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Synthesis and Proof of Structure of 2, 2-Dichloro-7H-Cyclobut-(A)-Indian-1-One: A New Route to 4, 5-Benzotropolone

Thomas Renwick Potts

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SYNTHESIS AND PROOF OF STRUCTURE OF
2,2-Dichloro-7H-cyclobut-(a)-indan-1-one:
A NEW ROUTE TO 4,5-Benzotropolone

by

Thomas Renwick Potts

A Thesis
Submitted to the
Faculty of The Graduate College
in partial fulfillment
of the
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Western Michigan University
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Thomas R. Potts

POTTS, Thomas Renwick
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A NEW ROUTE TO 4,5-BENZTROPOLONE.

Western Michigan University, M.A., 1971
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INTRODUCTION

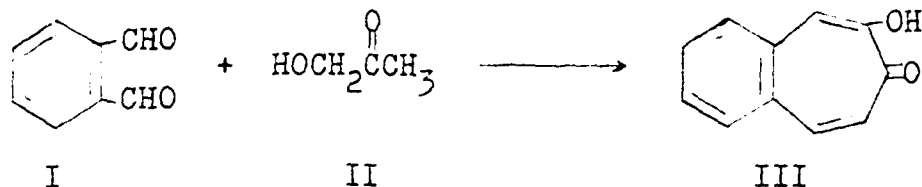
The objective of this work was to study the reaction of dichloroketene with indene and establish the structure of the adduct with spectral and chemical data. Further, it was to provide a facile synthesis to 4,5-benzotropolone via this adduct.

HISTORICAL

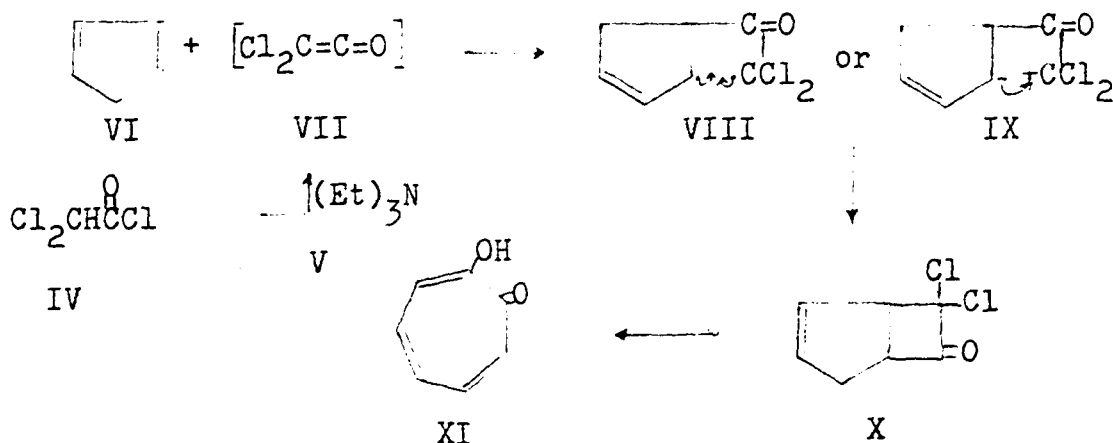
The occurrence of the seven-membered tropolone ring¹ in colchicine,² purpurogallin,³ and the thujaplicines⁴ has made the problem of synthesizing examples of this interesting non-benzenoid ring system and its analogs an attractive one.

In 1959, Eschenmoser⁵ and co-workers and van Tamelen² and co-workers achieved the total synthesis of colchicine, which as mentioned above, contains the seven-membered tropolone ring.

Tarbell⁶ and co-workers reported the synthesis of 4,5-benzotropolone, III, and some of its derivatives by the condensation of phthalaldehyde with hydroxyacetone. Preparation of an isomer of III, 3,4-benzotropolone has been reported by Cook and Somervilli.⁷

