl-5-oxo-4*H*-thiazolo[3,2-*a*]quinazolinium Hydroxides 24a,b with Alkynic Dipolarophiles[a]



compd	R	R^1	R^2	yield, %	mp °C	method	crystal habit	mol form.	ν_{CO}, cm^{-1}	$M^{+\cdot}$[b]	NMR data ($CDCl_3$), δ
26a	H	$COOCH_3$	$COOCH_3$	50	162–163	C	yellow needles (MeOH)	$C_{17}H_{14}N_2O_6$	1740, 1680	342	3.48 (s, 3, NCH_3), 3.87 (s, 3, $COOCH_3$), 3.90 (s, 3, $COOCH_3$), 7.2–8.4 (m, 5, arom)
26b	Ph	$COOCH_3$	$COOCH_3$	56	202–204	D	colorless needles (MeOH)	$C_{23}H_{18}N_2O_6$	1735, 1660	418	3.5 (s, 3, $COOCH_3$), 3.6 (s, 3, $COOCH_3$), 3.9 (s, 3, NCH_3), 7.2–8.6 (m, 9, arom)
26c	Ph	COPh	COPh	60	217–220 dec	C	colorless, irreg prisms (EtOH)	$C_{33}H_{22}N_2O_4$	1670	510	3.27 (s, 3, NCH_3), 7.13–10.23 (m, 19, arom)
26d	Ph	H	COOEt	40	167–168 dec	D	yellow needles (EtOH)	$C_{22}H_{18}N_2O_4$	1695, 1650	374	1.37 (t, 3, J = 7.2 Hz, OCH_2CH_3), 3.50 (s, 3, NCH_3), 4.40 (q, 2, J = 7.2 Hz, OCH_2CH_3), 7.2–8.6 (m, 10, arom)
26e	Ph	CN	CN	30	235–240 dec	D	orange irreg prisms (EtOH)	$C_{21}H_{12}N_4O_2$	1680, 2210 (CN)	352	3.52 (s, 3, NCH_3), 7.2–8.8 (m, 9, arom)

[a] Satisfactory analytical data (±0.4% for C, H, N) were reported for all compounds in the table. [b] All 100% relative intensity.

3.93 for the exo isomer **28c** and δ 4.54 for the endo isomer **29c**. All physical and spectral data were consistent with the assigned structures, but satisfactory analytical data could not be obtained for these products due to contamination by trace amounts of the H_2S elimination product formed thermally during recrystallization.

Maleic anhydride and both of the above mesoionic compounds gave no products corresponding to the 1:1 cycloadducts.

The reaction of **24b** with ethyl acrylate gave a 1:1 cycloadduct **30** (47% yield). The mass spectrum of **30** showed a low-intensity molecular ion (*m/e* 408, 10%), with the major fragment resulting from the loss of ethyl acrylate to give the radical cation of the initial mesoionic system **24b** (*m/e* 308, 100%). The 270-MHz ^1H NMR spectrum of the cycloadduct showed it to be a 45:55 mixture of exo and endo isomers, respectively. The NMR spectrum was also very complex, consisting of two ABX patterns for the CH_2CH groupings in each isomer as well as two 16-line ABX_3 patterns due to the prochiral nature of the methylene protons contained in the ester group attached to C_4.[20-23] The two isomers were separated by HPLC (Waters Prep 500A), and in the NMR spectrum of the exo isomer a 14-line pattern with the overlap of two additional peaks appearing as shoulders on two of the 14 peaks was observed. Simulation of the spectrum resulted in the best fit being obtained for an ABX_3 spin system for the 16-line pattern and an ABX spin system for the 12-line pattern of the CH_2CH groups.[24]

However, the NMR pattern for the endo isomer was more complicated due to overlapping of the patterns, making it difficult to assign coupling constants and chemical shifts with any degree of certainty.

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(24) Chemical shift values (Hz) of A = 859.47, B = 835.51, and X = 263.77, coupling constants J_{AB} = −10.85 Hz, J_{AX} = 7.15 Hz, and J_{BX} = 7.21 Hz, and a peak width of 1.0 Hz at half-height for the methylene protons of the C_4 ester. The ABX spin system gave chemical shift values (Hz) of A = 536.15, B = 645.78, and X = 713.41, coupling constants J_{AB} = −13.02 Hz, J_{AX} = 4.89 Hz, and J_{BX} = 7.99 Hz, and a peak width of 0.5 Hz at half-height.

Experimental Section[25]

2-(Trifluoromethyl)-4(3*H*)-quinazolinethione (1, R = CF_3). *o*-Aminothiobenzamide (10.0 g, 0.066 mol) was stirred in dry $CHCl_3$ (100 mL) with powdered molecular sieves and $(CF_3CO)_2O$ (15 mL). The mixture was refluxed for 2 h and after the reaction mixture cooled, the molecular sieves were removed by filtration. The filtrate was concentrated and the product obtained as bright yellow needles from EtAc: 9.1 g (90%); mp 215–127 °C; NMR (Me_2SO-d_6) δ 8.17–7.55 (m, 3, aromatic), 8.20–8.47 (m, 1, aromatic); $M^{+\cdot}$ 230 (100), 161 (47) [$M^{+\cdot} - CF_3$].

Anal. Calcd for $C_9H_5F_3N_2S$: C, 49.46; H, 2.19; N, 12.17. Found: C, 46.57; H, 2.01; N, 12.05.

Mesoionic Ring Formation: *anhydro*-3-Hydroxy-2-phenylthiazolo[3,2-*c*]quinazolin-4-ium Hydroxide (2b). Method A. α-Bromophenylacetyl chloride (11.7 g, 0.05 mol) in dry $CHCl_3$ (50 mL) was added dropwise with stirring to a suspension of 4(3*H*)-quinazolinethione (1 R = H) (8.3 g, 0.05 mol) in dry $CHCl_3$ (125 mL). After 15 min, Et_3N (10.1 g, 0.1 mol) was added slowly to the stirred reaction mixture at room temperature, and the dark red crystalline product which separated was collected and washed with water, followed by ether: 13.2 g (95%). Recrystallization from $CHCl_3$/cyclohexane afforded dark red needles, mp 242–244 °C (Table I).

