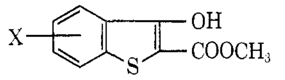
TABLE I

METHYL 3-HYDROXYBENZO[*b*]THIOPHENE-2-CARBOXYLATES



Registry no.	X	Mp, °C	Yield, %	Crystn solvent[a]	Temp, °C; time, hr
13134-76-4	H	109–110[b]	61	A	0, 0.5; 25, 2.5
33851-22-8	6-Cl	147–149	75	B	0, 0.5; 25, 1
33851-23-9	7-Cl	133–134	80	B	0, 0.5; 25, 2
42087-77-4	4-NO_2	185–186.5	85	B	0, 0.5
42087-78-5	7-NO_2	226–228	73	B	0, 0.5
42087-79-6	7-OCH_3	118–119	50	A	0, 0.5; 25, 3

[a] A, alcohol–water; B, alcohol. [b] Lit.[1] mp 104°.

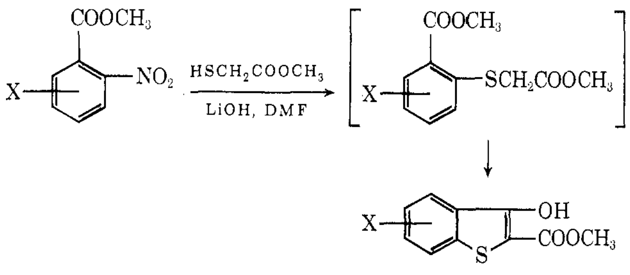
TABLE II

MICROANALYTICAL DATA

X	Empirical formula	Calcd, % C	Calcd, % H	Calcd, % N	Calcd, % S	Found, % C	Found, % H	Found, % N	Found, % S
H	$C_{10}H_8O_3S$	57.68	3.87		15.40	57.91	3.94		15.51
6-Cl	$C_{10}H_7ClO_3S$	49.48	2.91		13.21	49.31	2.82		13.16
7-Cl	$C_{10}H_7ClO_3S$	49.48	2.91		13.21	49.70	2.87		13.31
4-NO_2	$C_{10}H_7NO_5S$	47.43	2.79	5.53	12.66	47.47	2.77	5.52	12.76
7-NO_2	$C_{10}H_7NO_5S$	47.43	2.79	5.53	12.66	47.59	2.74	5.47	12.61
7-OCH_3	$C_{11}H_{10}O_4S$	55.45	4.23		13.46	55.67	4.14		13.59

The compound was formed by base-catalyzed cyclization of the bis methyl ester of *o*-[(carboxymethyl)thio]-benzoic acid, which was obtained in three steps from *o*-mercaptobenzoic acid. There are many modifications of this general synthesis, and these have been reviewed.[2] The free acids are readily decarboxylated to form benzo[*b*]thiophen-3(2*H*)-ones (thioindoxyls), which are precursors to thioindigo dyes. In a previous communication,[3] the author reported a direct synthesis of methyl 3-aminobenzo[*b*]thiophene-2-carboxylates from *o*-nitrobenzonitriles and methyl benzo[*b*]thiophene-2-carboxylates from *o*-nitrobenzaldehydes. This synthesis has now been extended for the conversion of methyl *o*-nitrobenzoates to methyl 3-hydroxybenzo[*b*]thiophene-2-carboxylates (Scheme I).

SCHEME I



Under the conditions of the reaction, the nitro group, activated by the adjacent carbomethoxyl function, is readily displaced by methyl thioglycolate anion (lithium salt) in DMF, and this is followed by a base-catalyzed cyclization as in the Friedlander synthesis. The conditions are mild and the yields, which are based upon crystallized products, are high (Table I). The major side reaction appears to be hydrolysis of the starting ester, and this can probably be overcome by rigorous drying of the DMF and lithium hydroxide. Other examples of the synthetic utility of activated nitro displacement will be the subject of further communications.

Experimental Section[4]

Materials.—All benzoic acids utilized are commercially available from the Aldrich Chemical Co. The methyl esters were prepared by standard procedures in the literature.

