TABLE I

COMPARISON OF MASS SPECTRA

m/e	CF_2HCHCl_2[a] I	$CF_2ClCHCl_2$[a] III	CF_2ClCCl_3[b] VI	Mixture	Ion	Expected for[c] CHF_2CCl_3
51	16.3	0.6	0.09	10.2	CHF_2^+	1
82	1.6	2.0	27.6	6.0	CCl_2^+	s
83	100.0	100.0	0.4	100.0	$CHCl_2^+$	—
84	1.7	2.4	17.7	4.9	CCl_2^+	s
85	64.3	77.4	43.4	74.9	$CHCl_2^+$	—
					CF_2Cl^+	
87	10.5	14.4	13.8	13.7	$CHCl_2^+$	—
					CF_2Cl^+	
117	1.6	0.41	100.0	26.1	CCl_3^+	1
119	0.3	0.25	94.9	24.2	CCl_3^+	1
121	—	0.08	30.5	7.6	CCl_3^+	1
132	0.1	0.6	14.6	1.1	$C_2F_2Cl^+$	s
133	2.7	19.2	0.36	46.7	$C_2F_2HCl_2^+$	1
134	21.5	0.75	9.4	3.9	$C_2H_2F_2Cl_2^+$	s
					$C_2F_2Cl_2^+$	
135	2.1	12.1	0.19	29.6	$C_2HF_2Cl_2^+$	1
136	13.6	0.3	1.5	2.0	$C_2F_2HCl_2^+$	s
					$C_2F_2Cl_2^+$	
167	—	0.02	97.9	4.0	$C_2F_2Cl_3^+$	s
169	—	0.06	93.6	4.0	$C_2F_2Cl_3^+$	s
171	—	0.04	29.8	1.3	$C_2F_2Cl_3^+$	s

[a] Peak strength relative to m/e at 83 = 100. [b] Peak strength relative to m/e at 117 = 100. [c] "1" indicates a major peak predicted, "s" a minor peak predicted.

= 133 and 135 particularly indicate the presence of II.

The infrared spectrum of the mixture confirmed the presence of III and indicated the presence of another compound which was neither I nor VI. The weak peaks at m/e = 134, 136, 167, 169, and 171 in the mass spectrum of the mixture could be due to small amounts of I and VI in the mixture. However, as is indicated in Table I, all of the fragments could be derived from II so there is no reason to assume, by necessity, that I or VI are present. Conversely, there is no reason to assume that I and VI are entirely absent either.

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ORGANIC CHEMICALS DEPARTMENT
JACKSON LABORATORY
E. I. DU PONT DE NEMOURS AND CO.
WILMINGTON, DEL.

Synthesis and Configuration of *cis*-8-Methylhydrindane

HAROLD CONROY[1] AND ELLIOTT COHEN[2]

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In connection with the determination of the skeletal structure of picrotoxinin we have described a synthesis of DL-*cis*-5-isopropyl-8-methylhydrin-4,6-diene (picrotoxadiene);[3] we now wish to detail the observations made in a repetition of part of this synthesis with optically active materials. Although an extension of this work will make possible the assignment of absolute configuration in the picrotoxin series the results herein are sufficient to allow such assignment for an important reference compound, *cis*-8-methylhydrindane, as well as some of its ketonic derivatives.

Cis-2-methyl-2-carboxycyclopentane-1-acetic acid (I),[4] prepared *via* 2-methyl-2-carbethoxycyclopentylidenecyanoacetic ester,[3,5] was resolved with the aid of its brucine salt; after twenty-one recrystallizations of this salt from water the rotation ($[\alpha]_D^{21}$ +37°) of the regenerated acid showed no further increase. Partially resolved (−) acid was obtained from the mother liquors. The remaining transformations (to IX) indicated in the diagram were carried out in a manner similar to that described previously for the corresponding racemic series; the compounds were characterized by their infrared spectra, in all cases identical with those of the racemic series. The optically active bicyclic hydrocarbon (X) was prepared from IX by the Huang-Minlon modification of the Wolff-Kishner reduction.

