heights at 0.36 and 0.50 ppm) was again 71:29.

(b) By Sodium Methoxide. The title compound (40 mg, 0.22 mM; *Z,Z*:*E,E* = 65:35) was dissolved in $CDCl_3$ (0.5 mL). 1, 2, 5, 10, and 20 μL of a 0.81 M sodium methoxide solution in methanol were added. Relative amounts of isomers were determined by measuring the peak heights of their silicon methyl signals. $k'(k)$ values, in s^{-1}, were found to be 1.77×10^{-5} (5.62×10^{-6}) for [NaOMe] = 1.63×10^{-3} M, 2.91×10^{-5} (9.23×10^{-6}) for [NaOMe] = 3.25×10^{-3} M, 5.32×10^{-5} (1.68×10^{-5}) for [NaOMe] = 8.07×10^{-3} M, 5.83×10^{-5} (1.84×10^{-5}) for [NaOMe] = 1.60×10^{-2} M, and 6.21×10^{-5} (1.95×10^{-5}) for [NaOMe] = 3.13×10^{-2} M.

Acknowledgment. Support of our work by the Australian Research Grants Commission is gratefully acknowledged. We thank Mr. V. Alberts for experimental assistance and Professor M. D. Sutherland (University of Queensland) for providing analytical facilities. Mass spectra were recorded by Mr. G. A. Macfarlane and Dr. R. F. Evans. We gratefully acknowledge the cooperation of the National NMR Center, Canberra, and of Mr. K. Penman and Miss L. Lambert, University of Queensland, in recording ^{13}C and ^{19}F spectra. We also thank Ing. H. Begutter and W. Deimbacher, Tobacco Research Institute, Vienna, Austria, for GC/MS information.

Registry No. 1, 71518-75-7; (*E,E*)-1-chloro-1,2,5-trimethyl-1-silacyclopentane, 71518-76-8; (*E,Z*)-1-chloro-1,2,5-trimethyl-1-silacyclopentane, 71564-07-3; (*Z,Z*)-1-chloro-1,2,5-trimethyl-1-silacyclopentane, 71564-08-4; (*E,E*)-1-methoxy-1,2,5-trimethyl-1-silacyclopentane, 71518-77-9; (*E,Z*)-1-methoxy-1,2,5-trimethyl-1-silacyclopentane, 71564-09-5; (*Z,Z*)-1-methoxy-1,2,5-trimethyl-1-silacyclopentane, 71564-10-8; (*E,E*)-1-fluoro-1,2,5-trimethyl-1-silacyclopentane, 71564-11-9; (*E,Z*)-1-fluoro-1,2,5-trimethyl-1-silacyclopentane, 71564-12-0; (*E,E*)-1-acetoxy-1,2,5-trimethyl-1-silacyclopentane, 71605-99-7; (*E,Z*)-1-acetoxy-1,2,5-trimethyl-1-silacyclopentane, 71606-00-3; (*Z,Z*)-1-acetoxy-1,2,5-trimethyl-1-silacyclopentane, 71518-78-0; (*E,E*)-1,2,5-trimethyl-1-silacyclopentane, 68212-43-1; (*E,Z*)-1,2,5-trimethyl-1-silacyclopentane, 71564-13-1; sodium methoxide, 124-41-4.

Facile Synthesis of 6,7-Dichloro-1-oxo-5-indanylalkanoic Acids and Related Compounds via Triflate Displacement

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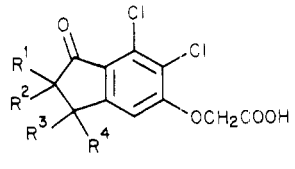
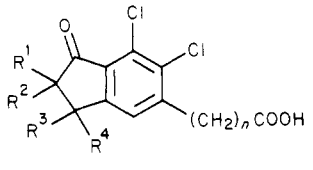
Substitution of the triflate group in 6,7-dichloro-1-oxo-5-indanyl trifluoromethanesulfonates, by a conjugative addition–displacement mechanism, provides a new route to 1-indanones with a variety of substituents in the 5-position.

