phosphoric acid at 100°. Heating of V with potassium hydrogen sulfate in toluene gave a high melting (above 300°) product which may be a dimeric lactone (VII).

The acid (I) was finally obtained in an overall yield of 53% by the following conventional method: Hydrindene-2-carboxylic acid (VIII), which is available from *o*-xylylene dibromide and ethyl acetoacetate[5] or diethyl malonate[6] in 55 and 69% yield, respectively, was subjected to the Arndt-Eistert reaction and yielded in 88% yield 2-hydrindylacetic acid (IX). Its methyl ester gave with *N*-bromosuccinimide the methyl ester of I in 80% yield.

EXPERIMENTAL

2-Carbethoxymethyl-1-hydrindone (IV). A mixture of 1 mole of 1-hydrindone, 2 moles of pyrrolidine and 600 ml. of benzene was subjected to azeotropic distillation. The enament (III) boiled at 142–144° (2 mm.); 165° (5 mm.); yield, 65 g. (35%). As the product proved to be unstable, it was immediately treated as follows: A mixture of 61 g. of the enamine, 55 g. of ethyl bromoacetate, and 180 ml. of benzene was heated on the water bath at 80° for 15 min. Water (90 ml.) was added and the benzene layer separated and distilled. B.p. 127–133° (0.01 mm.); yield, 30 g. (41%).

Anal. Calcd. for $C_{13}H_{14}O_3$: C, 71.6; H, 6.4. Found: C, 70.2; H, 6.5.

1-Hydroxy-2-hydrindylacetic acid (V) was prepared according to the literature[1] and recrystallized from chloroform or water, m.p. 131°.

The methyl ester was prepared with diazomethane, b.p. 118° (0.005 mm).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8. Found: C, 69.8; H, 6.5.

We also prepared the following derivatives of V.

1-Hydroxy-2-hydrindylacetamide. A mixture of 6 g. of the methyl ester of V and concentrated ammonia was kept at room temperature for 2 days and the solid product recrystallized from ethanol; m.p. 170–171°, yield, 3 g. (55%).

Anal. Calcd. for $C_{11}H_{13}NO_2$: C, 69.1; H, 6.8. Found: C, 69.2; H, 7.5.

1-Hydroxy-2-hydrindylacetonitrile. A mixture of 6 g. of the amide and 6 g. of phosphorus pentoxide was distilled *in vacuo* (b.p. 170–200°, 20 mm.) and the distillate dissolved in benzene. The solution was washed with water, dried, and concentrated and the solid residue recrystallized from ethanol, m.p. 73°.

Anal. Calcd. for $C_{11}H_{11}NO$: C, 76.3; H, 6.4. Found: C, 76.1; H, 5.8.

The lactone (VI), m.p. 73° from toluene or petroleum ether, b.p. 100° (0.5 mm), was formed in the following experiments: (a) from 20 g. of the acid (V) in 100 ml. of anhydrous alcohol with gaseous hydrogen bromide for 6 hr.; yield, 15 g. (83%); (b) from 5 g. of the acid (V) and 10 g. of oxalic acid in 125 ml. of boiling toluene; (c) from 5 g. of the acid (V), 0.75 g. of red phosphorus, 0.25 g. of iodine, 12.5 ml. of glacial acetic acid, and 0.25 ml. of water at boiling temperature for 3 hr.; yield, 3.5 g. (78%); (d) from 10 g. of the methyl ester of V with 7 ml. of phosphorus oxychloride in 16 ml. of pyridine; (e) from 11 g. of the methyl ester of V with 4 g. of thionyl chloride in 4 g. of pyridine at 100° for 1 hr.; yield, 7 g. (77%).

Dimeric anhydride (VII) (?). A mixture of 10 g. of the acid (V), 10.6 g. of potassium hydrogen sulfate, and 200 ml. of toluene was refluxed azeotropically for 4 hr. The resulting product was washed with water, dried, and concentrated and the remaining solid product (4 g.; 40%) recrystallized from chloroform m.p. about 300°.

Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.9; H, 5.8. Found: C, 75.7; H, 6.1.

Hydrindene-2-carboxylic acid (VIII), from water, m.p. 130, was obtained in 55% yield from *o*-xylylene dibromide, ethyl acetoacetate, and sodium ethoxide according to Scherks[4] and in 69% yield with diethyl sodiomalonate *via* hydrindene-2,2-dicarboxylic acid, m.p. 193°, according to Baeyer and Perkin.[6]

Chloride. A mixture of 22.5 g. of VIII and 50 ml. of thionyl chloride was gently heated until dissolution. Then the excess of thionyl chloride was removed *in vacuo* and the residue twice dissolved in benzene and again concentrated *in vacuo*, b.p. 90–94° (0.7 mm); 108° (2.5 mm). The chloride crystallized upon standing; m.p. 38°. Yield, 19.5 g. (83%).

2-Hydrindylacetic acid (IX). At a temperature of −10°, 18.5 g. of the chloride of VIII was added slowly to an ethereal solution of excess diazomethane (from 61.8 g. of nitrosomethylurea). After 12 hr. at room temperature, the ether was evaporated. The remaining yellowish needles of the diazoketone melted at 47° dec.. It was dissolved in a mixture of 35 ml. of benzyl alcohol and 35 ml. of collidine and decomposed in batches of 5 ml. at 180°. To the combined resulting solutions, 100 ml. of benzene was added and the solution washed with dilute hydrochloric acid and water and freed from benzene. The product was hydrolyzed for 4 hr. with 25 ml. of 50% aqueous potassium hydroxide and 50 ml. of methanol, diluted with water and, after extraction with ether, acidified. Yellowish crystals, which melted at 91° after recrystallization from petroleum ether (b.p. 60–80°) or nitromethane. Yield, 14.5 g. (88%).

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.0; H, 6.8. Found: C, 75.4; H, 7.3.

The *methyl ester* was prepared from 17.9 g. and diazomethane in 75% yield (14.5 g.), b.p. 90° (0.7 mm); $n_D^{26.5}$ 1.5168.

Anal. Calcd. for $C_{12}H_{14}O_2$: C, 75.8; H, 7.4. Found: C, 75.4; H, 7.7.

Methyl 2-indenylacetate (as I). A mixture of 13.6 g. of the foregoing ester, 12.8 g. of *N*-bromosuccinimide and 125 ml. of carbon tetrachloride was refluxed for 90 min., filtered, and concentrated. The residue was refluxed for 2 hr. with 15 ml. of pyridine and 40 ml. of benzene. The solution was washed with dilute hydrochloric acid and water and concentrated, and the product distilled *in vacuo*, b.p. 95–96° (0.01 mm.);[2] $n_D^{26.5}$ 1.5441. Yield, 11 g. (80%).

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.6; H, 6.4. Found: C, 76.3; H, 6.3.

2-Indenylacetic acid (I), obtained by alkaline hydrolysis of the ester, was recrystallized from nitromethane and melted at 124°(lit.,[2] m.p. 116–117°); yield, practically quantitative.

Anal. Calcd. for $C_{11}H_{10}O_2$: C, 75.9; H, 5.8. Found: C, 75.9; H, 5.9.

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The Synthesis of Some *vic*-Dihalo-1,2-dihydrodicyclopentadienenitroso Halides

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Received January 9, 1961

During the course of an investigation of the monomerization of the nitroso chloride dimer (I) of *endo*-dicyclopentadiene, we had occasion to prepare

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(5) E. Scherks, *Ber.*, **18**, 378 (1885).

(6) A. N Baeyer and H. W. Perkin, *Ber.*, **17**, 122 (1884).

