Annulation to the Phthalazine Ring System Utilizing Mesoionic Ring Systems

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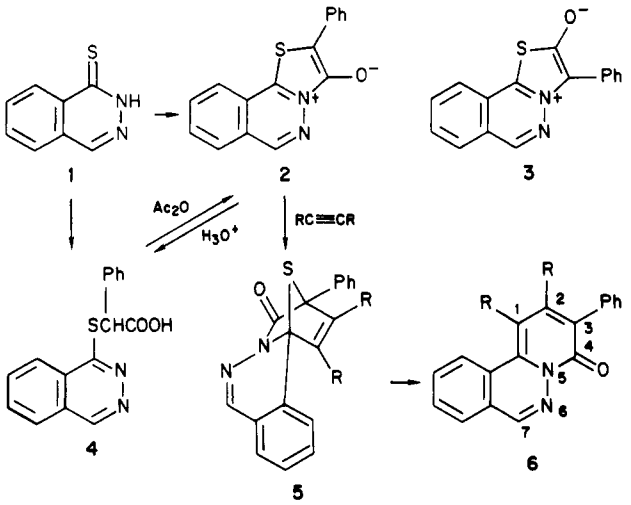
anhydro-3-Hydroxy-2-phenylthiazolo[2,3-*a*]phthalizinium hydroxide, prepared from 1(2*H*)-phthalazinethione and α-bromophenylacetyl chloride or by Ac_2O/Et_3N ring closure of *S*-(1-phthalazinyl)-α-phenylthioglycolic acid, and dimethyl acetylenedicarboxylate in refluxing xylene (17 h) gave dimethyl 4-oxo-3-phenyl-4*H*-pyrido[2,1-*a*]phthalazine-1,2-dicarboxylate (85%). Fumaronitrile gave the corresponding 1,2-dicyano product (93%), whereas *N*-ethylmaleimide and maleic anhydride gave the initial 1:1 cycloadducts, again in high yields. Ethyl acrylate, however, resulted in a pyrrolo[2,1-*a*]phthalazine derivative, a complex rearrangement being involved. Several other representatives of those tricyclic systems are described.

The use of mesoionic ring systems for ring annulations is becoming a well-established procedure, resulting in either five- or six-membered annulated systems.[2-4] This paper describes our results establishing this approach as the most convenient for annulation of a pyridinone to the *a* side of phthalazine.

1(2*H*)-Phthalazinethione (**1**), readily prepared from 1-(2*H*)-phthalazinone and P_4S_{10} in dry pyridine, gave with α-bromophenylacetyl chloride in anhydrous ether in the presence of Et_3N (2 mol) *anhydro*-3-hydroxy-2-phenylthiazolo[2,3-*a*]phthalazinium hydroxide (**2**) (90%). The

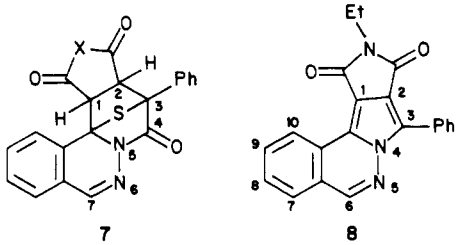


alternative structure **3** for the condensation product was excluded by an alternative synthesis of **2**. 1(2*H*)-Phthalazinethione[6] (**1**) with α-bromophenylacetic acid[7] readily gave the thioglycolic acid **4**. Cyclodehydration of **4** gave **2**. Conversely, hydrolysis of **2** with dilute acid gave the thioglycolic acid **4**. Analytical and spectral data were consistent with the assigned structure **2**, especially M^+· 278, ν_{CO} 1633 cm^{-1}, and ^{13}C NMR δ 156.04 (ν_{CO}). In addition, the thiobenzoylium ion [$PhCS^+$], *m/e* 121, in the mass spectrum of **2** can only be accounted for on the basis of the assigned structure.

Dimethyl acetylenedicarboxylate (DMAD) reacted cleanly with **2** in refluxing xylene (17 h), the pyridinone **6** (R = $COOCH_3$) being obtained in 85% yield. As in other cycloadditions of this type,[2-4] sulfur is postulated to be extruded from the initial cycloadduct **5**.

Alkenic dipolarophiles also underwent ready reaction with **2**. Fumaronitrile required a 96-h reaction period in boiling xylene for complete reaction to occur, and the pyridinone **6** (R = CN) was obtained (93%) by loss of H_2S from the initial 1:1 cycloadduct corresponding to **5**. The chemical shift of the C_{11} proton of **6** (R = CN) was at δ 9.5, an appreciable downfield shift from the chemical shifts of the other aromatic protons. However, in **6** (R = $COOCH_3$), the corresponding proton did not undergo this shift to lower field. A similar phenomenon has been observed[8] with 4-cyanophenanthrene in which the corresponding proton was found as a multiplet at δ 9.9–9.5. In 4-(methoxycarbonyl)- or 4-(ethoxycarbonyl)phenanthrene, no downfield shift of the corresponding proton was observed.[9] These data find a satisfactory rationalization in terms of the deshielding effect exerted by the cyano group and steric interaction altering the preferred conformation of the ester group so that no deshielding of the appropriate proton is observed.