A number of compounds from the 6,7-dichloro-1-oxo-5-indanyloxyacetic acid series (**1**) possess interesting pharmacological activities. The diuretic and uricosuric properties of some members of this series have been described,[1] and more recently, biological activities of potential therapeutic value have been found in other compounds of the series.[2]



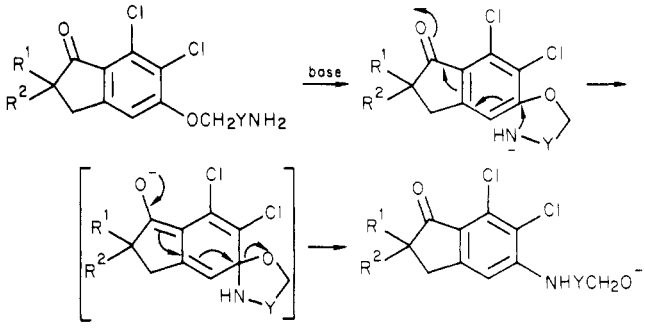
1



2

To the medicinal chemist the related series of compounds lacking the ether linkage between the aromatic ring and the side chain (**2**) is of interest as a component in the structure/activity pattern in this area, but hitherto only arduous methods of synthesis for compounds in this second series have been available. A new approach to this problem was suggested by the observation that the ether linkage in derivatives of compounds of general formula **1** could be substituted by a nitrogen under strongly basic conditions.[3] This rearrangement presumably takes place via a conjugative addition–displacement mechanism as outlined in Scheme I, and finds a parallel in a recent publication.[4]

Scheme I



Y = CH_2 or CO

The first idea of exploiting the unusual reactivity of this system for the preparation of compounds of formula **2** was to try to bring about the intramolecular displacement of the 5-oxygen by a carbanion. Several possible O-derivatives could be envisaged as candidates for this type of rearrangement. However, before we embarked on this

(1) (a) O. W. Woltersdorf, Jr., S. J. de Solms, E. M. Schultz, and E. J. Cragoe, Jr., *J. Med. Chem.*, **20**, 1400 (1977). (b) S. J. de Solms, O. W. Woltersdorf, Jr., E. J. Cragoe, Jr., L. S. Watson, and G. M. Fanelli, Jr., *J. Med. Chem.*, **21**, 437 (1978).

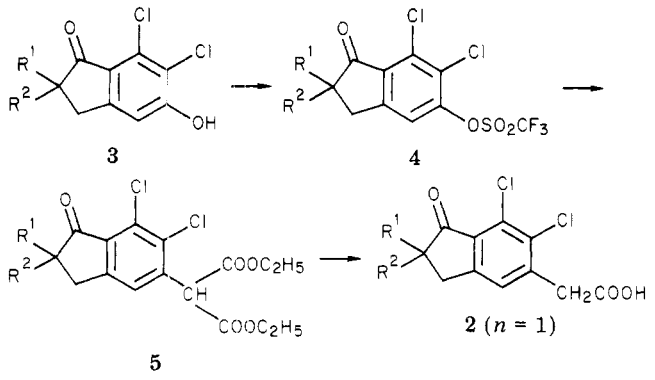
(2) Unpublished work in our laboratories

(3) H. W. R. Williams and O. W. Woltersdorf, Jr., unpublished results.

(4) R. Bayles, M. C. Johnson, R. F. Maisey, and R. W. Turner, *Synthesis*, 31, 33 (1977).

0022-3263/79/1944-4060$01.00/0

Scheme II

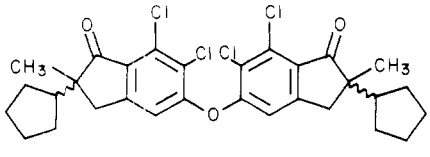


a, $R^1 = CH_3$; R^2 = cyclopentyl; b, $R^1 = R^2 = CH_3$; c, $R^1 = CH_3$; $R^2 = C_6H_5$

approach, the substitution reactions of nitroaryl triflates by Atkinson and co-workers[5] were made known to us, and this information made possible the straightforward route described below.