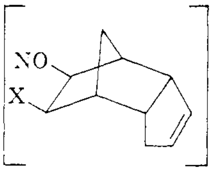
TABLE I

Compound	Yield, %	M.P.	Calcd.		Found	
			% C	% H	% C	% H
III	53	203–205 dec.	44.72	4.51	45.09	4.53
IV	54[a]	189–189.5	33.59	3.92	33.84	3.57
V	37	163–164	38.37	3.87	38.42	3.90
VI	46	159–164[b]	29.88	3.01	29.42	3.10
IX	48	159–160	44.72	4.51	44.38	4.68
X	47	168–169.5	33.59	3.92	33.15	3.56
XI	83	148–148.5	38.37	3.87	37.86	3.75
XII	43	170–171.5	29.88	3.01	30.14	3.29

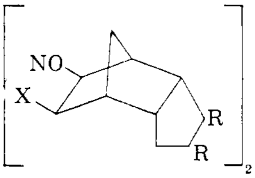
All products were difficult to recrystallize because of their insolubility in low boiling solvents and their tendency to monomerize and/or decompose at higher temperatures. The higher boiling solvents (>100°) seem to give purer products but loss during recrystallization is often considerable. Unless otherwise indicated, the compounds reported here were recrystallized from chloroform, a solvent which does not cause decomposition of the nitrosohalides. [a] Recrystallized from toluene. [b] Reported,[3] m.p. 211° from amyl alcohol.

the dibromo derivative IV by direct addition of bromine to the cyclopentenyl double bond. This compound which contains an incipient nitrogen mustard moiety in the $O{=}N{-}\overset{|}{C}H{-}\overset{|}{C}H{-}X$ function has been extensively tested as a nitrogen mustard agent in the antitumor screening program of the Cancer Chemotherapy National Service Center, National Institutes of Health. In this communication we are reporting the synthesis of the dibromonitroso chloride IV and the nitroso bromide dimer (VIII) of *exo*-dicyclopentadiene and the subsequent preparation for testing of seven *vic*-dihalo-1,2-dihydrodicyclopentadienenitroso halides.

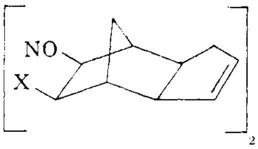
The dichloro derivative (III) of the dimeric *endo*-nitroso chloride I was prepared by direct chlorination and by the same general route the dichloro (V) and dibromo (VI) derivatives of the dimeric *endo*-nitroso bromide II were prepared. In the *exo*-dicyclopentadiene series the dichloro (IX and XI) and dibromo (X and XII) derivatives of the nitroso chloride (VII) and nitroso bromide (VIII) dimers have also been prepared.[1]



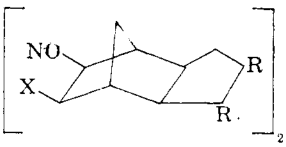
I. X = Cl
II. X = Br



III. X = Cl; R = Cl
IV. X Cl; R = Br
V. X = Br; R = Cl
VI. X = Br; R = Br



VII. X = Cl
VIII. X = Br



IX. X = Cl; R = Cl
X. X = Cl; R = Br
XI. X = Br; R = Cl
XII. X = Br; R = Br

EXPERIMENTAL

Analyses are by Dr. Ing. A Schoeller, Mikroanalytisches Laboratorium, West Germany.

Preparation of the nitroso halides. The nitroso halide dimers, I, II, VII, and VIII, were prepared from the olefins by the usual method[2] using isoamyl nitrite and either concd. hydrochloric or concd. hydrobromic acid to generate the desired nitrosyl halide. The nitrosobromide of *exo*-dicyclopentadiene VIII, not previously reported in the literature, was obtained by dropwise addition of a solution of 45 ml. of 95% ethanol and 45 ml. of concd. hydrobromic acid to a stirred, ice cold solution of 60 g. (0.45 mole) of *exo*-dicyclopentadiene, 57 g. of isoamyl nitrite, 45 ml. of glacial acetic acid, and 45 ml. of 95% ethanol. The solid product was filtered, washed thoroughly with 95% ethanol and then with ether to yield 93 g. (84%) of the nitroso bromide VIII. A sample was further purified by recrystallization from chloroform; m.p. 157–158°, mixed melting point with a sample of the *endo* isomer (reported[3] m.p. 157°) was 149–153°.

