reflux, the water was distilled from the reaction mixture. The residue was cooled, washed several times with ether, and recrystallized from absolute ethanol.

2-Phthalimido-1-indanone (XII).—The method of Curtin and Schmukler (11) was used. To 3.89 Gm. (0.021 mole) of potassium phthalimide in 15 ml. of *N,N*-dimethylformamide was added 6.34 Gm. (0.03 mole) of 2-bromo-1-indanone (crude). The mixture was heated on a steam bath with stirring for 8 hr. At the end of this period, the reaction mixture was poured into 120 ml. of water. The product (3.0 Gm., 36%) was removed by filtration and recrystallized several times from ethanol, m.p. 200–201°.

Anal.—Calcd. for $C_{17}H_{11}NO_3$: C, 73.62; H, 4.00; N, 5.05. Found: C, 73.79; H, 4.03; N, 5.07.

REFERENCES

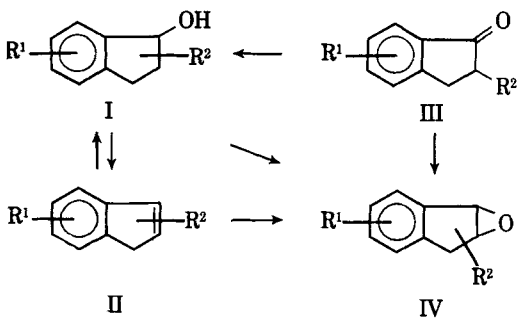
(1) Sam, J., and Thompson, A. C., *J. Pharm. Sci.*, **53**, 535(1964).
(2) Nobles, W. L., and Blanton, C. D., Jr., *ibid.*, **53**, 115(1964); Blanton, C. D., Jr., and Nobles, W. L., *ibid.*, **51**, 878(1962).
(3) Knoll, J., *et al.*, *Magy. Tud. Akad. Biol. Orvosi Tud. Csszt. Koszlemen.*, **11**, 329(1960); through *Chem. Abstr.*, **55**, 2892*i*(1961).
(4) Chauvette, R. R., *et al.*, *J. Am. Chem. Soc.*, **84**, 3401 (1962).
(5) Blicke, F. F., *Org. Reactions*, **1**, 303(1942).
(6) Delepine, M., *Compt. Rend.*, **124**, 292(1897); *Chem. Zentr.*, **1**, 539(1897); Covello, M., Abignente, E., and Piscopo, E., *Ann. Chim. Rome*, **52**, 213(1962); through *Chem. Abstr.*, **57**, 2114*b*(1962).
(7) Wilds, A. L., *J. Am. Chem. Soc.*, **64**, 1421(1942).
(8) Sheehan, J. C., and Bolhofer, W. A., *ibid.*, **72**, 2786(1950).
(9) Takahashi, T., Hori, M., and Tsuruha, H., *J. Pharm. Soc. Japan*, **76**, 56(1956); through *Chem. Abstr.*, **50**, 12849*b* (1956).
(10) Fry, E. M., *J. Org. Chem.*, **10**, 259(1945).
(11) Curtin, D. Y., and Schmukler, S., *J. Am. Chem. Soc.*, **77**, 1105(1955).

Synthesis of 1,2-Epoxyindans

By JOSEPH SAM and T. C. SNAPP*

Several substituted 1,2-epoxyindans have been prepared either by dehydrobromination of bromoindanols or by the peracid oxidation of indenes. It was observed that the course of ring opening of the epoxides with piperazine was dependent upon neighboring substituents. Preliminary screening of several of the compounds for antineoplastic activity has not revealed significant activity.

ALTHOUGH EXTENSIVE investigations have been reported on cyclopentane- (1), cyclohexane- (2), and tetralin-1,2-epoxides (3), few reports (4–6) involving 1,2-epoxyindans (IV) have been published. The synthesis of substituted 1,2-epoxyindans was investigated through three methods: (*a*) dehydrobromination of 2-bromo-1-indanols (I, R^2 = 2-Br) by potassium hydroxide (7), (*b*) epoxidation of substituted indenes (II) with peracids (5), and (*c*) reduction of 2-bromo-1-indanones (III, R^2 = Br). (Scheme I.)