N-Ethylmaleimide (boiling toluene, 65 h) and maleic anhydride (boiling xylene, 24 h) gave thermally stable 1:1 cycloadducts represented by **7** (X = NEt) and **7** (X = O),



respectively, both in 88% yield. The α-imido protons in **7** (X = NEt) occurred as a singlet at δ 4.20, suggesting that they are in an exo configuration where they are deshielded by the bridge sulfur atom.[10] The corresponding protons

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(2) Potts, K. T.; Kanemasa, S. *J. Org. Chem.* **1979**, *44*, 3808.
(3) Potts, K. T.; Kanemasa, S. *J. Org. Chem.* **1979**, *44*, 3803.
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(9) Bartle, K. D.; Smith, J. A. S. *Spectrochim. Acta, Part A* **1967**, *23A*, 1715.
(10) Cava, M. P.; Pollack, N. M. *J. Am. Chem. Soc.* **1966**, *88*, 4112. Potts, K. T.; Baum, J.; Houghton, E. *J. Org. Chem.* **1974**, *39*, 3631.

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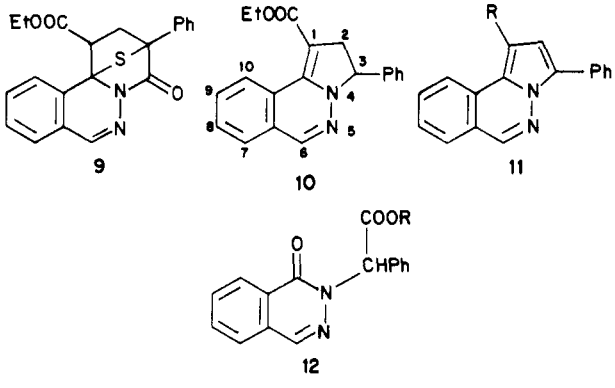
in **7** (X = O) also occurred at δ 4.64.

Cycloadducts of this type usually lose H_2S on heating[2,3] or on treatment with base. For example, the 1:1 cycloadduct from **2** and fumaronitrile was smoothly converted by heat into **6** (R = CN). In refluxing xylene **7** (X = NEt) did not lose H_2S but rather underwent an unanticipated loss of CH_2OS. The resultant product had molecular formula $C_{21}H_{15}N_3O_2$, established from analytical and mass spectral data (M^+· 341 (100%)]. Carbonyl absorptions occurred at 1740 and 1690 cm^{-1}, and NMR data [δ 1.24 (t), 3.62 (q)] indicated the retention of the *N*-ethylmaleimide moiety. Other chemical shifts were all in the aromatic region, with two being found at δ 8.9 (m) and 9.1 (s), significant downfield shifts from the other aromatic protons. These data are consistent with structure **8**, the singlet proton at δ 9.1 being the phthalazine proton adjacent to the nitrogen atom and the multiplet at δ 8.9 being that in the peri position of the phthalazine nucleus being deshielded by the imido carbonyl group. Structure **8** is that anticipated from the reaction of the isomeric mesoionic system **3** and *N*-ethylmaleimide after loss of COS and subsequent aromatization. However, the cycloadditions above exclude structure **3** and as it is highly unlikely that CO would be extruded from the pyridinone system **6**, the elements of COS were most likely extruded as that compound. This would require an oxidation of the initial 1:1 cycloadduct and a subsequent rearrangement similar to that observed previously in the *anhydro*-1-hydroxythiazolo[3,2-*a*]quinolinium hydroxide system.[11]

Reaction of the mesoionic system **2** with ethyl acrylate in boiling xylene (20 h) gave two products, the normal 1:1 cycloadduct **9** and very small amounts of a second product

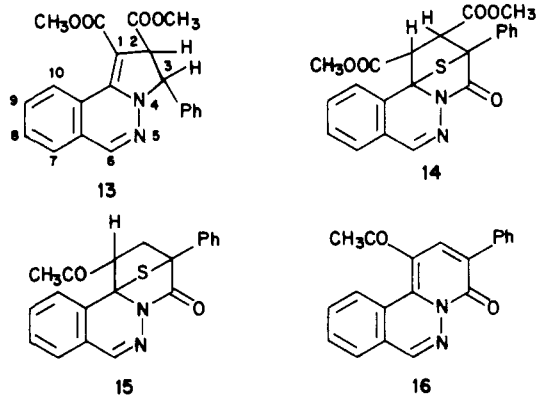


which was related to **9** by loss of the elements of COS. (In one experiment the latter product predominated, but despite repeated attempts, compound **9** was always formed in greater amount.)

The structure of the 1:1 cycloadduct **9** was established from its ^1H NMR spectrum, which consisted of an ABX pattern for the CH_2CH grouping as well as a 16-line ABX_3 pattern due to the prochiral nature of the methylene protons contained in the C_1 ester. By use of *J*-resolved 2-D NMR and ultimate computer simulation of the spectrum,[12] the chemical shifts of the peaks due to the CH_2CH moiety as well as the methylene protons of the C_1 ester were established. 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] (Experimental Section).

The structure of the minor product **10** obtained in the ethyl acrylate reaction was established as follows. Treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) gave the pyrrole ester **11** (R = COOEt), which was hydrolyzed and decarboxylated to **11** (R = H). Due to the small quantity available, only limited spectral and analytical characterizations were possible which did substantiate the assigned structure. Thus, the carboxylic acid **11** (R = COOH) was found to have a consistent molecular formula, by analytical and mass spectral data, and ν_{CO} 1670 cm^{-1}. The decarboxylated product **11** (R = H) gave M^+· 244 (100%), and its NMR spectrum showed that the C_{10}-H shifted back into the normal aromatic region. The structure of **10** was confirmed by the synthesis of its DDQ oxidation product **11** (R = COOEt) in an alternative manner by ring closure of (3,4-dihydro-4-oxophthalazin-3-yl)phenylacetic acid (**12**, R = H) with acetic anhydride in the presence of ethyl propiolate. An intermediate *anhydro*-2-hydroxy-3-phenyloxazolo[2,3-*a*]phthalazinium hydroxide was involved in this reaction followed by loss of CO_2 from the initial 1:1 cycloadduct.