General Procedure for Methyl 3-Hydroxybenzo[*b*]thiophene-2-carboxylates.—To a well stirred, cold solution (ice bath) containing 30 mmol of the substituted methyl *o*-nitrobenzoate and 4.0 ml of methyl thioglycolate in 60 ml of DMF was added slowly, portionwise, 2.5 g of lithium hydroxide. The mixture was stirred in the cold for 0.5 hr and then at room temperature for the time period shown in Table I. It was poured into ice water and the solution was acidified. The crude product was collected and crystallized from the appropriate solvent (Table I). Microanalytical data are summarized in Table II.

Acknowledgments.—The author wishes to thank Mr. Paul Unger and associates for spectral measurements and Mr. George Maciak and associates for microanalytical data.

Registry No.—Methyl *o*-nitrobenzoate, 606-27-9; methyl 4-chloro-2-nitrobenzoate, 42087-80-9; methyl 3-chloro-2-nitrobenzoate, 42087-81-0; methyl 2,6-dinitrobenzoate, 42087-82-1; methyl 2,3-dinitrobenzoate, 42087-83-2; methyl 3-methoxy-2-nitrobenzoate, 5307-17-5; methyl thioglycolate, 2365-48-2.

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(2) (a) H. D. Hartough and S. L. Meisel, "The Chemistry of Heterocyclic Compounds," A. Weissberger, Ed., Interscience, New York, N. Y., 1954, pp 67, 138; (b) B. Iddon and R. M. Scrowston, *Advan. Heterocycl. Chem.*, **11**, 229 (1970).

(3) J. R. Beck, *J. Org. Chem.*, **37**, 3224 (1972).

(4) Melting points were determined on a Mel-Temp apparatus and are uncorrected.

Synthesis and Properties of 3,3,6,6-Tetramethyl-1-oxacycloheptane-4,5-dione

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Our interest in charge-transfer phenomena in heteroatom containing medium ring ketone[1a] and α-dione[1b,c] substrates has led us to synthesize oxa α-dione **1**[2] in order to compare its uv spectra, mass spectral frag-

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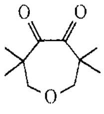
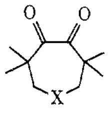
(1) (a) P. Y. Johnson and G. A. Berchtold, *J. Org. Chem.*, **35**, 584 (1970); (b) P. Y. Johnson, *Tetrahedron Lett.*, 1991 (1972); (c) P. Y. Johnson and I. Jacobs, *Chem. Commun.*, 925 (1972).

(2) Since submitting this manuscript a second report of the synthesis of **1** has been published. See A. Krebs and G. Eurgdorfer, *Tetrahedron Lett.*, 2063 (1973).

mentation pattern, and photochemical reactions with its sulfur, **2**,[1b,3] nitrogen, **3**,[4] and carbon, **4**,[3,5] analogs.



