Methyl 2-Pyrone-6-carboxylate.—This ester was prepared by adding 25.0 g. (0.157 mole) of 2-pyrone-6-carbonyl chloride to 100 ml. (0.248 mole) of dry methanol. After the initial vigorous reaction, the reaction mixture was refluxed 15 minutes. The excess methanol was evaporated and the residue recrystallized from benzene to give 23.7 g. (98% of the theoretical amount) of methyl 2-pyrone-6-carboxylate, rectangular plates, m.p. 124–125°. Analytical data are given in Table I.

Cyclohexyl 2-Pyrone-6-carboxylate.—This ester was prepared by heating 5.0 g. (0.032 mole) of 2-pyrone-6-carbonyl chloride with 3.2 g. (0.032 mole) of cyclohexanol at 100° for one-half an hour. The solid which formed on cooling the reaction mixture was recrystallized from ethanol-water to give 4.8 g. (48% of the theoretical amount) of cyclohexyl 2-pyrone-6-carboxylate, white needles, m.p. 108–109°. Analytical data are given in Table I.

Isobutyl, *n*-amyl and dodecyl 2-pyrone-6-carboxylates were prepared by the same procedure used for the preparation of the cyclohexyl ester. Yields, properties and analytical data are given in Table I.

Pentaerythrityl Tetrakis-(2-pyrone-6-carboxylate).—This ester was prepared by heating a mixture of 3.5 g. (0.022 mole) of 2-pyrone-6-carbonyl chloride and 0.75 g. (0.0055 mole) of powdered pentaerythritol at 150° to the solution. The solid which formed on cooling was recrystallized from hot acetic acid and dried to give 1.4 g. (40% of the theoretical amount) of white crystals of pentaerythrityl tetrakis-(2-pyrone-6-carboxylate), m.p. 218–221°. Analytical data are given in Table I.

Decamethylene Glycol Bis-(2-pyrone-6-carboxylate).—This ester was prepared by heating 5.0 g. (0.032 mole) of 2-pyrone-6-carbonyl chloride with 2.8 g. (0.016 mole) of 1,10-decanediol (decamethylene glycol) at 100° for one-half hour. The solid which formed on cooling was triturated with 50 ml. of ethanol, collected on a filter, and recrystallized from toluene to give 4.6 g. (70% of the theoretical amount) of 1,10-decanediol bis-(2-pyrone-6-carboxylate), m.p. 146–148°. Analytical data are given in Table I.

Ethylene glycol, trimethylene glycol,[5] pentamethylene glycol, diethylene glycol[5] and triethylene glycol[5] bis esters of 2-pyrone-6-carboxylic acid were prepared by the same procedure used for the preparation of the 1,10-decanediol bis ester. Analytical and yield data are given in Table I.

***p*-Methoxyphenyl 2-Pyrone-6-carboxylate.**—A mixture of 5.0 g. (0.032 mole) of 2-pyrone-6-carbonyl chloride and 4.0 g. (0.032 mole) of *p*-methoxyphenol was heated slowly to 150° and held at 150–160° for five hours. The solid that formed on cooling the reaction mixture was recrystallized from acetone–water to give 5.2 g. (67% of the theoretical amount) of *p*-methoxyphenyl 2-pyrone-6-carboxylate, m.p. 140–142° (after several recrystallizations). Analytical data are given in Table I.

Phenyl and 2,6-dimethoxyphenyl 2-pyrone-6-carboxylate were prepared by the procedure given for the preparation of the *p*-methoxyphenyl ester. The 2,6-dimethoxyphenyl ester was prepared by heating the reactants at 180–190° for one hour. Analytical data are given in Table I.

None of the aryl esters gave positive ferric chloride enol tests or were readily soluble in cold, dilute sodium hydroxide.

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[5] The authors wish to thank Carbide and Carbon Chemicals Corporation for generously providing samples of these glycols.

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NOTES

4-Nitrophthalimide. II. Di-(4-nitrophthalimido)-alkanes and Bis-(4-nitrophthalimidoalkyl) Ethers[1]

By John H. Billman and R. Vincent Cash

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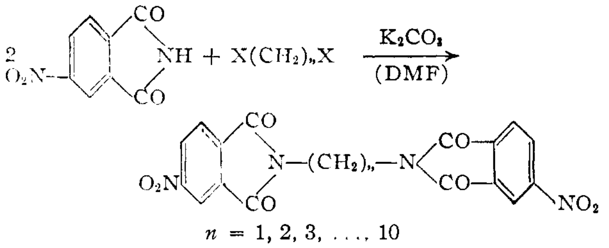
In a previous article[2] it was shown that N-alkyl-4-nitrophthalimides may be prepared by the reaction of 4-nitrophthalimide and potassium carbonate with the corresponding monohaloalkane in a medium of dimethylformamide. It seemed a logical extension of this work to attempt the preparation of a number of α,ω-di-(4-nitrophthalimido)-alkanes from dihaloalkanes with terminal halogen atoms.



