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(13) We thank Dr. J. J. D'Amico for this procedure which ensures complete elimination of 2-benzothiazolyl disulfide often present as a contaminant.
(14) Criteria for identity were superimposable IR spectra, no depression in mmp, and identical r_f values.

Notes

Mesoionic Compounds. 44. Synthesis and Cycloaddition Reactions of the *anhydro*-1-Hydroxythiazolo[3,2-*a*]quinolinium Hydroxide System[1]

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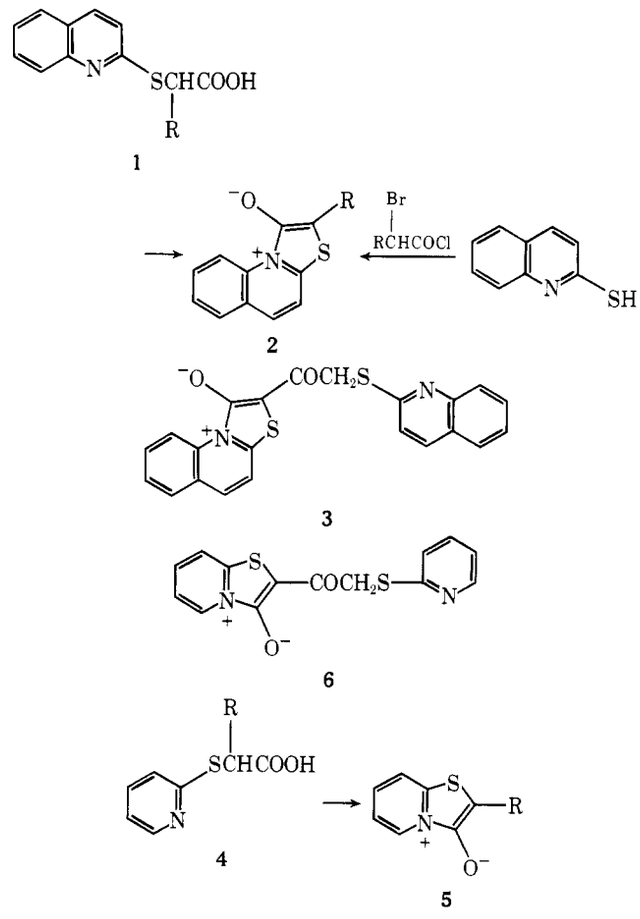
In an accompanying publication,[2] we reported the ready cycloaddition of the isomeric *anhydro*-2- and 3-hydroxythiazolo[2,3-*b*]benzothiazolium hydroxides with acetylenic dipolarophiles to the pyrrolo[2,1-*b*]benzothiazole and the 1*H*-pyrido[2,1-*b*]benzothiazol-1-one ring systems, respectively. As sulfur is isoelectronic with a double bond, we anticipated that the *anhydro*-1-hydroxythiazolo[3,2-*a*]quinolinium hydroxide system **2** should also be of interest as a substrate for cycloaddition reactions. The results obtained with this ring system are described below.

anhydro-1-Hydroxythiazolo[3,2,-*a*]quinolinium hydroxide (**2**, R = H) has been reported earlier,[3] prepared by the cyclodehydration of the 2-quinolinylthioglycolic acid (**1**, R = H) with Ac_2O. On repetition of this procedure, a dark-brown-bronze product was obtained which was difficult to isolate in a pure state despite repeated recrystallizations. However, the observed spectral data were inconsistent with structure **2** (R = H); although infrared carbonyl absorptions at 1610 and 1600 cm^{-1} are compatible with the C_1-carbonyl group, an absorption at 1660 cm^{-1} suggests attachment of a carbonyl group to C_2. The NMR spectrum, in addition to the aromatic multiplet at δ 7.93–7.26, showed a singlet at δ 4.98 which is consistent with structure **3** for this product (vide infra). Similar results were also obtained in the attempted preparation of *anhydro*-3-hydroxythiazolo[3,2-*a*]pyridinium hydroxide (**5**, R = H) from 2-pyridinylthioglycolic acid (**4**, R = H) with Ac_2O under the previously reported conditions.[3] The yellow crystalline product obtained showed ν_{CO} 1680, 1620, and 1600 cm^{-1} and a singlet at δ 4.16 in its NMR spectrum in addition to an aromatic multiplet. Its molecular weight was shown to be 302, and these data require revision of the assigned structure **5** (R = H) to that of **6**, The same product was also obtained from the reaction of bromoacetyl chloride and 2-mercaptopyridine and the formation of **6** is indicative of a high electron density at the 2 position of **5** (R = H). Authentic samples of this ring system have been prepared by the reaction of 2-mercaptopyridine with δ-bromophenylacetyl chloride[4] and 2-bromo-2-ethoxycarbonylacetyl chloride[5] giving **5** (R = Ph) and **5** (R = COOEt), respectively. With a variety of electron-deficient dipolarophiles, no cycloaddition of **5** (R = Ph, COOEt) was observed.