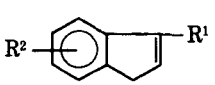


Scheme I

DISCUSSION

The substituted indenes (II) utilized in this work were prepared by the dehydration of 1-indanols (I). The latter were derived from indanones (III) by the reduction with sodium borohydride or by the reaction with a Grignard reagent. Table I lists the novel indenes involved in this study.

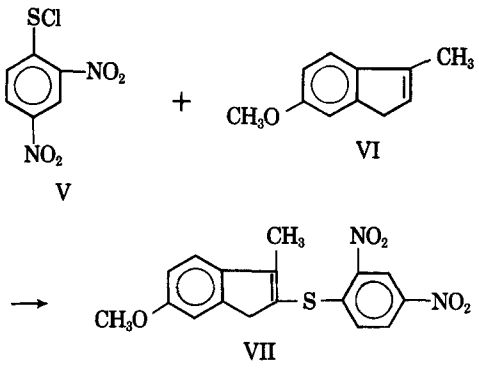
TABLE I.—INDENES



R^1	R^2
H	6-CH_3O (trimer)[a]
C_6H_5	7-Cl
H	6-CH_3O-5-$C_6H_5CH_2O$
C_6H_5	6-$C_6H_5CH_2O$
CH_3	6-CH_3O

[a] The monomer has been described by Süs (8).

Received January 11, 1965, from the Department of Pharmaceutical Chemistry, The University of Mississippi, University.
Accepted for publication February 24, 1965.
Presented to the Scientific Section, A.PH.A., Detroit meeting, March 1965.
Abstracted in part from a thesis submitted by Thomas C. Snapp to the Graduate School, The University of Mississippi, University, in partial fulfillment of Doctor of Philosophy degree requirements.
This investigation was supported by grant CY 5290 from the National Institutes of Health, U. S. Public Health Service, Bethesda, Md.
* Present address: Texas Eastman Co., Division of Eastman Kodak Co., Longview, Tex.



Scheme II

The use of 2,4-dinitrophenylsulfenyl chloride (V) was investigated for the identification of 6-methoxy-3-methylindene (VI). Whereas V normally gives an addition product on reaction with ethylenic compounds (9), a dehydrohalogenated product was obtained with VI which, on the basis of elemental and infrared analysis, was assigned structure VII. (Scheme II.)

The preparation of 2-bromo-1-indanols (Table II) from the corresponding indenes was effected by two methods: (*a*) treatment of the substituted indenes with an aqueous solution of bromine and sodium bromide and (*b*) the reaction of *N*-bromosuccinimide in an aqueous mixture with the indene. Whitmore and Gebhart (10) synthesized 2-bromo-1-indanol by treating an emulsion of indene and water with a saturated aqueous solution of bromine and sodium bromide. Satisfactory results were obtained from this reaction only when the solution was emulsified. In the preparation of bromohydrins of substituted indenes, this method was unsuccessful, perhaps due to the difficulty encountered in the formation of an emulsion.

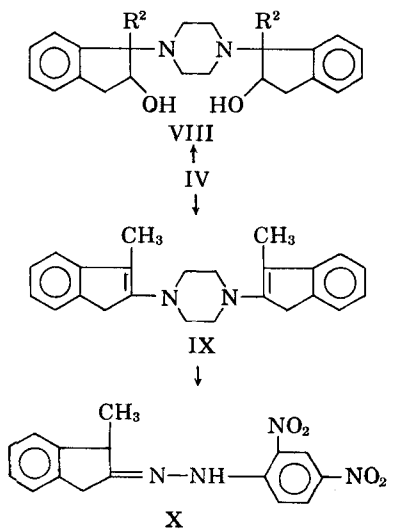
A synthetic route to 2-bromo-1-indanol (I, R^1 = H; R^2 = 2-Br) from indene and *N*-bromosuccinimide was reported by Guss and Rosenthal (11). This method was found to be more applicable to substituted indenes (II) than the method of Whitmore and Gebhart.

While the dehydrohalogenation of the bromohydrins (I, R^2 = 2-Br) to the 1,2-epoxyindans (IV) was achieved in good yields, this synthetic route was hampered by the low yields obtained in the preparation of the bromohydrins.

The epoxidation of indenes with perbenzoic acids appeared to be the most successful approach to indene oxides. We observed that *m*-chloroperbenzoic acid could be substituted for perbenzoic acid in the epoxidation of indene without affecting the yield of 1,2-epoxyindan.