Anal. Calcd. for $(C_{10}H_{12}BrNO)_2$: C, 49.60; H, 5.00 Found: C, 49.78; H, 5.12.

Chlorination of the nitroso halides. A suspension of 10 g. of dimer in 200 ml. of chloroform was cooled in a Dry ice–acetone bath and stirred vigorously while chlorine gas was bubbled through. In every case, the solid dissolved within 30–50 min. giving a bright yellow chlorine saturated solution. After the solid had disappeared, stirring was continued with slow addition of chlorine for about 30 min. Then excess chlorine was removed by evacuating a stirred solution with an aspirator. The cooling bath was allowed to warm slowly to room temperature. The yellow color disappeared slowly and a white suspension resulted. The sides of the reaction flask were washed with 95% ethanol, which also tended to precipitate the product, and the solid was collected by filtration. In all cases additional product was obtained from the filtrate after it had been allowed to remain at room temperature for about 24 hr. All of the compounds were obtained as colorless solids after washing with 95% ethanol and with ether. Analyses were performed on samples recrystallized from chloroform. Yields, melting points and analytical data are given in Table I.

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(1) There is ambiguity in the position of the double bond in the nitroso halides and consequently in the dihalo products. It is not known whether the olefinic center exercises steric control in the halonitrosation reaction.

(2) G. Kraemer and A. Spilker, *Ber.*, **29**, 552 (1896).

(3) A. Rule, *J. Chem. Soc.*, 1339 (1906).

Bromination of the nitroso halides. Ten grams of the dimer was suspended in 200 ml. of chloroform. To the nitroso chlorides, 8.88 g. of bromine in 20 ml. of chloroform was added slowly with stirring. To the nitroso bromides, 6.6 g. of bromine in 20 ml. of chloroform was added. The reaction was stirred for 1 hr. after the addition of bromine was complete, and then the solution was evacuated at the aspirator at room temperature with vigorous stirring. The solution became colorless and the product precipitated. The reactions were worked-up in exactly the manner described for the chlorination reactions. Pertinent data are given in Table I.

Acknowledgment. The support of this investigation by a Research Grant (CY-4298) of the National Institutes of Health, Public Health Service, is greatly appreciated.

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On the Preparation of Codeinone

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Received January 10, 1961

The methods of Rapoport and Reist[2] and Highet and Wildman[3] for the preparation of codeinone, although the best yet devised for this ketone, require a lengthy preparation of either silver carbonate[2] or manganese dioxide.[3] From our experience, a modification of the original conditions of Rapoport eliminates the silver carbonate preparation and shortens the reaction time. We have found commercial silver carbonate in only 300 mole per cent excess to be as effective as the specially prepared reagent in 500 mole per cent excess. Although oxidation did not take place in boiling benzene, the reaction in refluxing toluene or xylene was complete within ten to fifteen minutes and yielded 80–85% of crude codeinone, m.p. 178–180°. The same yield was obtained with or without mechanical stirring.

Conditions also have been found for several Michael-type additions of nitrogen, carbon, and sulfur compounds to the conjugated carbonyl system of codeinone in benzene solution. In particular, adducts of piperidine, morpholine, nitromethane, and *N,N*-diethyldithiocarbamic acid were prepared. When these reactions were attempted in ethanol solution extensive darkening and decomposition were observed.

