Anal. Calcd. for $C_{16}H_{14}O$: C, 86.5; H, 6.3. Found: C, 87.2; H, 6.0.

The *2,4-dinitrophenylhydrazone* derivative melted at 197–198°.[15]

B. From 2-chloro-1-tetralone. The reaction of 27 g. (0.15 mole) of 2-chloro-1-tetralone with 100 cc. of 1.5*M* phenylmagnesium bromide solution in ether (0.15 mole) under conditions of Procedure C gave 14 g. (43%) of 2-phenyl-1-tetralone with 10.0 g. chlorotetralone recovered. Recrystallization of the ketone from alcohol yielded 12.0 g. crystals, m.p. 71–74°.

Reaction of 2-chloro-1-tetralone with excess Grignard reagent. Under the conditions of Procedure C, 27 g. (0.15 mole) of 2-chloro-1-tetralone was treated with 200 cc. of 1.5*M* phenylmagnesium bromide solution in ether (0.30 mole) to give a product consisting of 10 g. of recovered 2-chloro-1-tetralone and 24 g. of residue which would not distill at 1 mm. No fraction corresponding to 2-phenyl-1-tetralone was obtained.

2-Chloro-1-phenyl-1,2,3,4-tetrahydro-1-naphthol. Eighteen g. (0.1 mole) of 2-chloro-1-tetralone was treated with 100 cc. of 1.5*M* phenylmagnesium bromide solution in ether (0.15 mole) according to Procedure A to give 15.5 g. (60%) of 2-chloro-1-phenyl-1,2,3,4-tetrahydro-1-naphthol (140–160° at 0.5 mm.) m.p. 90–95°, with 6.0 g. chlorotetralone recovered. A sample of the chlorohydrin recrystallized several times from ligroin melted at 98–99°.

Anal. Calcd. for $C_{16}H_{15}OCl$: C, 74.3; H, 5.8. Found: C, 74.2; H, 5.8.

This experiment was repeated and the reaction mixture was carbonated by adding powdered Dry Ice before hydrolysis. No benzoic acid was obtained. The product consisted of 42% 2-chloro-1-tetralone and 58% chlorohydrin.

Rearrangement of 2-chloro-1-phenyl-1,2,3,4-tetrahydro-1-naphthol. A. With Phenylmagnesium bromide. Under conditions of Procedure B, 10 g. (0.039 mole) of 2-chloro-1-phenyl-1,2,3,4-tetrahydro-1-naphthol was added to 26 cc. (0.039 mole) of 1.5*M* phenylmagnesium bromide solution to give 7.0 g. (81%) of 2-phenyl-1-tetralone, m.p. 71–74°.

B. With sodium hydride. Thirteen g. (0.05 mole) of the chlorohydrin, when refluxed for 3 hr. with 1.3 g. (0.055 mole) of sodium hydride In dry benzene ether, gave 12.0 g. of starting material unchanged, m.p. 85–90°.

(15) A. A. Plentl and M. T. Bogert, *J. Am. Chem. Soc.*, **63**, 989 (1941).

2-Chloroindanone. The procedure used was that described for 2-chloro-1-tetralone. Fractionation of the product obtained from 132 g. (1.0 mole) of 1-indanone gave 92 g. (55%) of 2-chloroindanone [with 28 g. (21%) of 1-indanone recovered]; m.p. 34–38°, from petroleum heptane.[16]

2-Chloro 1-phe l-1-indanol. Under the conditions of Procedure A 25 g. (0 15 mole) of 2-chloroindanone was treated with 100 cc. of 2.1*M* phenylmagnesium bromide solution in ether (0.21 mole) to give 25 g. (69%) of 2-chloro-1-phenyl-1-indanol, m.p. 81–84°. A sample for analysis melted at 87–88°.

Anal. Calcd. for $C_{15}H_{13}OCl$: C, 73.6; H, 5.3. Found: C, 73.3; H, 5.2.