The mesoionic system **2** also reacted with dimethyl fumarate in refluxing xylene (24 h). The residue was separated by HPLC (Prep 500 A, chloroform) into two products. The first compound eluted crystallized as lemon yellow needles (15%), and spectral and analytical data established the structure **13**, which is consistent with the



loss[14] of COS from an initial 1:1 cycloadduct. The second compound isolated (7%) was the 1:1 cycloadduct **14**, and spectral data that established this structure are in the Experimental Section.

The reaction of **2** with methyl vinyl ketone also gave two products. The residue was separated by HPLC (Prep 500 A, chloroform), and the first compound eluted (48%) was the 1:1 cycloadduct **15**. Spectral and analytical data verified this structural assignment, especially the regiochemistry of the cycloaddition. The mass spectrum of **15** had M^+· 348 (22%), and loss of methyl vinyl ketone from the molecular ion gave a fragment corresponding to the radical cation of *anhydro*-3-hydroxy-2-phenylthiazolo-[2,3-*a*]phthalazinium hydroxide (**2**) (*m/e* 278, 100%).

The second compound isolated was obtained as yellow microprisms from ethanol (91% yield). The mass spec-

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

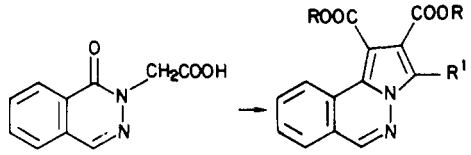
(12) The ^1H NMR simulations were accomplished with the program available for the Varian XL-200 NMR spectrometer. This utilizes the program LAME, which is LACOON with magnetic equivalence added. See Varian Publication No. 87-146-000 Rev. B 780 and references listed therein.

(13) The best fit was obtained for the ABX spin system with chemical shifts (Hz) of A = 538.87, B = 661.91, and X = 741.35 and coupling constants J_{AB} = −12.71, J_{AX} = 7.87, and J_{BX} = 5.00 Hz. The best fit was obtained for the ABX_3 spin system with chemical shifts (Hz) of A = 799.31, B = 766.43, and X = 185.22, coupling constants J_{AB} = −10.84, J_{AX} = 7.17, and J_{BX} = 7.18 Hz, and a peak width of 1.0 Hz at half-height.

(14) Bubbling effluent gases through an alcoholic piperidine solution failed to detect any evolution of carbonyl sulfide in these reactions (Seibert, W. *Angew. Chem.* **1959**, *71*, 194).

trum of **16** showed $M^{+\cdot}$ 314 (100%), and the formation of **16** is consistent with the loss of the elements of H_2S (*m/e* 34) from the initial 1:1 cycloadduct.

The synthesis of (3,4-dihydro-4-oxophthalazin-3-yl)-phenylacetic acid (**12**, R = H) was accomplished from the phthalazinone, NaH in benzene, and ethyl α-bromophenylacetate at reflux temperature overnight. (Use of α-bromophenylacetic acid/dimethylacetamide[15] was unsuccessful.) The N-alkylated product (**12**, R = Et) was hydrolyzed (90%) to the acid **12** (R = H) in a hot 1:1 mixture of dioxane and concentrated HCl. In contrast, (3,4-dihydro-4-oxophthalazin-3-yl)acetic acid (**17**) was ob-



17 **18**

tained from 1(2*H*)-phthalazinone with 2 equiv of NaH in DMF and bromoacetic acid in 90% yield. These substituted acetic acids on heating with Ac_2O in the presence of DMAD or DEAD (diethyl acetylenedicarboxylate) readily gave the corresponding dialkyl pyrrolo[2,1-*a*]-phthalazine-1,2-dicarboxylate **18** (R = Me; R^1 = H) and **18** (R = Et; R^1 = H and Ph) (Experimental Section).

Experimental Section[16]

***anhydro*-3-Hydroxy-2-phenylthiazolo[2,3-*a*]-phthalazinium Hydroxide (2). Method A.** α-Bromophenylacetyl chloride (18.0 g, 0.077 mol) in dry ether (150 mL) was added dropwise with stirring to a solution of 1(2*H*)-phthalazinethione[6] (**1**; 12.5 g, 0.077 mol) in dry ether (900 mL). After 15 min, Et_3N (15.6 g, 0.154 mol) was added slowly with stirring at room temperature. The dark red crystalline product that separated was washed with 10% aqueous Na_2CO_3 solution (100 mL), followed by distilled water (3 × 100 mL), finally yielding after recrystallization from $CHCl_3$/cyclohexane dark red needles: 19.4 g (91%); mp 262–264 °C; IR (KBr) ν_{CO} 1633, $\nu_{C=N}$ 1590 cm^{-1}; λ_{max} (dioxane) 533 nm (log ε 4.12), 281 (4.18); ^1H NMR (Me_2SO-d_6) δ 6.8–8.7 (m, 9, aromatic), 9.4 (s, 1, C_6-H); mass spectrum, *m/e* (% relative intensity) 278 (32) $[M^{+\cdot}]$, 121 (100) $[PhCS]^+$.

Anal. Calcd for $C_{16}H_{10}N_2OS$: C, 69.05; H, 3.62; N, 10.06. Found: C, 69.11; H, 3.74; N, 10.03.