$n = 1, 2, 3, \ldots, 10$

In order to minimize the formation of N-(bromoalkyl)-4-nitrophthalimides, a ratio of 1:2.5 moles of the dibromide to the 4-nitrophthalimide was used in preparing the series of di-(4-nitrophthalimido)-alkanes (Table I) having one to ten (except eight) carbon atoms in the normal hydrocarbon chain. Bis-(4-nitrophthalimido)-ethyl ether and bis-(4-nitrophthalimido)-isopropyl ether (Table I) were obtained from the corresponding chloro ethers by a similar procedure. It should be noted that a longer period of heating of the reaction mixture gave higher yields.

The melting points of these di-(4-nitrophthalimido)-alkanes are of particular interest in that they follow the "sawtooth" effect with the compounds containing an even number of carbon atoms, in the chain, melting at a higher temperature than the next higher and lower homolog.

Experimental

Di-(4-nitrophthalimido)-alkanes and Bis-(4-nitrophthalimidoalkyl) Ethers.—In a 250-ml. round-bottomed flask with thermometer well were placed 9.6 g. (0.050 mole) of 4-nitrophthalimide, 4.2 g. (0.030 mole) of anhydrous potassium carbonate and 0.2 g. of potassium iodide. The dried dihalide (0.020 mole) and 40 ml. of dimethylformamide were added and a reflux condenser bearing a drying tube was attached. The mixture was heated at 135–140° for the period indicated in Table I. The flask was shaken occasionally. Carbon dioxide was evolved during the heating period.

The reaction mixture became solid on cooling to room temperature. It was introduced into 200 ml. of cold water, and the solid permitted to settle. After collecting the solid, it was washed with two 25-ml. portions of 2% sodium hydroxide, and finally with water. The dried crude product was recrystallized by dissolving it in a minimal volume of hot chloroform, filtering while hot, and then adding 95%

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[1] Contribution from the Chemistry Departments of Indiana University (No. 613) and Teachers College of Connecticut.

[2] J. H. Billman and R. V. Cash, This Journal, **75**, 2499 (1953).

TABLE I

DI-(4-NITROPHTHALIMIDO)-ALKANES AND BIS-(4-NITROPHTHALIMIDOALKYL) ETHERS

Dihalide	Heating time, hr.	Yield, %[a]	M.p., °C.[b]	Formula	Nitrogen, % Calcd.	Nitrogen, % Found
Dibromomethane	1.5	2.5	223–224	$C_{17}H_8N_4O_8$	14.14	14.21
	4.0	28.7	223–224			
1,2-Dibromoethane	3.0	44.6	289–290	$C_{18}H_{10}N_4O_8$	13.66	13.63
1,3-Dibromopropane	1.5	18.8	202.5–203.5	$C_{19}H_{12}N_4O_8$	13.20	13.16
1,4-Dibromobutane	1.5	65.0	263–264	$C_{20}H_{14}N_4O_8$	12.78	12.85
1,5-Dibromopentane	2.0	49.2	195–196	$C_{21}H_{16}N_4O_8$	12.39	12.36
1,6-Dibromohexane	1.5	55.4	213–214	$C_{22}H_{18}N_4O_8$	12.01	11.99
1,7-Dibromoheptane	1.5	16.5	169–170	$C_{23}H_{20}N_4O_8$	11.66	11.56
	3.0	62.1	169–170			
1,9-Dibromononane	1.5	29.9	146–147	$C_{25}H_{24}N_4O_8$	11.02	11.00
1,10-Dibromodecane	2.0	53.0	175–176	$C_{26}H_{26}N_4O_8$	10.72	10.82
Bis-(β-chloroethyl) ether	3.0	21.7	198.5–199.5	$C_{20}H_{14}N_4O_9$	12.33	12.43
Bis-(β-chloroisopropyl) ether	3.0	27.6	131–132	$C_{22}H_{18}N_4O_9$	11.61	11.52

[a] Yield after recrystallization, based on dihalide. [b] Melting points over 260° are uncorrected and taken on a Fisher-Johns apparatus.

ethyl alcohol nearly to the point of cloudiness. If the product would not largely dissolve in chloroform, dimethylformamide was used in a like manner. The purified products were cream-colored solids.