2-Phenylindanone. Ten g. (0.06 mole) of 2-chloroindanone was treated with 51 cc. (0.077 mole) of 1.5*M* phenylmagnesium bromide solution according to Procedure C to give 7.6 g. (60%) of 2-phenylindanone, m.p. 73–75°.[17] The *2,4-dinitrophenylhydrazone* derivative melted at 226–227°

Anal. Calcd. for $C_{21}H_{16}O_4N_4$: N, 14.4. Found: N, 14.1.

1-Keto-1,2,3,4,5,6,7,8-octahydroanthracene. This ketone was prepared as described by Krollpfeiffer and Schäfer.[18] A 75% yield of the ketone, m.p. 41–44°, was obtained.

2-Chloro-1-keto-1,2,3,4,5,6,7,8-octahydroanthracene. The procedure used was that described for the chlorination of 1-tetralone. Twenty-six g. of the ketone gave 20 g. (66%) of the chloroketone, m.p. 61–65°, after crystallization from alcohol. A sample for analysis melted at 66–67°.

Anal. Calcd. for $C_{14}H_{15}OCl$: C, 71.6; H, 6.4. Found: C, 71.1; H, 6.4.

2-Phenyl-1-keto-1,2,3,4,5,6,7,8-octahydroanthracene. Under the conditions of Procedure C, 16.5 g. (0.07 mole) of the chloroketone was treated with 33 cc. of 2.1*M* phenylmagnesium bromide solution in ether (0.07 mole) to give 10.0 g. (52%) of the phenyl ketone, m.p. 132–140°. A sample for analysis melted at 144–145°.

Anal. Calcd. for $C_{20}H_{20}O$: C, 87.0; H, 7.2. Found: C, 87.1; H, 7.3.

The *2,4-dinitrophenylhydrazone* derivative melted at 209–210°.

Anal. Calcd. for $C_{26}H_{24}O_4N_4$: N, 12.2. Found: N, 11.7.

EVANSTON, ILL.

(16) C. Courtot, A. Fayet, and P. Parant, *Compt. rend.*, **186**, 372 (1928).

(17) P. A. Plattner, R. Sandrin, and J. Wyss, *Helv. Chim. Acta*, **29**, 1604 (1946).

(18) F. Krollpfeiffer and W. Schäfer, *Ber.*, **56**, 620 (1923).

[CONTRIBUTION FROM THE RESEARCH DIVISION, AMERICAN CYANAMID CO.]

Triacylhalomethanes: 2-Halo-2-acyl-1,3-indandiones

K. C. MURDOCK[1]

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Various 2-halo-2-acyl-1,3-indandiones were prepared for evaluation as blood anticoagulants. Stability and activity paralleled the degree of branching in the acyl group. A halogenation procedure was developed which was particularly useful for the synthesis of the more labile products. The structures of some anomalous bromination products are discussed.

Certain 3-alkyl-4-hydroxycoumarins and 2-acyl-1,3-indandiones have been found to be potent blood anticoagulants[2] and are in general use for the treatment of thrombo-embolism. Somewhat erratic dose-response relationships present the alternative hazards of embolism or hemorrhage and have required that such therapy be very carefully controlled. In a search for improved anticoagulants there have been prepared a number of 2-halo-2-acyl-1,3-indandiones (I), novel triacylhalomethanes.

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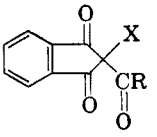
(2) W. H. Seegers, *Pharm. Rev.*, **3**, 278 (1951).