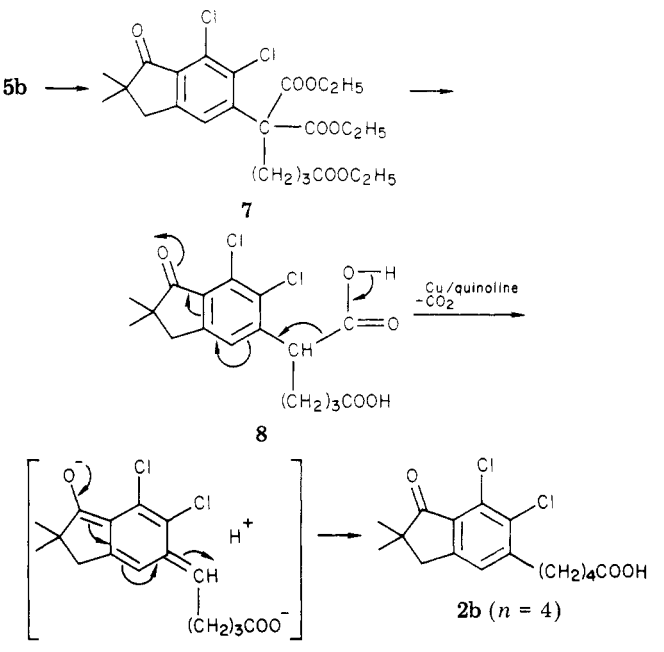
The hydroxyindanone **3a**[1] was treated with anhydrous potassium carbonate in acetone and then with trifluoromethanesulfonyl chloride to give the triflate **4a** in 94% crude yield as an oil (see Scheme II). Reaction of **4a** with 4 equiv of the sodium salt of diethyl malonate in dimethylformamide at 0–5 °C (rising to room temperature), followed by acidification and workup, afforded **5a** in 77% yield. Hydrolysis and decarboxylation of **5a** gave the desired compound **2a** (n = 1). In this sequence all of the compounds were obtained as oils, but the physical data (NMR, IR, and TLC) were in good agreement for structure and purity, and the final compound was characterized as the dicyclohexylammonium salt.

A small quantity of the ether **6** was isolated during the chromatographic purification of **5a**. Presumably this byproduct arose from a small amount of hydrolysis of the triflate **4a** followed by reaction of the resulting phenoxide ion with more triflate.

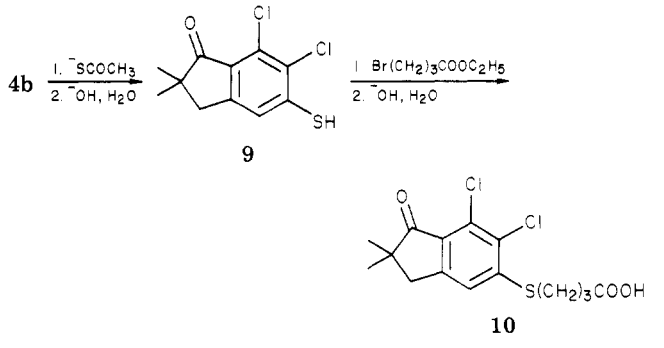


A parallel series of reactions was carried out by starting with hydroxyindanone **3c**, and the ultimate compound **2c** was obtained as a solid. Likewise, hydroxyindanone **3b** gave triflate **4b** which was converted similarly to malonic ester **5b**. Hydrolysis and decarboxylation of **5b** afforded the substituted acetic acid **2b** (n = 1). In this series, malonic ester **5b** served as an intermediate for the preparation of higher homologous acids in the series **2** (Scheme III). Thus, alkylation of **5b** with ethyl 4-bromobutyrate gave the tricarboxylic ester **7** which on saponification and acidic workup afforded dicarboxylic acid **8**. This acid underwent a surprisingly facile decarboxylation when heated at 140 °C in quinoline with copper powder to yield 90% of the pentanoic acid **2b** (n = 4). The ease of decarboxylation may be attributed to the extended β-keto acid character of the intermediate monocarboxylic acid **8**, which, while it does not provide a cyclic transition state for the loss of CO_2, nevertheless provides a means of electron flow to facilitate such a reaction.

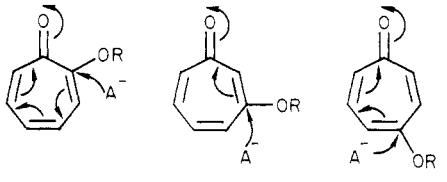
Scheme III



Scheme IV



Scheme V



An obvious extension of this chemistry is the preparation of sulfides by the displacement of the trifluoromethylsulfonyloxy group in triflates **4** by mercaptide anions. Such a displacement is the basis for the synthesis of a thio analogue of **2b** (n = 4) (compound **10**, Scheme IV). Triflate **4b** reacted with sodium thiolacetate in dimethylformamide to yield, after hydrolysis of the *S*-acetyl group, the thiophenol **9**. Alkylation of **9** with ethyl 4-bromobutyrate and subsequent ester hydrolysis gave **10**.

