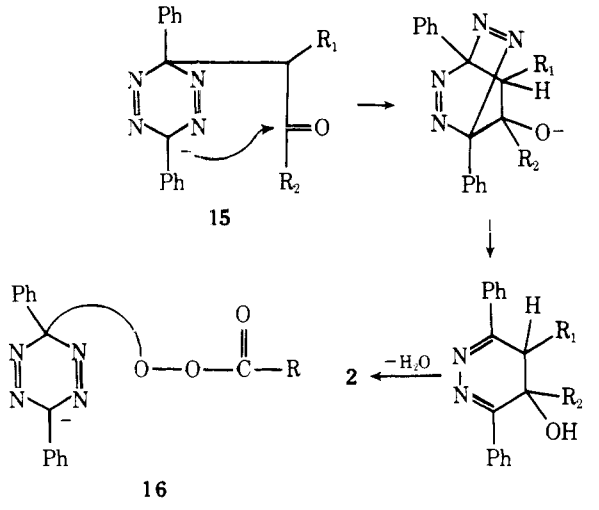
Scheme I



reactivity of the cyclic ketones increased with decreasing ring size. Moreover, cyclic ketones were more reactive than their open-chain analogues, but less reactive than aldehydes. Although we prefer a stepwise mechanism that involves intermediate **15** for the reaction of **1** with enolate anions (Scheme I), the possibility of a Diels–Alder reaction with "inverse" electron demand cannot be excluded. The latter has been advanced[2] as the mechanism through which vinyl ethers, vinyl esters, ketene acetals, ketene aminals, and enamines react with **1**.

Furthermore, we found that **1** (R = Ph) reacted instantaneously with peracids or peroxides, in base, to give 2,5-diphenyl-1,3,4-oxadiazole in good yield. The latter compound was obtained by Hancock[5] and co-workers in a reaction of **1** (R = Ph) were peracetic acid (24 h). It is likely that the remarkable enhancement of the rate of the former reaction is due to the availability of the peracid anion, which initiates the nucleophilic attack on the relatively electron-poor tetrazine to give intermediate **16**. The hydrolysis of **1** (R = Ph) with base to give benzoylbenzaldehyde hydrazone (PhCH=NNHCOPh) can be envisaged to proceed by an analogous mechanism and therefore renders the mechanism of Libman and Slack[6] untenable.

The merits of the present method become apparent when compared with some of the literature methods for the preparation of pyridazines **3, 4,** and **7,** which were obtained after heating for 50, 70 h, and 3 days, respectively.[1,3,4]

The generality of the reaction of **1** (R = Ph or 2-pyridyl) with enolate anion seems to be subject to steric effects. It was found that pinacolone and 1-adamantyl methyl ketone did not react with **1** under the conditions of the reaction. Nevertheless, the present method provides a convenient route into the preparation of a large number of substituted pyridazines, some of which are inaccessible by other methods.

Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were taken as KBr discs using Perkin-Elmer 257 or 621 grating infrared spectrophotometers. Merck silica gel $60PF_{254}$ was used in TLC. Elemental analyses were performed by F. Pascher, W. Germany.

3,6-Diphenyl-1,2,4,5-tetrazine (1, R = Ph) was prepared in 37% yield according to the literature[7] method with a slight modification where the product was leached with carbon disulfide to remove elemental sulfur.

General Procedure for the Preparation of Pyridazines 3–14. 3,6-Diphenyl-1,2,4,5-tetrazine (0.25 g, 1.1 mmol) and the appropriate aldehyde or ketone (2.2 mmol) were mixed with dry peroxide-free tetrahydrofuran (10 mL). The mixture was magnetically stirred at room temperature, and a solution (1 mL) of 2.5% methanolic potassium hydroxide was added to it. In most of the cases the reaction ensued immediately, and the termination of the reaction was indicated by the cessation of nitrogen evolution and the discharge of the violet-red color of the tetrazine. The solvent was evaporated, and the resulting residue was washed with water (40 mL), collected by suction filtration, dried, and recrystallized from the appropriate solvent, usually ethanol or methanol–water.