Method B. *S*-(1-Phthalazinyl)-α-phenylthioglycolic Acid (4). 1(2*H*)-Phthalazinethione (**1**; 1.6 g, 0.01 mol) was dissolved in dry THF (25 mL). α-Bromophenylacetic acid (2.2 g, 0.01 mol) dissolved in dry THF (10 mL) was added with stirring followed by Et_3N (1.0 g, 0.01 mol). After 1 h, the reaction mixture was concentrated and partitioned between ether and water; the ether layer was washed with water and then saturated with aqueous NaCl. After drying (Na_2SO_4), the ether was concentrated. The residue crystallized from isopropyl alcohol, affording pale orange prisms: 1.2 g (40%); mp 165–166 °C dec; IR (KBr) ν_{OH} 3600–3300 (br), ν_{CO} 1710 cm^{-1}; λ_{max} (dioxane) 295 nm (log ε 2.96), 258 (sh) (2.77); ^1H NMR (Me_2SO-d_6) δ 5.93 (s, 1, C_α-H), 7.2–8.4 (m, 9, aromatic), 9.50 (s, 1, C_4-H); mass spectrum, *m/e* (% relative intensity) 296 (0.2) $[M^{+\cdot}]$, 219 (100).

Anal. Calcd for $C_{16}H_{12}N_2O_2S$: C, 64.85; H, 4.08; N, 9.45. Found: C, 64.60; H, 4.28; N, 9.27.

The above thioglycolic acid **4** (0.25 g, 0.0084 mol) was added to a mixture of Ac_2O (2 mL) and Et_3N (2 mL). After the mixture was stirred for 15 min, anhydrous ether was added (10 mL). The dark red crystals of **2** (0.2 g, 85%) crystallized from $CHCl_3$/cyclohexane, giving dark red needles, mp 261–263 °C, identical[17] with **2** above.

Hydrolysis of *anhydro*-3-Hydroxy-2-phenylthiazolo[2,3-*a*]phthalazinium Hydroxide (2). The mesoionic system **2** (2.0 g, 0.0072 mol) was refluxed for 24 h in 1 M HCl (25 mL). After evaporation of the acid, the residue crystallized from isopropyl alcohol, affording pale orange prisms: 0.9 g (43%); mp 165–167 °C dec, identical[17] with **4** above.

Dimethyl 4-Oxo-3-phenyl-4*H*-pyrido[2,1-*a*]phthalazine-1,2-dicarboxylate (6, R = $COOCH_3$). The ester **6** (R = $COOCH_3$) was obtained from **2** (2.8 g, 0.01 mol) and DMAD (1.5 g, 0.011 mol) after 17-h reflux in dry xylene (50 mL). The xylene was evaporated, and the residue was crystallized from methanol and then from ethyl acetate, affording yellow prisms: 3.3 g (85%); mp 268–270 °C dec; IR (KBr) ν_{CO} 1740, 1700, 1665 cm^{-1}; λ_{max} (dioxane) 404 nm (log ε 4.23), 304 (4.21), 297 (4.15); ^1H NMR (Me_2SO-d_6) δ 3.58 (s, 3, CH_3), 3.87 (s, 3, CH_3) 7.2–8.4 (m, 9, aromatic), 9.1 (s, 1, C_7-H); mass spectrum, *m/e* (% relative intensity) 388 (59) $[M^{+\cdot}]$, 329 (100).

Anal. Calcd for $C_{22}H_{16}N_2O_5$: C, 68.04; H, 4.15; N, 7.21. Found: C, 68.07; H, 4.09; N, 7.35.

1,2-Dicyano-3-phenyl-4*H*-pyrido[2,1-*a*]phthalazin-4-one (6, R = CN). The dicyano compound **6** (R = CN) was obtained from **2** (4.0 g, 0.014 mol) and fumaronitrile (1.2 g, 0.015 mol) after 96-h reflux in dry xylene (50 mL). The xylene was evaporated, and the residue was recrystallized from methanol, affording bright yellow needles: 4.2 g (93%); mp 283–284 °C; IR (KBr) ν_{CN} 2210, ν_{CO} 1700 cm^{-1}; λ_{max} (dioxane) 430 (sh) nm (log ε 4.19), 412 (4.25), 308 (4.04), 288 (4.02); ^1H NMR (Me_2SO-d_6) δ 7.3–8.5 (m, 8, aromatic), 9.3 (s, 1, C_7-H), 9.5 (m, 1, C_{11}-H); mass spectrum, *m/e* (% relative intensity) 322 (49) $[M^{+\cdot}]$, 43 (100).

Anal. Calcd for $C_{20}H_{10}N_4O$: C, 74.53; H, 3.13; N, 17.38. Found: C, 74.45; H, 3.18; N, 17.35.

***N*-Ethylmaleimide Cycloadduct of 2.** The mesoionic system **2** (2.5 g, 0.009 mol) and *N*-ethylmaleimide (1.3 g, 0.01 mol) were refluxed in dry toluene (50 mL) for 65 h. The toluene was evaporated, and the residue was recrystallized from isopropyl acetate and then from methanol, affording pink prisms of **7** (X = NEt): 3.2 g (88%); mp 237–238 °C dec; IR (KBr) ν_{CO} 1780, 1720, 1690 cm^{-1}; λ_{max} (dioxane) 322 nm (log ε 3.21), 285 (3.10); ^1H NMR (Me_2SO-d_6) δ 0.8–1.3 (t, 3, CH_3), 3.2–3.8 (q, 2, CH_2), 4.2 (s, 2, C_1-H, C_2-H), 7.2–8.0 (m, 9, aromatic), 8.2 (s, 1, C_7-H); mass spectrum, *m/e* (% relative intensity) 403 (2) $[M^{+\cdot}]$, 278 (100).

Anal. Calcd for $C_{22}H_{17}N_3O_3S$: C, 65.49; H, 4.25; N, 10.41. Found: C, 65.33; H, 4.14; N, 10.29.

