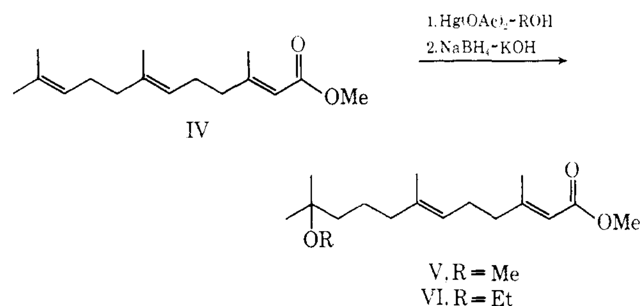
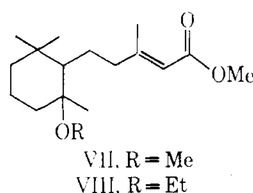
The bulk around C-11 might be the cause of the enhancement of JH activity of I–III over that of methyl farnesate (IV). This hypothesis was tested by preparing methyl 11-methoxy-3,7,11-trimethyl-2,6-dodecadienoate (V) and methyl 11-ethoxy-3,7,11-trimethyl-2,6-dodecadienoate (VI) by the alkoxymercuration of methyl farnesate and then by demercuration with $NaBH_4$.[7]



Two points were noteworthy in the reaction. The first was the rapidity of the alkoxymercuration. Earlier reports gave reaction times of 36 hr for methyl cinnamate,[8] several hours for ethylene,[9] and 14 hr for one double bond in methyl linoleate.[10] We have observed that the reaction was over in 30 min and probably much sooner. In fact, $Hg(OAc)_2$ must be added to methyl farnesate; reverse addition invariably led to a mixture of the starting material, monoadduct, and diadduct. Brown has remarked on the speed of the related hydroxymercuration reaction.[7]

The second point was that cyclization to form products such as VII or VIII was not an important reaction.



The nuclear magnetic resonance spectra of V and VI retained the signal at τ 8.42 for Me at C-7; the highest field signal was at τ 8.95, which would seem too low for the *gem*-Me_2 in VII and VIII; also, there were signals for two vinylic protons, at τ 4.43 (H on C-2) and 4.95 (H on C-6), which conclusively ruled out structures VII and VIII.

When *Tenebrio molitor* L. was used as the test insect, V and VI were less than one-third as active as farnesyl methyl ether and about $^1/_{300}$ as active as the mixture of synthetic JH and its isomers.[3] Apparently, the causative factor(s) for the enhanced activities of I–III reside(s) in something other than the mere bulk effect of the oxygen or chlorine atoms.

Experimental Section

Analytical and preparative glpc were made with an Aerograph A-700 Autoprep on a 152 cm × 6.4 mm column of 5% SE-30 on base-washed Chromosorb P at 225° and a flow of 60 ml/min. Nmr spectra were obtained on a Varian HA-100 by E. L. Gooden of this Division. The *Tenebrio* test[11] was used for bioassays with assistance from Mrs. R. B. Henegar and Mrs. P. Hall of the Biological Invesigations Unit of this Division. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

The methyl farnesate was prepared by the condensation of *trans*-geranylacetone[12] and trimethyl phosphonoacetate and was a 70:30 mixture of methyl *trans,trans*-farnesate and methyl *cis,trans*-farnesate.

Methyl 11-Methoxy-3,7,11-trimethyl-2,6-dodecadienoate (V).—A solution of $Hg(OAc)_2$ (2.6 g, 7.6 mmoles) in 50 ml of MeOH was added to a stirred, ice-cold solution of methyl farnesate (2.0 g, 7.6 mmoles) in 20 ml of MeOH during 15 min; then the mixture was allowed to stand for 30 min. A solution of KOH (1.27 g, 53 mmoles) in 20 ml of MeOH was added next. Then $NaBH_4$ (0.14 g, 3.8 mmoles) was added in small portions, and stirring was continued for 30 min. The solution was decanted from Hg, concentrated to half-volume under reduced pressure, diluted with 100 ml of H_2O, and extracted with three 50-ml portions of Et_2O. The combined Et_2O phase was extracted twice with 20-ml portions of H_2O and dried ($MgSO_4$). The removal of the ether yielded the desired product (1.66 g, 74%). The complete absence of methyl farnesate was demonstrated by gas chromatograms that had major peaks at 2.6 and 3.1 min (88% combined) and minor peaks at 3.5 (10%) and 3.8 min (2%). Analytical and nmr samples consisted of the two major peaks and were collected by preparative glpc. *Anal.* ($C_{17}H_{30}O_3$) C, H.