1



2, X = S
3a, X = *N*-*t*-Bu
b, X = *N*-phenyl
4, X = CH_2

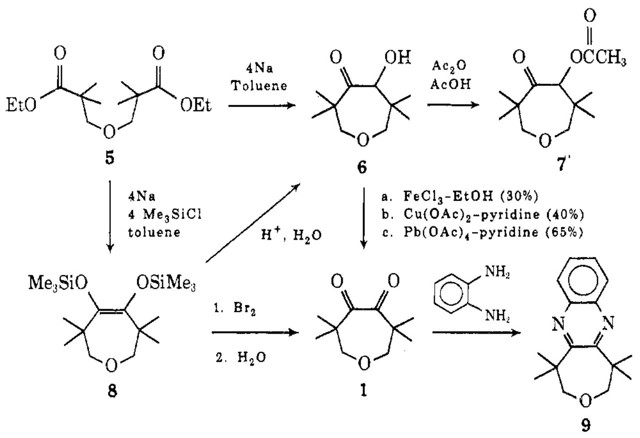
Initial attempts to synthesize oxa dione **1** by an acyloin ring closure procedure from the appropriate 3,3′-oxa diester, **5**,[6] were only partially successful. While the acyloin product, hydroxy ketone **6**, could be obtained in high yield (~85%) using either the normal[7a] or the chlorotrimethylsilane modification[7b] of the acyloin reaction, we were unable to oxidize it to **1** in greater than 50% yield using procedures which worked well in our hands for similar molecules. The following procedures were employed: $FeCl_3$–ethanol, 24-hr reflux (~30% **1** + **6**); $Cu(OAc)_2$–pyridine, 15 hr at 25° (~40% **1** + **6**); and $Pb(OAc)_4$–pyridine, 160 hr at 25° (~50% **1** + **6**). In all cases vpc analysis showed no further reaction with increased time. The addition of more oxidant and/or solvent did not seem to improve the yields of these reactions. The differences between the oxidation of **6** and its sulfur analog **2**[1b,8] cannot be accounted for.[9] Acyloin **6** was, however, oxidized by $Pb(OAc)_4$–pyridine in 65% yield when the reaction was run at reflux temperatures for 12 hr under a nitrogen atmosphere.

Hydroxy ketone **6** was converted to its acetate derivative, **7**, by standard procedures. The decomposition noticed (see Experimental Section, procedure A) during the distillation of **6**, leaving a viscous, nondistillable oil, was not noticed during the distillation of acetate **7**.

The desired oxa α-dione **1** was also obtained in 70% yield using a simplification of a procedure involving the bromine oxidation of the disiloxene intermediate, **8**, which was generated in the chlorotrimethylsilane modification of the acyloin reaction.[10] We found it to be experimentally easier to oxidize the disiloxene intermediate in the original reaction flask than to try to isolate it first as is the reported procedure. In our case, bromine was added to the cooled reaction mixture until a red color persisted. Usually slightly more than 1 equiv of bromine was required, probably owing to reaction of the bromine with traces of unreacted sodium.

Oxa dione **1** was characterized as its quinoxaline derivative **9**. The reactions described are shown in Scheme I.

SCHEME I



In contrast to α-diones **2**[1b] and **3**,[4] **1** showed no absorption band in its uv spectra attributable to charge transfer interaction. On the contrary, its uv spectrum was similar to that of its carbon analog **4**[5] [**4**, uv max (EtOH) 337 nm (ε 33), 292 (34), shoulder 288 (28); **1**, uv max (EtOH) 326 nm (ε 26), 292 (26), shoulder 283 (20)].

The lack of apparent charge-transfer interaction (uv spectra) leads us to believe that the photolysis of **1** will not parallel that of **2**.[1b]

Experimental Section

Melting points were taken on a calibrated Mel-Temp apparatus. Infrared spectra were taken on a Perkin-Elmer 337 spectrometer; nmr spectra were recorded on a Varian A-60 spectrometer using TMS as an internal standard. Mass spectra were obtained on a Hitachi RMU6D mass spectrometer. Ultraviolet spectra were recorded on a Cary 14 instrument. Vpc analyses were performed using program temperature control on a Hewlett-Packard 5750 gas chromatograph equipped with 8 ft × 0.25 in. 10% Carbowax on Chrom-P and 8 ft × 0.25 in. 10% SE-30 on Chrom-P stainless steel columns. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn.

3,3,6,6-Tetramethyl-5-hydroxy-1-oxacycloheptan-4-one (**6**).—Hydroxy ketone **6** was synthesized from diester **5** using both the normal (A) and the chlorotrimethylsilane modification (B) of the acyloin reaction.