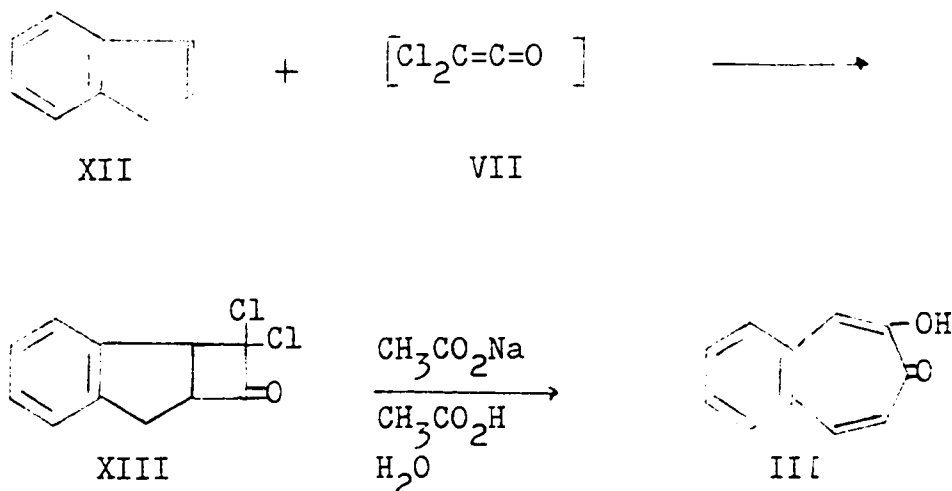


Stevens⁸ and co-workers reported the synthesis of tropolone by the hydrolysis of the adduct of cyclopentadiene, VI, and dichloroketene, VII, and Gosez⁹ and co-workers proposed that the addition could proceed by one of the two intermediates.



An alternative route to tropolone has been reported by Drysdale¹⁰ and co-workers and involves the adduct of tetrafluoroethylene and cyclopentadiene. However, a pyrolytic step at 700-750° and 5 mm is required to convert the adduct to an isomeric mixture of tetrafluoroheptadienes prior to hydrolysis to tropolone.

Turner and Seden¹¹ reported the reaction of indene, XII, with, VII, and obtained 2,2-dichloro-7H-cyclobut-(a)-indan-1-one, XIII, in 20% yield and established its structure by n.m.r. They then treated, XIII, with sodium acetate in aqueous acetic acid and obtained 4,5-benz-tropolone in 80% yield.



EXPERIMENTAL

All melting points, expressed in degrees centigrade, are corrected. The elemental analyses were performed by Galbraith Microanalytical Laboratories, Inc., of Knoxville, Tennessee. The analytical samples were dried in vacuo over phosphorous pentoxide for a minimum of two days before analysis. Chemicals were used as obtained, unless stated otherwise. Thin-layer chromatography was carried out on microslides using Silica Gel-G (Darmstadt) and column chromatography was accomplished in a column 30 cm. in length and with an inside diameter of 2 cm. using Silica Gel-G (Darmstadt) as an absorbant. Gas-liquid phase chromatography data was obtained on a Model 720, Dual Column, F & M Gas Chromatograph equipped with a disc integrator. The liquid phase was SE-30. Infrared spectra were measured with a Beckman IR-8 Spectrophotometer and the assignments were made according to Rao.¹² The ultraviolet spectra were measured on a Cary-14 spectrophotometer. The nuclear magnetic resonance spectra were determined with a Varian A-60 and a HA-100 spectrometer and all assignments were made according to Bible.¹³

Preparation of 2,2-Dichloro-7H-cyclobut-(a)-indan-1-one (XIII)

A solution containing 116g. (1.0 mole) of XII and 7.40g. (0.74 mole) of triethylamine in 200 ml. of anhydrous ether was added dropwise with stirring to a solution containing 100g. (0.68 mole) of dichloroacetyl chloride in one liter of anhydrous ether. The addition was completed in 30 min., and the mixture was then heated at reflux for 15 hrs. The solution was cooled to 10°, filtered and washed five times with 200 ml. portions of distilled water.

The brown solution was dried over anhydrous Na_2SO_4 for 10 hrs., filtered, and the ether removed at reduced pressure. The resulting black oil was flash-distilled at 0.1 mm. yielding a light-yellow viscous liquid which crystallized on standing, yielding 64.0g. (42% crude yield) of a yellowish-white crystalline product. Recrystallization three times from petroleum ether (30-60°) afforded an analytical sample m.p. 80-81° (lit.¹¹ 78-79°). The product gave one spot on a thin-layer chromatogram, Silica Gel-G (Darmstadt) using benzene or dioxane as a carrier solvent, and one peak in glpc.

Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{Cl}_2\text{O}$: C, 58.18; H, 3.55.
Found: C, 58.23; H, 3.59.