Methyl 11-Ethoxy-3,7,11-trimethyl-2,6-dodecadienoate (VI).—The compound was prepared in a similar manner with EtOH substituted for MeOH and with the following differences. $Hg(OAc)_2$ was added as a suspension in the EtOH, and the mixture was allowed to stand 2 hr before the addition of $NaBH_4$. The crude yield was 110%. Glpc (percentages given are exclusive of solvent peaks) demonstrated the absence of methyl farnesate, minor peaks at 2.1 and 2.3 min (12% combined), VI at 3.4 and 4.0 min (78% combined), and a minor peak at 4.5 min (10%). *Anal.* ($C_{18}H_{32}O_3$) C, H.

(7) H. C. Brown and P. Geoghegan, Jr., *J. Am. Chem. Soc.*, **89**, 1522 (1967).
(8) G. F. Wright, *ibid.*, **57**, 1993 (1935).
(9) M. M. Kreevoy and M. A. Turner, *J. Org. Chem.*, **30**, 373 (1965).
(10) E. Jantzen and H. Andreas, *Chem. Ber.*, **94**, 628 (1966).
(11) W. S. Bowers and M. J. Thompson, *Science*, **142**, 1469 (1963).
(12) Commercial geranylacetone was separated by the procedure of O. Isler, R. Ruegg, L. Chopard-dit-Jean, H. Wagner, and K. Bernhard, *Helv. Chim. Acta*, **39**, 897 (1956).

An Analog of Doisynolic Acid. 3-Hydroxy-16,17-seco-16-norestra-1,3,5(10)-trien-17-oic Acid

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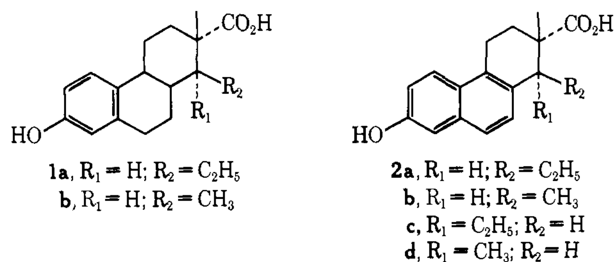
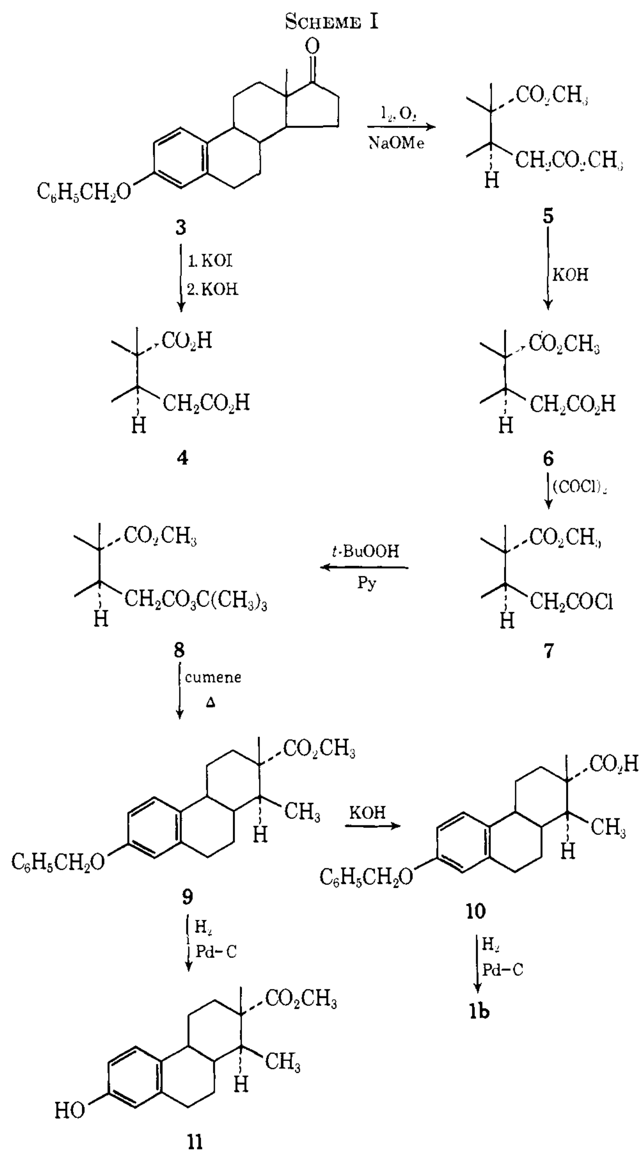
Many analogs of the potent estrogen *l-cis*-bisdehydrodoisynolic acid (**2c**) have been synthesized.[1,2] Although the replacement of the side-chain ethyl with a methyl group (**2c** → **2d**) caused no change in activity, a corresponding change (**2a** → **2b**) with the closely related, but much less active, *d-trans*-bisdehydrodoisynolic acid resulted in a more active compound (tested as the methyl ester).[1] Since *d-trans*-doisynolic acid (**1a**) is related in configuration to the less active bisdehydrodoisynolic acid **2a**, but is itself a potent estrogen, a similar transformation (**1a** → **1b**) would be of interest. This note describes the synthesis and estrogenic activity of **1b**.