Procedure A.—Into a dry Morton flask set up for high-speed stirring under N_2 was added 400 ml of toluene and 13.34 g (0.58 mol) of sodium. The mixture was refluxed and 39.6 g (0.145 mol) of diester **5** in 100 ml of toluene was added to it over several hours. After 2 hr additional reflux, the mixture was cooled to 0° and the reaction was quenched with aqueous NH_4Cl [7.8 g (0.145 mol) in 200 ml of water]. The organic layer was separated, washed with H_2O, dried with $MgSO_4$, filtered, and evaporated to give 27 g (~100%)[11] of a crude oil. Vpc analysis of the crude oil showed it to be mostly desired hydroxy ketone **6** (based on the mass spectrum of a collected sample) and some starting diester. Attempts to solidify this oil by cooling it or by cooling it in the presence of acetic acid[8] or ethanol failed. Finally, distillation of the oil gave a low yield, 7.4 g (28.0%), of **6**, bp 92–96° (0.2 mm), which solidified upon standing. Recrystallization from low petroleum ether (bp 30–60°) gave **6** as a white solid: mp 58.5–59.5°; ir (CCl_4) 3450, 2952, 2935, 2865, 1700, 1470, 1385, 1360, 1262, 1123, 1048 cm^{-1}; nmr (CCl_4) δ 0.69 (s, 3), 0.91 (s, 6), 1.27 (s, 3), 3.2–3.7 (m, 5), 4.19 (d, 1, J = 5 Hz, collapses to singlet in D_2O); mass spectrum (70 eV) m/e (rel intensity) 186 (trace, M^+), 158 (7), 131 (11), 114 (16), 103 (59), 101 (18), 85 (15), 73 (30), 72 (23), 71 (30), 59 (10), 57 (30), 56 (100), 55 (17), 43 (24), 41 (37); uv λ_{max} (EtOH) 261 nm (ε 43). When the reaction was run in the same manner as described above but the crude oil was kept under high vacuum for 24 hr in order to remove

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[3] A second report on the photolysis of the sulfur, **2**, and the carbon, **4**, analogs of **1** has been published. See J. Kooi, H. Wynberg, and R. M. Kellogg, *Tetrahedron*, **29**, 2135 (1973).

[4] P. Y. Johnson and I. Jacobs, unpublished results.

[5] N. J. Leonard and P. M. Mader, *J. Amer. Chem. Soc.*, **72**, 5388 (1950).

[6] (a) J. Zitsman and P. Y. Johnson, *Tetrahedron Lett.*, 4201 (1971); (b) P. Y. Johnson and J. Zitsman, *J. Org. Chem.*, **38**, 2346 (1973).

[7] (a) K. Y. Finley, *Chem. Rev.*, **64**, 573 (1964); (b) J. J. Bloomfield, *Tetrahedron Lett.*, 587 (1968).

[8] Ae De Groot and H. Wynberg, *J. Org. Chem.*, **31**, 3954 (1966).

[9] For a large list of oxidants employed in the oxidation of α-hydroxy ketones and a discussion of their usefulness for reaction with hindered systems, see G. E. Gream and S. Wortley, *Tetrahedron Lett.*, 3319 (1968), and references cited therein.

[10] For a review of this procedure, see J. Strating, S. Reiffers, and H. Wynberg, *Synthesis*, 209 (1971).

[11] In our hands the yields of these and other acyloin reactions have been found to fall 10–20% when a *Morton flask* is not used.

all of the reaction solvents, it was found to solidify after standing at 0° for 24 hr. Recrystallization from low petroleum ether twice gave pure **6** (85%),[11] mp 59–59.5°.

Procedure B.—The reaction was run as above but 4 equiv of chlorotrimethylsilane were added to the reaction mixture dropwise along with diester **5**. After the additional 1 hr of reflux the reaction mixture was cooled. No attempt was made to isolate the disiloxene intermediate **8**, but rather aqueous NH_4Cl was added to the reaction mixture. The organic–aqueous mixture was stirred for 1 hr and the organic layer was treated as described in procedure A. The yield of **6** was 80–85% over several runs.