The strong bands of the infrared spectra of the new pyridazines are as follows. **5**: 1583, 1443, 1397, 772, 756, 694 cm^{-1}. **6**: 1449, 1398, 1106, 1058, 990, 779, 761, 715, 708 cm^{-1}. **8**: 1400, 769, 740, 706 cm^{-1}. **9**: 1380, 1020, 760, 710 cm^{-1}. **10**: 1375, 780, 707 cm^{-1}. **12**: 2915, 1375, 756, 694 cm^{-1}. **13**: 1548, 1478, 1447, 1070, 790, 720, 697 cm^{-1}. **14**: 2940, 1376, 742, 688 cm^{-1}.

Registry No.—**1** (R = Ph), 6830-78-0; **3,** 891-22-5; **4,** 2242-68-4; **5,** 3238-12-8; **6,** 68629-91-4; **7,** 2272-58-4; **8,** 68629-92-5; **9,** 23063-11-8; **10,** 68629-73-2; **11,** 2272-61-9; **12,** 68629-74-3; **13,** 68629-75-4; **14,** 68629-76-5; acetaldehyde, 75-07-0; propanal, 123-38-6; butanal, 123-72-8; 1,1-dimethoxy-2-propanone, 6342-56-9; benzeneacetaldehyde, 122-78-1; acetophenone, 98-86-2; acetone, 67-64-1; benzenepropanal, 104-53-0; 2-butanone, 78-93-3; 3-pentanone, 96-22-0; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; cyclooctanone, 502-49-8.

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1-Benzoyl-2-thiobiuret: Rearrangement and Cyclization

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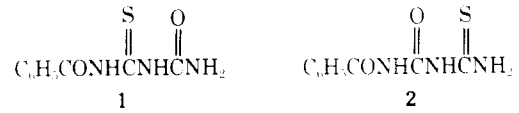
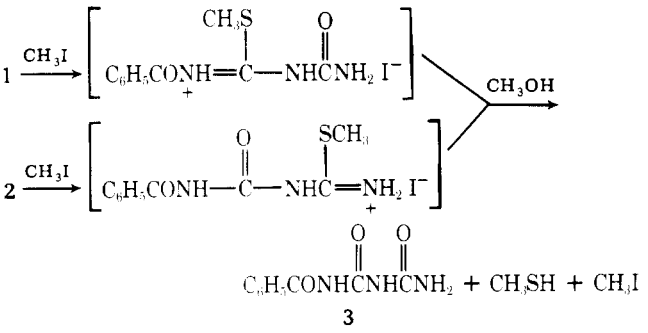
Received September 19, 1978

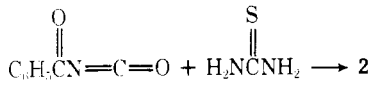
In attempting a water recrystallization of 1-benzoyl-2-thiobiuret (**1**), a yellow crystalline compound melting at 171–173 °C, we observed the formation of a white material (**2**) melting at 230–231 °C. Complete conversion of **1** to **2** could be effected by heating an aqueous suspension of the former compound for ca. 16 h. Elemental analysis and mass spectrometry established that the white compound was isomeric with **1** whereas a positive ammoniacal silver nitrate test indicated the retention of the thioureido moiety. These considerations suggested that the new isomer might be 1-benzoyl-4-thiobiuret (**2**).

The arrangement of the carbon–nitrogen skeleton of the isomer was established by conversion of **1** and **2** to their *S*-methiodide derivatives which then underwent methanolysis to yield 1-benzoylbiuret (**3**). This type of reaction has been observed to occur in activated thioureas.[1]