(1) J. Heer and K. Miescher, *Helv. Chim. Acta*, **28**, 1506 (1945).
(2) For an excellent summary of the work on doisynolic acids and the nomenclature employed see L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp 487–494.



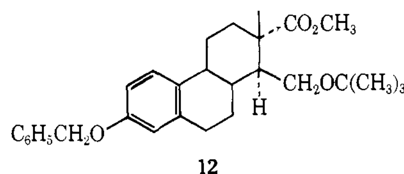
Decarboxylation of the monoester **6** was chosen as the most convenient synthetic route to **1b** (Scheme I).

SCHEME I



The preparation of **6** was expected to offer little difficulty. Oxidative cleavage of the D ring of 17-keto steroids by base and iodine was employed earlier[3,4] to give the prerequisite diacid **4**. Esterification of **4** gave the diester **5** which upon partial hydrolysis[4,5] yielded the monoester **6**.

However, in our hands the oxidative cleavage of **3** by the above procedure gave erratic results and the diacid **4** was difficult to isolate. In a series of experiments the yield of diacid **4** varied from 0 to 60%. A recent investigation of the mechanism of this reaction revealed that molecular oxygen is involved,[6] and a new procedure incorporating aeration was devised. By employing methanolic NaOMe as the solvent-base system the diester **5** was obtained in one step in 43% yield. The other products were a mixture of diacid **4** and the two possible monoesters.[6] Partial hydrolysis of **5** with KOH gave the crude monoester **6**, which on treatment with oxalyl chloride[5] furnished the acid chloride **7**. Reaction of the latter (**7**) with dry *t*-butyl hydroperoxide and pyridine in benzene yielded the perester **8**. The perester was decomposed[7] in boiling cumene during 1 hr and the solvent was removed by distillation. Chromatography separated 1,2-diphenyltetramethylethane and gave the desired product **9** in 40% yield based on **6**. Also isolated was a minor product which has tentatively been assigned structure **12** on the basis of its nmr and ir spectra.



Finally, saponification of **9** gave **10**. Both **9** and **10** were readily debenzylated by hydrogenolysis over Pd–C to give **11** and **1b**, respectively, thus completing the synthetic sequence.

Biological Data.—The estrogenicity of these compounds was determined by two different methods: assessing uterotropic and vaginal cornification activities. Uterotropic activity in mice after subcutaneous injection was measured using the assay described by Dorfman,[8] and vaginal cornification activity in rats was measured using essentially the procedure reported by Tschopp.[9] Slight modification of the latter assay included larger size of rats (weighing 240 ± 15 g) and a 4-day examination of vaginal smears. The compounds were given subcutaneously in sesame oil on two consecutive days.

In the uterotropic test **1b** was found to be most active, followed by **1a** and **11**. Compounds **9** and **10** were least active and displayed only a marginal estrogenicity (Table I).

The threshold values for estrone (used as a reference compound) and **1a** in the vaginal cornification assay were approximately the same as those reported by Tschopp.[9] Compound **1a** in this assay was 50% more potent than **1b**. Compound **11**, however, had only one-ninth the activity of **1a** (Table II).