Preparation of 2-Chloro-7H-cyclobut-(a)-indan-1-one (XV)

A solution containing 4.0g. (0.017 mole) of XIII, 2g. of 10% Pd-C and 2.0g. of anhydrous CaCO_3 in 250 ml. of anhydrous dioxane was shaken with hydrogen at 60 psi in a Parr medium-pressure hydrogenation apparatus for 3.5 hrs. The Pd-C, CaCl_2 and CaCO_3 were removed by vacuum filtration through celite, and the product isolated by removal of the dioxane at reduced pressure. The resulting white solid was recrystallized from petroleum ether (30-60°) yielding 3.1g. (94%) of white crystals, m.p. 111.5-112.0°. A positive test for chlorine was observed when a sodium fusion was performed, and a grey precipitate was observed when the compound was added to alcoholic silver nitrate. The product gave one spot on a thin-layer chromatogram, Silica Gel-G (Darmstadt), using benzene or cyclohexane as a carrier solvent, and one peak in glpc.

Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{ClO}$: C, 68.58; H, 4.70; Cl, 18.41. Found: C, 68.62; H, 4.68; Cl, 18.49.

Preparation of Methyl trans-1-(dichloromethyl)-indan-2-carboxylate (XVII)

To a solution containing 3.0g. of sodium metal dissolved in 120 ml. of absolute methanol at -5° , was added 3.0g. (0.013 mole) of XIII. The mixture was stirred for 30 min. and then allowed to warm to room temperature. The solution was then neutralized with glacial acetic acid, and evaporated to dryness at reduced pressure. The resulting solid was dissolved in 50 ml. of distilled water and extracted five times with 100 ml. portions of ether. The ether solution was dried over anhydrous Na_2SO_4 for 12 hrs., filtered, and the ether removed at reduced pressure. The resulting yellow oil was crystallized from petroleum ether ($30-60^{\circ}$)-ether, 10:1, yielding 2.7g. (79%) m.p. $45-46^{\circ}$. The product gave one spot on a thin-layer chromatogram, Silica Gel-G (Darmstadt), using benzene or chloroform-methanol, 20:1, as a carrier solvent, and one peak in glpc.

Anal. Calcd. for $\text{C}_{12}\text{H}_{12}\text{Cl}_2\text{O}_2$: C, 55.61; H, 4.66; Cl, 27.36. Found: C, 55.40; H, 4.77; Cl, 27.61.

Preparation of trans-1-Methylindan-2-carboxylic acid (XIX)

A solution containing 50mg. (0.193 mmoles) of XVII and 12.3mg. (0.193 mmoles) of powdered zinc in 25 ml. of glacial acetic acid was heated at reflux for 2 hrs. The solution was cooled to room temperature, and the precipitate removed by filtration. The acetic acid was removed at reduced pressure and the resulting yellow oil was dissolved in 10 ml. of ether and washed five times with 5 ml. portions of 10% NaHCO_3 . The ether solution was dried over anhydrous Na_2SO_4 for 5 hrs., filtered, and the ether removed at reduced pressure yielding 31mg. of a yellow oil. The oil was chromatographed over 75g. of Silica Gel-G (Darmstadt).

Washing with 150 ml. of benzene gave 23mg. of a pale yellow oil which when treated with 10% aq. NaOH solution and poured into a small amount of ice-water containing concentrated hydrochloric acid resulted in 13mg. (41%) of a white solid m.p. 78-79° (lit.¹⁴ 79°).

Preparation of 4,5-Benzotropolone (III)

To a stirred solution containing 3.6g. (0.044 mole) of sodium acetate in 100 ml. of 50% acetic acid was added 5.0g. (0.022 mole) of XIII. The solution was heated on a steam bath for 72 hrs. and upon gradual cooling to room temperature, yellow crystals formed. Filtration and recrystallization from 95% ethanol yielded 3.1g. (82%) of yellow needles m.p. 157-159° (lit.⁶ 158.5-160°).