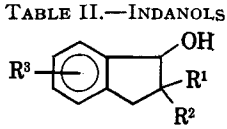
The 1,2-epoxyindans, because of difficulties encountered in their purification, were identified as the products obtained from their reaction with piperazine (Table III).

Whereas the reaction of piperazine with excess 1,2-epoxyindan (IV, R^1 = R^2 = H) gave the bisindanylpiperazine derviative, (VIII, R^2 = H) (4), the reaction with 1-methyl-1,2-epoxyindan (IV, R^1 = H; R^2 = 1-CH_3) yielded the enamine (IX). The ring opening of unsubstituted 1,2-epoxyindan with amines has been shown to yield 1-amino-2-indanol derivatives (6, 12). The enamine (IX)



Scheme III

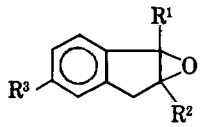
TABLE II.—INDANOLS



R^1	R^2	R^3	Method	Reaction Temp., °C.	Yield, %	M.p., °C. (B.p., °C./mm.)	Molecular Formula	Anal., % Calcd.	Found
H	H	4-Cl	*A*	30	73	67–68	C_9H_9ClO[a]	...	...
H	H	5-CH_3O-6-$C_6H_5CH_2O$	*A*	30	81	91–92	$C_{17}H_{18}O_3$	C, 75.53	75.91
								H, 6.71	7.05
H	H	5-$C_6H_5CH_2O$	*A*	30	97	72–73	$C_{16}H_{14}O_2$	C, 79.92	79.48
								H, 6.71	6.82
Br	H	H	*A*	70	82	129–130	C_9H_9BrO[b]	C ...	...
								H ...	...
Br	CH_3	H	*B*	30	53	61–63	$C_{10}H_{11}BrO$[c]	C, 52.88	53.20
								H, 4.88	4.76
Br	H	4-Cl	*A*, *B*	30	13	112–114	C_9H_8ClBrO	C, 43.72	43.74
								H, 3.02	3.24
H	H	5-CH_3O	*A*	30	83	(104–106/0.1)	$C_{10}H_{12}O_2$	C, 73.14	72.84
								H, 7.37	7.46

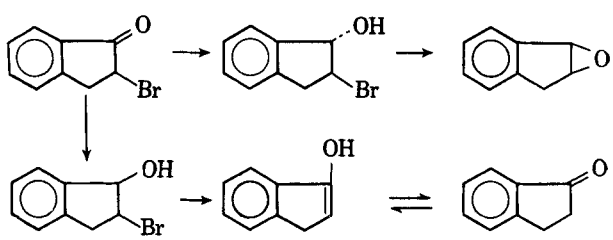
[a] *Reference 22.* [b] *Reference 10.* [c] $\gamma_{max.}^{KBr}$ 9.5 μ, characteristic of secondary alcohols.

TABLE III.—EPOXYINDANS



R¹	R²	R³	Method	Yield, %	M.p., °C. (B.p., °C./mm.)	Molecular Formula	Anal., % Calcd.	Found
H	H	H	*C, D*	70, 72	(105–108/8)	C_9H_8O[a]	C ...	...
							H ...	...
							N ...	...
H	H	H	*E*	72	254–255[b]	$C_{22}H_{26}N_2O_2$[c,d]	C ...	...
							H ...	...
							N ...	...
CH_3	H	H	*C*	61	(77–79/18)	$C_{10}H_{10}O$[e]	C ...	...
							H ...	...
							N ...	...
CH_3	H	H	*E*	62	172–173[b]	$C_{24}H_{26}N_2$[d,f]	C, 84.23	84.05
							H, 7.68	7.79
							N, 8.18	8.10
C_6H_5	H	H	*C*	41	56–58[g]	$C_{15}H_{12}O$[e]	C ...	...
							H ...	...
							N ...	...
C_6H_5	H	H	*E*	85	233–234[b]	$C_{32}H_{34}N_2O_2$[d]	C, 81.04	80.92
							H, 6.81	6.12
							N, 5.57	5.49
C_6H_5	H	CH_3O	*C*	41	(127–129/0.1)	$C_{16}H_{14}O_2$[e]	C ...	...
							H ...	...
							N ...	...
C_6H_5	H	CH_3O	*E*	51	227–229[b]	$C_{20}H_{24}N_2O_2$[h]	C, 74.43	74.68
							H, 7.48	6.85
							N, 8.61	8.47
H	CH_3	H	*D*	65	37–38 (67–70/0.8)	$C_{10}H_{10}O$[e]	C ...	...
							H ...	...
							N ...	...
H	CH_3	H	*E*	72	246–247[i]	$C_{24}H_{30}N_2O_2$[d]	C, 76.10	75.98
							H, 7.92	8.02
							N, 7.41	7.35