Experimental Section[10]

3-Benzyloxy-16,17-secoestra-1,3,5(10)-triene-16,17-dioic Acid Dimethyl Ester (5).—A methanolic NaOMe solution was pre-

(3) A. Wettstein, H. Fritzsche, F. Hunziker, and K. Miescher, *Helv. Chim. Acta*, **24**, 332E (1941).

(4) J. Heer and K. Miescher, *ibid.*, **28**, 156 (1945).

(5) C. von Seemann and G. A. Grant, *J. Am. Chem. Soc.*, **72**, 4073 (1950)

(6) L. A. Freiberg, *ibid.*, **89**, 5297 (1967).

(7) (a) P. D. Bartlett and R. R. Haitt, *ibid.*, **80**, 1398 (1958); (b) L. A. Freiberg [French Patent 1,509,769 (1967)] employed this procedure in the androstane series.

(8) R. I. Dorfman, *Methods Hormone Res.*, **2**, 713 (1962).

(9) E. Tschopp, *Helv. Physiol. Pharmacol. Acta*, **4**, 272 (1946).

(10) Melting points are corrected. Optical rotations were measured in about 1% $CHCl_3$ solutions at 23–24° unless stated otherwise. Uv, ir, and nmr spectra were obtained for all new compounds. Most spectra were as expected and are therefore omitted. Analytical tlc was carried out on silica gel G from Brinkmann Instruments, Inc. Elemental analyses reported as symbols were within 0.4% of the theoretical values.

TABLE I

ESTROGEN POTENCIES. UTEROTROPIC ASSAY

Compd	Rel potency[a]
Estrone	100.00
1b	4.10
1a	2.90
11	0.90
10	0.03
9	0.02

[a] Estrone was used as a reference compound and the response to it was assigned the value of 100%. The per cent response (potency) of the other substances was related to that of estrone using a standard curve.

TABLE II

ESTROGEN ACTIVITY. VAGINAL CORNIFICATION ASSAY

Compd	Threshold value, μg[a]
Estrone	1.0
1a	1.0
1b	1.5
11	9.0

[a] The threshold value is defined as the amount of substance (in μg) needed to cause vaginal cornification in at least 50% of the animals employed in the test.[9]

pared from 12.74 g (0.554 g-atom) of Na and 3.0 l. of MeOH. Estrone benzyl ether (3)[11] (20.00 g, 55.4 mmoles) was added and the mixture was stirred for 1 hr to obtain a finely divided suspension. After cooling to 5° with dry air bubbling through the stirred mixture to maintain oxygen saturation, a solution of 28.10 g (110.8 mmoles) of I_2 in 320 ml of MeOH was added during 1 hr. After 3 hr the dark red mixture was homogeneous. Stirring and aeration were stopped and the flask was stored at 5° for 16 hr. The resulting yellow solution was acidified with 40 ml of concentrated HCl and MeOH was removed under vacuum to a final volume of 150 ml. The residue was partitioned between 700 ml of H_2O and 700 ml of Et_2O. The aqueous phase was separated and extracted with 200 ml of Et_2O. The combined Et_2O layers were washed (H_2O, three 300-ml portions of 10% sodium thiosulfate, H_2O). The acidic products were removed by extraction with two 250-ml portions of 5% NaOH. These extracts were subsequently processed as described below. The Et_2O layer and 200 ml of 10% sodium thiosulfate solution were exposed to light and periodically agitated for 1.5 hr when the color of I_2 ceased to reappear. The aqueous layer was separated. The Et_2O solution was washed (H_2O), dried (Na_2SO_4), and evaporated to give 17.0 g of crude 5 as a yellow oil which crystallized on standing. Colored impurities separated as an oil from C_6H_{14}. The supernatant liquid was decanted and the C_6H_{14} was evaporated. The residue was crystallized from MeOH to give 10.55 g (43%) of 5 as colorless needles, mp 80–83° (lit.[12] mp 80–82°), $[\alpha]_D$ +63°.

The basic extracts obtained above were acidified with HCl and the acids were extracted with Et_2O. The acids (7.10 g), obtained after evaporation of the Et_2O, were refluxed for 5 days in 1.0 l. of 0.4% (v/v) H_2SO_4–MeOH to give an additional 3.40 g of **5**.