TABLE I
INFRARED SPECTRAL DATA^a

COMPOUND	ABSORPTION BANDS ^b IN MICRONS
2,2-Dichloro-7H-cyclobut-(a)-indan-1-one (XIII)	carbonyl, 5.5(S) adjacent ring hydrogens, 11.9(M), 12.5(M), carbon-chlorine, 15.3(S)
2-Chloro-7H-cyclobut-(a)-indan-1-one (XV)	carbonyl, 5.6(S) adjacent ring hydrogens, 12.0(M), 12.8(M), 13.1(M) carbon-chlorine, 15.6(S)
Methyl <u>trans</u> -1-(dichloromethyl)-indan-2-carboxylate (XVII)	ester carbonyl, 5.75(S) adjacent ring hydrogens, 12.0(M), 12.7(M), 13.3(M) carbon-chlorine, 13.7(S)
<u>trans</u> -1-Methylindan-2-carboxylic acid (XIX)	hydroxyl, 3.5(M) carbonyl, 5.8(S) four adjacent ring hydrogens, 9.22(M), 9.8(M), 10.8(M)
4,5-Benzotropolone (III)	hydroxyl, 3.15(W) carbonyl, 6.15(S) four adjacent ring hydrogens, 9.4(M), 10.2(M), 10.8(M)

^aInfrared spectra were determined as Nujol mulls.

^bS = strong absorption, M = medium absorption,
W = weak absorption

TABLE II
ULTRAVIOLET SPECTRAL DATA

COMPOUND	λ^a	ϵ^b
2,2-Dichloro-7H-cyclobut-(a)-indan-1-one ^c (XIII)	213(S) ^e	8,600
	205	16,400
2-Chloro-7H-cyclobut-(a)-indan-1-one ^c (XV)	216(S)	7,600
	207	14,200
Methyl <u>trans</u> -1-(dichloromethyl)-indan-2-carboxylate ^d (XVII)	280(S)	10,400
	267	20,000
	236(S)	19,500
	232	21,000
4,5-Benzotropolone ^c (III)	274	15,400
	267	13,000
	260	8,500
	217	61,500
	212	34,600

^aThe wavelength of absorption (λ) is expressed in millimicrons.

^bMolar extinction coefficient

^cThe solvent used for these compounds was absolute ethyl alcohol.

^dThe solvent used for this compound was absolute methyl alcohol.