The assignment of the *cis* configuration in this series has rested on the obtention by Errington and

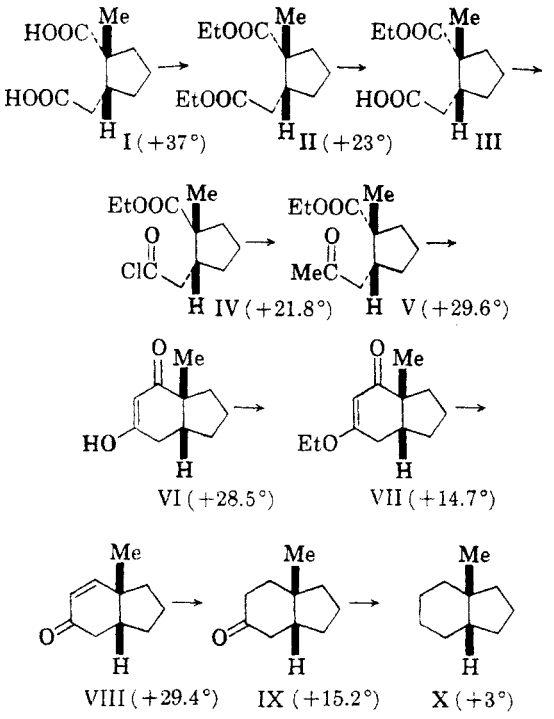
(1) Present address: Department of Chemistry, Brandeis University, Waltham 54, Mass.

(2) Present address: Lederle Laboratories, Pearl River, N. Y. Abstracted from the Ph.D. Thesis of Elliott Cohen, Columbia University, 1956.

(3) H. Conroy, *J. Am. Chem. Soc.*, **73**, 1889 (1951); **74**, 491 (1952); **74**, 3046 (1952).

(4) K. D. Errington and R. P. Linstead, *J. Chem. Soc.*, 666 (1938).

(5) P. Bagchi and D. K. Banerjee, *J. Ind. Chem. Soc.*, **24**, 12 (1947).



Figures in parentheses are $[\alpha]_D$.

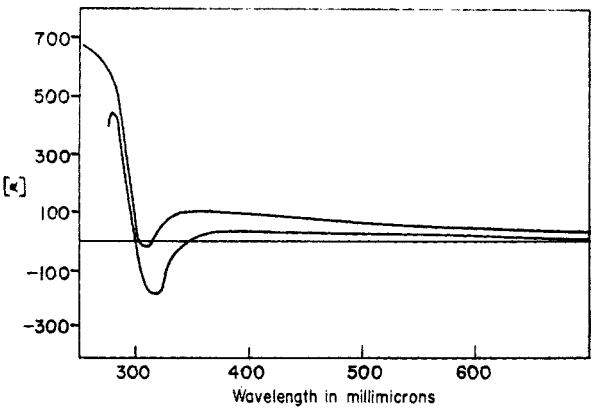


Fig. 1. Rotatory dispersion curves for coprostanone-3 (in methanol; upper curve) and (+)*cis*-8-methylhydrindan-5-one (in dioxane; lower curve)

Linstead[4] of the diacid (I) from a bicyclo[3.3.0]-octanone derivative believed for good reason to contain the *cis* ring junction. Nevertheless the evidence may not be entirely convincing, and apparently has been the subject of recent doubt.[6] The infrared spectrum of our hydrocarbon (X) was identical in all respects with that of the cis-8-methylhydrindane (3a-methyl-*cis*-hexahydroindan) reported recently by Kronenthal and Becker[7] and different from that of their *trans* modification. Their synthesis was based upon a Diels-Alder addition and is stereochemically unequivocal.

We owe the assignment of absolute configurations depicted in the diagram for the dextrorotatory materials to the powerful method of rotatory dispersion as elaborated by Djerassi *et al.* (*Cf.* ref. 6, etc.). A comparison of the curves for (+) *cis*-8-methylhydrindan-5-one (IX) and coprostanone-3 (A/B *cis*) leaves no doubt that the immediate steric environments of the respective carbonyl groupings are similar in the absolute sense.