EXPERIMENTAL

Codeinone. To a solution of 10 g. (0.033 mole) of codeine in 150 ml. of toluene (reagent or technical grade) in a 500-ml., three necked flask fitted with a condenser was added 25 g. (0.091 mole) of commercial silver carbonate (Baker and Adamson). The olive-gray mixture was heated to reflux under a slow stream of nitrogen. After the color had changed to gray and then black (about 5 min.), reflux was continued for another 5 min. The insoluble mixture of silver and silver salts was removed by filtration and was washed with hot benzene. The combined organic solutions were concentrated with addition of petroleum ether (b.p. 69°) until crystallization began. Filtration gave 4.0 g., of codeinone m.p. 185°. A second crop of 4.2 g., m.p. 178–180°, brought the yield to 8.2 g. (82%), λ_{max}^{KBr} 6.0 μ.

Piperidine adduct. Codeinone (4.0 g.) was heated to reflux for 1 hr. in 75 ml. of dry benzene containing 9 ml. of piperidine. The solvent was evaporated and the residue was recrystallized from 95% ethanol to give 2.6 g. of colorless rhombic crystals, m.p. 190–191° dec., λ_{max}^{KBr} 5.85 μ.

Anal. Calcd. for $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.90; N, 7.32. Found: C, 72.08; H, 8.20; N, 7.87.

Morpholine adduct. Codeinone (2.0 g.) was heated to reflux for 2 hr. in 75 ml. of dry benzene containing 10 ml. of morpholine. The organic solution was washed twice with water and evaporated to dryness. Recrystallization from absolute ethanol gave colorless crystals, m.p. 208–210° dec., λ_{max}^{KBr} 5.86 μ.

Anal. Calcd. for $C_{22}H_{28}N_2O_4$: C, 68.72; H, 7.34; N, 7.28 Found: C, 68.67; H, 7.26; N, 7.33.

Nitromethane adduct. Nitromethane (3 ml.) was added to a solution of 1 g. of sodium in 50 ml. of absolute ethanol. The excess solvent was decanted from the white precipitate which was then washed by decantation with absolute alcohol, dry ether, and finally dry benzene. A solution of 1.5 g. of codeinone in 50 ml. of dry benzene was added to the sodium salt. The mixture was heated to reflux for 2 hr. and filtered. The filtrate was evaporated and the residue recrystallized from benzene and then from ethanol to give 0.45 g. (25%) of white powder, m.p. 199–200°, λ_{max}^{KBr} 5.83, 6.48, and 7.30 μ (NO_2).

Anal. Calcd. for $C_{19}H_{24}N_2O_5$: C, 63.33; H, 6.70; N, 7.71. Found: C, 63.51; H, 6.83; N, 7.74.

N,N-Diethyldithiocarbamic acid adduct. Triethylammonium *N,N*-diethyldithiocarbamate was prepared according to the procedure of Buess[4] from 1.9 ml. of triethylamine, 0.8 ml. of carbon disulfide, and 1.4 ml. of diethylamine. A solution of 2.0 g. of codeinone in 50 ml. of benzene was added to the reagent. A day later the solvent was removed at room temperature. The product, washed with water and dried, weighed 2.6 g. (86%). Recrystallization from a mixture of benzene and petroleum ether gave a white microcrystalline powder, m.p. 80–85° dec., which decomposed slowly on standing.

Anal. Calcd. for $C_{23}H_{30}N_2O_3S_2$: C, 61.85; H, 6.76; N, 6.29. Found: C, 60.78; H, 7.12, N, 6.27.

Acknowledgment. We would like to acknowledge the experimental advice of Dr. E. W. Warnhoff and the assistance of Mr. D. Lawson in determining infrared spectra.

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[1] Chemical Laboratory, Los Angeles Police Department.

[2] H. Rapoport and H. N. Reist, *J. Am. Chem. Soc.*, **77**, 490 (1955).

[3] R. J. Highet and W. C. Wildman, *J. Am. Chem. Soc.*, **77**, 4399 (1955).

[4] C. M. Buess, *J. Am. Chem. Soc.*, **77**, 6613 (1955).