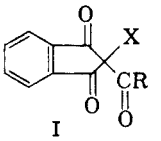
TABLE I

2-HALO-2-ACYL-1,3-INDANDIONES



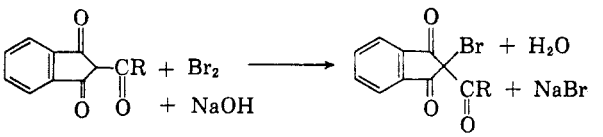
R	X	Method	Yield, %	M.P., °C.[a]	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Halogen, % Calcd.	Halogen, % Found
C_6H_5	Br	A[b]	62	119	58.4	58.2	2.76	2.66	24.2	24.4
2-HOOC-C_6H_4	Br		25	120–132[c]	54.8	54.2[d]	2.43	2.40[d]	21.4	22.0
$(C_6H_5)_2CH$	Br	A[e]	80	139–140	66.0	66.0	3.62	3.29	19.1	19.0
$(C_6H_5)_2CH$	Br	B[f]	79	136–139						
$(C_6H_5)_2CH$	Cl	B[e]	20	157	73.7	73.1	4.03	4.01	9.46	9.75
$(C_6H_5)_2COH$	Br	A[e]	2[g]	160	63.5[h]	63.0	3.48	3.46	18.4	18.9
$C_6H_5CH_2$	Br	B[e]	42	86	59.5	59.5	3.23	3.19	23.3	23.0[d]
CH_3CH_2	Br	B[e]	7	74–75	51.3	51.4	3.23	3.45	28.4	28.1[d]
$(CH_3)_2CH$	Br	B[e]	78	60–61	53.0	52.9	3.76	3.79	27.1	27.2
$(CH_3)_3C$	Br	B[e]	66	103	54.4	54.4	4.24	4.19	25.8	26.1

[a] All melting points are corrected. [b] Product recrystallized from carbon tetrachloride. [c] Lit. (ref. 3): no m.p. reported. [d] Average of two determinations. [e] Product recrystallized from a mixture of benzene and *n*-hexane. [f] Product was not recrystallized. [g] Obtained as a by-product. See text. [h] Calcd.: O, 14.7. Found: O, 15.5.



I

II. R = 2-C_6H_4COOH, X = Br
III. R = $CH(C_6H_5)_2$, X = Br
IV. R = $C(CH_3)_3$, X = Br



The only halogen compound of this type previously described in the literature was 2-bromo-2-(2-carboxybenzoyl)-1,3-indandione (II). This was an unstable substance for which no physical constants were reported.[3] In the present investigation early attempts to brominate 2-pivalyl-1,3-indandione resulted in the formation of 2,2-dibromo-1,3-indandione, a product of brominative cleavage. This result paralleled the findings of Hunter and Yackel who obtained the same product from the action of bromine on 2-benzoyl-1,3-indandione; they recommended this method of degradation as a proof of structure for 2-acyl-1,3-indandiones.[4]

Two bromination methods have been developed which have enabled the synthesis of the 2-bromo-2-acyl-1,3-indandiones listed in Table I. In the first method (A), the reaction was carried out in refluxing chloroform with two equivalents of bromine being preferred. The second method (B) was generally applicable and was the only method successfully used for the preparation of the more sensitive bromo compounds. This method involved a two-phase reaction at 0° of a chloroform solution of the triketone with bromine dissolved in an equivalent amount of aqueous sodium hydroxide. Stirring was adjusted so as to mix the two phases only slightly; thus, the sensitive brominated product, in the organic layer, was less subject to hydrolysis. 2-Chloro-2-diphenylacetyl-1,3-indandione was prepared with a commercial sodium hypochlorite solution.

The conditions of time and temperature and the use of an inert solvent for recrystallization were found to be important. Stability of the brominated products paralleled the degree of branching in the acyl side chain. The brominated 2-propionyl and 2-phenylacetyl compounds decomposed extensively on standing overnight. The 2-bromo-2-diphenylacetyl-1,3-indandione (III) and 2-bromo-2-pivalyl-1,3-indandione (IV) did not evidence decomposition for months. The 2-chloro analog of III was stable. This stability of the chloro analog as compared with the bromo compound parallels the reported relationship between the corresponding 2-halo-2-carbethoxy-1,3-indandiones.[5]

With those 2-acyl-1,3-indandiones having an α-hydrogen atom in the acyl group, it was necessary to consider the possibility that halogenation replaced this hydrogen atom rather than that in the 2-position of the indandione nucleus. In the bromination of the somewhat analogous ethyl acetoacetate the α-bromo derivative is the primary product, but it gradually rearranges to form the more stable γ-bromo isomer.[6] After one bromination of 2-diphenylacetyl-1,3-indandione the reaction mixture was allowed to stand at 100° for several hours

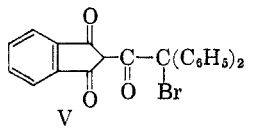
(3) W. Wislicenus and H. Schlichenmaier, *Ann.*, **460**, 278 (1928).