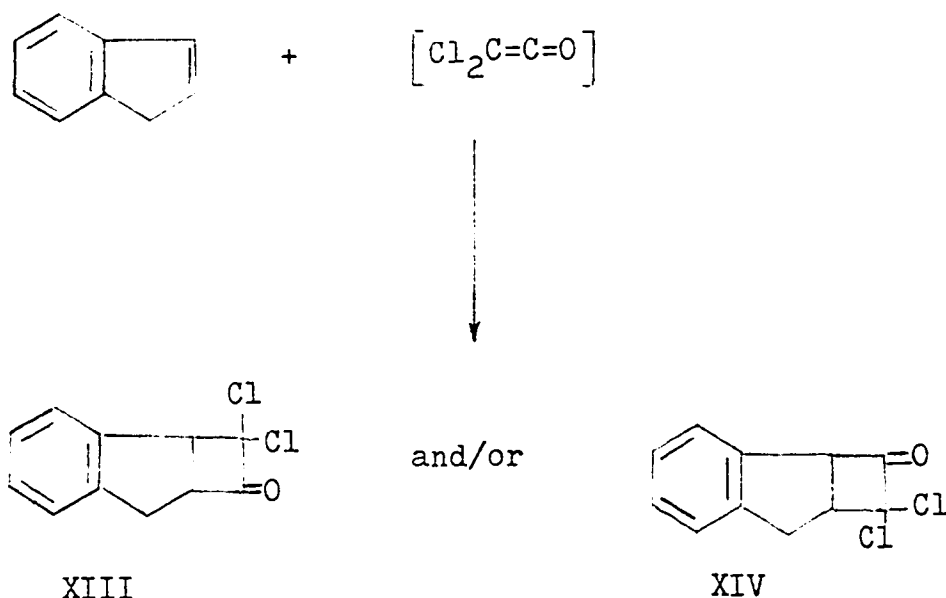
^eS = Shoulder

TABLE III
NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA

COMPOUND	τ VALUES	ASSIGNMENTS
2,2-Dichloro-7H-cyclobut-(a)-indan-1-one (XIII)	2.71(singlet)	four adjacent ring hydrogens
	5.50-5.65(complex multiplet)	fusion carbon hydrogen atom
	6.70-7.15(complex multiplet)	benzylic hydrogens
2-Chloro-7H-cyclobut-(a)-indan-1-one (XV)	2.72(singlet)	four adjacent ring hydrogens
	4.65-4.81(two doublets)	-CHCl
	5.45-6.28(complex multiplet)	fusion carbon hydrogen atom
	6.67-6.88(complex multiplet)	benzylic hydrogens
Methyl <u>trans</u> -1-(dichloro-methyl)-indan-2-carboxylate (XVII)	2.8(singlet)	four adjacent ring hydrogens
	3.81-3.89(doublet)	-CHCl ₂
	5.50-5.68(triplet)	H adjacent to -CHCl ₂
	6.18(singlet)	-CH ₃
	6.37-6.83(complex multiplet)	H adjacent to -CO ₂ CH ₃ and benzylic hydrogens
4,5-Benzotropolone (III)	2.10	-OH
	2.31	four adjacent ring hydrogens
	2.46	β -H
	2.75	α -H to C=O
	2.98	α -H to C-OH

DISCUSSION

The addition of dichloroketene to indene could occur in two ways, and could result in the following possibilities. First, the addition could result in the formation of structures XIII and XIV; and second, it could result in the formation of structure XIII or XIV.



Chromatographic evidence would rule out the first since only one spot was observed on a thin-layer chromatogram, Silica Gel-G (Darmstadt), using different solvent systems, and only one peak in gas-liquid phase chromatography.

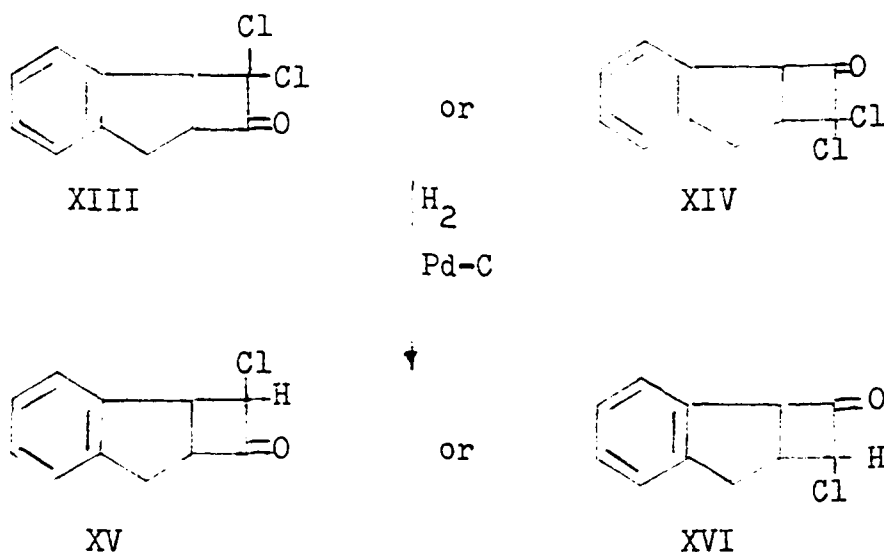
The infrared spectrum showed a strong carbonyl absorption at 5.5μ , which is characteristic of a four-membered ring ketone bearing alpha halogens,¹⁵ absorptions at 11.9 and 12.5μ , which are characteristic of adjacent ring hydrogens, and an absorption at 15.3μ , which is characteristic for carbon-chlorine stretching.

The n.m.r. spectrum of the addition product, determined on a 60 Mc. and a 100 Mc. instrument, exhibited a singlet at 2.71τ which was assigned to the four adjacent aromatic ring hydrogens, a complex multiplet ranging from $5.50-5.65\tau$ which was tentatively assigned to the fusion carbon hydrogen atom, and a complex multiplet ranging from $6.70-7.15\tau$ which was tentatively assigned to the benzylic hydrogens.

The analysis was consistent for $C_{11}H_8Cl_2O$.

Hydrogenolysis of the adduct, using 10% Pd-C in dioxane at 60 psi, resulted in a 94% yield of a chromatographically pure compound. A sodium fusion was performed and a positive test was obtained for halogen. The elemental analysis was consistent for $C_{11}H_9ClO$.