[a] *Reference 7.* [b] Recrystallized from isoamyl alcohol. [c] *Reference 4.* [d] Disubstituted piperazine. [e] Analyzed as a piperazine derivative. [f] 1,4-Di-(1-methyl-1-indenyl)piperazine. [g] Recrystallized from ethanol–water. [h] Monosubstituted piperazine. [i] Recrystallized from ethanol.



Scheme IV

was identified by elemental and infrared analysis and also by the identification of the product of the reaction of IX and 2,4-dinitrophenylhydrazine in dilute acid as the hydrazone (X) of 1-methyl-2-indanone. (Scheme III.) The reverse ring opening of the epoxide, followed by dehydration to provide IX, may be attributed to steric hindrance caused by the methyl group.

The reaction of 1-phenyl-1,2-epoxyindan (IV, R^1 = H; R^2 = 1-C_6H_5) with piperazine, on the other hand, gave the normal ring opening product, *i.e.*, the 2-indanol derivative (VIII, R^2 = C_6H_5). The electronic factor involved in the proposed mechanism of the ring opening reaction of 1,2-epoxyindan (6) is increased by the introduction of a phenyl group in position 1 and, therefore, must be more important than the steric factor in the ring opening of 1-phenyl-1,2-epoxyindan.

In recent years, the synthesis of epoxy steroids has become of increasing importance. The preparation of these compounds has been accomplished by reduction of steroid bromoketones. Since the reductions of α-chloro- and α-bromoketones with sodium borohydride have resulted in the synthesis of epoxy steroids, this method was employed in the reduction of 2-bromo-1-indanones. The reduction of 2-bromo-1-indanone with sodium borohydride, at temperatures of 0–60°, however, produced 1-indanone and 1-indanol. Apparently *cis*-2-bromo-1-indanol was formed since the *trans* isomer is necessary for the formation of 1,2-epoxyindan and the *cis* isomer for 1-indanone. (Scheme IV.) The use

of an excess of sodium borohydride accounted for the occurrence of 1-indanol as a product in the reaction. Various authors (13, 14) have verified the transformation of the *cis*- and *trans*-bromohydrins in an alkali medium to ketones and epoxides, respectively.

The reduction of 2-bromo-4-chloro-1-indanone with sodium borohydride in ethanol at room temperature yielded a mixture from which 10% of *trans*-2-bromo-4-chloro-1-indanol was isolated.

Preliminary screening of several of the compounds for antineoplastic activity has not revealed significant activity.

EXPERIMENTAL[1]

Indene and 1,2-epoxyindan were purchased from Neville Chemical Co., Pittsburgh, Pa. 2-Methylindene (15), 3-methylindene (16), and 3-phenylindene (17) were prepared according to published procedures.

2-Bromo-4-chloro-1-indanone.—The procedure employed by Wilds (18) for the preparation of 2-bromo-1-keto-1,2,3,4-tetrahydrophenanthrene was followed. To a solution of 16.5 Gm. (0.1 mole) of 4-chloro-1-indanone (19) in 200 ml. of ether was added dropwise with stirring 16.0 Gm. (0.1 mole) of bromine. The mixture was stirred for 4 hr. and allowed to stand overnight at room temperature. Evaporation of the solvent and recrystallization of the residue from heptane yielded 32.0 Gm. (97%) of 2-bromo-4-chloro-1-indanone, m.p. 42–43°.

Anal.—Calcd. for C_9H_6ClBrO: C, 44.03; H, 2.46; Cl, 14.44; Br, 32.95. Found: C, 43.81; H, 2.61; Cl, 13.76; Br, 32.78.

5-Methoxy-6-benzyloxy-1-indanone.—The procedure described by Donbrow (20) for the preparation of 5-benzyloxy-1-indanone was employed. From 17.6 Gm. (0.1 mole) of 5-methoxy-6-hydroxy-1-indanone (21) there was obtained, after recrystallization from an ethanol–water mixture, 26.5 Gm. (95%) of product, m.p. 130–131°.