3-Benzyloxy-16,17-secoestra-1,3,5(10)-triene-16,17-dioic Acid (4).—In another experiment, similar to that above, the crude mixture of acids (2.5 g) was hydrolyzed during 20 hr with 3.3 g of KOH in 150 ml of refluxing MeOH–H_2O (4:1). Crystallization from EtOAc–n-C_6H_{14} gave 1.5 g of **4** as colorless prisms, mp 215–220° with softening at 210° (evac tube), $[\alpha]_D$ +84° (EtOH) [lit.[4] mp 226–227 dec, $[\alpha]_D$ +83° (EtOH)].

3-Benzyloxy-16,17-secoestra-1,3,5(10)-triene-16,17-dioic Acid 17-Methyl Ester (6).—To a solution of 10.0 g of **5** in 500 ml of warm MeOH was added 12.75 g of KOH in 50 ml of H_2O. The solution was refluxed for 4 hr, concentrated to 100 ml under vacuum, and poured into 600 ml of H_2O. The alkaline solution was washed (Et_2O) and then acidified with HCl. The product was extracted with 500 ml of Et_2O, the Et_2O layer was washed (H_2O) and dried (Na_2SO_4), and the Et_2O was evaporated to give 9.5 g of **6** as a colorless oil. The presence of a minor amount of **4** was shown by the tlc.[13]

An analytical sample was prepared from 1.00 g of crude **6** by chromatography on 30 g of silica gel prepared in C_6H_6–n-C_6H_{14} (1:1). All eluents contained 0.1% AcOH to prevent trailing. The column was eluted with C_6H_6–n-C_6H_{14}, C_6H_6, and finally C_6H_6–EtOAc (99:1, 98:2, and 97:3) to give pure (tlc) **6** as 0.62 g of colorless oil. Solvated crystals were obtained from both $CHCl_3$–n-C_6H_{14} (mp 78–82° with softening at 72°) and Me_2CO–n-C_6H_{14} (mp 70–72°), but the samples reverted to colorless glasses on drying at 40° *in vacuo*; $[\alpha]_D$ +65°. *Anal.* ($C_{26}H_{30}O_5$) C, H.

3-Benzyloxy-16,17-seco-16-norestra-1,3,5(10)-trien-17-oic Acid Methyl Ester (9).—To a solution of 8.64 g of crude **6** in 150 ml of dry C_6H_6 was added two 8-ml portions of oxalyl chloride. The mixture was stirred at 25° for 2.5 hr. Excess oxalyl chloride and C_6H_6 were distilled under vacuum leaving 8.7 g of the acid chloride **7** as an oil.

The crude acid chloride was dissolved in 150 ml of dry C_6H_6. To the stirred solution cooled to 10° was added 11 ml of t-butyl hydroperoxide[14] followed by dropwise addition of 12 ml of dry pyridine during 5 min. Pyridine hydrochloride began to precipitate and the mixture was stirred at room temperature overnight. The mixture was partitioned between 200 ml of Et_2O and 200 ml of H_2O. The organic layer was separated and washed with 1 N HCl, 10% KOH solution, and H_2O. After drying over Na_2SO_4 the solvent was evaporated to give 7.9 g of oily perester **8**.

The perester was dissolved in 270 ml of freshly distilled cumene. The solution was thoroughly purged with N_2 and refluxed for 1 hr under N_2. The cumene was distilled under vacuum leaving 8.9 g of partially crystalline residue. The product was chromatographed on 500 g of Florisil prepared in C_6H_6. 1,2-Diphenyltetramethylethane (1.96 g) was eluted with C_6H_6. The desired product **9** was eluted with C_6H_6–Et_2O (99:1, 98:2, 97:3, 95:5), giving 3.06 g of colorless crystalline material (40% from **6**) with mp 86–94°. An analytical sample was obtained by crystallization from n-C_5H_{12}; mp 96–98°, $[\alpha]_D$ +53°. *Anal.* ($C_{25}H_{30}O_3$) C, H.