EXPERIMENTAL

Resolution of cis-2-methyl-2-carboxycyclopentane-1-acetic acid (I). The racemic acid[3] (m.p. 110–111°) (459.5 g.; 2.46 moles) was dissolved in a minimum amount of hot water and 1948 g. (2.46 moles) of brucine was added with enough hot water to dissolve it. The brucine salt separated when the solution was cooled; twenty-one such recrystallizations of the salt were carried out before the diacid regenerated by treatment of the salt with 10% hydrochloric acid and extraction with ether gave a constant rotation. The resolved diacid (70.5 g.) had the m.p. 114° and $[\alpha]_D^{21°}$ +37° (4% in chloroform). Racemic acid (186 g.) recovered from the mother liquor and put through a similar treatment with extensive recrystallization of the brucine salt gave an additional 18.5 g. of resolved acid, making a total of 89 g. Partially resolved (−) acid (109 g.) $[\alpha]_D^{25°}$ −6.4° was also obtained from the mother liquor.

(+) *Ethyl cis-2-methyl-2-carbethoxycyclopentane-1-acetate* (II). The diester (70 g.; 68% yield) was obtained from 89 g. of the diacid (I) with ethanol and sulfuric acid after a long reflux period. It distilled at 87–89° (0.5 mm.) $[\alpha]_D^{25°}$ +23° (7% in chloroform).

(+)*cis-2-Methyl-2-carbethoxycyclopentane-1-acetyl chloride* (IV). The oily half-ester (III) obtained by partial hydrolysis of 70 g. of II with 11.5 g. of sodium hydroxide in aqueous ethanol was dried by distillation with 150 ml. of benzene and then refluxed together with 41.8 g. of thionyl chloride until the gas evolution ceased. After distillation, 59 g. (88.6%) of acid chloride, b.p. 75–78° (0.35 mm.), $n_D^{27°}$ 1.4635 and $[\alpha]_D^{27°}$ +21.8° (7% in chloroform) was obtained.

(+)*cis-2-Methyl-2-carbethoxycyclopentane-1-acetone* (V). The preparation was conducted as described previously.[3] From 58 g. of acid chloride (IV) and the sodium salt from 101 g. of diethyl malonate and 15 g. of sodium hydride in benzene there was obtained after hydrolysis-decarboxylation 30 g. of V, b.p. 77–85° (0.4–0.8 mm.), n_D^{27} 1.4505, $[\alpha]_D^{27°}$ +29.6° (4% in chloroform). The 2,4-dinitrophenylhydrazone, recrystallized from ethanol, melted at 72°.

(+)*cis-8-Methylhydrindan-5,7-dione* (VI). The preparation was conducted as described previously. From 36.3 g. of the acetonyl derivative (V), 8.3 g. of sodium hydride in 30 ml. of benzene there was obtained 20.5 g. (70%) of VI, m.p. 151–152° with $[\alpha]_D^{26°}$ +28.5° (3% in chloroform).

(+)*cis-5-Ethoxy-8-methylhydrind-5-ene-7-one* (VII). A mixture of the diketone (VI), 100 ml. of benzene, 40 ml. of absolute ethanol, and 0.5 g. of *p*-toluenesulfonic acid was distilled slowly through a column packed with helices. The vapor temperature rose to 67° at the completion of the reaction when water was no longer formed. The solvents were removed on the steam bath, finally *in vacuo*, and the product was distilled. The yield of material, b.p. 83–84° (0.2 mm.), was 20.2 g. (84%); $n_D^{25°}$ 1.5085, $[\alpha]_D^{26°}$ +14.7° (chloroform).

(+)*cis-8-Methylhydrind-6-ene-5-one* (VIII). Lithium aluminum hydride reduction of VII (20.1 g.) followed by mild acid hydrolysis, as previously described, gave 13.1 g. (84.5%) of the unsaturated ketone with b.p. 57–59° (0.8 mm.), $n_D^{25°}$ 1.4995 and $[\alpha]_D^{25°}$ +29.4° (4% in chloroform).

(+)*cis-8-Methylhydrindan-5-one* (IX). Four grams of the unsaturated ketone (VIII) in 40 ml. of methanol with 200 mg. of platinum oxide was hydrogenated at atmospheric

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(7) R. L. Kronenthal and E. I. Becker, *J. Am. Chem. Soc.*, **79**, 1095 (1957).

pressure; gas absorption was complete in 2.5 hr. The catalyst was removed by filtration and the solvent evaporated on the steam bath. The residue had $n_D^{25°}$ 1.4790 and $[\alpha]_D^{25°}$ +15.2°. The dibenzylidene derivative had the m.p. 124–125°.