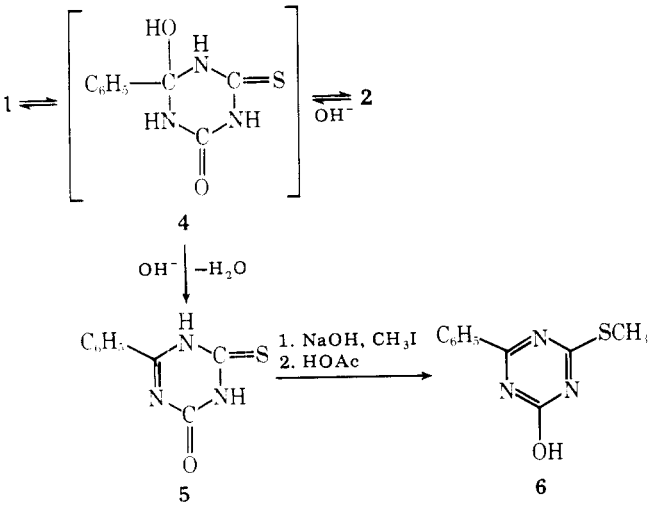
The unequivocal synthesis of 1-benzyl-4-thiobiuret was undertaken employing the method of Nuridzhanyan and Kuznetsova[2] in which benzoyl isocyanate[3] was allowed to react with thiourea. The material obtained by us was identical in all respects to **2**. However, the product did not melt at 165–166



°C as reported by the Soviet authors but rather almost 70 °C higher. No obvious explanation has been found to account for this discrepancy.

The formation of **2** may be rationalized as occurring by the intermediacy of the cyclic structure **4** resulting from attack of the terminal amino group on the benzoyl carbonyl carbon followed by ring opening. The failure of the cycloreversion of **2** to **1** is probably due to the lower nucleophilicity of the thiourea-type amino group in **2** relative to the urea type in **1**. Evidence for this difference in nucleophilicities is our observation that benzoyl isothiocyanate reacts with urea to give **1** but is unreactive toward thiourea.

Under basic catalysis, however, both **1** and **2** cyclized to 2-hydroxy-6-phenyl-4-thio-1,3,5-triazine (**5**), apparently by dehydration of the common tetrahedral intermediate **4**. Compound **5** was alkylated with iodomethane to 2-hydroxy-4-(methylthio)-6-phenyl-1,3,5-triazine (**6**) which had been prepared previously by another method.[5]



Experimental Section

IR spectra were recorded on a Perkin-Elmer Model 283 grating spectrophotometer. Mass spectra were obtained with a Finnigan 3100D spectrometer operated in the CI mode using methane as the reagent gas. Microanalyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, MI. Melting points were determined with a Fisher-Johns melting point apparatus and are uncorrected.

1-Benzoyl-2-thiobiuret (1):[1] IR (KBr) 3365, 3305, 3220, 3020, 1742, 1700, 1540, 1495, 1255, 1200, 707, and 555 cm^{-1}; mass spectrum (CH_4,CI) *m/e* (rel intensity) 224 (M + 1, 13), 181 (18), 122 (13), and 105 (100).

1-Benzoyl-4-thiobiuret (2). Method A: A suspension of 500 mg (2.24 mmol) of 1-benzoyl-2-thiobiuret in 5 mL of H_2O was heated at ca. 95 °C for 16 h, by which time the yellow starting material was completely converted to white crystals. The crystals were collected and washed with EtOH affording 460 mg (92%) of the rearranged product **2**, mp 219–222 °C. An analytical sample, mp 230–231 °C, was prepared by recrystallization from CH_3CN: IR (KBr) 3375, 3310, 3260, 3170, 1710, 1680, 1620, 1517, 1470, 1425, 1355, 1260, 1195, 1165, 1045, 1033, 965, 895, 850, 767, 705, 685, and 650 cm^{-1}; mass spectrum (CH_4, CI) *m/e* (rel intensity) 224 (M + 1, 53), 148 (23), 131 (48), 122 (100), 105 (65), and 77 (51).

Anal. Calcd for $C_9H_9N_3O_2S$: C, 48.42; H, 4.06; N, 18.82; S, 14.33. Found: C, 48.49; H, 4.05; N, 18.82; S, 14.38.

Method B: A suspension of 1.06 g (14 mmol) of thiourea in 20 mL of benzene was treated with a solution of 2.5 g (17 mmol) of benzoyl isocyanate[3] in 10 mL of benzene and stirred at room temperature for 36 h. The white crystals which formed were collected and washed with benzene, giving 2.3 g (74%) of **2**, mp 230–231 °C (from CH_3CN). The IR spectrum was identical to that of the rearranged product obtained by method A.