Further elution with C_6H_6–Et_2O (95:5, 90:10, 80:20, 50:50) gave a total of 1.12 g of yellow oil. Tlc showed the presence of a major component, a minor-to-trace amount of **9**, and trace amounts of several more polar components. The major component was not further purified, but has been tentatively assigned structure **12** on the basis of the ir (1718 cm^{-1}) and nmr spectra [69 Hz, 18-H and $C(CH_3)_3$; 223, OCH_3; 305, $ArCH_2O$-], and by analogy with a similar product in the androstane series which was purified and fully characterized.[15]

3-Hydroxy-16,17-seco-16-norestra-1,3,5(10)-trien-17-oic Acid Methyl Ester (11).—The hydrogenolysis of the benzyl group was carried out on 1.00 g of **9** at 25° and atmospheric pressure in 100 ml of absolute EtOH with 0.3 g of 5% Pd–C. The product was crystallized from Me_2CO–n-C_6H_{14} to give 0.54 g (71%) of **11** as colorless needles: mp 163.5–165.5° (evac tube), $[\alpha]_D$ +67°. *Anal.* ($C_{18}H_{24}O_3$) C, H.

3-Benzyloxy-16,17-seco-16-norestra-1,3,5(10)-trien-17-oic Acid (10).—To a solution of 1.51 g of **9** in 120 ml of MeOH was added 18 g of KOH in 30 ml of H_2O. The solution was refluxed under N_2 for 48 hr. Most of the MeOH was removed under vacuum and 1.0 l. of H_2O was added. The mixture was extracted with Et_2O to remove a small amount of neutral material. The basic phase was acidified with HCl and extracted with Et_2O, the Et_2O solution was washed (H_2O) and dried (Na_2SO_4), and the Et_2O was evaporated to give 1.15 g of colorless solid. Crystallization from Me_2CO–n-C_6H_{14} gave 0.74 g (50%) of **10** as colorless plates: mp (transition 155–165°) 172.5–174° (evac tube), $[\alpha]_D$ +52°; $\nu_{max}^{7\%\ CHCl_3}$ 2800–2400, 1720 (sh, monomer), and 1690 (dimer).[16] *Anal.* ($C_{24}H_{28}O_3$) C, H.

(11) M. N. Huffman and M. H. Lott, *J. Biol. Chem.*, **172**, 325 (1948).

(12) M. Levitz and J. R. Spitzer, *ibid.*, **222**, 979 (1956).

(13) Neither a shorter reaction time nor the use of K_2CO_3 in place of KOH reduced the amount of this impurity.

(14) The available samples of t-butyl hydroperoxide contained an appreciable amount of H_2O which was removed by distillation at 25° and 5 mm. The residue from this treatment produced no turbidity on addition to C_6H_6. The necessary safety precautions were taken.

(15) Unpublished results of L. A. Freiberg.

(16) Consistent with this interpretation a 0.5% $CHCl_3$ solution showed an increase in the intensity of the high-frequency absorption while the intensity of the low-frequency absorption decreased.

3-Hydroxy-16,17-seco-16-norestra-1,3,5(10)-trien-17-oic Acid (1b).—The hydrogenolysis of the benzyl group of 1.00 g of **10** was accomplished as described in the preparation of **11**. The solid residue was crystallized from Me_2CO–n-C_6H_{14} to give 0.63 g (84%) of **1b**, mp 195–198° (evac tube). The analytical sample was obtained from C_6H_6 as thick needles, mp 198.5–200.5° (evac tube), $[\alpha]_D$ +69° (EtOH). *Anal.* ($C_{17}H_{22}O_3$) C, H.

Doisynolic Acid (1a).—Doisynolic acid was prepared by the method of Heer and Miescher.[4] From 4.0 g of estrone there was obtained, after four crystallizations from $MeOH$–H_2O and one from Me_2CO–n-C_6H_{14}, 0.179 g of colorless needles, mp 198.5–200° (evac tube), $[\alpha]_D$ +105° (c 0.470, EtOH) [lit.[4] mp 199–200°, $[\alpha]_D$ +102° (c 0.475, in EtOH)].

Acknowledgments.—The authors are indebted to Drs. Leslie A. Freiberg, Wayne Cole, and Paul Kurath for helpful discussions, and to Dr. R. E. Mauer and Thomas Kallal for biological evaluation. We are also grateful to Brigitte Fruehwirth, Evelyn Baker, Ruth Stanaszek, Victor Rauschel, and David Williamson for spectroscopic and analytical services.