Anal.—Calcd. for $C_{17}H_{16}O_3$: C, 76.01; H, 6.00. Found: C, 75.83; H, 5.73.

Indanols (Table II).—*Method A.*—The procedure described by Tamayo and Robles (22) was modified using sodium borohydride in place of lithium aluminum hydride. To a solution of 0.2 mole of indanone in 300 ml. of ethanol or diglyme was added gradually 11.4 Gm. (0.3 mole) of sodium borohydride. The reaction mixture was stirred for 8–12 hr. at 25–80°. (See Table II.) The solvent was distilled *in vacuo* and the residue treated with 200 ml. of water and extracted with ether. The ether extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness. The product was recrystallized from a suitable solvent.

Method B.—The procedure described by Guss and Rosenthal (11) for the preparation of styrene bromohydrin was followed. A mixture of 0.05 mole of indene, 9.1 Gm. (0.05 mole) of *N*-bromosuccinimide, and 50 ml. of water was stirred vigorously at room temperature for 6 hr. The bromohydrin was isolated by filtration, washed with petroleum ether (b.p. 30–60°), and recrystallized.

[1] Melting and boiling points are uncorrected. Melting points were determined on a Fisher-Johns apparatus. Infrared spectra were determined on a Perkin-Elmer model 137G Infracord spectrophotometer.

3-Methyl-6-methoxyindene.—The general method of Solmssen and Wenis (23) was employed. A solution of 100 ml. of dry tetrahydrofuran and 65 ml. of 3 *M* ethereal solution of methyl magnesium bromide was cooled and treated dropwise with a solution of 16.3 Gm. (0.1 mole) of 5-methoxy-1-indanone (21) in 200 ml. of dry tetrahydrofuran. After the addition was complete, the mixture was refluxed on a steam bath for 2 hr. The solvent was evaporated *in vacuo* with heating, and the cooled black residue was treated dropwise with a saturated aqueous solution of ammonium chloride.

The brown oil which separated was extracted with three 100-ml. portions of ether; the combined ethereal layers were washed with water and dried with anhydrous sodium sulfate. Evaporation of the ether and distillation of the residual oil gave 12 Gm. (75%) of product, b.p. 76–80°/0.2 mm.

A 2,4-dinitrobenzenesulfenyl chloride derivative [VII, 2-(2,4-dinitrophenylthio)-3-methyl-6-methoxyindene] was prepared in the usual manner (8) and recrystallized from an acetic acid–ethanol mixture, m.p. 180–181°. The infrared spectrum posssesed a band at 1615 cm.$^{-1}$ (6.15 μ), which is characteristic of a conjugated ethylenic linkage.

Anal.—Calcd. for $C_{17}H_{14}N_2O_5S$: C, 56.98; H, 3.90; N, 7.78; S, 8.95. Found: C, 56.97; H, 3.94; N, 7.82; S, 8.95.

7-Chloro-3-phenylindene.—The procedure described for the preparation of 3-methyl-6-methoxyindene was followed using 33.2 Gm. (0.2 mole) of 4-chloro-1-indanone (19), 65 Gm. (0.42 mole) of bromobenzene, and 9.6 Gm. (0.4 mole) of magnesium turnings. The concentrated Grignard complex was decomposed by the dropwise addition of 250 ml. of 1 *N* sulfuric acid. Nine grams (35%) of 7-chloro-3-phenylindene was obtained, b.p. 134–136°/0.75 mm. One-tenth gram of 2,5-di-*tert*-butylhydroquinone was added to the compound after distillation.

The 2,4,7-trinitrofluorenone derivative was prepared in the usual manner (24) and recrystallized from an ethyl acetate–ethanol mixture.

Anal.—Calcd. for $C_{27}H_{16}ClN_3O_7$: C, 62.05; H, 2.97; N, 7.75. Found: C, 62.69; H, 2.99; N, 7.94.

3-Phenyl-6-benzyloxyindene.—The procedure described for the preparation of 7-chloro-3-phenylindene was followed using 4.8 Gm. (0.2 mole) of magnesium turnings and 22.5 Gm. (0.09 mole) of 5-benzyloxy-1-indanone (20). The product was refluxed in 150 ml. of 20% sulfuric acid for 1 hr. The mixture was cooled, and the solid was isolated by filtration and recrystallized from an ethanol–water mixture to yield 20.4 Gm. (78%) of product, m.p. 88–89°.