Maleic Anhydride Cycloadduct of 2. The mesoionic compound **2** (2.8 g, 0.01 mol) and maleic anhydride (1.1 g, 0.011 mol) were refluxed in dry xylene (50 mL) for 24 h. The xylene was evaporated, and the residue was crystallized from methanol and then from ethyl acetate, affording salmon prisms of **7** (X = O): 3.0 g (88%); mp 208–209 °C dec; IR (KBr) ν_{CO} 1870, 1830, 1780, 1720 cm^{-1}; λ_{max} (dioxane) 318 nm (log ε 3.84), 284 (3.75); ^1H NMR (Me_2SO-d_6) δ 7.1–7.8 (m, 9, aromatic), 8.07 (s, 1, C_7-H), 4.64 (s, 2, C_1-H, C_2-H); mass spectrum, *m/e* (% relative intensity) 376 (0.2) $[M^{+\cdot}]$, 54 (100).

Anal. Calcd for $C_{20}H_{12}N_2O_4S$: C, 63.82; H, 3.21; N, 7.44. Found: C, 63.91; H, 3.18; N, 7.42.

Thermal Decomposition Product of 7 (X = NEt). The cycloadduct **7** (X = NEt) (1.0 g, 0.002 mol) was refluxed in dry xylene (50 mL) for 19 h. The solvent was evaporated, the residue crystallizing from isopropyl acetate, affording light brown needles of **8**: 0.2 g (24%); mp 208–210 °C; IR (KBr) ν_{CO} 1740, 1690 cm^{-1}; λ_{max} (dioxane) 358 nm (log ε 3.96), 270 (4.60); ^1H NMR (Me_2SO-d_6) δ 1.24 (t, 3, CH_3), 3.62 (q, 2, NCH_2), 7.0–8.7 (m, 8, aromatic), 8.9 (m, 1, C_{10}-H), 9.1 (s, 1, C_6-H); mass spectrum, *m/e* (% relative intensity) 341 (100) $[M^{+\cdot}]$, 326 (50).

Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.64; H, 4.59; N, 12.14.

(15) Huisgen, R.; Funke, E.; Schaefer, F. C.; Gotthardt, H.; Brunn, E. *Tetrahedron Lett.* **1967**, 1809. Funke, E.; Huisgen, R.; Schaefer, F. C. *Chem. Ber.* **1971**, *104*, 1550. Smith, R. C.; Otremba, E. D. *J. Org. Chem.* **1962**, *27*, 879.

(16) Spectral characterizations were carried out with the following instrumentation: IR, Perkin-Elmer 467 spectrophotometer; NMR, Varian HA-100 and XL-200 spectrometers using Me_4Si as an internal standard; UV, Cary 15 spectrophotometer; MS, JEOL JMS-01SC mass spectrometer at 70 eV using a direct-insertion probe with a source temperature of 200 °C; ^{13}C, Jeol FX 60 spectrometer using Me_4Si as an internal standard. Evaporations were done under reduced pressure using a Rotovap apparatus, and melting points were determined in capillaries. Analyses were by Galbraith Laboratories, Inc., Knoxville, TN.

(17) Identity was established by using superimposable IR spectra, mixture melting points, and R_f values as criteria.

Reaction of 2 with Ethyl Acrylate. Formation of 9 and 10. The mesoionic system **2** (2.78 g, 0.01 mol) and ethyl acrylate (1.00 g, 0.01 mol) were refluxed for 20 h in dry xylene (50 mL). The xylene was removed under reduced pressure and the residue separated by HPLC ($CHCl_3$ eluent). Two compounds were isolated. The 1:1 cycloadduct **9** was obtained as colorless needles from EtOH: 2.27 g (60%); mp 190–192 °C dec; IR (KBr) ν_{CO} 1725 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.93 (t, 3, J_{AX} = 7.17 Hz, J_{BX} = 7.18 Hz, OCH_2CH_3), 2.69 (dd, 1, J_{AB} = −12.71 Hz, J_{AX} = 7.87 Hz, CH_2CH), 3.31 (dd, 1, J_{AB} = −12.71 Hz, J_{BX} = 5.00 Hz, CH_2CH), 3.71 (dd, 1, J_{AX} = 7.17 Hz, J_{BX} = 5.00 Hz, CH_2CH), 3.83 (2 q, 1, J_{AB} = −10.84 Hz, J_{BX} = 7.18 Hz, OCH_2CH_3), 4.00 (2 q, 1, J_{AB} = −10.84 Hz, J_{AX} = 7.17 Hz, OCH_2CH_3), 7.25–7.62 (m, 9, aromatic), 7.72 (s, 1, C_7-H); ^{13}C NMR ($CDCl_3$) 170.6, 169.7, 142.8, 133.7, 131.8, 130.4, 129.3, 128.9, 128.7, 128.4, 127.3, 125.4, 124.1, 76.9, 67.0, 61.3, 65.6, 38.3, 13.7 ppm; ^{13}C APT 2 × CO, 1 × HC=N, 5 × C, 7 × aromatic CH, 1 × aliphatic CH, 2 × CH_2, 1 × CH_3; 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, 66.65; H, 4.80; N, 7.38.