3,3,6,6-Tetramethyl-5-acetoxy-1-oxacycloheptan-4-one (**7**).—Hydroxy ketone **6** (2.5 g, 0.014 mol) was refluxed in 10 ml of acetic acid and 10 ml of acetic anhydride for 12 hr and cooled. Water was added and the mixture was stirred for 30 min. It was then extracted with ether which was washed with 10% K_2CO_3, dried, and evaporated to give an oil which did not solidify. Short-path distillation of the oil gave 2.6 g of liquid which solidified upon standing. Recrystallization from ethanol gave 2.4 g (78%) of pure acetate **7**: bp 91–93° (1.00 mm); mp 69.5–71°; ir (CCl_4) no OH, 2960, 2940, 2860, 1749, 1725, 1380, 1365, 1250, 1120 cm^{-1}; nmr (CCl_4) δ 0.85 (s, 3), 0.91 (s, 3), 0.98 (s, 3), 1.18 (s, 3), 2.08 (s, 3), 3.3–3.8 (m, 4), 5.32 (s, 1); mass spectrum (70 eV) *m/e* (rel intensity) 228 (1, M$^+$), 185 (3), 173 (31), 157 (7), 145 (8), 131 (17), 115 (10), 113 (8), 86 (9), 85 (38), 73 (15), 72 (15), 57 (24), 56 (59), 55 (14), 43 (100), 41 (32); uv λ_{max} (EtOH) 273 nm (ϵ 40).

Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 62.99; H, 8.71.

3,3,6,6-Tetramethyl-1-oxacycloheptane-4,5-dione (**1**).—Dione **1** was synthesized according to procedure B described above for the synthesis of **6** with the following changes. To the cooled reaction mixture containing disiloxene **8** was added about 1 equiv of Br_2 in CCl_4 over 10 min with cooling. Additional Br_2 was added until its characteristic red color persisted. After the mixture was allowed to warm to 25° over 30 min, aqueous NH_4Cl was added and stirring was continued for 1 hr. The organic layer was separated, washed with a minimum amount of 10% sodium bisulfite, 10% K_2CO_3, and 10% HCl, dried, filtered, and evaporated to give an oil which was distilled to give 60–70% (several runs) of pure dione **1**: bp 52–54° (0.1 mm) and 62–63° (0.5 mm) (this oxa dione was a low-melting solid when pure); ir (CCl_4) 2955, 2940, 2855, 1720 (shoulder 1700), 1395, 1365, 1200, 1187, 1108 cm^{-1}; nmr (CCl_4) δ 1.10 (s, 12), 3.51 (s, 4); mass spectrum (70 eV) *m/e* (rel intensity) 184 (12, M$^+$), 101 (56), 73 (19), 59 (11), 57 (19), 56 (100), 55 (22), 43 (11), 42 (11), 41 (44); uv λ_{max} (EtOH) 283 nm (ϵ 20), 292 (26), 326 (26).

3,3,6,6-Tetramethyl-1-oxacycloheptane-4,5-dione (**1**) **Using Pb(OAc)$_4$.**—Hydroxy ketone **6**, 3.16 g (0.017 mol), and lead tetraacetate, 9.04 g (0.020 mol), were refluxed in 35 ml of pyridine, under nitrogen, for 12 hr. The reaction mixture was cooled and poured into 120 ml of cold 6 *N* HCl and the resulting solution was extracted with ether. The ether was washed with 10% aqueous K_2CO_3, dried over anhydrous K_2CO_3, and evaporated to give an oily liquid. Distillation gave 1.90 g (65%) of pure dione **1** as a pale yellow, oily liquid which solidified to a low-melting solid on cooling, mp 41.5–43.5°.

Dione **1** was characterized as its quinoxaline derivative, **9**, which was synthesized by standard procedures, mp (EtOH) 74–75°.

Anal. Calcd for $C_{16}H_{20}N_2O$: C, 74.96; H, 7.86; N, 10.93. Found: C, 74.98; H, 7.74; N, 10.94.

Acknowledgment.—We wish to thank the National Institutes of Health for partial support of this work.

Registry No.—**1**, 42031-65-2; **5**, 34506-36-0; **6**, 42031-67-4; **7**, 42031-68-5; **8**, 42133-38-0; **9**, 42031-69-6.