Blocking of the 2 position in **2** with a phenyl substituent proved to be the most effective way of obtaining an authentic example of this ring system and reaction of 2-mercaptoquinoline with α-bromophenylacetyl chloride gave an 82% yield of **2** (R = Ph) as deep-red plates. A carbonyl absorption at 1610 cm^{-1} is consistent with this structure which was confirmed by an alternative synthesis by ring closure of 2-quinolinyl-α-phenylthioglycolic acid (**1**, R = Ph).

Reaction of **2** (R = Ph) with dimethyl acetylenedicarboxylate in refluxing toluene for 6 h gave a yellow crystalline product anticipated to be **8** (R = R^1 = $COOCH_3$). However, the infrared spectrum indicated only ester carbonyl bands at 1725 and 1705 cm^{-1} and no absorption due to the ring carbonyl group was present. The mass spectrum showed M^+· 359



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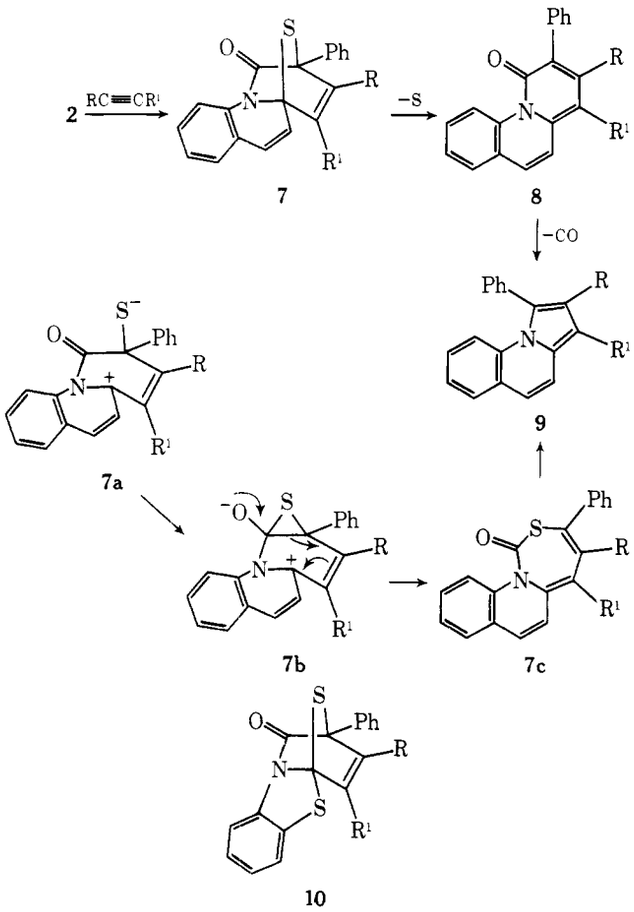
and, in conjunction with analytical data, established the structure of the product as methyl 1-phenylpyrrolo[1,2-*a*]-quinoline-2,3-dicarboxylate (**9**) (R = R^1 = $COOCH_3$). The physical and spectral characteristics of **9** (R = R^1 = $COOCH_3$) were in agreement with reported values.[4]