The second compound, **10**, was generally isolated as a minor product from the above reaction. In one reaction, however, the mesoionic system **2** (4.0 g, 0.014 mol) and ethyl acrylate (1.5 g, 0.015 mol) were refluxed for 20 h in dry xylene (50 mL). The solvent was evaporated, the residue crystallizing from isopropyl acetate, affording orange prisms of **10**: 2.0 g (42%); mp 124–126 °C; IR (KBr) ν_{CO} 1655, $\nu_{C=N}$ 1580 cm^{-1}; λ_{max} (dioxane) 390 nm (log ϵ 3.14), 298 (4.01), 291 (3.98), 270 (3.84), 255 (2.86); ^1H NMR ($CDCl_3$) δ 1.24 (t, 3, CH_3), 2.91 (q, 1, J = 16.0 Hz, C_2-H), 3.54 (q, 1, J = 16.0 Hz, C_2-H), 4.14 (q, 2, J = 8.0 Hz, OCH_2), 5.30 (q, 1, J = 8.0 Hz, C_3-H), 6.98–7.91 (m, 9, aromatic), 9.78 (m, 1, C_{10}-H); mass spectrum, *m/e* (% relative intensity) 318 (92) [M^{+}·], 245 (100).

Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.15; H, 5.74; N, 8.72.

Ethyl 3-Phenylpyrrolo[2,1-*a*]phthalazine-1-carboxylate (11, R = COOEt). The product **10** (0.213 g, 0.000 67 mol) and DDQ (0.16 g, 0.0074 mol) were refluxed in dioxane (20 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 obtained as tan plates from *i*-PrOH: 0.2 g (94%); mp 108–110 °C; IR (KBr) ν_{CO} 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (t, 3, J = 7.10 Hz, OCH_2CH_3), 4.44 (q, 2, J = 7.10 Hz, OCH_2CH_3), 8.10–7.32 (m, 9, aromatic), 8.52 (s, 1, C_2-H), 10.02–9.68 (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, 75.69; H, 5.24; N, 8.79.

Alternative Synthesis of Ethyl 3-Phenylpyrrolo[2,1-*a*]phthalazine-1-carboxylate (11, R = COOEt). A mixture of (3,4-dihydro-4-oxophthalazin-3-yl)phenylacetic acid (**12**, R = H) (0.5 g, 0.0018 mol), Ac_2O (0.4 g, 0.004 mol), and ethyl propiolate (0.4 g, 0.004 mol) was refluxed in dry xylene (15 mL) under an atmosphere of dry N_2 for 18 h. The solvent was removed, and the residue was recrystallized from EtOH, affording the product as fawn microprisms: 0.4 g (70%); mp 108–110 °C, identical[17] with **11** (R = COOEt) above.

3-Phenylpyrrolo[2,1-*a*]phthalazine-1-carboxylic Acid (11, R = COOH). Ethyl 3-phenylpyrrolo[2,1-*a*]phthalazine-1-cawrboxylate (**11**, R = COOEt) (80 mg, 0.000 25 mol) was dissolved in EtOH (20 mL) with warming. To this solution was added 10% NaOH in 50% EtOH/H_2O (excess) and the mixture heated 1 h on a steam bath. Upon acidification with concentrated HCl and cooling, a precipitate formed, which was collected by filtration and washed with water. Recrystallization from EtOH afforded the product as yellow microcrystals: 60 mg (75%); mp 241 °C dec; IR (KBr) ν_{CO} 1670 cm^{-1}.

Anal. Calcd for $C_{18}H_2N_2O_2$: C, 74.99; H, 4.20; N, 9.72. Found: C, 74.94; H, 4.20; N, 9.71.

3-Phenylpyrrolo[2,1-*a*]phthalazine (11, R = H). The above carboxylic acid (**11**, R = COOH) (32 mg, 0.000 11 mol) was heated to 240 °C under aspirator vacuum until evolution of CO_2 ceased. The residue was separated by HPLC ($CHCl_3$ eluent): ^1H NMR ($CDCl_3$) δ 8.23–7.15 (m, 11, aromatic), 8.35 (s, 1, C_6H); mass spectrum, *m/e* (% relative intensity) 244 (100) [M^{+}·].

Ethyl α-Phenyl(1-oxophthalazin-2-yl)acetate (12, R = Et). 1(2*H*)-Phthalazinone (5.0 g, 0.03 mol) and NaH (1.6 g, 0.03 mol) were refluxed together in dry benzene (50 mL) for 1 h. The reaction mixture was cooled to room temperature, ethyl α-bromophenylacetate (8.3 g, 0.03 mol) was added, and the mixture was refluxed overnight. After the usual reaction workup the product was obtained as colorless irregular prisms from anhydrous ether: 5.2 g (50%); mp 103–104 °C; IR (KBr) ν_{CO} 1715, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (t, 3, J = 7.2 Hz, OCH_2CH_3), 4.28 (q, 2, J = 7.2 Hz, OCH_2CH_3), 6.90 (s, 1, CH), 7.2–8.5 (m, 9, aromatic); mass spectrum, *m/e* (% relative intensity) 308 (100) [M^{+}·].

Anal. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.08. Found: C, 70.05; H, 5.25; N, 9.07.

α-Phenyl(1-oxophthalazin-2-yl)acetic Acid (12, R = H). The above ester **12** (R = Et) (5.0 g, 0.016 mol) was added to a 10% solution of NaOH and warmed until all the solid had dissolved. The product separated upon acidification with concentrated HCl. The product was recrystallized from a 1:1 mixture of ethanol and H_2O: IR (KBr) ν_{OH} 2650–2100, ν_{CO} 1680 cm^{-1}; ^1H NMR (unisolv) δ 6.77 (s, 1, CH), 7.2–8.5 (m, 10, aromatic); mass spectrum, *m/e* (% relative intensity) 280 (100) [M^{+}·].

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 9.99. Found: C, 68.43; H, 4.36; N, 9.96.