(+)*cis-8-Methylhydrindane* (X). The ketone (IX) (3.5 g.) was refluxed for two hr. at 135° with 4.0 g. of potassium hydroxide, 80 ml. of diethyleneglycol, and 7.0 g. of 85% hydrazine hydrate. The water was distilled off and then the temperature was raised to 200° for 4 hr. The mixture was cooled, taken up in water, extracted with pentane, and the pentane layer washed with concentrated sulfuric acid until the acid no longer became colored. The pentane solution was washed with water, dried over magnesium sulfate, and the pentane removed, leaving two grams of an oil whose infrared spectrum showed no carbonyl band and was identical with that given in ref. 7. The oil crystallized on cooling, m.p. 5°, $[\alpha]_D^{26°}$ +3° (6% in chloroform).

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DEPARTMENT OF CHEMISTRY
COLUMBIA UNIVERSITY
NEW YORK 27, N. Y.

A New Synthesis of *cis*-1,2-Cyclohexanediol

FREDERICK V. BRUTCHER, JR.,[1] AND GEORGE EVANS III

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cis-1,2-Cyclohexanediol (I) has found considerable use as a model compound for synthetic and mechanistic studies. In discussing methods of preparing I, Criegee and Stanger[2] have recommended a four-step method starting with cyclohexene. As pointed out by Winstein, Hess, and Buckles,[3] however, its success is dependent on the reaction conditions of the replacement reaction.

We have developed a much simpler two-step synthesis of I from cyclohexene which requires about a day's time and which is amenable to large scale work. The method employed is that developed[4] for *cis*-hydroxylation in the synthetic steroid series. It involves the interaction of an olefin with iodine, silver acetate, and wet acetic acid to give, by way of a neighboring group replacement reaction,[3] *cis*-hydroxy acetate in one operation. Subsequent hydrolysis yields the free diol.

Using this technique, we have obtained after one recrystallization quite pure I in 66% yield. Considerable variation of the reaction conditions did not improve the yield. The use of iodine monochloride in place of iodine decreased the yield of I to 32%.

EXPERIMENTAL[5]

cis-1,2-Cyclohexanediol (I). To a slurry of 16 g. (0.096 mole) of silver acetate in 150 ml. of glacial acetic acid in a three-neck flask equipped with a condenser, thermometer, and stirrer was added 3.42 g. (0.0416 mole) of freshly distilled cyclohexene, b.p. 83–85°. Accompanied by vigorous stirring, 11.7 g. (0.046 mole) of powdered iodine was added over a 30-min. period at room temperature. Finally, 0.67 g. (0.042 mole) of water was added and the reaction mixture was heated with vigorous stirring for 3 hr. at 90–95°. After the reaction mixture was cooled, filtered, and the silver iodide precipitate washed well with hot benzene and ethyl acetate, the combined filtrates were evaporated at the water pump to give a yellow viscous oil which was taken up in methanol and filtered. The filtrate was neutralized with a few ml. of alcoholic potassium hydroxide, treated with 3.5 g. of potassium hydroxide in 20 ml. of methanol and hydrolyzed by refluxing for 1.5 hr. (darkening occurred). After evaporation of the methanol at the water pump, the residue was taken up in 500 ml. of warm diethyl ether and filtered. The filtrate was evaporated yielding 3.92 g. (81%) of crude glycol. Recrystallization from carbon tetrachloride yielded 3.2 g. (66%) of white *cis*-1,2-cyclohexanediol, m.p. 97–98°, lit.[2] m.p. 96–98°.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA 4, PA.

(5) All melting points are uncorrected.

Some 4-Substituted Thiourazoles[1]

C. K. BRADSHER, FRANCES C. BROWN, AND SIDNEY T. WEBSTER[2]

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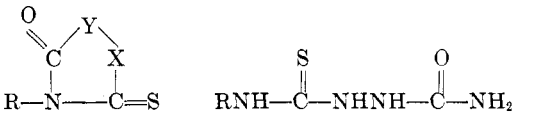
It was shown that 3-substituted rhodanines (I) possess pronounced antimicrobial activity.[3–5] The present work deals with the synthesis of some related 4-substituted thiourazoles (II). The thioura-



I, X = S, Y = CH_2
II, X = Y = NH

III

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(2) Monsanto Chemical Co. Fellow 1956–1957.

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(1) Thanks are due the Du Pont Co. for a Summer Faculty Fellowship.

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