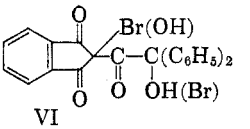
(4) W. H. Hunter and E. C. Yackel, *J. Am. Chem. Soc.*, **58**, 1395 (1936).

(5) L. Flatow, *Ber.*, **34**, 2145 (1901).

(6) A. Hantzsch, *Ber.*, **27**, 3168, 355 (1894).

during the removal of solvent. Though none of the usual monobromo derivative was isolated, there was obtained a small amount of an isomeric monobromide, along with what appears to be a *bis* compound from two molecules of starting material. In the infrared absorption spectrum of this isomeric monobromide twin maxima were seen[7] in the carbonyl region at 5.74 and 5.83μ. These set it apart from the other monobromides (Table I) in which the location of the bromine atom was in question. The latter compounds, like 2-bromo-2-pivalyl-1,3-indandione (IV) in which the bromine atom is necessarily *alpha* to all three carbonyl groups, exhibited only a single strong maximum in that region (5.79μ). They were accordingly designated as 2-bromo derivatives while the above, abnormal product was designated as V, 2-diphenylbromoacetyl-1,3-indandione.


V


VI

From the normal bromination of 2-diphenylacetyl-1,3-indandione there was isolated in addition to the 2-bromo derivative about 2% of another brominated substance. This compound exhibited an infrared absorption maximum at 2.98μ (Nujol mull), indicating the presence of a hydrogen-bonded hydroxyl group. From the location of the absorption peaks in the carbonyl region (5.63 and 5.77μ), the alternative locations of the bromine and hydroxyl groups of this bromohydroxy-2-diphenylacetyl-1,3-indandione (VI) could not be firmly established.

An aminolysis of the bromine atom in 2-bromo-2-diphenylacetyl-1,3-indandione (III) was effected with piperidine, forming the corresponding 2-piperidino compound.

Most of the compounds of Table I were active as anticoagulants. In general their activities paralleled the degree of branching in the acyl side chain and were about the same as those[8] of the corresponding unhalogenated precursors. Toxicities were somewhat lower. The pharmacological evaluations were made by Mr. Vincent Downing and his associates at the Lederle Laboratories and are to be reported in detail elsewhere.[9]

EXPERIMENTAL

2-Acyl-1,3-indandiones. 2-Benzoyl-, 2-propionyl-, 2-isobutyryl-, 2-pivalyl-,[10] 2-diphenylacetyl-,[11] and 2-phenylacetyl-1,3-indandione were prepared by the acylation of the appropriate methyl ketone with diethyl phthalate in the presence of sodium methoxide. The synthesis of 2-phenylacetyl-1,3-indandione[12] does not appear to have been described previously: m.p. 84°.

Anal. Calcd. for $C_{17}H_{12}O_3$: C, 77.3; H, 4.58. Found: C, 77.1; H, 4.63.

2-(2-Carboxybenzoyl)-1,3-indandione. Instead of following the reported synthetic sequence for the preparation of this compound,[3] which requires four steps after the preparation of 1,3-indandione, the magnesium salt of 1,3-indandione was acylated with phthalic anhydride. To a warm slurry of 0.16 mole of finely powdered magnesium methoxide in 80 ml. of dry benzene, protected from moisture, was added with stirring a solution at 50° of 23.4 g. (0.16 mole) of 1,3-indandione[13] in 320 ml. of benzene. (The magnesium methoxide, 19.4 g., had been dried *in vacuo* at 100° and appeared to be free of methanol, but from the apparently excessive yield obtained in its preparation it did not contain more than 63% of the desired compound.) A deep brown color developed with the addition. After 5 min. of stirring the mixture was chilled to 5° with an ice bath. There was then added with chilling and stirring a hot solution of 23.4 g. (0.16 mole) of phthalic anhydride in 240 ml. of benzene, at such a rate that the temperature of the reaction mixture did not rise above 10°. With the reaction flask initially chilled in the ice bath, stirring was continued for 42 hr. It was estimated that the ice bath used would require 3–4 hr. to come to room temperature.