It would be very unusual for **8** (R = R^1 = $COOCH_3$), formed by thermal extrusion of sulfur from the initial 1:1 adduct **7** (R = R^1 = $COOCH_3$), to lose CO at 110 °C forming the tricyclic system **9** (R = R^1 = $COOCH_3$) and this pathway can be definitely excluded on the basis of the thermal stability of **12** described below as well as by the formation of COS in the reaction. Also it should be noted that in the reaction of *anhydro*-3-hydroxy-2-phenylthiazolo[2,3-*b*]benzothiazolium hydroxide with acetylenic dipolarophiles the anticipated pyridones were obtained.[2]

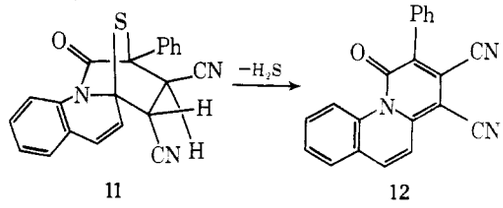
Trapping of COS from the reaction of **2** (R = Ph) with dimethyl acetylenedicarboxylate suggests the formation of **7c** as an intermediate via the sequence **7a** → **7b** → **7c**. A similar intermediate is not formed from **10** presumably due to the difference in stabilities between the intermediate carbonium ions **7a** and the analogous one derived from **10**. It should be noted that **9** would also be obtained if the structure of the initial mesoionic system **2** (R = Ph) were actually that of the 3-hydroxy isomer. This possibility can be excluded by the alternative synthesis of **2** (R = Ph) and the cycloaddition with fumaronitrile described below.

Ethyl propiolate reacted readily with **2** (R = Ph) giving the corresponding derivative of **9** (R = H; R^1 = COOEt). The



chemical shift of H_2 (δ 7.13) is in agreement with that reported[7] for a pyrrole proton in a similar fused ring environment. Dibenzoylacetylene, however, did not give any cycloaddition product even in refluxing xylene, most likely a consequence of severe steric crowding in **7** (R = R^1 = COPh) rather than any lack of reactivity in **2** (R = Ph) with dibenzoylacetylene.

Fumaronitrile also reacted readily with **2** (R = Ph) giving the fused pyridone **12,** presumably formed by loss of H_2S from



the primary cycloadduct **11.** The stability of **12** in boiling xylene excludes any possibility of the loss of CO from **8** (R = R^1 = $COOCH_3$) above to give **9** (R = R^1 = $COOCH_3$).

Experimental Section[8]

2-Mercaptoquinoline was purified as follows. The thiol (10.0 g) was dissolved in NaOH solution (50 mL of 10% solution) and the undissolved material was filtered. The filtrate was refluxed with charcoal for 30 min and filtered hot and the cooled filtrate was acidified with aqueous HCl (20% solution). The precipitated thiol was collected, washed with water, and dried.

Cyclodehydration of 2-Quinolinylthioglycolic Acid (1, R = H). 2-Mercaptoquinoline (3.22 g, 20 mmol) and bromoacetic acid (2.78 g, 20 mmol) in anhydrous benzene (50 mL) were treated with Et_3N (2.8 mL, 20 mmol) and stirred for 15 h. The reaction mixture was washed with water (2 × 20 mL) and dried (Na_2SO_4) and the benzene was evaporated in vacuo.

One-half of the above oil was dissolved in dry benzene (5 mL), cooled to 0 °C, and treated with an ice-cold mixture of Ac_2O (1.5 mL) and Et_3N (1.5 mL). After stirring for 15 min, the reaction mixture was allowed to warm to room temperature and anhydrous ether was added, precipitating an orange solid. This was recrystallized from $CHCl_3$–Et_2O, separating as an unstable orange powder which decomposed on standing: mp 162–163 °C dec; IR (KBr) 1700, 1655, 1605 cm^{-1}.

The remaining portion of the oil was treated with Ac_2O (1.5 mL) and Et_3N (1.5 mL) at room temperature, an exothermic reaction resulting. The brown needles that separated after 15 min and the additional solid precipitated by addition of anhydrous ether were collected: mp 174 °C; IR (KBr) 1700, 1660, 1615 cm^{-1}.