Anal.—Calcd. for $C_{22}H_{18}O$: C, 88.56; H, 6.09. Found: C, 88.51; H, 6.16.

6-Methoxyindene Trimer.—A mixture of glacial acetic acid, 10 ml. of concentrated hydrochloric acid, and 6.0 Gm. (0.04 mole) of 5-methoxy-1-indanol was refluxed for 30 min. Most of the solvent was distilled *in vacuo*, and the residual mixture, after cooling, was neutralized with sodium carbonate. The solid was removed by filtration, washed with water, and recrystallized from an ethanol–water mixture. Two grams (62%) of product, melting at 131–132°, was obtained.

Anal.—Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.90. Found: C, 82.41; H, 6.73.

A molecular weight determination of 430 by the Rast method indicated the formation of a trimer.

5-Benzyloxy-6-methoxyindene.—The dehydration procedure from Johnson and Kon (25) was utilized. A mixture of 4.5 Gm. (0.02 mole) of 5-methoxy-6-benzyloxy-1-indanol and 8 Gm. (0.08 mole) of acetic anhydride was heated on a steam bath with stirring. After heating for 20 min., the solution was poured onto 25 Gm. of crushed ice. The solid that separated was collected by filtration. Recrystallization from an ethanol–water mixture yielded 2.6 Gm. (68%) of 5-benzyloxy-6-methoxyindene, m.p. 81–82°.

Anal.—Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.40. Found: C, 80.47; H, 6.57.

Epoxyindans (Table III).—*Method C.*—The general procedure outlined by Hibbert and Burt (26) for the synthesis of 1,2-epoxyethylbenzene was employed. To a solution of 0.05 mole of requisite indene in 50 ml. of dry chloroform was added dropwise a solution of 10.3 Gm. (0.06 mole) of *m*-chloroperbenzoic acid in 200 ml. of dry chloroform. Thereafter, the reaction mixture was stirred for 8 hr. in an ice bath and for 12 hr. at room temperature. The mixture was filtered, and the chloroform solution was washed with three 100-ml. portions of cold 10% sodium hydroxide solution, followed by two 100-ml. portions of water, then dried with anhydrous sodium sulfate. The chloroform solution was evaporated to dryness and the residual material either crystallized from a suitable solvent or distilled. The infrared spectra of the products exhibited a band at 1250 cm.$^{-1}$ (8.00 μ) characteristic of an epoxy group.

Method D.—A mixture of 50 ml. of 13 *N* aqueous potassium hydroxide and 0.04 mole of desired 2-bromo-1-indanol was stirred at room temperature for 30 min. The resulting mixture was extracted with ether and the ether layers washed with two 50-ml. portions of water. After drying over anhydrous sodium sulfate, the ether was evaporated, and the residue was either distilled or crystallized from a suitable solvent.

Piperazine Derivatives of Epoxides (Table III).—*Method E.*—To a solution of 0.01 mole of epoxyindan in 5 ml. of absolute ethanol was added 0.9 Gm. (0.005 mole) of piperazine hexahydrate. The mixture was refluxed on a steam bath for 5 hr. and thereafter cooled. The product (disubstituted piperazine) was removed by filtration and recrystallized from a suitable solvent.

A monosubstituted piperazine derivative may result if an equimolar ratio of epoxyindan and piperazine are used.

The examine (IX) showed a strong infrared maximum (KBr) at 1675 cm.$^{-1}$ characteristic of the C=C—N group (27).

Ethyl 4-(2-Hydroxy-2-methylindanyl)aminobenzoate.—A solution of 5.3 Gm. (0.04 mole) of 2-methyl-1,3-epoxyindan and 5.9 Gm. (0.03 mole) of ethyl 4-aminobenzoate in 25 ml. of ethanol was refluxed on a steam bath for 24 hr. The solvent was distilled *in vacuo*, and the solid was recrystallized from ethanol to give 5.1 Gm. (56%) of product, m.p. 170–171°.

Anal.—Calcd. for $C_{19}H_{21}NO_3$: C, 73.29; H, 6.80; N, 4.50. Found: C, 73.59; H, 6.72; N, 4.71.