Reaction of 1 with Iodomethane in Methanol. A suspension of 223 mg (1 mmol) of **1** in 5 mL of MeOH was treated with 0.5 mL (1.15 g, 8 mmol) of CH_3I and heated at reflux. Heating was continued until moistened lead acetate paper placed in the mouth of the condenser no longer turned yellow (~10 h). The white crystals were collected and washed with methanol, affording 10 mg (48%) of **3**, mp 223–224 °C (from MeOH), which gave a negative ammoniacal silver nitrate test; IR was identical to that of an authentic sample of **3**; mp 224–225 °C.[4]

Reaction of 2 with Iodomethane in Methanol. The same procedure was employed starting with **2**, giving **3**, mp 224–225 °C, in 43% yield.

1-Benzoylbiuret (3). A solution of 0.60 g (10 mmol) of urea in 5 mL of CH_3CN was stirred overnight with 1.5 g (10.2 mmol) of benzoyl isocyanate, affording 1.4 g (68%) of **3**, mp 223–225 °C (from EtOH) (lit.[4] mp 224–225 °C): IR (KBr) 3403, 3360, 3245, 1715, 1670, 1475, 1400, 1265, 1217, and 775 cm^{-1}; mass spectrum (CH_4,CI) *m/e* (rel intensity) 208 (M + 1, 7), 207 (8), 191 (10), 179 (5), 162 (5), 136 (7), 122 (10), 106 (10), 105 (100), 104 (15), 101 (10), 93 (12), 87 (5), and 77 (18).

2-Hydroxy-6-phenyl-4-thio-1,3,5-triazine (5). A suspension of 1.1 g (4.9 mmol) of 1-benzoyl-2-thiobiuret in 5 mL of H_2O was treated with 10 drops of 50% NaOH solution. The yellow solid was converted immediately to a mass of white needles. Neutralization with glacial HOAc converted the white needles to a yellow product which was collected and washed with MeOH, affording 1.0 g (99%) of **5**. An analytical sample was prepared by two recrystallizations from DMF: mp 256–258 °C dec; IR (KBr) 3100, 1685, 1605, 1505, 1497, 1457, 1418, 1388, 1325, 1233, 1217, 1205, 1028, 819, 770, and 700 cm^{-1}; mass spectrum (CH_4,CI) *m/e* (rel intensity) 206 (M + 1, 100), 205 (45), 147 (38), 130 (11), 103 (45), and 102 (25).

Anal. Calcd for $C_9H_7N_3OS$: C, 52.67; H, 3.44; N, 20.47; S, 15.62. Found: C, 52.75; H, 3.31; N, 20.36; S, 15.57.

The identical procedure as above, starting with **2**, also gave **5**, mp 257 °C dec, in 92% yield.

2-Hydroxy-4-(methylthio)-6-phenyl-1,3,5-triazine (6). A solution of 250 mg (1.22 mmol) of **5** was dissolved in 3 mL of 10% NaOH solution. The solution was diluted with 5 mL of MeOH and treated with 0.5 mL (1.15 g, 8 mmol) of iodomethane to give white crystals. The suspension was neutralized with glacial HOAc and the white precipitate was collected affording 200 mg (75%) of **6**. An analytical sample was prepared by two recrystallizations from DMF: mp 280–281 °C (lit.[5] mp 275–276 °C); IR (KBr) 1681, 1611, 1600, 1555, 1540, 1500, 1440, 1330, 1275, 1175, 1105, 1018, 855, 807, 781, 718, and 689 cm^{-1}.

Anal. Calcd for $C_{10}H_9N_3OS$: C, 54.78; H, 4.14; N, 19.16; S, 14.62. Found: C, 54.79; H, 4.03; N, 19.07; S, 14.76.

Acknowledgment. We thank Carl J. Mason for obtaining the mass spectra.