When a sample of the thioglycolic acid was treated with Ac_2O, rapidly heated to boiling and then cooled quickly, the addition of EtOH deposited a dark solid. It crystallized from pyridine–ethanol as dark-brown prisms: mp 178–182 °C dec (lit[3] mp 194 °C); IR (KBr) 1660, 1610, 1600 cm^{-1}; NMR ($CDCl_3$) δ 7.93–7.26 (m, 8, aromatic), 4.98 (s, 1, CH_2).

Cyclodehydration of 2-Pyridinylthioglycolic Acid (4; R = H). A mixture of the acid (0.75 g, 4.44 mmol) and Ac_2O (4 mL) was heated quickly to boiling and cooled immediately. The deposited solid was recrystallized from EtOH forming yellow plates of **6:** 75%; mp 187 °C (lit.[3] mp 180 °C); IR (KBr) 1680, 1620, 1600 cm^{-1} (CO); NMR ($CDCl_3$) δ 8.46–6.63 (m, 8, aromatic), 4.16 (s, 2, CH_2); M^+· 302 (31). Anal. Calcd for $C_{14}H_{10}N_2O_2S_2$: C, 55.62; H, 3.33; N, 9.26. Found: C, 56.11; H, 3.57; N, 9.10.

Reaction of 2-Mercaptopyridine with Bromoacetyl Chloride. The thiol (0.55 g, 5 mmol) in dry $CHCl_3$ (30 mL) was treated dropwise with bromoacetyl chloride (0.78 g, 5 mmol). After stirring for 5 min, Et_3N (1.4 mL, 10 mmol) was added and the reaction mixture was stirred for an additional hour. The $CHCl_3$ solution was washed with H_2O (2 × 10 mL), dried (Na_2SO_4), and concentrated. Addition of Et_2O precipitated a greenish-yellow product that crystallized from EtOH as yellow needles, 78%, mp 187 °C, identical[9] with **6** prepared above.

***anhydro*-1-Hydroxy-2-phenylthiazolo[3,2-*a*]quinolinium Hydroxide (2, R = Ph). A.** A solution of 2-mercaptoquinoline (1.61 g, 10 mmol) in dry $CHCl_3$ (50 mL) was treated dropwise with α-bromophenylacetyl chloride (2.34 g; 10 mmol) at room temperature. After stirring for 10 min, Et_3N (2.02 g; 20 mmol) was added dropwise and stirring was continued for a further 30 min. The reaction mixture was washed with cold water (2 × 15 mL), dried (Na_2SO_4), and concentrated. Addition of a small amount of anhydrous Et_2O gave a deep-red solid that crystallized from $CHCl_3$–Et_2O as deep-red plates: 82%; mp 199–200 °C dec; IR (KBr) 1610 cm^{-1}; λ_{max} (CH_3OH) 482 (log ε 4.14), 306 (3.92), 270 nm (3.84); NMR ($CDCl_3$–Me_2SO-d_6) δ 8.13–7.07 (m, aromatic); M^+· 277 (64). Anal. Calcd for $C_{17}H_{11}NOS$: C, 73.62; H, 4.00; N, 5.05. Found: C, 73.74; H, 3.94; N, 4.88.

B. A stirred mixture of 2-mercaptoquinoline (3.22 g, 20 mmol) in

benzene (50 mL) and α-bromophenylacetic acid (4.3 g, 20 mmol) was treated dropwise with Et_3N (2.02 g, 20 mmol) and stirred for 6 h at room temperature. Insoluble material was filtered and the filtrate was diluted with $CHCl_3$, washed with H_2O (2 × 20 mL), dried (Na_2SO_4), and concentrated. Addition of benzene gave 2-quinolinyl-2-phenylthioglycolic acid (**1**, R = Ph) as a colorless solid which crystallized from $CHCl_3$–benzene as colorless prisms: mp 140 °C dec; IR (KBr) 1705 cm^{-1} (CO); NMR (Me_2SO-d_6) δ 8.21–7.28 (m, 11, aromatic), 5.85 (s, 1, CH). Anal. Calcd for $C_{17}H_{13}NO_2S$: C, 69.11; H, 4.43; N, 3.74. Found: C, 69.36; H, 4.42; N, 4.73.