The solid in the reaction mixture was collected by filtration and washed with benzene, giving 14.9 g. of a dark material (A) which did not melt by 360° (see below). The dark gray filtrate was extracted with 500 ml. of water. The intensely purple, aqueous extract was neutralized just to the disappearance of the purple color by the gradual addition with swirling of 95 ml. of 1*N* hydrochloric acid. The mixture was allowed to stand 1 hr. as the precipitate agglomerated. The precipitate was collected (saving the dark brown filtrate—see below), washed with water, dried, and recrystallized from dioxane. The produt separated as yellow-orange granules, m.p. 208–211° (dec.). Wislicenus and Kötzle[14] reported the m.p. of 2-(3-oxo-1-indanylidene)-1,3-indandione ("bindone") as 206–208°.

Anal. Calcd. for $C_{18}H_{10}O_3$: C, 78.8; H, 3.68. Found: C, 78.6; H, 3.22.

After thorough extraction with water of the above-mentioned dark solid (A) present in the reaction mixture there remained after drying 4.0 g. of a green, infusible salt. This appeared to be inert to the action of dilute acid. Upon stirring with concentrated hydrochloric acid, however, the green color was discharged, leaving 3.4 g. of a yellow-orange solid, m.p. 205–207°. The melting point of this material was not depressed after admixture with bindone.

The above-mentioned filtrate remaining after removal of the bindone was acidified by the portionwise addition of *ca.* 150 ml. of 1*N* hydrochloric acid. A solid slowly separated during the next 1.5 hr. This solid was collected and washed with water; 2.2 g., m.p. 160–162°. Recrystallization from ethanol-water followed by drying *in vacuo* at 60° over phosphorus pentoxide gave a tan powder, m.p. (taken rapidly) 156–160°, with sudden gassing at about 180°; lit.,[3] m.p. 155–160°.

Anal. Calcd. for $C_{17}H_{10}O_5$: C, 69.4; H, 3.43. Found: C, 68.3, 68.0; H, 3.37, 3.45.

2-Halo-2-acyl-1,3-indandiones. The two halogenation methods used for the preparation of the 2-halo-2-substituted-1,3-indandiones of Table I involved the use of: (A) bromine in refluxing chloroform or (B) a two-phase mixture at 0°

(7) All infrared absorptions were determined in chloroform solution unless specified otherwise.

(8) J. T. Correll, L. L. Coleman, S. Long and R. F. Willy, *Proc. Soc. Exp. Biol. Med.*, **80**, 139 (1952).

(9) V. Downing, *et al.*, to be published.

(10) L. B. Kilgore, J. H. Ford, and W. B. Wolfe, *Ind. Eng. Chem.*, **34**, 494 (1942).

(11) D. G. Thomas, U. S. Patent **2,672,483** (1954).

(12) Prepared by Dr. R. L. Horton.

(13) W. Teeters and R. Shriner, *J. Am. Chem. Soc.*, **55**, 3026 (1933).

(14) W. Wislicenus and A. Kötzle, *Ann.*, **252**, 72 (1889).

of chloroform and a solution of bromine in an equivalent amount of aqueous sodium hydroxide.

The following examples are illustrative: *Method A. 2-Bromo-2-diphenylac tyl-1,3-indandione* (III). To a solution of 136.2 g. (0.4 mole) of 2-diphenylacetyl-1,3-indandione in 600 ml. of chloroform was added 41.9 ml. (127.8 g., 0.8 mole) of bromine. The mixture was heated under reflux for 6 hr. The hydrogen bromide evolved was trapped in a beaker of water. The solvent and excess bromine were distilled off until the rate of distillation diminished. To avoid overheating the sensitive product, the remaining volatile material was then distilled under aspirator pressure until the residue just began to crystallize. Immediately, 320 ml. of dry, boiling benzene was added. The resulting red solution was filtered through a plug of cotton, 800 ml. of warm *n*-hexane was added to the filtrate, and the resulting solution was allowed to cool to room temperature. On top of the main crop of large, white prisms which separated there were observed clumps of light tan, fine needles. The product was collected by filtration and thoroughly washed on the Büchner funnel with ethanol, thus removing the contaminating needles. (The isolation of this by-product, bromohydroxy-2-diphenylacetyl-1,3-indandione, VI, is described below.) After drying at 60° the product weighed 133.7 g. (80%), m.p. 139–140°.