Two reactions with similar mechanisms have been described in the literature since our work was completed. One involves the substitution of the tosyloxy group of 3-tosyloxytropone by alkoxide,[6] and the second is the reaction of lithium amide derivatives with 2-(2-methoxyphenyl)-4,4-dimethyloxazoline,[7] although in the latter example chelation of the cation plays an important part in the course of the reaction. The tropolone series is of interest in two respects: first, the coplanarity of the carbonyl group must be a factor in promoting the electron shifts

(5) J. G. Atkinson, B. K. Wasson, J. J. Fuentes, Y. Girard, E. L. Engelhardt, and C. S. Rooney, *Tetrahedron Lett.*, in press.

(6) M. Cavazza, R. Cabrino, and F. Pietra, *Synthesis*, 298 (1977).
(7) A. I. Meyers and R. Gabel, *J. Org. Chem.*, **42**, 2653 (1977).

involved in the reaction (as it probably does with indanones also), and second, it may be noted that, theoretically, derivatives of all three tropolones can undergo the electron shifts necessary for this type of substitution (Scheme V), whereas only suitably substituted ortho and para phenol derivatives can react in this way.

Although there are limitations to the scope of the triflate displacement reaction even within the classes of compound in which the necessary electron shifts can theoretically occur, the reaction can provide an easy synthetic route to a compound which otherwise would be very difficult to prepare. The synthetic utility is demonstrated by the cases described above.

Experimental Section

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 257 spectrometer and NMR spectra on a Varian EM 360 spectrophotometer. Mass spectra were provided by Morgan Schaffer Corp. of Montreal.

Preparation of 2-Cyclopentyl-6,7-dichloro-2-methyl-1-oxo-5-indanyl Trifluoromethanesulfonate (4a). A mixture of 2-cyclopentyl-6,7-dichloro-5-hydroxy-2-methyl-1-indanone (20.93 g, 0.07 mol), anhydrous potassium carbonate (25.95 g, 0.188 mol), and dry acetone (350 mL) was stirred at room temperature for 20 min and then treated with a solution of trifluoromethanesulfonyl chloride (12.70 g, 0.0754 mol) in acetone (20 mL) added portionwise. Reaction was complete (by TLC) in 15 min. The mixture was filtered and evaporated to dryness in vacuo. The residue was dissolved in methylene chloride and the solution dried ($MgSO_4$) and again evaporated in vacuo [finally at 50 °C (0.05 torr)] to an oil: 28.45 g (94%); IR (KBr) 2945, 2860, 1720, 1430 cm^{-1}; NMR ($CDCl_3$) δ 7.42 (s, 1 H, aromatic H), 3.15 and 2.77 (2 d, J = 18 Hz, 2 H, benzyl CH_2), ~2.5–1 (m, 9 H, cyclopentyl H's), 1.23 (s, 3 H, CH_3).

Anal. Calcd for $C_{16}H_{15}Cl_2F_3O_4S$: C, 44.56; H, 3.51; S, 7.43. Found: C, 45.31; H, 3.59; S, 6.96.

Preparation of 6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl Trifluoromethanesulfonate (4b). A mixture of 6,7-dichloro-5-hydroxy-2,2-dimethyl-1-oxoindan (10.00 g, 0.0408 mol), potassium carbonate (16.92 g, 0.1224 mol), and dimethylformamide (40 mL) was treated, dropwise during 30 min, with trifluoromethanesulfonyl chloride (7.91 g, 0.0469 mol) while the temperature was not allowed to rise to about 30 °C. Stirring was continued at ambient temperature.

After 30 min, the mixture was poured into cold water (200 mL). The resulting oil was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give the title compound as a light tan solid: yield 14.36 g (93%), mp 63–65 °C. Recrystallization from hexane gave light orange rods, mp 65–66.5 °C.

Anal. Calcd for $C_{12}H_9Cl_2F_3O_4S$: C, 38.21; H, 2.41. Found: C, 38.49; H, 2.28.