Method B. 4(3*H*)-Quinazolinethione (1, R = H) (8.1 g, 0.05 mol) was suspended in dry THF (300 mL), and α-bromophenylacetic acid (10.8 g, 0.05 mol) dissolved in dry THF (25 mL) was added with stirring, followed by Et_3N (5.0 g, 0.05 mol). After 1 h, the reaction mixture was concentrated and partitioned between Et_2O and H_2O; the Et_2O extract was washed with H_2O and then saturated NaCl solution. The Et_2O extract was dried over Na_2SO_4 and concentrated in vacuo. The residue crystallized from methanol: 3.3 g (22%). Recrystallization from isopropyl acetate afforded tan prisms of S-(4-quinazolinyl)-α-phenylthioglycolic acid (3, R = H; R^1 = Ph): mp 177–178 °C; IR (KBr) 2500–2400 (br), 1720, 1570 cm^{-1}; λ_{max} (dioxane) 329 nm (log ε 3.92), 317 (3.97), 288 (3.90), 277 (3.95), 268 sh (3.89); NMR (Me_2SO-d_6) δ 5.8 (s, 1, C_α-H), 7.3–8.2 (m, 9, aromatic), 8.9 (s, 1, C_2-H); $M^{+\cdot}$ 296 (54), 129 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; N, 9.45. Found: C, 64.77; H, 4.08; N, 9.67.

The above thioglycolic acid 3 (R = H; R^1 = Ph) (0.5 g, 0.0017 mol) was added to a mixture of Ac_2O (2 mL) and Et_3N (2 mL). After the mixture was stirred 15 min, anhydrous Et_2O was added (10 mL). The dark red crystals (0.3 g, 64%) were recrystallized from chloroform/cyclohexane, mp 242–244 °C, and the product was identical with that prepared above.

Hydrolysis of *anhydro*-3-Hydroxy-2-phenylthiazolo[3,2-*c*]quinazolin-4-ium Hydroxide (2b). The mesoionic system **2b** (1.0 g, 0.004 mol) was refluxed for 17 h in distilled H_2O (50 mL). After cooling, the product was separated, washed with water, and dried at 60 °C in vacuo, giving 0.7 g (66%) of a hydrolysis product 4 (R = H). Recrystallization from methanol afforded pink plates: mp 214–218 °C dec; IR (KBr) 1680, 1580 cm^{-1}; λ_{max} (dioxane) 375 nm (log ε 4.33), 272 (4.10) [cf. 2,5-diphenyl-4-hydroxythiazole[7] 363 nm (log ε 4.28), 267 (3.88)]; NMR (Me_2SO-d_6) δ 7.1–7.8 (m, 9, aromatic), 8.5–8.7 (m, 2, NHCHO), 9.9 (s, 1, OH); $M^{+\cdot}$ 296 (18), 121 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; N, 9.45. Found: C, 64.67; H, 4.45; N, 9.48.

***S*-(2-Methylquinazolin-4-yl)thioglycolic Acid (3, R = CH_3; R^1 = H).** 2-Methyl-4(3*H*)-quinazolinethione (1, R = CH_3) (10.0 g, 0.6 mol) and bromoacetic acid (7.9 g, 0.06 mol) were mixed in dry benzene (75 mL), treated with Et_3N (10 mL, 0.07 mol), and stirred overnight. The solution was filtered to remove all Et_3N·HBr, and the solvent was removed. The product was finally obtained as small yellow needles by recrystallization from EtOH: 57.4 g (43%); mp 174–175 °C; IR (KBr) 1735 (CO) cm^{-1}; NMR (CF_3COOH) δ 3.05 (s, 3, CH_3), 4.48 (s, 2, CH_2), 8.52–7.80 (m, 4, aromatic); mass spectrum, *m/e* (% relative intensity) 234 (14) [$M^{+\cdot}$], 190 (100) [$M^{+\cdot} - CO_2$], 143 (93) [$M^{+\cdot} - SCH_2CO_2H$].

α-Phenyl-*S*-(2-methylquinazolin-4-yl)thioglycolic Acid (3, R = CH_3; R^1 = Ph). The quinazolinethione (1, R = CH_3) (3.94 g, 0.02 mol) and α-phenylbromoacetic acid (4.82 g, 0.02 mol) were mixed in dry toluene (50 mL), treated with Et_3N (10 mL, 0.07 mol), and stirred overnight. The solution was filtered to remove Et_3N·HBr, and the solvent was removed under vacuum. The residue was dissolved in 10% $NaHCO_3$ and filtered, and the solution was then neutralized with dilute HCl. The precipitated product was finally obtained as off-white microcrystals from EtOH: 6.28 g (91%); mp 206–207 °C dec; IR (KBr) 1705 (CO) cm^{-1}; NMR (CF_3COOH) δ 3.10 (s, 3, CH_3), 6.07 (s, 1, C_α-H), 8.53–7.35 (m, 9, aromatic); mass spectrum, *m/e* (% relative intensity) 310 (4) [$M^{+\cdot}$], 176 (100) [$M^{+\cdot} - H_2O$ - PhCS].

***S*-(2-(Trifluoromethyl)quinazolin-4-yl)thioglycolic Acid (3, R = CF_3; R^1 = H).** The quinazolinethione 1 (R = CF_3) (1.15 g, 0.005 mol) and bromoacetic acid (0.70 g, 0.005 mol) were mixed in dry toluene (50 mL) and treated with Et_3N (10 mL, 0.071 mol). When all starting material was consumed (ca. 3 h) the solution was filtered to remove the Et_3N·HBr formed. The solid was washed with water until no more dissolved, and the remaining residue was added to the filtrate. The solvent was removed, the residue dissolved in 10% $NaHCO_3$ and filtered, and the solution then neutralized with dilute HCl. The product precipitated and was finally obtained as off-white microcrystals from EtOH/H_2O: 1.15 (80%); mp 225–227 °C dec; IR (KBr) 1715 (CO) cm^{-1}; NMR (CF_3COOH) δ 4.30 (s, 2, CH_2), 8.43–7.73 (m, 4, aromatic); mass spectrum, *m/e* (% relative intensity) 288 (10) [$M^{+\cdot}$], 244 (100) [$M^{+\cdot} - CO_2$], 69 (46) [CF_3^+].

Anal. Calcd for $C_{11}H_7F_3N_2O_2S$: C, 45.84; H, 2.45; N, 9.72. Found: C, 45.87; H, 2.48; N, 9.68.