Reaction of 2 with Dimethyl Fumarate. Formation of 13 and 14. The mesoionic systems **2** (1.0 g, 0.0036 mol) and dimethyl fumarate (0.8 g, 0.006 mol) were refluxed in dry xylene (50 mL) for 24 h. The xylene was removed and the residue separated by HPLC ($CHCl_3$ eluent). Two compounds were isolated. The first eluted compound, **13**, was obtained as lemon yellow needles from CH_3OH: 0.2 g (15%); mp 145–146 °C; IR (KBr) ν_{CO} 1735, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.71 (s, 3, $COOCH_3$), 3.80 (s, 3, $COOCH_3$), 4.07 (d, 2, J = 5.4 Hz, C_2-H), 5.41 (d, 2, J = 5.4 Hz, C_3-H), 7.94–7.08 (m, 9, aromatic), 10.15–9.72 (m, 1, C_{10}-H); mass spectrum, *m/e* (% relative intensity) 362 (31) [M^{+}·], 303 (100), [M^{+}· − $COOCH_3$)].

Anal. Calcd for $C_{21}H_{18}N_2O_4$: C, 69.60; H, 5.01; H, 7.73. Found: C, 69.54; H, 5.03; N, 7.70.

The second compound, **14**, was obtained as colorless prisms from CH_3OH: 0.1 g (7%); mp 148 °C dec; IR (KBr) ν_{CO} 1750, 1730 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.47 (s, 3, $COOCH_3$), 3.63 (s, 3, $COOCH_3$), 4.08 (d, 2, J = 5.0 Hz, CH), 4.59 (d, 2, J = 5.0 Hz, CH), 7.28–7.16 (m, 1, aromatic), 7.60–7.42 (m, 6, aromatic), 7.92–7.78 (m, 3, aromatic); mass spectrum, *m/e* (% relative intensity) 422 (16) [M^{+}·], 278 (100).

Anal. Calcd for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N, 6.63. Found: C, 62.58; H, 4.35; N, 6.59.

Reaction of Methyl Vinyl Ketone with 2. Formation of 15 and 16. The mesoionic system **2** (1.0 g, 0.0036 mol) was refluxed in methyl vinyl ketone (40 mL) (excess) until all red color disappeared (6 h). The solvent was removed and the residue separated by HPLC ($CHCl_3$ eluent). Two compounds were isolated. The first product eluted, compound **15**, was obtained as colorless needles from EtOH: 0.6 g (48%); mp 168–174 °C dec; IR (KBr) ν_{CO} 1730, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.73 (s, 3, $COCH_3$), 2.53 (dd, 1, C_2-H), 3.27 (dd, 1, C_2-H), 3.97 (dd, 1, C_1-H), 7.93–7.12 (m, 10, aromatic); mass spectrum, *m/e* (% relative intensity) 348 (7) [M^{+}·], 278 (100).

Anal. Calcd for $C_{20}H_{16}N_2O_2S$: C, 68.95; H, 4.63; N, 8.04. Found: C, 68.90; H, 4.67; N, 8.03.

The second product, compound **16**, was obtained as yellow microcrystals from EtOH: 0.1 g (9%), mp 274–276 °C dec; IR (KBr) ν_{CO} 1700, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.92 (s, 3, COCH3), 8.10–7.08 (m, 9, aromatic), 8.47–8.16 (m, 1, C_{11}-H), 8.73 (s, 1, C_7-H); mass spectrum, *m/e* (% relative intensity) 314 (100) [M^{+}·].

Anal. Calcd for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.30; H, 4.55; N, 8.55.

(3,4-Dihydro-4-oxophthalazin-3-yl)acetic Acid (17). A mixture of NaH (3.3 g, 0.14 mol) in dry DMF (50 mL) was treated with 1(2*H*)-phthalazinone (5.0 g, 0.034 mol) in small portions while the temperature was maintained below 35 °C. After the evolution of H_2 gas had subsided, bromoacetic acid (4.75 g, 0.034 mol) was added in small portions with occasional cooling in an ice–water bath to maintain the temperature below 35 °C. The reaction mixture was stirred overnight and then poured into an ice–water mixture; the material that separated was filtered off. The filtrate was cooled in an ice–water bath and acidified with concentrated

HCl. The product was collected and dried: 6.2 g (90%). The white powder crystallized from methanol as colorless needles: mp 227–228 °C; IR (KBr) ν_{OH} 2880, ν_{CO} 1730, 1630 cm^{-1}; ^{1}H NMR (unisolv) δ 5.13 (s, 2, CH_2), 8.09–8.60 (m, 5, aromatic); mass spectrum, m/e (% relative intensity) 204 (33) [M$^{+\cdot}$], 159 (100) [M$^{+\cdot}$ – CO_2H].

Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.83; H, 3.95; N, 13.71. Found: C, 58.86; H, 3.95; N, 13.71.

Dimethyl Pyrrolo[2,1-*a*]phthalazine-1,2-dicarboxylate (18, R = CH_3; R^1 = H). In a flame-dried reaction flask that was flushed with dry N_2, (3,4-dihydro-4-oxophthalizin-3-yl)acetic acid (**17**) (1.0 g, 0.0049 mol), DMAD (0.69 g, 0.0049 mol), and Ac_2O (0.5 g, 0.0049 mol) were refluxed in dry xylene under an atmosphere of dry N_2 for 3–4 h. The xylene was removed by vacuum distillation. Trituration of the residue with anhydrous ether yielded a yellowish powder. Filtration and recrystallization from methanol gave colorless spears: 1.2 g (86%); mp 146–147 °C; IR (KBr) ν_{CO} 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.84 (s, 3, OCH_3), 3.95 (s, 3, OCH_3), 7.5–8.6 (m, 4, aromatic); mass spectrum, m/e (% relative intensity) 284 (100) [M$^{+\cdot}$], 257 (94) (M$^{+\cdot}$ – HCN).