The above acid (2.0 g, 7 mmol) in anhydrous benzene (2 mL) was treated with a mixture of Ac_2O (4 mL) and Et_3N (4 mL) and stirred for 1 h at room temperature. Addition of anhydrous Et_2O precipitated a deep-red solid that crystallized from $CHCl_3$–Et_2O as deep-red plates: 88%; mp 198–199 °C dec, identical[9] with that prepared above.

Reaction of *anhydro*-1-Hydroxy-2-phenylthiazolo[3,2-*a*]quinolinium Hydroxide (2, R = Ph) with Dimethyl Acetylenedicarboxylate. The above mesoionic compound (0.81 g; 3 mmol), dimethyl acetylenedicarboxylate (0.5 g; 35.2 mmol), and toluene (30 mL) were refluxed for 6 h. Evaporation of the toluene in vacuo and trituration of the residue with hot EtOH gave a yellow solid that crystallized from $CHCl_3$–EtOH as yellow needles of methyl 1-phenylpyrrolo[1,2-*a*]quinoline-2,3-dicarboxylate (**9**, R = R^1 = $COOCH_3$): 66%; mp 160–161 °C (lit.[6] mp 161–162 °C); IR (KBr) 1725, 1705 cm^{-1}; λ_{max} (CH_3OH) 350 (log ε 4.06), 277 (4.03), 227 nm (sh, 4.39); NMR ($CDCl_3$) δ 8.28–7.16 (m, 11, aromatic), 3.91 (s, 3, $COOCH_3$), 3.71 (s, 3, $COOCH_3$); M^+· 359 (100). Anal. Calcd for $C_{22}H_{17}NO_4$: C, 73.53; H, 4.77; N, 3.90. Found: C, 73.68; H, 4.64; N, 3.76.

In one experiment dry N_2 was passed through the reaction mixture and the effluent gases condensed in an alcoholic solution of piperidine. Concentration of this solution resulted in colorless needles of *N,N'*-pentamethylenethiocarbamic acid, recrystallized from acetone, mp 112–113 °C (lit.[10] mp 113–115 °C), identical[9] with an authentic sample.

Ethyl 1-phenylpyrrolo[1,2-*a*]quinoline-3-carboxylate (9, R = H; R^1 = COOEt) was obtained as yellow needles from $CHCl_3$–EtOH from **2** (R = Ph) and ethyl propiolate in refluxing toluene over 7 h: 95%; mp 98 °C; IR (KBr) 1700 (CO), 1660 cm^{-1}; λ_{max} (CH_3OH) 420 (log ε 3.75), 370 (4.0), 285 (4.16), 240 (sh, 4.40), 227 nm (sh, 4.42); NMR ($CDCl_3$) δ 8.28 (d, 1, *J* = 9.0 Hz, aromatic), 7.77–7.26 (m, 10, aromatic), 7.13 (s, 1, H_2), 4.4 (q, 2, *J* = 7.0 Hz, $\mathbf{CH_2}CH_3$), 1.4 (t, 3, *J* = 7.0 Hz, $CH_2\mathbf{CH_3}$); M^+· 315 (100). Anal. Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 4.53; N, 4.44. Found: C, 79.59; H, 5.25; N, 4.37.

Reaction of 2 (R = Ph) with Fumaronitrile. The mesoionic compound (0.53 g, 2 mmol), fumaronitrile (0.16 g, 2 mmol), and toluene (30 mL) were refluxed for 24 h. Evaporation of the toluene in vacuo and trituration of the residue with hot ethanol gave a solid that crystallized from $CHCl_3$: EtOH as golden yellow needles of 3,4-dicyano-2-phenyl-1*H*-pyrido[1,2-*a*]quinolin-1-one (**12**): 28%; mp 304–305 °C; IR (KBr) 2210 (CN), 1685 cm^{-1} (CO); M^+· 321 (80). Anal. Calcd for $C_{21}H_{11}N_3O$: C, 78.49; H, 3.45; N, 13.08. Found: C, 78.20; H, 3.24; N, 12.93.