α-Phenyl-*S*-(2-(trifluoromethyl)quinazolin-4-yl)thioglycolic Acid (3, R = CF_3; R^1 = Ph). The thioquinazoline 1 (R = CF_3) (1.07 g, 0.005 mol) and α-phenylbromoacetic acid (1.00 g, 0.005 mol) were mixed in dry benzene (15 mL) and treated with Et_3N (1.5 mL, 0.001 mol). An exothermic reaction occurred immediately. The solution was filtered to remove all Et_3N·HBr formed, and the solvent was removed. The product solidified and was finally obtained as colorless prisms from EtOH/H_2O: 1.2 g (71%), mp 232–236 °C dec; IR (KBr) 1710 (CO) cm^{-1}; NMR (CF_3COOH) δ 6.03 (s, 1, C_α-H), 7.72–7.27 (m, 5, aromatic), 8.58–7.92 (m, 4, aromatic); mass spectrum, *m/e* (% relative intensity) 364 (98) [$M^{+\cdot}$], 346 (100) [$M^{+\cdot} - H_2O$], 69 (21) [$CF_3^{+\cdot}$].

Anal. Calcd for $C_{17}H_{11}F_3N_2O_2S$: C, 56.03; H, 3.04; N, 7.69. Found: C, 55.78; H, 2.94; N, 7.62.

Methyl 3-[(2-(Trifluoromethyl)quinazolin-4-yl)thio]-3-(methyoxycarbonyl)acrylate (5). 2-(Trifluoromethyl)-4-(3*H*)-quinazolinethione (1, R = CF_3) (0.5 g, 0.002 mol) and α-bromophenylacetyl chloride (0.51 g, 0.002 mol) were stirred together in dry toluene (5 mL) at room temperature for 30 min. The resultant suspension was then added dropwise to a refluxing solution of Et_3N (2 mL, 0.014 mol) and DMAD (0.6 g, 0.004 mol) in dry toluene (50 mL). On addition of each drop a deep purple color formed which disappeared in approximately 30 s. After complete decolorization, the solvent was removed under reduced pressure and the residue triturated with cyclohexane. The resultant crystalline product separated as shiny, colorless plates from EtOH: 0.45 g (56%); mp 148–149 °C dec; IR (KBr) 1720 (CO) cm^{-1}; NMR ($CDCl_3$) δ 3.70 (s, 3, CO_2CH_3), 3.73 (s, 3, CO_2CH_3), 7.23 (s, 1, C=CH), 8.40–7.63 (m, 4, aromatic); mass spectrum, *m/e* (% relative intensity) 313 (100) [$M^{+\cdot} - CO_2CH_3$].

(25) Spectral characterizations were performed on the following instruments: IR spectra, Perkin-Elmer Model 337 spectrophotometer; ^1H NMR spectra, Varian T-60, Hitachi Perkin-Elmer R600 high-resolution NMR spectrometer, and Varian XL-200, with Me_4Si as an internal standard; ^{13}C NMR, Varian XL-200, with Me_4Si as an internal standard; mass spectra, Hitachi Perkin-Elmer RMU-6E mass spectrometer utilizing a direct insertion probe for solid samples or a variable-leak gas/liquid inlet and operated with a source temperature of 175 °C. Melting points were determined with a Thomas Hoover capillary melting point apparatus for samples melting below 220 °C and a Mel-Temp capillary melting point apparatus for those melting above 22 °C. Evaporations were carried out under reduced pressure using a Buchi Rotovap apparatus. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN and Instranal Laboratories, Inc., Rensselaer, NY. Reagent grade solvents were dried in the following manner: benzene, toluene, xylene, and absolute ether were stored over sodium wire for a minimum of 12 h; tetrahydrofuran (THF) was refluxed with, and distilled under nitrogen from, potassium prior to use.

(26) Michaelis, A.; Ginbarn, H. V. *Ber.* **1894**, *27*, 272.

Anal. Calcd for $C_{15}H_{11}F_3N_2O_4S$: C, 48.39; H, 2.98; N, 7.52. Found: C, 48.48; H, 2.94; N, 7.36.

Methyl 3-[(2-(Trifluoromethyl)quinazolin-4-yl)thio]-3-(methoxycarbonyl)propionate (6). The above substituted acrylate **5** (0.2 g, 0.0005 mol) and a catalytic amount of 10% Pd/C were stirred in absolute EtOH (50 mL). Hydrogen, introduced at atmospheric pressure (13.2 mL, 0.0005 mol), was consumed quickly. The mixture was stirred for 2 h at room temperature, heated to boiling, and then filtered hot. The solvent was removed and the product finally obtained as colorless microcrystals by sublimation: 0.18 g (90%); mp 74–76 °C; IR (KBr) 1725 (CO) cm^{-1}; NMR ($CDCl_3$) δ 3.25 (d, 2, J = 6.30 Hz, CH_2), 3.75 (s, 3, $COOCH_3$), 3.80 (s, 3, $COOCH_3$), 5.19 (t, 1, J = 6.30 Hz, CH), 8.34–7.52 (m, 4, aromatic); mass spectrum, m/e (% relative intensity) 374 (14) [M^+·], 315 (23) [M^+· – $COOCH_3$], 230 (100).

Anal. Calcd for $C_{15}H_{13}F_3N_2O_4S$: C, 48.13; H, 3.50; N, 7.48. Found: C, 48.19; H, 3.70; N, 7.46.

α-Phenyl-*S*-(2-phenylquinazolin-4-yl)thioglycolic Acid (3, R = R^1 = Ph). 2-Phenyl-4(3*H*)-quinazolinethione (1, R = Ph) (10.0 g, 0.042 mol) and α-phenylbromoacetic acid (9.0 g, 0.042 mol) were mixed in dry benzene (100 mL), treated with Et_3N (6.0 mL, 0.042 mol), and stirred overnight. The solution was filtered to remove the Et_3N·HBr formed. The solvent was removed, the Et_3N·HBr that was filtered was washed with H_2O, and the solid that remained was added to the residue above. The combined solid was dissolved in 10% $NaHCO_3$ and filtered, and the solution was then neutralized with dilute HCl. The precipitated product was finally obtained as colorless needles from CH_3OH: 13.3 g (85%); mp 209–210 °C dec; IR (KBr) ν_{CO} 1710 cm^{-1}; ^1H NMR (Unisolv) δ 5.90 (1, s, C_α-H), 7.2–8.86 (m, 14, aromatic); mass spectrum, m/e (% relative intensity) 372 (50) [M^+·].

Anal. Calcd for $C_{22}H_{16}N_2O_2S$: C, 70.95; H, 4.33; N, 7.52. Found: C, 70.93; H, 4.33; N, 7.48.