Preparation of 6,7-Dichloro-2-methyl-1-oxo-2-phenyl-5-indanyl Trifluoromethanesulfonate (4c). To a stirred solution of 6,7-dichloro-5-hydroxy-2-methyl-2-phenyl-1-indanone (12.28 g, 0.04 mol) in acetone (150 mL) was added potassium carbonate (13.18 g, 0.095 mol).

After 10 min a solution of trifluoromethanesulfonyl chloride (11.81 g, 0.07 mol) in acetone (150 mL) was added over 10 min. After 15 min of stirring the precipitated salts were filtered, and the acetone was evaporated at reduced pressure to leave an oil which upon trituration with hexane gave 15 g (85%) of product which melted at 105–107 °C.

Anal. Calcd for $C_{17}H_{11}Cl_2F_3O_4S$: C, 46.48; H, 2.52. Found: C, 46.72; H, 2.72.

Preparation of Diethyl (2-Cyclopentyl-6,7-dichloro-2-methyl-1-oxo-5-indanyl)malonate (5a). A solution of diethyl malonate (19.2 g, 120 mmol) in dimethylformamide (30 mL) was added dropwise to a cooled (ice bath) stirred suspension of sodium hydride (2.88 g, 120 mmol) in dimethylformamide (20 mL) under dry nitrogen. The mixture was cooled again in the ice bath, and a solution of **4a** (12.93 g, 30 mmol) in dimethylformamide (25 mL) was added dropwise during 1.5 h. The reaction mixture was stirred at room temperature overnight and then poured into a mixture of ice–water (750 mL), methylene chloride (200 mL), and 6 N hydrochloric acid (20 mL). The organic layer was separated and the aqueous layer extracted with methylene chloride (50 mL). The combined extract was washed with water (500 mL), dried ($MgSO_4$), and evaporated in vacuo [finally at 70 °C (0.05 torr)] to give an oil (18.3 g). The crude product was divided in half (for convenience) and purified by chromatography on two 500-g columns of Merck silica gel with 1,1,1-trichloroethane as the solvent. The product was accompanied by some diethyl malonate which was removed by distillation at 125 °C (0.05 torr), leaving **5a** as a viscous oil: 10.25 g (77%); IR (KBr) 2945, 2860, 1749, 1732, 1720, 1300 cm^{-1}; NMR ($CDCl_3$) δ 7.52 (s, 1 H, aromatic H), 5.30 (s, 1 H, COCHCO), 4.30 (q, J = 8 Hz, 4 H, 2 CH_2O), 3.13 and 2.91 (2 d, J = 18 Hz, 2 H, benzylic CH_2), 1.8–0.9 (m, 9 H, cyclopentyl H's), 1.33 (t, J = 8 Hz, 6 H, 2 CH_3), 1.26 (s, 3 H, CH_3).

Anal. Calcd for $C_{22}H_{26}Cl_2O_5$: C, 59.87; H, 5.94; Cl, 16.06. Found: C, 59.87; H, 6.00; Cl, 15.84.

Isolation of Bis(2-cyclopentyl-6,7-dichloro-2-methyl-1-oxo-5-indanyl) Ether (6). A very minor byproduct isolated by preparative plate chromatography from a probe run of the above reaction proved to be compound **6**: mp 186–188 °C (from ethyl acetate); IR (KBr) 2960, 2855, 1715, 1270, cm^{-1}; NMR ($CDCl_3$) δ 6.89 (s, 1 H, aromatic H), 3.67 and 2.60 (2 d, 2 H, benzylic CH_2), 2.0–0.8 (m, 9 H, cyclopentyl), 1.21 (s, 3 H, CH_3). Mass spectrum, m/e 510 (M^+ – cyclopentane).