Registry No.—**1**, 34277-78-6; **2**, 41835-24-9; **3**, 6291-91-4; **4**, 68475-04-7; **5**, 32622-40-5; **6**, 1917-43-7; thiourea, 62-56-6; benzoyl isocyanate, 4461-33-0; iodomethane, 74-88-4; urea, 57-13-6.

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Monothioanthraquinones

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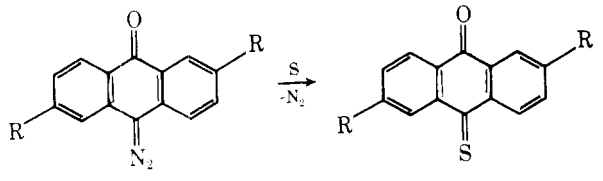
Received September 11, 1978

Substances thought to be dithioanthraquinone[2] and 2,5-diamino-1,4-dithiobenzoquinone[3] have been reported, but no monothioquinones appear to have been recorded, though unsuccessful attempts to prepare them have been made[4,5] and they have been postulated as reaction intermediates in the rearrangement of monothiobisphenols.[6,7]

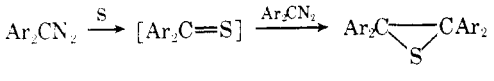
Monothioanthraquinones (**2**) have now been synthesized by the reaction of 10-diazoanthrones (**1**) with sulfur in dimethylformamide at 130–150 °C. The compounds are green with absorption in the visible region at 697 nm for **2a** and 685 nm for **2b** in chloroform.



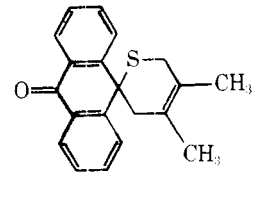
1a, R = H
b, R = CH_3O

2a, R = H
b, R = CH_3O

This is a new method of preparing thiocarbonyl compounds. In previous work, reaction of sulfur with diazo compounds, including 9-diazofluorene, has given thiiranes,[8,9] but thioketones have been postulated as reaction intermediates in this synthesis.



Like other thiocarbonyl compounds,[10] monothioanthraquinone undergoes Diels–Alder reactions. Reactions of **2a** with 2,3-dimethylbutadiene and with cyclopentadiene form **3** and **4**. Crystals of the latter slowly dissociate back to **2a** and cyclopentadiene at 22 °C.



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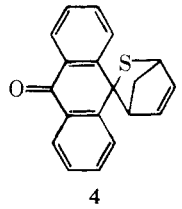
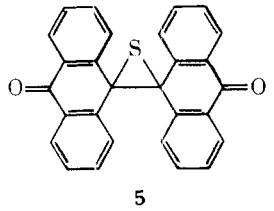


4

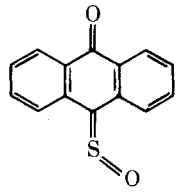
Reaction of monothioanthraquinone with trimethyl phosphite yields the thiirane **5**.

Thiiranes have been proposed as intermediates in the reaction of thiocarbonyl compounds with phosphites,[11–13] but the above case appears to be the first in which the thiirane was isolated. Trimethyl phosphite does not remove sulfur from **5** under the reaction conditions, so the reaction stops at the thiirane stage rather than proceeding to the olefin. The structure of **5** was confirmed by its synthesis by reaction of **1a** with **2a**, which represents a 1,3-dipolar addition to the thiocarbonyl group followed by loss of nitrogen.[14] Compounds **3**, **4**, and **5** are new ring systems.

In common with other thioketones, monothioanthraquinone can be oxidized to a sulfine[15] (**6**).



5



6

Experimental Section

The ^1H NMR spectra were determined on a Varian A-60 instrument using tetramethylsilane as an internal standard. IR spectra were taken on a Perkin-Elmer Model 21 spectrometer. Melting and boiling points are uncorrected.