Anal. Calcd. for $C_{23}H_{15}O_3Br$: C, 66.0; H, 3.62; Br, 19.1. Found: C, 66.0; H, 3.29; Br, 19.0.

After 2 months in a brown bottle at room temperature the melting point of a sample of this compound was not lower, nor were there observed any other signs of decomposition. But after 9 months the external surfaces had become yellow and the melting point had dropped to 129–136°.

Method B. 2-Bromo-2-pivalyl-1,3-indandione (IV). To an ice-cold solution of 4.5 g. (0.02 mole) of 2-pivalyl-1,3-indandione in 25 ml. of chloroform was added an ice-cold solution of 0.8 g. (0.02 mole) of sodium hydroxide and 3.2 g. (0.02 mole) of bromine in 25 ml. of water. The mixture was stirred for 5 hr. while chilling the reaction flask with an ice bath. The chloroform layer was separated, diluted with 25 ml. of cold chloroform, extracted rapidly with an ice-cold solution of 0.4 g. (0.01 mole) of sodium hydroxide in 25 ml. of water, washed with two ice-cold portions of water, and dried over anhydrous calcium chloride. The chloroform solution was filtered, then concentrated to dryness *in vacuo*. The pale yellow crystalline residue was dissolved in 11 ml. of warm, dry benzene and 25 ml. of *n*-hexane was added. Crystallization began rapidly and was allowed to continue, finally at 5°. The product was collected by filtration, washed with *n*-hexane, and dried at room temperature; 4.1 g. (66%), elongated prisms, m.p. 103°.

Anal. Calcd. for $C_{14}H_{13}O_3Br$: C, 54.4; H, 4.24; Br, 25.8. Found: C, 54.4; H, 4.19; Br, 26.1.

Brominative cleavage of 2-pivalyl-1,3-indandione: 2,2-dibromo-1,3-indandione. To a solution of 1.0 g. of 2-pivalyl-1,3-indandione in 2.5 ml. of chloroform was added portionwise about 1.5 ml. of bromine. The evolution of hydrogen bromide was accompanied by the separation of a crystalline material which, however, redissolved upon the addition of the last 0.5 ml. of bromine. The mixture was allowed to stand for 1 hr., whence the solvent and unreacted bromine were removed *in vacuo*. The residue, after four recrystallizations from ethanol, gave a small quantity of a white solid, m.p. 179–181°; lit.,[4] m.p. 178–179°.

Anal. Calcd. for $C_9H_4O_2Br_2$: C, 35.6; H, 1.33; Br, 52.5. Found: C, 35.0, 35.0; H, 1.53, 1.80; Br, 52.6, 52.4.

Abnormal products from the action of bromine on 2-diphenylacetyl-1,3-indandione. In an early attempt to prepare 2-bromo-2-diphenylacetyl-1,3-indandione by the procedure described in Method A, the molar ratio of bromine to 2-diphenylacetyl-1,3-indandione (96.1 g.) was only 1.2:1, rather than 2:1. After heating the reaction mixture under reflux for 3 hr., the chloroform and unreacted bromine were distilled off over the steam bath, allowing the distillation residue to stand over the steam bath for an additional 3 hr. Although this residue was thoroughly investigated by a series of fractional crystallizations, none of the desired product was isolated. In addition to 33% of recovered starting material there were finally isolated, on the basis of the solubilities mentioned below, the following two compounds:

1. *2-Diphenylbromoacetyl-1,3-indandione* (V). This compound separated from a mixture of benzene and *n*-hexane as white platelets, 3.6 g., m.p. 184° (orange melt). In contrast to the starting material it was relatively insoluble in carbon tetrachloride, though soluble in benzene and dioxane.