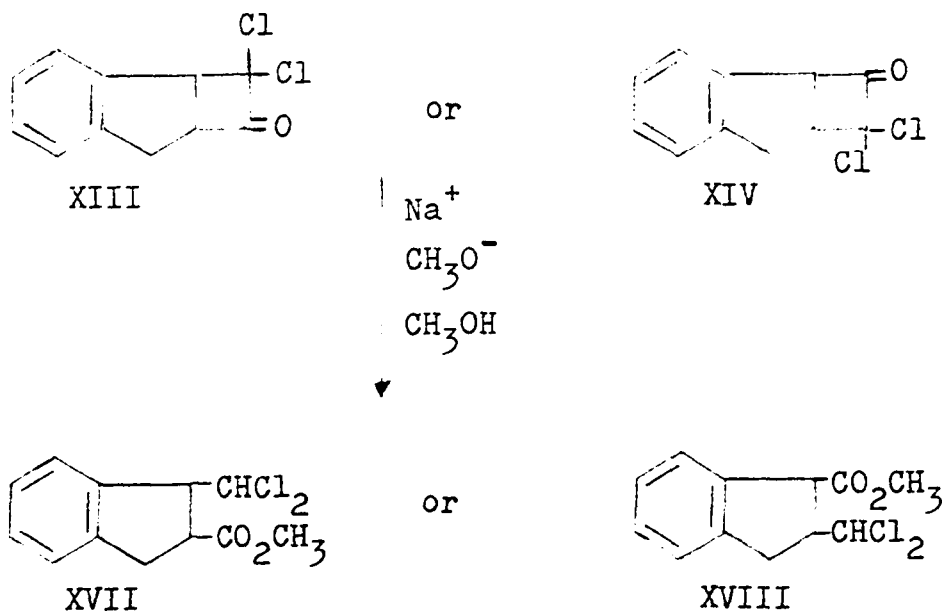
Construction of a molecular model showed that only one chlorine was favorably oriented for removal. Therefore, the product obtained after hydrogenolysis could be structure XV or XVI.



The infrared spectrum exhibited a strong carbonyl absorption at 5.6μ , which is a slight shift from the starting material, absorptions at 12.0 , 12.8 , and 13.3μ , which are characteristic of adjacent ring hydrogens, and an absorption at 15.6μ , which is characteristic for carbon-chlorine stretching.

The n.m.r. spectrum of the mono-chloro cyclobut-(a)-indanone was quite complex, and exhibited a singlet at 2.72τ which was assigned to the four adjacent aromatic ring hydrogens, a pair of doublets ranging from 4.65 - 4.81τ which was assigned to the hydrogen which replaced the chlorine on hydrogenolysis, a complex multiplet ranging from 5.45 - 6.28τ which was tentatively assigned to the fusion carbon hydrogen atom, and another complex multiplet ranging from 6.67 - 6.88τ which was tentatively assigned to the benzylic hydrogens.

Treatment of XIII or XIV with sodium methoxide at -5° followed by neutralization with acetic acid afforded a low melting solid which gave only one spot on a thin-layer chromatogram, Silica Gel-G (Darmstadt), using different solvent systems and one peak in gas-liquid phase chromatography.



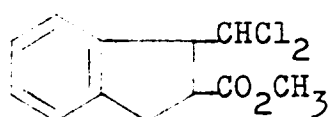
The infrared spectrum showed an ester carbonyl at 5.75μ , absorptions at 12.0 , 12.7 , and 13.3μ which are characteristic of four adjacent ring hydrogens, and an absorption at 13.7μ which is characteristic of carbon-chlorine stretching.

The n.m.r. spectrum of the methanolysis product exhibited a singlet at 2.8τ which was assigned to four adjacent ring hydrogens, a doublet at 3.81 - 3.89τ which was assigned to the $-\text{CHCl}_2$ group, a triplet at 5.50 - 5.68τ which was assigned to the hydrogen adjacent to the $-\text{CHCl}_2$ group, a singlet at 6.18τ which was assigned to the methyl ester group, and a complex multiplet at 6.37 - 6.83τ which was assigned to the hydrogen adjacent to the carboxylate group and to the benzylic hydrogens.

The analysis was consistent for $\text{C}_{12}\text{H}_{12}\text{O}_2\text{Cl}_2$.

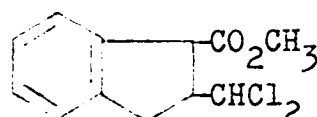
At this point, a preliminary conclusion could be made as to the structure of the methanolysis product. The n.m.r. spectrum would favor XVII since a triplet was observed which was assigned to the hydrogen adjacent to the $-\text{CHCl}_2$ group. In XVIII, a triplet would not be expected anywhere in the spectrum.