Preparation of Diethyl (5,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)malonate (5b). A stirred suspension of sodium hydride (9.34 g, 0.3890 mol) in dimethylformamide (125 mL), under nitrogen, was cooled in an ice bath and treated with a solution of diethyl malonate (62.31 g, 0.3890 mol) in dimethylformamide (100 mL), dropwise, during 30 min. Stirring was continued for 15 min with cooling and then for 30 min without cooling. The mixture was again cooled in an ice bath, and a solution of 6,7-dichloro-2,2-dimethyl-1-oxo-5-indanyl trifluoromethanesulfonate (75.35 g, 0.1945 mol) in dimethylformamide (150 mL) was added dropwise during 1 h. The ice bath was removed, and stirring was continued for 16 h. The dark reaction solution was poured into a mixture of ice–water (3750 mL) and 6 N hydrochloric acid (100 mL). The organic layer was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give 85.4 g of a semisolid residue. This residue was stirred with petroleum ether, and the resulting white solid, 6,7-dichloro-5-hydroxy-2,2-dimethyl-1-oxoindan (yield 8.32 g, mp 268–273 °C), was removed by filtration. The petroleum ether filtrate was diluted with ether, washed with aqueous sodium bicarbonate solution and then with water, and dried over anhydrous magnesium sulfate. The solvents were removed under vacuum to give 68.6 g of a mixture of hard solid and some oil. The oil was decanted and the solid recrystallized from hexane to give the title compound as white prisms: yield 49.05 g (65%), mp 72–74 °C. Further purification from hexane gave a melting point of 75–76 °C.

Anal. Calcd for $C_{18}H_{20}Cl_2O_5$: C, 55.83; H, 5.21. Found: C, 55.71; H, 5.39.

Preparation of (2-Cyclopentyl-6,7-dichloro-2-methyl-1-oxo-5-indanyl)acetic Acid (2a, n = 1). A mixture of **5a** (1.50 g, 3.40 mmol), ~9 N hydrochloric acid (1.5 mL), and acetic acid (15 mL) was heated under reflux (oil bath at 125 °C) for 36 h. The mixture was evaporated in vacuo, and the syrupy residue was dissolved in methylene chloride (50 mL). The solution was washed with water (4 × 25 mL), dried ($MgSO_4$), and evaporated in vacuo to a foam: 1.161 g (100%); NMR (CD_3CN) δ 9.0 (s, 1 H, COOH), 7.47 (s, 1 H, aromatic H), 3.93 (s, 2 H, CH_2CO), 3.13 and 2.70 (2 d, J = 18 Hz, 2 H, benzylic CH_2), 2.0–0.8 (m, 9 H, cyclopentyl H's), 1.18 (s, 3 H, CH_3). The spectrum also showed traces of methylene chloride and acetic acid. The acid could not be induced to crystallize and was converted to the dicyclohexylamine salt for further characterization. The salt, recrystallized from acetonitrile, had mp 167–167.5 °C dec.

Anal. Calcd for $C_{17}H_{18}Cl_2O_3 \cdot C_{12}H_{23}N$: C, 66.66; H, 7.91; N, 2.68. Found: C, 66.70; H, 8.13; N, 2.62.

Preparation of (6,7-Dichloro-2,2-dimethyl-1-oxoindan-5-yl)acetic Acid (2b, n = 1). A mixture of diethyl (6,7-dichloro-2,2-dimethyl-1-oxoindan-5-yl)malonate (12.04 g, 0.0311 mol), acetic acid (200 mL), and 9 N hydrochloric acid (20 mL) was heated under reflux for 40 h. The cooled reaction solution was poured

into cold water (1000 mL). The title compound separated as a tan solid: yield 6.93 g (77%), mp 165–178 °C. Recrystallization from benzene gave white platelets, mp 183–185 °C. Further purification from toluene gave a solid, mp 184–186 °C.

Anal. Calcd for $C_{13}H_{12}Cl_2O_3$: C, 54.38; H, 4.21. Found: C, 54.37; H, 4.03.

Preparation of (6,7-Dichloro-1-oxo-2-methyl-2-phenyl-5-indanyl)acetic Acid (2c, *n* = 1). To a stirred suspension of sodium hydride (1.43 g, 0.06 mol) in 50% benzene/dimethylformamide (25 mL) cooled in ice was added a solution of diethyl malonate (9.6 g, 0.075 mol) over a 1-h period. After the mixture was stirred for 10 min after the evolution of hydrogen had ceased, **4c** (6.69 g, 0.015 mol) dissolved in 50% benzene/dimethylformamide (15 mL) was added over a 15-min period, and the reaction mixture was stirred at ambient temperature for 18 h. The solution was poured into water (300 mL) and concentrated hydrochloric acid (10 mL). An ether extract, after being washed with water and then with brine, was dried over magnesium sulfate. Evaporation of the ether left the diethyl indanylmalonate **5c** which was hydrolyzed by refluxing for 60 h in a mixture of acetic acid (70 mL), water (20 mL), and concentrated hydrochloric acid (3 mL) to give **2c** which melts at 133 °C after crystallization from butyl chloride–hexane.