Cycloadditions with Alkynic Dipolarophiles. Method C. Dimethyl 6,9-Diphenyl-8-oxo-8*H*-pyrido[1,2-*c*]quinazoline-10,11-dicarboxylate (8d). A mixture of the *S*-quinazolinylthioglycolic acid (**3**, R = R^1 = Ph) (0.40 g, 0.003 mol) and DMAD (0.40 g, 0.003 mol) in dry benzene (50 mL) was treated with DCC (0.55 g, 0.002 mol), and the reaction mixture was heated under relux for 3 h. The insoluble dicyclohexylurea was filtered off and the filtrate evaporated. Trituration of the residue with EtOH and recrystallization from ethanol yielded yellow needles: 1.0 g (80%); mp 222–223 °C (Table II). Alternatively, if crystallization did not occur, the product was chromatographed on silica gel with $CHCl_3$ as eluent (compound **8g**).

Method D. Dimethyl 6-Methyl-8-oxo-9-phenyl-8*H*-pyrido[1,2-*c*]quinazoline-10,11-dicarboxylate (8b). The mesoionic compound **2d** (0.72 g, 0.0002 mol) and DMAD (0.55 g, 0.003 mol) were refluxed in dry toluene overnight. The solution was cooled and, after trituration with petroleum ether F, the product crystallized. The product was obtained as small yellow needles by recrystallization from EtOAc, the product decomposing in refluxing MeOH: 0.64 g (65%); mp 228–230 °C (Table II).

Reaction of the Mesoionic Compound 2d with *N*-Ethylmaleimide. The mesoionic compound **2d** (1.00 g, 0.003 mol) and *N*-ethylmaleimide (9.80 g, 0.006 mol) were refluxed in dry toluene (50 mL) for 6 h. The solution was cooled and, after trituration with petroleum ether F, the product **12a** crystallized. It crystallized from EtOH as off-white microcrystals: 1.16 g (81%); mp 214–215 °C dec; IR (KBr) 1740, 1705, 1690 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.13 (t, 3, J = 7.0 Hz, NCH_2CH_3), 2.52 (s, 3, CH_3), 3.50 (q, 2, J = 7.0 Hz, NCH_2CH_3), 3.89 (AB d, J = 6.0 Hz, H_{12c}), 3.85 (AB d, 1, J = 6.0 Hz, H_{3a}), 7.50–7.12 (m, 9, aromatic); mass spectrum, m/e (% relative intensity) 417 [M^+·].

Base-Catalyzed Elimination of H_2S from 12a. Formation of 11. The 1:1 cycloadduct **12a** (0.52 g, 0.0013 mol) was treated with potassium *tert*-butoxide (0.14 g, 0.0013 mol) in dry toluene (25 mL) at room temperature for 10 min. The mixture was then acidified with dilute HCl to expel H_2S. The organic layer was washed with H_2O and dried over anhydrous Na_2SO_4, and the solvent was removed. The residue showed an 8:3 mixture of product to startng material. The product **11** was separated from the mixture by chromatography on silica gel (toluene eluent) and was finally obtained as yellow microcrystals from EtAc: 0.20 g (67%); mp 209–211 °C; IR (KBr) 1675 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.25 (t, 3, J = 7.0 Hz, NCH_2CH_3), 2.83 (s, 3, CH_3), 3.55 (q, 2, J = 7.0 Hz, NCH_2CH_3), 7.82–7.37 (m, 9, aromatic); mass spectrum, m/e (% relative intensity), 383 (100) [M^+·], 284 (23) [M^+· – OCNCO].

Anal. Calcd for $C_{23}H_{17}N_3O_3$: C, 72.05; H, 4.47; N, 10.96. Found: C, 71.81; H, 4.43; N, 10.91.

***N*-Ethylmaleimide Cycloadduct of 2e.** A mixture of the *S*-quinazolinylthioglycolic acid (**3**, R = R^1 = Ph) (1.0 g, 0.003 mol) and *N*-ethylmaleimide (0.33 g, 0.003 mol) in dry benzene (50 mL) was treated with DCC (0.55 g, 0.003 mol). The reaction mixture was heated under reflux for 1 h and the insoluble dicyclohexylurea was filtered from the cooled mixture and the filtrate evaporated. Trituration of the residue with ethanol and recrystallization from ethanol yielded colorless needles of **12c**: 1.13 g (87%); mp 225–226 °C; IR (KBr) 1745, 1695 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.19 (t, 3, J = 7.20 Hz, NCH_2CH_3), 3.59 (dd, 2, J = 7.2 Hz, H_a and H_b), 4.05 (q, 2, J = 7.20 Hz, NCH_2CH_3), 7.49–8.50 (m, 14, aromatic); mass spectrum, m/e (% relative intensity) 479 (5) [M^+·], 354 (100).

Ethyl Acrylate Adduct of 2e. A mixture of the mesoionic compound **2e** (1.0 g, 0.003 mol) and ethyl acrylate (0.30 g, 0.003 mol) in dry xylene (50 mL) was heated under reflux overnight. After evaporation of the xylene, the residue was triturated with ethanol and the resultant crystalline product **14** (R = Ph) crystallized from ethanol as colorless needles: 0.50 g (39%); mp 204–206 °C; IR (KBr) ν_{CO} 1720, 1660 cm^{-1}; NMR ($CDCl_3$) δ 1.0 (t, 3, J = 7.2 Hz, OCH_2CH_3), 2.83 (dd, 1, J = 8.4 Hz, C_2-H), 3.42 (dd, 1, J = 4.2 Hz, C_2-H), 4.00 (q, 2, J = 7.2 Hz, OCH_2CH_3), 4.05 (dd, 1, J = 13.2 Hz, C_1-H), 7.38 (brs, 14, aromatic); mass spectrum, m/e (% relative intensity) 454 (6) [M^+·], 354 (100) [M^+· – $CH_2CHCOOEt$].

Anal. Calcd for $C_{27}H_{22}N_2O_3S$: C, 71.36; H, 4.88; N, 6.16. Found: C, 71.07; H, 4.93; N, 6.09.