1-Methyl-2-indanone 2,4-Dinitrophenylhydrazone (X).[2]—The usual procedure for the preparation of 2,4-dinitrophenylhydrazones was followed using 0.16 Gm. of 1,4-di-(1-methyl-1-indenyl)piperazine in place of the ketone. The product (0.06 Gm., 38%) was recrystallized from ethanol, m.p. 184–185.5°. The infrared spectrum was similar to that of 2,4-dinitrophenylhydrazones.

Anal.—Calcd. for $C_{16}H_{14}N_4O_4$: C, 58.89; H, 4.32; N, 17.17. Found: C, 58.70; H, 4.50, N, 16.83.

REFERENCES

(1) Mousseron, M., Winternitz, F., and Combes, G., *Compt. Rend.*, **222**, 1503(1946); through *Chem. Abstr.*, **41**, 102*d*(1947).
(2) Mousseron, M., *et al.*, *Bull. Soc. Chim. France*, **1947**, 850; through *Chem. Abstr.*, **42**, 3377*i*(1948).
(3) van Tamelen, E. E., Van Zyl, G., and Zuidema, G. D., *J. Am. Chem. Soc.*, **72**, 488(1950).
(4) Mousseron, M., *Bull. Soc. Chim.*, **51**, 782(1932); through *Chem. Abstr.*, **26**, 5567(1932).
(5) Hückel, W., and Bollig, F. J., *Ber.*, **86**, 1137(1953).
(6) Sam, J., Plampin, J. N., and Alwani, D. W., *J. Org. Chem.*, **27**, 4543(1962).
(7) Böeseken, J., and van Loon, C., *Proc. Acad. Sci. Amsterdam*, **20**, 1186(1918); through *Chem. Abstr.*, **13**, 314 (1919).
(8) Süs, O., *Ann.*, **599**, 133(1953).
(9) Kharasch, N., and Buess, C. M., *J. Am. Chem. Soc.*, **71**, 2724(1949).
(10) Whitmore, W. F., and Gebhart, A. I., *ibid.*, **64**, 912 (1942).
(11) Guss, C. O., and Rosenthal, R., *ibid.*, **77**, 2549(1955).
(12) Levin, N., Graham, B. E., and Kolloff, H. G., *J. Org. Chem.*, **9**, 380(1944).
(13) Fieser, L. F., and Ettorre, R., *J. Am. Chem. Soc.*, **75**, 1700(1953).
(14) James, D. R., and Shoppee, C. W., *J. Chem. Soc.*, **1954**, 4224.
(15) Alexander, E. R., and Mudrak, A., *J. Am. Chem. Soc.*, **73**, 59(1951).
(16) Parham, W. E., Reiff, H. E., and Swartzentruber, P., *ibid.*, **78**, 1437(1956).
(17) Plattner, P. A., Sandrin, R., and Wyss, J., *Helv. Chim. Acta*, **29**, 1604(1946); through *Chem. Abstr.*, **41**, 2026 (1947).
(18) Wilds, A. L., *J. Am. Chem. Soc.*, **64**, 1421(1942).
(19) Mayer, F., *et al.*, *Ber.*, **61**, 1966(1928).
(20) Donbrow, M., *J. Chem. Soc.*, **1959**, 1613.
(21) Johnson, W. S., and Shelberg, W. E., *J. Am. Chem. Soc.*, **67**, 1853(1945).
(22) Tamayo, M. L., and Robles, N. D., *Anales Real Soc. Espan. Fis. Quim. Madrid*, **52B**, 117(1956); through *Chem. Abstr.*, **50**, 14676(1956).
(23) Solmssen, U. V., and Wenis, E., *J. Am. Chem. Soc.*, **70**, 4197(1948).
(24) Orchin, M., Reggel, L., and Woolfolk, E. O., *ibid.*, **69**, 1225(1947).
(25) Johnson, J. D. A., and Kon, G. A. R., *J. Chem. Soc.*, **1926**, 2748.
(26) Hibbert, H., and Burt, C. P., *J. Am. Chem. Soc.*, **47**, 2240(1925).
(27) Blomquist, A. T., and Moriconi, E. J., *J. Org. Chem.*, **26**, 3761(1961).

[2] The authors are grateful to A. K. Bej, Department of Pharmaceutical Chemistry, The University of Mississippi, for conducting this experiment.