Treatment of XVII or XVIII with zinc and acetic acid followed by chromatography over Silica Gel-G (Darmstadt) and hydrolysis gave a crystalline solid, m.p. 78 - 79° .

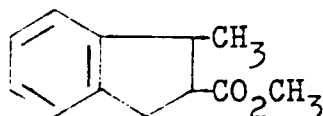
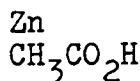


XVII

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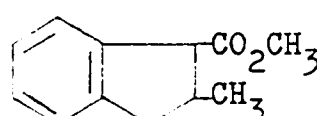


XVIII

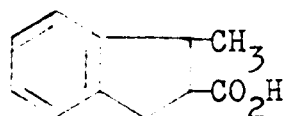
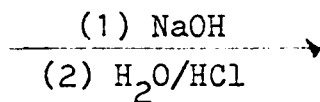


XIX

or

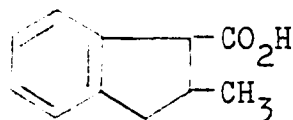


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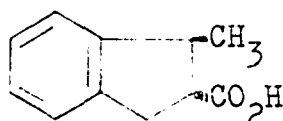
XXI

or

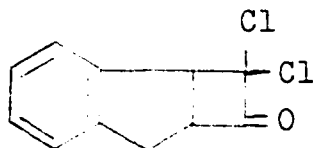


XXII

This melting point is identical with that reported by Lahiri and Pathak¹⁴ for the following structure.



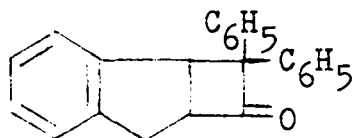
Therefore, the structure of the adduct could only be XIII.



XIII

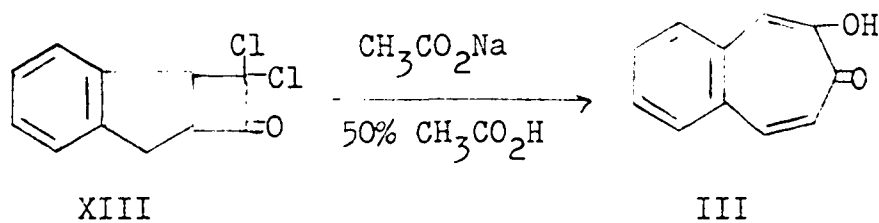
Since the adduct XIII from its mode of formation must be cis, it follows that epimerization must have occurred during ring-fission.

Campbell and Heller¹⁶ reported that when the adduct of indene and diphenylketene was treated with sodium methoxide and neutralized with acetic acid, the product isolated was the trans acid.



However, the evidence is not conclusive.

The hydrolysis of XIII with sodium acetate in 50% acetic acid proceeded smoothly, and 4,5-benzotropolone was isolated in 82% yield.



SUMMARY

The addition of dichloroketene to indene to yield 2,2-dichloro-7H-cyclooct-(a)-indan-1-one gave cleanly one adduct and not a mixture of isomers. The structure of the adduct has been proven unequivocally, and a new and efficient route to 4,5-benzotropolone has been established.

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VITA

Thomas Renwick Potts was born August 27, 1941, in Sturgis, Michigan. After completing his secondary education in the White Pigeon School System, White Pigeon, Michigan, he enrolled at Western Michigan University in September 1959. He received a B.S. degree with a major in chemistry in June 1964.

From September 1964, through May 1966, the author was a research assistant on a grant from the Michigan Cancer Foundation and from June 1966, through August 1966, he was a research assistant on a grant from the National Institutes of Health.

From September 1966, through December 1966, he was employed as part-time laboratory assistant in the Herbicides and Plant Growth Regulators section, Agriculture Products and Research at The Upjohn Company.

From January 1967, through May 1970, he was a research assistant at Wayne State University, Detroit, Michigan on a grant from the National Institutes of Health, and from June 1970, through February 1971, he continued as a research assistant at Wayne State University.

Since March 1971, the author has been employed as a chemical engineer with Union Carbide Corporation, Consumer Products Division.

The author is married and the father of one daughter.

He is a member of the American Chemical Society and Phi Lambda Upsilon.