Ethyl Acrylate Adduct of 2b. Formation of 15. The mesoionic system (4.0 g, 0.014 mol) and ethyl acrylate (1.5 g, 0.015 mol) were refluxed for 2 h in dry xylene (50 mL). The solvent was evaporated in vacuo and the residue crystallized from isopropyl acetate: 2.6 g (54%). Recrystallization from isopropyl alcohol afforded bright yellow prisms of **15**: mp 148–149 °C; IR (KBr) 1670, 1620 cm^{-1}; λ_{max} (dioxane) 367 nm (log ϵ 4.17), 293 (4.10), 283 (4.00), 270 (3.84), 255 (3.97); NMR ($CDCl_3$) δ 1.23 (t, 3, OCH_2CH_3), 3.04 (dd, 1, J = 16.0 Hz, C_2-H), 3.57 (dd, 1, J = 16.0 Hz, C_2-H), 4.17 (q, 2, J = 8.0 Hz, OCH_2CH_3), 5.20 (dd, 1, J = 8.0 Hz, C_1-H), 7.0–7.65 (m, 9, aromatic), 9.55 (m, 1, C_{11}-H); mass spectrum, m/e (% relative intensity) 318 (75) [M^+·], 245 (100).

Anal. Calcd for $C_{20}H_{28}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.54; H, 5.92; N, 8.73.

Ethyl 3-Phenylpyrrolo[1,2-*c*]quinazoline-1-carboxylate (16). The cycloadduct **15** (0.5 g, 0.002 mol) and DDQ (0.36 g, 0.0012 mol) were refluxed in dioxane (50 mL) for 18 h. The solvent was removed under reduced pressure and the resulting solid partitioned between 10% K_2CO_3 and Et_2O. The Et_2O solution was washed with H_2O and then dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the product **16** finally obtained as tan microcrystals from EtOH: 0.33 g (66%); mp 124–125 °C; IR (KBr) 1690 (CO) cm^{-1}; NMR ($CDCl_3$) δ 1.43 (t, 3, J = 7.0 Hz, OCH_2CH_3), 4.43 (q, 2, J = 7.0 Hz, OCH_2CH_3), 7.20–8.02 (m, 9, aromatic), 8.90 (s, 1, C_2-H), 9.53–9.89 (m, 1, C_{10}-H); mass spectrum, m/e (% relative intensity) 316 (100) [M^+·].

Anal. Calcd for $C_{20}H_{16}N_2O_2$: C, 75.93; H, 5.10; N, 8.85. Found: C, 75.81; H, 5.21; N, 8.80.

Hydrolysis of 16 to 19 (R = COOH) and Decarboxylation to 3-Phenylpyrrolo[1,2-*c*]quinazoline (20). The ester **16** (80 mg) was heated with ethanolic NaOH (excess) for 1 h. After acidification with concentrated HCl, the precipitate was collected, washed with water, and air-dried. Crystallization from EtOH gave cream needles: 60 mg (75%); mp 241 °C dec; IR (KBr) ν_{CO} 1670 cm^{-1}; mass spectrum, m/e (% relative intensity) 288 (100) [M^+·], 244 (10) [M^+· – CO_2].

Anal. Calcd for $C_{18}H_{12}N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.94; H, 4.20; N, 9.71.

The above acid (32 mg) was heated at its melting point (bath temperature 240 °C) under water pump vacuum until gas evolution ceased. The cooled melt was purified by HPLC (Prep 500A; $CHCl_3$): ^1H NMR ($CDCl_3$) δ 8.22–7.15 (m, 11, aromatic), 8.35 (s, 1, C_6-H); M^+· 244 (100).

Reaction of 2b with Ethyl Acrylate in the Absence of Solvent. The mesoionic compound **2b** (1.0 g, 0.004 mol) was

boiled with ethyl acrylate (10 mL) for 5 h. A small amount of gray solid was filtered from the reaction mixture and the filtrate concentrated. The residue was triturated with ethanol, and the product **14** (R = H) crystallized from ethanol as colorless prisms: 0.20 g (15%); mp 179–180 °C dec; IR (KBr) ν_{CO} 1720, 1670 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.99 (t, 3, J_{AX} = 6.73 Hz, J_{BX} = 7.65 Hz, OCH_2CH_3), 2.69 (dd, 1, J_{AB} = −12.87 Hz, J_{AX} = 7.87 Hz, CH_2-CH), 3.29 (dd, 1, J_{AB} = −12.87, J_{BX} = 4.97, CH_2-CH), 3.70 (dd, 1, J_{AX} = 7.87 Hz, J_{BX} = 4.97 Hz, CH_2CH), 3.92 (2 q, 1, J_{AB} = 10.86 Hz, J_{BX} = 7.65 Hz, OCH_2CH_3), 4.07 (2 q, 1, J_{AB} = −10.86 Hz, J_{AX} = 6.73 Hz, OCH_2CH_3), 7.2–7.52 (m, 9, aromatic), 7.80 (s, 1, C_6-H); mass spectrum, *m/e* (% relative intensity) 378 (11) [M^+·], 278 (100).

Anal. Calcd for $C_{21}H_{18}N_2O_3S$: C, 66.65; H, 4.79; N, 7.40. Found: C, 66.59; H, 4.80; N, 7.38.

Ethyl α-Phenyl(4-oxoquinazolin-3-yl)acetate (17, R = Et). To a mechanically stirred solution of potassium *tert*-butoxide (3.84 g, 0.034 mol) in dry THF (200 mL) was added 4(3*H*)-quinazolinone (5.0 g, 0.034 mol), and the mixture refluxed for 1 h. After the mixture cooled to room temperature, ethyl α-bromophenylacetate (8.31 g, 0.034 mol) was added and the reaction mixture refluxed overnight. The THF was evaporated, and the residue was extracted with $CHCl_3$ and washed with acidic water. The organic layer was separated, dried (Na_2SO_4), and evaporated to a thick oil. The oil was chromatorgaphed on silica gel (CC7; $CHCl_3$); however, the product still remained as an oil. The oil was placed under high vacuum and heated to 230 °C to remove all traces of solvent and starting material. A small portion of this oil was set aside and after standing for a week yielded colorless prisms. The bulk of the thick oil was carried through the next reaction without further purification: 5.3 g (50%); mp 86–87 °C; IR (KBr) ν_{CO} 1740, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (t, 3, *J* = 7.0 Hz, OCH_2CH_3), 4.37 (q, 2, *J* = Hz, OCH_2CH_3), 6.79 (s, 1, CH), 7.26–8.5 (m, 9, aromatic); mass spectrum, *m/e* (% relative intensity) M^+· 308 (41), 262 (100).

Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.09. Found: C, 70.00; H, 5.25; N, 9.08.