Anal. Calcd for $C_{18}H_{14}Cl_2O_3$: C, 61.91; H, 4.04. Found: C, 62.37; H, 4.46.

Preparation of Diethyl 2-(6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)-2-(ethoxycarbonyl)adipate (7). A stirred suspension of sodium hydride (2.78 g, 0.1155 mol) in a solvent mixture of benzene (55 mL) and dimethylformamide (55 mL) was treated, dropwise, over 30 min with a solution of diethyl (6,7-dichloro-2,2-dimethyl-1-oxoindan-5-yl)malonate (40.68 g, 0.105 mol) in a solvent mixture of benzene (25 mL) and dimethylformamide (25 mL). Stirring was continued for an additional 30 min, and then ethyl 4-bromobutyrate (23.55 g, 0.1208 mol) was added, dropwise, over 15 min. A trace of sodium iodide was added, and the mixture was heated at 85–86 °C for 20 h. The cooled reaction mixture was treated with water (500 mL), and the organic layer was separated. The aqueous layer was extracted with ether. The combined organic solutions were washed with water and saturated sodium chloride solution and then dried over anhydrous magnesium sulfate. The solvents were removed under vacuum to give the title compound as a light orange, residual oil: yield 52.64 g (97%); NMR ($CDCl_3$) δ 7.35 (s, 1 H, aromatic H), 4.5–4.0 (m, 6 H, 3 CH_2O), 2.95 (s, 2 H, benzylic CH_2), 2.7–2.0 (m, 4 H, 2 CH_2), 1.6–1.1 (m, 17 H, 5 CH_3 and CH_2).

Preparation of 2-(6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)adipic Acid (8). Diethyl 2-(6,7-dichloro-2,2-dimethyl-1-oxoindan-5-yl)-2-(ethoxycarbonyl)adipate (42.64 g, 0.105 mol) was added to a solution of sodium hydroxide (24.20 g, 0.630 mol) in water (78 mL) and methanol (500 mL). The resulting solution was heated under reflux for 2 h. Most of the methanol was removed under vacuum. The residual solution was diluted with water (500 mL), extracted once with ether, and acidified with concentrated hydrochloric acid to the Congo Red endpoint. The resulting white solid was collected and dried: yield 34.62 g (88%), mp 165–187 °C. After trituration with boiling toluene and recrystallization from acetonitrile, the title compound was obtained as white prisms, mp 208–210 °C.

Anal. Calcd for $C_{17}H_{18}Cl_2O_5$: C, 54.71; H, 4.86. Found: C, 54.85; H, 5.05.

Preparation of 5-(6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)pentanoic Acid (2b, *n* = 4). A mixture of 2-(6,7-dichloro-2,2-dimethyl-1-oxoindan-5-yl)adipic acid (16.83 g, 0.045 mol), quinoline (144 mL), and copper powder (6 g) was heated at 130–135 °C for 25 min. The cooled reaction mixture was poured into cold water (720 mL) and acidified with concentrated hydrochloric acid to the Congo Red endpoint. The resulting oil was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give the title compound as a tan solid: yield 14.82 g (100%), mp 116–121 °C. Recrystallization from acetonitrile gave off white needles, mp 123.5–124.5 °C.

Anal. Calcd for $C_{16}H_{18}Cl_2O_3$: C, 58.37; H, 5.51. Found: C, 58.72; H, 5.52.

Preparation of 6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl Thioacetate. A stirred suspension of sodium hydride (1.57 g, 0.0653 mol) in dimethylformamide (25 mL), under nitrogen, was cooled in an ice bath and treated with a solution of thiolacetic acid (5.53 g, 0.0726 mol), dropwise, during 1 h. Stirring was continued with cooling for 15 min. Then a solution of 6,7-dichloro-2,2-dimethyl-1-oxo-5-indanyl trifluoromethylsulfonate (13.70 g, 0.0363 mol) in dimethylformamide (30 mL) was added, dropwise, during 1 h. The ice bath was removed, and stirring was continued for 1 h longer. The dark reaction solution was poured into a mixture of ice–water (750 mL) and 6 N hydrochloric acid (20 mL). The organic layer was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give the title compound as a dark, reddish brown residual oil, yield 10.9 g (99%).