Anal. Calcd. for $C_{23}H_{15}O_3Br$: C, 66.0; H, 3.62; Br, 19.1. Found: C, 66.2, 66.2; H, 3.47, 3.44; Br, 19.0.

2. *"Bis(2-diphenylacetyl-1,3-indandione)."* This second compound was recrystallized with much loss from dimethylformamide (2 ml./g.). There was obtained 8.6 g. of deeply yellow prisms, m.p. 190–195°, with gassing. This material was almost insoluble in most solvents, although it was moderately soluble in hot 2-ethoxyethanol. It gave a negative Beilstein test for halogen. Though soluble in 2*N* methanolic potassium hydroxide, it was apparently insoluble in and did not color 20% aqueous sodium hydroxide.

Anal. Calcd. for $C_{46}H_{30}O_3$: C, 81.5; H, 4.46. Found: C, 80.9, 81.2; H, 4.14, 4.05.

Bromohydroxy-2-diphenylacetyl-1,3-indandione (VI). This compound was isolated, as indicated above in the example illustrating Method A, as a by-product from the synthesis of 2-bromo-2-diphenylacetyl-1,3-indandione. In three runs there was brominated a total of 680 g. (2.0 moles) of 2-diphenylacetyl-1,3-indandione. From the crude solids obtained by chilling and concentrating the mother liquor and alcoholic washes of the main product, there was obtained a total of 18.7 g. (2%) of the by-product. Its extraction from these crude solids was enabled by its ready solubility in unheated alcohol. The alcoholic extracts were concentrated to dryness *in vacuo* and the residue was recrystallized from mixtures of benzene and *n*-hexane. The product separated as fine, white needles, m.p. 160°.

Anal. Calcd. for $C_{23}H_{15}O_4Br$: C, 63.5; H, 3.48; Br, 18.4; O, 14.7. Found: C, 63.0; H, 3.46; Br, 18.9; O, 15.5.

From the above crude solids there was also obtained about 10% of unreacted starting material and 3.1 g. of "bis(2-diphenylacetyl-1,3-indandione)."

2-Chloro-2-diphenylacetyl-1,3-indandione. To a solution at 0° of 68.0 g. (0.2 mole) of 2-diphenylacetyl-1,3-indandione in 200 ml. of chloroform was added 94.0 ml. of a cold sodium hypochlorite solution (containing 15.1 g. of active chlorine per 100 ml. of solution. This hypochlorite was later found to contain free sodium hydroxide, which would be expected to convert some of the starting material to its sodium salt, thus lowering the yield in the chlorination). The mixture was kept cold with an ice bath and stirred for 7.5 hr. The yellow solid then present was removed by filtration and washed once with chloroform. The chloroform layer from the combined filtrate and wash was washed once with water and dried over anhydrous calcium chloride. The solvent was removed *in vacuo*, the yellowish residue dissolved in 180 ml. of hot benzene, 200 ml. of hot *n*-hexane added to the filtrate, and the solution allowed to cool, finally at 5°. The solid which separated was collected, washed with a mixture of benzene and *n*-hexane (3:1), and dried at 60°. There was thus obtained 16.7 g. of a pale, pink solid, m.p. 157°. After two more recrystallizations from mixtures of benzene (3 ml./g.) and *n*-hexane (6 ml./g.), using decolorizing charcoal, there was obtained 14.5 g. (20%) of a pinkish white solid, m.p. still 157°. After 1.5 months at room temperature a sample had become slightly yellow on the surface, where it was exposed to diffuse light, but the melting point had not dropped.

Anal. Calcd. for $C_{23}H_{15}O_3Cl$: C, 73.7; H, 4.03; Cl, 9.46. Found: C, 73.1; H, 4.01; Cl, 9.75.