α-Phenyl(4-oxoquinazolin-3-yl)acetic Acid (17, R = H). The above ester (2.7 g, 0.008 mol) was heated under reflux for 2 h in a mixture of concentrated HCl (10 mL) and dioxane (10 mL). The reaction mixture was then evaporated to dryness, giving a tan product, which, after washing with ether, was recrystallized from a 1:1 mixture of ethanol and water to form colorless needles: 2.2 g (90%); mp 195–196 °C; IR (KBr) ν_{OH} 2650–2100 cm^{-1} ν_{CO} 1680 cm^{-1}; NMR (Me_2SO-d_6) δ 6.53 (s, 1, CH), 7.2–8.4 (m, 9, aromatic); mass spectrum, *m/e* (relative intensity) 280 (80) [M^+·], 262 (100) [M^+· − H_2O].

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 9.99. Found: C, 68.36; H, 4.35; N, 9.97.

Alternative Synthesis of Ethyl 3-Phenylpyrrolo[1,2-*c*]quinazoline-1-carboxylate (16). A mixture of α-phenyl(4-oxoquinazolin-3-yl)acetic acid (**17**, R = H) (0.5 g, 0.008 mol), Ac_2O (excess), and ethyl propiolate (excess) was refluxed in dry xylene under an atmosphere of dry N_2. After 2 h of reflux the mixture became homogeneous with a yellow tint, and the TLC showed evidence for the cycloaddition product; it was then refluxed for an additional 18 h. The xylene was evaporated, and the residue was recrystallized from ethanol forming, gray needles: 0.3 g (54%); mp 124–125 °C, identical with that of the sample prepared above.

Reaction of 2b with Dimethyl Fumarate. Formation of 21 and 22. The mesoionic compound **2b** (1.0 g, 0.004 mol) and dimethyl fumarate (0.52 g, 0.004 mol) were refluxed in dry xylene (50 mL) overnight. The xylene was removed by vacuum distillation and the resiude was chromatographed (Prep 500-A; hexane/ethyl acetate). The product **21** crystallized from methanol as colorless microprisms: 0.31 g (40%); mp 170–174 °C dec (decomposition starts at 120 °C); IR (KBr) ν_{CO} 1730 cm^{-1}; NMR ($CDCl_3$) δ 3.54 (s, 3, OCH_3), 3.65 (s, 3, OCH_3), 3.94 (d, 1, *J* = 6.0 Hz, CHCH), 4.51 (d, 1, *J* = 6.0 Hz, CHCH), 7.05–8.0 (m, 10, aromatic); mass spectrum, *m/e* (% relative intensity) 422 (100) [M^+·].

Anal. Calcd for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N, 6.63. Found: C, 62.53; H, 4.32; N, 6.58.

The rearranged product **22** crystallized from methanol as pale yellow, fine needles: 0.15 g (12%); mp 210–212 °C dec; IR (KBr) ν_{CO} 1730, 1690 cm^{-1}; NMR ($CDCl_3$) δ 3.15 (s, 3, OCH_3), 3.69 (s, 3, OCH_3), 4.48 (d, 1, *J* = 12.0 Hz, CHCH), 5.61 (d, 1, *J* = 12.0 Hz, CHCH), 7.1–7.8 (m, 9, aromatic), 9.54–9.70 (m, 1, C_{10}-H); mass spectrum, *m/e* (% relative intensity) 362 (100) [M^+·].

Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.61; H, 5.01; N, 7.73. Found: C, 69.67; H, 5.06; N, 7.73.

***S*-(3-Methyl-4-oxoquinazolin-2-yl)thioglycolic Acid (23, R = H).** A mixture of 3,4-dihydro-3-methyl-4-oxo-2(1*H*)-quinazolinethione[4] (5.0 g, 0.026 mol) and α-bromoacetic acid (3.6 g, 0.026 mol) in dry benzene (150 mL) was treated dropwise with Et_3N (2.62 g, 0.026 mol) and stirred overnight at room temperature. The insoluble Et_3N·HBr was filtered off, and the filtrate was washed with water and the benzene solution dried over anhydrous Na_2SO_4. Removal of the solvent and trituration of the residue with 95% ethanol gave a colorless powder: 5.8 g (90%); mp 188–189 °C (lit.[4] mp 184–185 °C); IR (KBr) 1710 (acid CO), 1665 (amide CO) cm^{-1}; NMR (TFA) δ 3.95 (s, 3, NCH_3), 4.50 (s, 2, SCH_2), 7.65–8.50 (m, 4, aromatic).

Similarly, ***S*-(3-methyl-4-oxoquinazolin-2-yl)-α-phenylthioglycolic acid (23, R = Ph)** was obtained when the quinazolinethione (5.0 g, 0.03 mol) and α-phenylbromoacetic acid (5.6 g, 0.03 mol) in dry benzene (150 mL) was treated dropwise with Et_3N (2.62 g, 0.03 mol) and worked up as above. The thioglycolic acid crystallized from $CHCl_3$ as colorless, irregular prisms: 5.5 g (65%); mp 169–171 °C; IR (KBr) 1720, 1650 (CO) cm^{-1}; NMR (TFA) δ 3.9 (s, 3, NCH_3), 6.1 (s, 1, C_α-H), 7.4–8.6 (m, 9, aromatic).

Anal. Calcd for $C_{17}H_{16}N_2O_3S$·0.6$CHCl_3$: C, 53.11; H, 3.60; N, 7.04. Found: C, 53.42; H, 3.84; N, 7.27.

***anhydro*-1-Hydroxy-4-methyl-5-oxo-4*H*-thiazolo[3,2-*a*]quinazolinium Hydroxide (24a).** Ac_2O (10 mL) was added at room temperature to a solution of *S*-(3-methyl-4-oxo-2-quinazolinyl)thioglycolic acid (**23**, R = H; 1.0 g, 4 mmol) in pyridine (10 mL). The mixture was immediately warmed on a steam bath for 4–5 min. The color of the solution quickly changed from light to deep yellow in the cold and finally to reddish brown when the reaction was virtually complete. The mixture was cooled to room temperature and the excess Ac_2O decomposed with 95% ethanol (10 mL). The pale yellow mesoionic compound separated on keeping the reaction mixture in an ice bath for 2 h. The product was recrystallized from ethyl acetate, forming yellow needles: 0.39 g (43%); mp 232 °C dec (lit.[4] mp 232 °C dec); IR (KBr) 1695 (CO), 1665 (amide CO) cm^{-1}; NMR (Me_2SO-d_6) δ 3.62 (s, 3, NCH_3), 7.2–8.0 (m, 5, aromatic); mass spectrum, *m/e* (% relative intensity) 232 (100) [M^+·].