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Preparation of Ethylenethioketals

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Previous methods for effecting the condensation of ketones with ethanedithiol or β-mercaptoethanol include use of zinc chloride and sodium sulfate,[1,2] hydrogen chloride in ether,[3,4] *p*-toluenesulfonic acid in benzene with azeotropic distillation[5,6] and an exchange method.[6] Two much simpler procedures that appear to be of comparable applicability utilize boron fluoride etherate as the condensing agent. In several instances addition of boron fluoride etherate to an acetic acid solution of ketone and excess mercaptan at room temperature results in prompt separation of the thioketal or hemithioketal derivative in high yield. An alternative procedure is to add boron fluoride etherate to a suspension or solution of the ketone in ethanedithiol; this reagent has remarkable power for dissolving steroid ketones. That the second procedure is more vigorous than the first is evidenced by the observation that B-norcoprostane-3,6-dione gave only oils when treated with ethanedithiol and boron fluoride etherate in acetic acid or methanol but afforded the bis-ethylenethioketal in high yield in the absence of solvent.[7] Neither procedure seems to be applicable to the condensation of ethylene glycol with such ketones as the 3-one, 3,6-dione and Δ^4-3,6-dione derivatives of cholestane.[8]

The possibility of investigating the structure of an unknown diketone by converting it into a monoethylenethioketal that could be degraded to recognizable products by desulfurization, or by Wolff–Kishner reduction followed by desulfurization, was tested with the model compounds cholestane-3,6-dione and Δ^4-cholestene-3,6-dione. Both diketones gave bis-ethylenethioketal derivatives in high yield with excess reagent, but on condensation with one equivalent of ethanedithiol in acetic acid in the presence of boron fluoride etherate each substance afforded a monoethylenethioketal, isolated by crystallization or by chromatography. Desulfurization of both mono derivatives with Raney nickel gave cholestane-6-one, and hence in each instance selective condensation with ethanedithiol occurs at the 3-keto group; desulfurization of Δ^4-cholestene-3,6-dione 3-monoethylenethioketal is attended with saturation of the double bond unless the Raney nickel is deactivated by refluxing it with acetone.[9] On reaction with excess ethanedithiol in acetic acid solution, benzil was found to yield only a monoethylenethioketal ketone. Whereas the 6β- and 6α-hydroxy derivatives of Δ^4-cholestene-3-one reacted with ethanedithiol to give cholestane-3,6-dione bis-ethylenethioketal (m.p. 220°) (as did Δ^5-cholestene-4α-ol-3-one acetate[10]), Δ^4-cholestene-6β-ol-3-one acetate gave an isomeric substance, m.p. 132°. An additional isomeric bis-ethylenethioketal (m.p. 280°) has been obtained from the condensation of ethanedithiol with Δ^4-cholestene-3β-ol-6-one acetate, and an investigation of the structure of these two isomers is in progress.

For exploration of possible molecular rotation relationships some additional cyclic ketal derivatives of monoketones were prepared and characterized, with the results summarized in Table I. Of the three derivatives of dehydroepiandrosterone acetate, the hemithioketal differs in *M*D more from the parent ketone than either of the symmetrical derivatives, and in the cholestanone series the hemithioketal shows a greater increment than the dithio

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(1) H. Hauptmann, THIS JOURNAL, **69**, 562 (1947).

(2) J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 4961 (1951).

(3) J. W. Rolls, R. M. Dodson and B. Riegel, *ibid.*, **71**, 3320 (1949).

(4) F. Kipnis and J. Ornfelt, *ibid.*, **71**, 3555 (1949).

(5) E. P. Oliveto, T. Clayton and E. B. Hershberg, *ibid.*, **75**, 486 (1953).

(6) C. Djerassi and M. Gorman, *ibid.*, **75**, 3704 (1953).

(7) L. F. Fieser, *ibid.*, **75**, 4386 (1953).

(8) However, H. Koster and H. H. Inhoffen, U. S. Patent 2,302,636 (1942), found that stannic chloride in carbon tetrachloride effectively catalyzes the reaction of ketones with ethylene oxide.

(9) O. B. Spero, A. V. McIntosh, Jr., and R. H. Levin, THIS JOURNAL, **70**, 1907 (1948); G. Rosenkranz, St. Kaufmann and J. Romo, *ibid.*, **71**, 3689 (1949).

(10) L. F. Fieser and R. Stevenson, manuscript submitted for publication.