10-Diazoanthrone (1a). Published directions[16] for preparing *p*-toluenesulfonyl azide were modified to eliminate the isolation of the explosive[17] azide. To 22.5 g (0.118 mol) of *p*-toluenesulfonyl chloride dissolved in 150 mL of ethanol was added 9.3 g (0.143 mol) of sodium azide dissolved in 27 mL of water. The mixture was stirred for 1 h, 150 mL of ethanol was added, and sodium chloride was filtered off. This solution of *p*-toluenesulfonyl azide was used directly in the procedure of Regitz[18] to prepare 10-diazoanthrone. Anthrone (19.4 g, 0.1 mol) was added and then 11.3 mL of piperidine over 30 min. After the mixture had been stirred for 5 h, the 10-diazoanthrone was filtered off and washed with ethanol, 19.6 g (89%). Recrystallization from dioxane left 17.7 g (80%).

Monothioanthraquinone [10-Thioxo-9(10*H*)-anthracenonel (2a)]. 10-Diazoanthrone (17.6 g, 0.08 mol), sulfur (3.07 g, 0.096 mol), and 170 mL of dimethylformamide were heated and stirred in a flask in an oil bath at 150 °C. Heating was continued for 10 min after evolution of nitrogen ceased. The green solution was cooled, and the product was filtered off and washed with acetone. It was then dissolved in dichloromethane, and 0.6 g of an orange substance was filtered off. The solution was evaporated to dryness and the residue sublimed at 0.5 mm and 190 °C. A fluffy residue remained behind. The sublimate was recrystallized from chloroform to give 9.8 g (57%) of green needles in two crops: mp 213–214 °C; IR 3077 (=CH), 1675, 1669 (doublet for conjugated ketone carbonyl), 1600 1580 (aromatic C=C), 1212 (medium band, C=S) cm^{-1}; UV ($CHCl_3$) 697 nm (ϵ 46.5), 334 (14 400), 270 (26 000); UV (CH_3CN) 690 nm (ϵ 48.6), 334 (13 900), 267 (25 800), 224 (24 200).

Anal. Calcd for $C_{14}H_8OS$: C, 74.98; H, 3.60; S, 14.29; M_r 224. Found: C, 75.31; H, 3.70; S, 14.11; M_r 220 (osmometric, C_6H_6, 37 °C), 217 (ebullioscopic, C_6H_6).

2,6-Dimethoxyanthrone. 2,6-Dimethoxyanthraquinone[19] (13.4 g, 0.05 mol) was added to a solution of 12 g (0.3 mol) of sodium hydroxide and 30 g (0.17 mol) of sodium hydrosulfite in 260 mL of water. The mixture was refluxed for 1.5 h and cooled, and the anthrone was filtered off and washed with water. Recrystallization from acetone gave 9.08 g (74%) of the pale yellow anthrone: mp 160–161 °C; NMR ($CDCl_3$) 3.88 (s, CH_3), 3.92 (s, CH_3), 4.24 (s, CH_2), 6.75–8.4 (m, 6 H, aromatic) ppm.

Impure 2,6-dimethoxyanthrone, mp 156 °C, prepared by stannous chloride reduction of the anthraquinone, has been reported.[20]

10-Diazo-2,6-dimethoxyanthrone (1b). This compound was prepared from 2,6-dimethoxyanthrone as described for 10-diazoanthrone and recrystallized from benzene: mp 137–138.5 °C dec (53%); NMR ($CDCl_3$) 3.84, 3.89 ppm (s, s, OCH_3).

Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.56; H, 4.32; N, 9.99. Found: C, 68.88; H, 4.46; N, 9.67.

2,6-Dimethoxymonothioanthraquinone (2b). 10-Diazo-2,6-dimethoxyanthrone (1.4 g, 0.005 mol), 0.19 g (0.006 mol) of sulfur, and 7 mL of dimethylformamide were heated and stirred in a flask in an oil bath at 130 °C. Nitrogen was evolved, and heating was continued for 10 min after evolution ceased. The mixture was cooled, and the thione (0.90 g) was filtered off and rinsed first with dimethylformamide and then with carbon tetrachloride. Recrystallization from chloroform gave 0.64 g (42.5%) of brown crystals of **2b**: mp 207 °C; NMR ($CDCl_3$) 3.97 ppm (OCH_3); UV ($CHCl_3$) 685 nm (ϵ 65.6), 390

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