***anhydro*-1-Hydroxy-4-methyl-5-oxo-2-phenyl-4*H*-thiazolo[3,2-*a*]quinazolinium hydroxide (24b)** was prepared in a similar fashion from the thioglycolic acid **23** (R = Ph). The orange mesoionic product separated on keeping the reaction mixture in an ice bath for 2 h, and the analytical sample was recrystallized from absolute ethanol from which it separated as bright red needles: 65%; mp 250–252 °C; IR (KBr) 1690, 1650 (CO) cm^{-1}; NMR ($CDCl_3$) δ 3.5 (s, 3, NCH_3), 6.8–8.4 (m, 9, aromatic); mass spectrum, *m/e* (% relative intensity) 308 (100) [M^+·].

Anal. Calcd for $C_{17}H_{12}N_2O_2S$: C, 66.23; H, 3.89; N, 9.09. Found: C, 66.23; H, 3.84; N, 9.05.

Cycloaddition with Alkynic Dipolarophiles. Method C. Dimethyl 1,6-Dioxo-5-methyl-5*H*,11*H*-pyrido[1,2-*a*]quinazoli[illegible]3,4-dicarboxylate (26a). A mixture of the *S*-quinazoli[illegible]oglycolic acid (**23**, R = H) (1.0 g, 0.004 mol) and DMAD ([illegible] 0.004 mol) in dry benzene (50 mL) was treated with DC[illegible], 0.004 mol). The reaction mixture was heated under re[illegible]rnight; the precipitated dicyclohexylurea was removed [illegible]ation and the solvent evaporated. Trituration of the res[illegible]ith methanol gave a crystalline product which upon recr[illegible]tion from methanol yielded yellow needles: 0.68 g (50%); [illegible]2–163 °C (Table III).

Metho[illegible]thyl 1,6-Dioxo-5-methyl-2-phenyl-5*H*,11*H*-pyrido[1,2[illegible]uinazoline-4-carboxylate (26d). The mesoionic system **24b** [illegible]0 g, 0.003 mol) and ethyl propiolate (0.30 g, 0.003 mol) were refluxed together in toluene (50 mL) overnight. The toluene was evaporated and the residue triturated with ethanol, with the solid material then being chromatographed on silica gel ($CHCl_3$). After recrystallization from ethanol it was obtained as yellow needles: 0.45 g (40%); mp 167–168 °C dec (Table III).

Reaction of 24a with *N*-Ethylmaleimide. Formation of 28a and 29a. A mixture of the *S*-quinazolinylthioglycolic acid **23** (R = H; 1.0 g, 0.004 mol) and *N*-ethylmaleimide (0.50 g, 0.004

mol) in dry benzene (50 mL) was treated with DCC (0.83 g, 0.004 mol). The reaction mixture was refluxed overnight. Removal of the dicyclohexylurea by filtration, evaporation of the solvent, and trituration of the residue with ethanol yielded a crystalline product, comprising a mixture of both the exo and endo products in approximately a 50:50 ratio by NMR. These were not separated. Recrystallization from ethanol gave colorless prisms: 1.1 g (80%); mp 177–178 °C dec; IR (KBr) ν_{CO} 1670 cm^{-1}; NMR ($CDCl_3$) δ 1.21 (t, 3, J = Hz, NCH_2CH_3), 3.22 (s, 3, NCH_3), 3.57 (s, 2, $C_{2a,5a}$-H) (exo isomer), 3.67 (q, 2, J = 7.2 Hz, NCH_2CH_3), 4.52 (s, 2, $C_{2a,5a}$-H) (endo isomer), 7.15–8.50 (m, 4, aromatic); mass spectrum, m/e (% relative intensity) 357 (4) [M$^{+\cdot}$].

Anal. Calcd for $C_{17}H_{15}N_3O_4S$: C, 57.14; H, 4.20; N, 11.76. Found: C, 57.07; H, 4.36; N, 11.73.

Reaction of 24b with *N*-Ethylmaleimide. Formation of 28b and 29b. A mixture of the *S*-quinazolinylthioglycolic acid **23** (R = Ph; 1.0 g, 0.003 mol) and *N*-ethylmaleimide (0.40 g, 0.003 mol) in dry benzene (50 mL) was treated with DCC (0.62 g, 0.003 mol). The reaction mixture was refluxed overnight and the dicyclohexylurea was then removed by filtration. The resiude was separated by preparative HPLC (hexane/ethyl acetate), the first fraction, after recrystallization from CH_2Cl_2/ethyl acetate, giving colorless rhombs of the endo isomer **29b**: 0.83 g (63%); mp 205–208 °C dec; IR (KBr) ν_{CO} 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (t, 3, J = 7.2 Hz, NCH_2CH_3), 3.30 (q, 2, J = 7.2 Hz, NCH_2CH_3), 3.40 (s, 3, NCH_3), 4.39 (s, 2, $C_{2a,5a}$-H), 7.1–8.5 (m, 9, aromatic); mass spectrum, m/e (% relative intensity) 433 (11) [M$^{+\cdot}$].

Anal. Calcd for $C_{23}H_{19}N_3O_4S$: C, 63.73; H, 4.42; N, 9.69. Found: C, 66.70; H, 4.43; N, 9.68.

The second fraction crystallized from CH_2Cl_2/ethyl acetate as colorless prisms of the exo isomer **28b**: 0.28 g (21%); mp 195–196 °C dec; IR (KBr) ν_{CO} 1700 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.13 (t, 3, J = 7.2 Hz, NCH_2CH_3), 3.29 (s, 3, NCH_3), 3.55 (q, 2, J = 7.2 Hz, NCH_2CH_3), 3.77 (s, 2, $C_{2a,5a}$-H), 7.2–8.5 (m, 9, aromatic); mass spectrum, m/e (% relative intensity) 433 (11) [M$^{+\cdot}$].

Anal. Calcd for $C_{23}H_{19}N_3O_4S$: C, 63.73; H, 4.42; 9.69. Found: C, 63.68; H, 4.45; N, 9.68.