Registry No.—1 (R = H), 56919-56-3; 1 (R = Ph), 66102-80-5; 2 (R = Ph), 43091-21-0; **3**, 66102-81-6; **4** (R = H), 10002-29-6; **6**, 66102-82-7; **9** (R = H; R = COOEt), 52249-53-3; **9** (R = R^1 = $COOCH_3$), 20958-83-2; **12**, 66102-83-8; 2-mercaptoquinoline, 2637-37-8; bromoacetic acid, 79-08-3; 2-mercaptopyridine, 2637-34-5; bromoacetyl chloride, 22118-09-8; α-bromophenylacetyl chloride, 19078-72-9; α-bromophenylacetic acid, 4870-65-9; dimethyl acetylenedicarboxylate, 762-42-5; ethyl propiolate, 623-47-2; fumaronitrile, 764-42-1.

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Synthesis of α-Methoxyaliphatic Acids from Chloroform and Aliphatic Aldehydes with Sodium Hydride as Catalyst in Tetrahydrofuran

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The preparations of α-methoxyaliphatic acids, which we report here, have not been reported previously by any other method. A number of earlier articles have reported the condensation of chloroform (or bromoform) with aryl aldehydes to produce either aryl trihalomethyl-substituted methanols[1] or the products of the reaction of such alcohols[2] with base and/or solvent. In the latter cases, α-substituted arylacetic acids are often produced, where the α substituent has been methoxyl[3] (or alkoxyl,[4] in general), hydroxyl,[5] amino,[6] and even chloro.[7]

Past attempts to carry out similar reactions with aliphatic aldehydes replacing the aryl aldehydes have met with little success,[8] resulting usually in the formation of tars (from aldol condensations) rather than the alkyl (trichloromethyl)-methanols (aliphatic ketones[8] do, however, condense with chloroform, usually in 80% yields). Thus, at moderate temperatures (10–15 °C), most aliphatic aldehydes undergo the aldol condensation in the presence of strong base. To avoid this competing reaction, we have devised a procedure described below involving the addition of the aldehyde in chloroform to sodium hydride at 0–5 °C. The resulting alkyl (trichloromethyl)methanol containing solution, on addition of methanolic potassium hydroxide and heat, is converted to the product α-methoxyaliphatic acid, allowing a "one-batch" conversion.

$$RCHO + HCCl_3 + THF \xrightarrow[(2)\ NaOH/CH_3OH]{(1)\ NaH/THF} \underset{\displaystyle OCH_3}{\overset{\displaystyle RCHCO_2H}{|}}$$

There is evidence[9] for a general mechanism for these related haloform condensations, a mechanism involving an epoxide intermediate, which undergoes ring opening with solvent (or base) nucleophile to produce the various α-substituted acids after hydrolysis:

$$RCHO + CHCl_3\ (\text{or } CHBr_3) \xrightarrow[\text{catalyst}]{\text{base}} \underset{\displaystyle OH}{\overset{\displaystyle RCHCCl_3}{|}}$$

$$\xrightarrow{KOH} RCH\underset{O}{\overset{Cl}{-C}}\underset{Cl}{} \xrightarrow{XH} \underset{X}{\overset{RCHC(=O)Cl}{|}} \xrightarrow{H_2O} \underset{X}{\overset{RCHCO_2H}{|}}$$

In our chloroform condensation, the yields of the α-methoxyaliphatic acids have been generally good, varying from 51 to 63%, in most cases (with one 24% exception).

Other variations tried were a mixture of Me_2SO and THF (Me_2SO–THF 1:10) and 1,4-dioxane as solvent systems. The use of bromoform (replacing chloroform), a variety of reactant stoichiometries and orders of addition, potassium hydroxide in methanolysis (replacing sodium hydroxide), and a number of temperature conditions were tried. The reaction did not work if bromoform was substituted for chloroform. Also, we were not able to modify the methodology to produce the α-hydroxy- or α-aminoaliphatic acids. However, alkyl (trichloromethyl)methanols were isolated in good (80%) yields in two trials (using isobutyraldehyde and *n*-pentanal) and thus we feel certain that given the right conditions these other α-substituted aliphatic acids should be achievable.

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