The yellow solid which separated from the reaction mixture, 33.8 g., was suspended in hot water, and concentrated hydrochloric acid was added dropwise until the mixture was

acidic to benzopurpurin paper. The solid present was collected, washed with water, dried, and recrystallized from 80 ml. of 2-ethoxyethanol to give 18.5 g. (27% recovery) of yellow needles, m.p. 147–148°. A mixture melting point determination with starting material showed no depression (148–149°).

2-Diphenylacetyl-2-piperidino-1,3-indandione. To a solution at 20° of 29.7 g. (0.071 mole) of 2-bromo-2-diphenylacetyl-1,3-indandione (III) in 1200 ml. of dioxane was added gradually with swirling 21.0 ml. (18.1 g., 0.213 mole) of piperidine. The mixture warmed spontaneously to 43°. After standing overnight the piperidinium bromide which had separated was removed by filtration and washed with dioxane and acetone; 5.5 g. (47%), m.p. and mixture m.p. 240–241°. The bright orange mother liquor and the dioxane wash were combined, evaporated under reduced pressure, and the dark, viscous residue allowed to crystallize at 5° from 140 ml. of carbon tetrachloride. The solid which separated, after washing with carbon tetrachloride and water, amounted to 11.6 g., m.p. 181–187 . Recrystallization from methyl ethyl ketone gave 6.6 g. (22%) of bright yellow rods, m.p. 192–193°.

Anal. Calcd. for $C_{28}H_{25}O_3N$: C, 79.41; H, 5.95; N, 3.31. Found: C, 79.8; H, 6.12; N, 3.35.

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Decarboxylation of Thetin Salts

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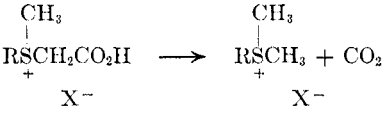
Dialkyl thetin salts, $R_1R_2\overset{+}{S}CH_2CO_2H\cdot X^-$, undergo facile decarboxylation to the corresponding trialkylsulfonium salts. The presence of an electron-donating (methyl) group on the alpha-carbon tends to suppress the reaction.

To the ever-increasing accounts of differences in reactivity,[1] conjugative ability[2,3] and the like between numerous sulfonium and ammonium compounds should be added another example of considerable interest. In the course of a study of various long-chain thetin salts (I), it was discovered that facile decarboxylation occurrred under relatively mild conditions to give the corresponding trialkyl sulfonium salts.



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This reaction is virtually unknown in the corresponding betaine (ammonium) series, in which the compounds are ordinarily stable at temperatures below their melting points which often run in excess of 200°. A noteworthy exception[4] has been reported with the betaine derived from 2,5-dimethylpyrazine, in which case decarboxylation is facilitated by an intermediate capable of resonance stabilization.

The reaction was first encountered in alkaline hydrolysis of carbethoxymethyl(dodecyl)methylsulfonium *p*-toluenesulfonate. The identity of the product as dodecyldimethylsulfonium *p*-toluenesulfonate was shown by (1) analysis, (2) the infrared spectrum which indicated the absence of carboxyl ion and the presence of *p*-toluenesulfonate ion, and (3) comparison with an authentic specimen. Dodecylmethylthetin, the expected product, was prepared by the action of silver oxide on the thetin hydrochloride and proved to be quite stable in contrast to the report of Werntz,[5] who used alkali to liberate this thetin from its salt. The thetin can also be reconverted to a salt, as shown by the reaction of dodecylmethylthetin with *p*-toluenesulfonic acid. The decarboxylation of the thetin salts is quite general, as was later confirmed in the cases of the decyl, tetradecyl, hexadecyl, and decamethylenebis analogs.

The ease with which decarboxylation of dodecyldimethylthetin *p*-toluenesulfonate occurs was shown by experiments carried out in refluxing acetone. At this relatively low temperature (56°), decarboxylation occurred readily and was complete within 2 hours in the presence of such mildly basic catalysts as piperidine, Amberlite IR-4B, and dodecylmethylthetin, itself. In the absence of a catalyst, no reaction was apparent after 1 hour, but, after 6 hours, a 94% yield of decarboxylated product was obtained. Evidently the reaction is extremely slow at first, until a sufficient quantity

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