Reaction of 24b with *N*-Phenylmaleimide. Formation of 28c and 29c. The mesoionic system **24b** (1.0 g, 0.003 mol) and *N*-phenylmaleimide (0.52 g, 0.003 mol) were refluxed in dry benzene (50 mL) overnight. The solvent was evaporated and the residue triturated wth alcohol. The ^{1}H NMR spectrum of the crude product showed the presence of both the endo and exo isomers in approximately a 2:1 ratio, respectively. Recrystallization from alcohol gave colorless needles: 1.1 g (80%). The two isomers were separated by fractional crystallization from either acetonitrile or chloroform. The endo isomer **29c** crystallized from CH_3CN, forming colorless needles: 0.28 g (20%); mp 225–228 °C dec; IR (KBr) ν_{CO} 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.43 (s, 3, NCH_3), 4.54 (s, 2, $C_{2a,5a}$-H), 6.7–8.7 (m, 14, aromatic); M$^{+\cdot}$ 481 (12). The exo isomer **28c** crystallized from $CHCl_3$/acetone, giving colorless prisms: 0.82 g (59%); mp 192–194 °C dec; IR (KBr) ν_{CO} 1715 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.33 (s, 3, NCH_3), 3.93 (s, 2, $C_{2a,5a}$-H), 7.2–8.6 (m, 14, aromatic); mass spectrum, m/e (% relative intensity) 481 (15) [M$^{+\cdot}$].

Reaction of 24b with Ethyl Acrylate. The above mesoionic compound **24b** (1.0 g, 0.003 mol) and ethyl acrylate (excess) were boiled in xylene for 20 h. Removal of the solvent and trituration of the resiude with ethanol gave a crystalline product. Recrystallization of the 1:1 adduct **30** from ethanol gave colorless irregular prisms. The 270-MHz ^{1}H NMR showed that the product was a 45:55 mixture [0.98 g (80%); mp 159–160 °C] of exo and endo isomers, which were separated by HPLC. The exo isomer had the following NMR characteristics: ^{1}H NMR (200 MHz) ($CDCl_3$) δ 1.32 (t, 3, J_{BX} = 7.15 Hz, J_{AX} = 7.21 Hz, OCH_2CH_3), 2.68 (dd, 1, J_{AB} = –13.02 Hz, J = –13.02 Hz, J_{AX} = 4.89 Hz, CH_2CH), 3.23 (dd, 1, J_{AB} = –13.02 Hz, J_{BX} = 7.99 Hz, CH_2CH), 3.57 (dd, 1, J_{AX} = 4.89 Hz, J_{BX} = 7.99 Hz, CH_2CH), 4.18 (2 q, 1, J_{AB} = –10.85 Hz, J_{BX} = 7.15 Hz, OCH_2CH_3), 4.30 (2 q, 1, J_{AB} = –10.85 Hz, J_{AX} = 7.21 Hz, OCH_2CH_3), 7.14–8.60 (m, 9, aromatic); mass spectrum, m/e (% relative intensity) 408 (10) [M$^{+\cdot}$].

Anal. Calcd for $C_{22}H_{20}N_2O_4S$: C, 64.69; H, 4.94; N, 6.86. Found: C, 64.55; H, 5.07; N, 6.91.

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Registry No. 1 (R = H), 3337-86-8; 1 (R = CH_3), 6484-28-2; 1 (R = Ph), 6483-99-4; 1 (R = CF_3), 35982-23-1; **2a**, 95616-34-5; **2b**, 91859-59-5; **2c**, 95616-35-6; **2d**, 94392-52-6; **2e**, 95616-36-7; **3** (R = H, R^1 = Ph), 95616-37-8; **3** (R = CH_3, R^1 = H), 95616-38-9; **3** (R = CH_3, R^1 = Ph), 95616-39-0; **3** (R = CF_3, R^1 = H), 95616-40-3; **3** (R = CF_3, R^1 = Ph), 95616-41-4; **3** (R = R^1 = Ph), 95616-42-5; **4** (R = H), 95616-43-6; **4** (R = CH_3), 95616-44-7; **5**, 95616-45-8; **6**, 95616-46-9; **8a**, 95616-47-0; **8b**, 95616-48-1; **8c**, 91534-03-1; **8d**, 95616-49-2; **8e**, 95616-50-5; **8f**, 95616-51-6; **8g**, 95616-52-7; **8h**, 95616-53-8; **8i**, 95616-54-9; **10** (R^1 = Et), 95616-55-0; **10** (R^1 = Ph), 95616-56-1; **11**, 95616-57-2; **12a**, 95616-58-3; **12b**, 95616-59-4; **12c**, 95616-60-7; **14** (R = Ph), 95616-61-8; **14** (R = H), 91534-00-8; **15**, 91533-97-0; **16**, 91533-98-1; **17** (R = Et), 16347-74-3; **17** (R = H), 91533-99-2; **19**, 95616-62-9; **20**, 95616-63-0; **21**, 91534-01-9; **22**, 91534-02-0; **23** (R = H), 63586-35-6; **23** (R = Ph), 95616-64-1; **24a**, 95616-65-2; **24b**, 94392-54-8; **26a**, 95616-66-3; **26b**, 95616-67-4; **26c**, 95616-68-5; **26d**, 95616-69-6; **26e**, 95616-70-9; **27** (R = H), 95616-71-0; **27** (R = Ph), 95616-72-1; **28a**, 95616-73-2; **28b**, 95616-74-3; **28c**, 95616-75-4; **29a**, 95721-08-7; **29b**, 95721-09-8; **29c**, 95721-10-1; **30** (isomer 1), 95616-76-5; **30** (isomer 2), 95721-11-2; 3,4-dihydro-3-methyl-4-oxo-2(1*H*)-quinazolinethione, 1705-09-5; α-bromophenylacetyl chloride, 19078-72-9; *N*-ethylmaleimide, 128-53-0; ethyl acrylate, 140-88-5; 4-(3*H*)-quinazolinone, 491-36-1; ethyl α-bromobenzeneacetate, 2882-19-1; ethyl propiolate, 623-47-2; dimethyl furmarate, 624-49-7; *N*-phenylmaleimide, 941-69-5; fumaronitrile, 764-42-1; dibenzoylacetylene, 1087-09-8; *o*-aminothiobenzamide, 2454-39-9; trifluoroacetic anhydride, 407-25-0; α-bromophenylacetic acid, 4870-65-9; bromoacetic acid, 79-08-3; DMAD, 762-42-5.

Supplementary Material Available: Figures 1–14 (NMR spectra) (10 pages). Ordering information is given on any current masthead page.