Anal. Calcd for $C_{15}H_{12}N_2O4$: C, 63.38; H, 4.26; N, 9.85. Found: C, 63.29; H, 4.26; N, 9.85.

Similarly, **diethyl pyrrolo[2,1-*a*]phthalazine-1,2-dicarboxylate (18, R = Et; R^1 = H)** was prepared from (3,4-dihydro-4-oxophthalazin-3-yl)acetic acid (**17**) (1.0 g, 0.0049 mol), DEAD (0.83 g, 0.0049 mol), and Ac_2O (0.50 g, 0.0049 mol). It crystallized from ethanol, yielding pale yellow spears: 0.61 g (40%); mp 102–103 °C; IR (KBr) ν_{CO} 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.37 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.42 (t, 3, J = 7.2 Hz, OCH_2CH_3), 4.37 (q, 2, J = 7.2 Hz, OCH_2CH_3), 4.49 (q, 2, J = 7.20 Hz, OCH_2CH_3), 7.24–8.55 (m, 6, aromatic); mass spectrum, m/e (% relative intensity) 312 (100) [M$^{+\cdot}$].

Anal. Calcd for $C_{17}H_{16}N_2O_4$: C, 65.38; H, 5.16; N, 8.97. Found: C, 65.35; H, 5.16; N, 8.97.

Diethyl 3-Phenylpyrrolo[2,1-*a*]phthalazine-1,2-dicarboxylate (18, R = Et; R^1 = Ph). Under reaction conditions analogous to those above, α-phenyl(3,4-dihydro-4-oxophthalazin-3-yl)acetic acid (**12**) (1.0 g, 0.004 mol), DEAD (0.68 g, 0.004 mol), and Ac_2O (0.6 mL, 0.004 mol) were refluxed in dry xylene under an atmosphere of dry N_2 for 6–8 h. On reaction workup the product was recrystallized from ethanol, yielding colorless spears: 1.3 g (85%); mp 114–115 °C; IR (KBr) ν_{CO} 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.19 (t, 3, J = 7.2 Hz, OCH_2CH_3), 1.43 (t, 3, J = 7.2 Hz, OCH_2CH_3), 4.24 (q, 2, J = 7.2 Hz, OCH_2CH_3), 4.47 (q, 2, J = 7.2 Hz, OCH_2CH_3), 7.50–7.83 (m, 8, aromatic), 8.45 (s, 1, C_6-H), 9.0 (m, 1, C_{10}-H); mass spectrum, m/e (% relative intensity) 388 (100) [M$^{+\cdot}$].

Anal. Calcd for $C_{23}H_{20}N_2O_4$: C, 71.12; H, 5.19; N, 7.21. Found: C, 71.09; H, 5.20; N, 7.18.

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Registry No. 1, 16015-46-6; 2, 94392-53-7; 4, 95647-35-1; 6 (R = CN), 95647-36-2; 6 (R = COOEt), 95647-53-3; 7 (X = NEt), 95647-37-3; 7 (X = O), 95647-38-4; 8, 95647-39-5; 9, 95647-40-8; 10, 95647-41-9; 11 (R = H), 82027-00-7; 11 (R = COOEt), 95647-42-0; 11 (R = CO_2H), 95647-44-2; 12 (R = H), 95647-43-1; 12 (R = Et), 95647-45-3; 13, 95647-46-4; 14, 95647-47-5; 15, 95647-48-6; 16, 95647-49-7; 17, 90689-39-7; 18 (R = CH_3, R^1 = H), 95647-50-0; 18 (R = Et, R^1 = H), 95647-51-1; 18 (R = Et, R^1 = Ph), 95647-52-2; DMAD, 762-42-5; DEAD, 762-21-0; PhCHBrCOCl, 19078-72-9; $PhCHBrCO_2H$, 4870-65-9; (*E*)-NCCH=CHCN, 764-42-1; CH_2=CHCOOEt, 140-88-5; HC≡CCOOEt, 623-47-2; PhCHBrCOOEt, 2882-19-1; (*E*)-CH_3OCOCH=CHCOOCH_3, 624-49-7; CH_2=CHCOCH_3, 78-94-4; $BrCH_2CO_2H$, 79-08-3; *N*-ethylmaleimide, 128-53-0; maleic anhydride, 108-31-6; 1(2*H*)-phthalazinone, 119-39-1.

Supplementary Material Available: Selected NMR spectra (1 page). Ordering information is given on any current masthead page.

Photochemistry of the Thioimide Systems: Imide–Thietanes[1]

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General photochemical behavior of cyclic thioimides, nitrogen–thiocarbonyl systems, was studied. The dithioimides were inert to the Norrish type I and II reactions in contrast to the behavior of their oxygen analogues (imides) and nitrogen-lacking counterparts (thiones). However, various aliphatic and aromatic di- and monothioimides underwent intermolecularly efficient photocycloaddition with olefins to afford the imide–thietanes in good yields.

The well-known carbonyl photochemistry has been extended to a nitrogen–carbonyl photochemistry by exploring excited reactivities of the imide system,[2] in which a carbonyl chromophore is in conjunction with an amide group. On the other hand, changing a key element in the ketone chromophore from oxygen to sulfur led to the unique thione photochemistry.[3,4] Obviously a new combination of functional groups leads to a new reactive system, also in excited-state pathways. To develop a frontier of organic photochemistry, we have explored a new amalgamation of such a key chromophore and a kety atom, i.e., imide and sulfur. In the present paper we wish to outline general photochemical behavior of cyclic thioimides, a nitrogen–thiocarbonyl system.

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