Preparation of 6,7-Dichloro-5-mercapto-2,2-dimethyl-1-oxoindan (9). 6,7-Dichloro-2,2-dimethyl-1-oxoindan-5-yl thioacetate (10.90 g, 0.0359 mol) was added to a solution of sodium hydroxide (2.87 g, 0.0718 mol) in water (26 mL) and methanol (165 mL). The resulting clear solution was allowed to stand at room temperature for 1 h. The methanol was removed under vacuum. The residue was dissolved in water (165 mL) and acidified with concentrated hydrochloric acid to the Congo Red endpoint. The resulting solid was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give the title compound as a brown solid: yield 6.77 g (72%), mp 113–121 °C; NMR ($CDCl_3$) δ 7.25 (s, 1 H, aromatic H), 4.25 (s, 1 H, SH), 2.87 (s, 2 H, CH_2), 1.22 (s, 6 H, 2 CH_3).

Preparation of Ethyl 4-[(6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)thio]butanoate. To a stirred solution of 6,7-dichloro-5-mercapto-2,2-dimethyl-1-oxoindan (6.77 g, 0.0259 mol) in dimethylformamide (28 mL) was added potassium carbonate (10.74 g, 0.0777 mol). Ethyl 4-bromobutyrate (5.55 g, 0.0285 mol) was added, and the mixture was heated at 55–60 °C for 3 h. The cooled reaction mixture was poured into water (140 mL). The organic layer was extracted into ether, washed well with water, and dried over anhydrous magnesium sulfate. The solvent was removed under vacuum to give 9.72 g of dark brown residual oil. The oil was purified by column chromatography on silica gel with chloroform as eluant. The title compound was obtained as a light orange oil, yield 5.92 g (61%), showing a single spot, R_f 0.83, on thin-layer chromatography on silica gel with chloroform saturated with ammonia as eluant. NMR ($CDCl_3$) δ 7.12 (s, 1 H, aromatic H), 4.14 (q, 2 H, CH_2O), 3.03 (t, 2 H, CH_2S), 2.90 (s, 2 H, benzylic CH_2), 2.52 (t, 2 H, CH_2COOH), 2.4–2.0 (m, 2 H, CH_2), 1.27 (t, 3 H, CH_3), 1.23 (s, 6 H, 2 CH_3).

Preparation of 4-[(6,7-Dichloro-2,2-dimethyl-1-oxo-5-indanyl)thio]butanoic Acid (10). A mixture of ethyl 4-[(6,7-dichloro-2,2-dimethyl-1-oxo-5-indanyl)thio]butanoate (5.92 g, 0.01577 mol), acetic acid (60 mL), and 5% hydrochloric acid (18 mL) was heated on a steam bath for 1 h. The reaction solution was allowed to cool, and the title compound separated as a tan, crystalline solid: yield 4.33 g (79%), mp 186–187.5 °C. Recrystallization from acetonitrile gave off-white needles, mp 187–188 °C.

Anal. Calcd for $C_{15}H_{16}Cl_2O_3S$: C, 51.88; H, 4.64. Found: C, 52.05; H, 4.64.

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Registry No. 2a (*n* = 1), 71500-84-0; **2a** (*n* = 1) dicyclohexylamine salt, 71500-85-1; **2b** (*n* = 1), 71500-86-2; **2b** (*n* = 4), 71500-87-3; **2c** (*n* = 1), 71500-88-4; **3a**, 54197-04-5; **3b**, 53107-40-7; **3c**, 57509-50-9; **4a**, 71500-89-5; **4b**, 71500-90-8; **4c**, 71500-91-9; **5a**, 71500-92-0; **5b**, 71500-93-1; **5c**, 71500-94-2; **6**, 71500-95-3; **7**, 71500-96-4; **8**, 71500-97-5; **9**, 71500-98-6; **10**, 71500-99-7; **10** ethyl ester, 71501-00-3; trifluoromethanesulfonyl chloride, 421-83-0; diethyl malonate, 105-53-3; ethyl 4-bromobutyrate, 2969-81-5; 6,7-dichloro-2,2-dimethyl-1-oxo-5-indanyl thioacetate, 71501-01-4; thiolacetic acid, 507-09-5.