New Compounds

An Aziridinone Derived from 1-Aminoadamantane

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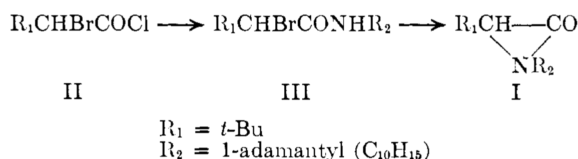
Although the physiological properties of aziridines have been extensively investigated, especially in connection with the nitrogen mustards, there is no report in the literature regarding the biological properties of aziridinones. We report here the preparation of an aziridinone (I), which is a derivative of 1-aminoadamantane, a compound in which there has been a considerable pharmacological interest since its antiviral activity was discovered.[2]



Experimental Section[3]

N-(1-Adamantyl)-2-bromo-3,3-dimethylbutyramide (III).—A solution of 1.00 g (8.6 mmoles) of 3,3-dimethylbutyric acid in $SOCl_2$ (1.0 ml) was refluxed for 30 min and excess $SOCl_2$ was removed under reduced pressure at 30°. The acid chloride was dissolved in 2.3 ml of CCl_4 and refluxed with Br_2 (0.53 ml, 9.6 mmoles) for 2.5 hr. The resulting bromo acid chloride was treated gradually with an ice-cold solution of 1.31 g (8.6 mmoles) of 1-aminoadamantane and 1.14 g (11 mmoles) of Et_3N in 60 ml of CH_2Cl_2. The reaction mixture was then treated with H_2O, extracted with CH_2Cl_2, and the combined CH_2Cl_2 layers were washed (5% HCl, 5% NaOH, H_2O, saturated NaCl solution) and dried (Na_2SO_4). The solvent was removed *in vacuo* to give crude III, which was recrystallized from heptane to furnish 2.30 g (82% over-all) of crystals, mp 182–183°. *Anal.* ($C_{16}H_{26}BrNO$) C, H, Br, N.

1-(1-Adamantyl)-3-t-butylaziridinone (I).—A solution of 1.00 g (3.1 mmoles) of III in 150 ml of dry Et_2O was stirred with 0.55 g (4.9 mmoles) of KO-t-Bu at 0° for 15 min (progress of the reaction was followed by ir spectroscopy). The reaction mixture was filtered through a sintered-glass funnel and the filtrate was removed under reduced pressure at room temperature. The solid residue was recrystallized from heptane to afford 0.51 g (68%) of the aziridinone I: mp 82–83°; ir, 1830 cm^{-1}; nmr, τ 7.32 (1 H, s), 7.73–8.42 (15 H, m), 9.02 (9 H, s). *Anal.* Calcd for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.46; H, 10.07; N, 5.55.

(1) Recipient of a Graduate Traineeship from the National Science Foundation.

(2) W. L. Davies, R. R. Grunert, R. F. Haff, J. W. McGahen, E. M. Neumayer, M. Paulshock, J. C. Watts, T. R. Wood, E. C. Hermann, and C. E. Hoffmann, *Science*, **144**, 862 (1964).

(3) Melting points were taken on a Mel-Temp apparatus and are uncorrected. Ir spectra were obtained in $CHCl_3$ on a Perkin-Elmer spectrophotometer, Model 337, and nmr spectra were recorded in CCl_4 as solvent on a Varian A-60 instrument (TMS as internal standard). Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

Some Aromatic Fluorine Compounds

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Fluorination of carcinogenic aminoazo dyes greatly enhances the activity of these compounds except when the sites involved in carcinogenesis are blocked by substitution with the halogen.[1,2] As these sites are on the diamine ring, various difluoroanilines are required for synthesis of the dyes. This communication reports some observations and new compounds of interest which have arisen during attempts to prepare 2,3-difluoroaniline.

Experimental Section[3]

2-Chloro-3-fluoronitrobenzene.—2,3-Dinitroaniline[4] (162 g) was suspended in HCl (5.5 N, 490 ml) and a solution of $NaNO_2$ (100 g) in H_2O (120 ml) was added slowly with constant stirring, the temperature being maintained below 0° by the addition of solid CO_2 to the mixture. The mixture was stirred for a further 30 min and then a slight excess (204 g) of solid sodium fluoroborate was added slowly with constant stirring. After a further 30 min, the precipitate was filtered off under vacuum, washed with a small volume of chilled saturated sodium fluoroborate solution, and allowed to dry in the dark. The product, **2-chloro-3-nitrobenzenediazonium fluoroborate**, was a bright yellow solid (193 g, 80%) which darkened upon exposure to light. The diazonium salt was dried further in a desiccator (NaOH, silica gel) and then decomposed by intimately mixing small portions (10 g) with washed, dried sand (20 g) in a 500 ml round-bottomed flask fitted with a condenser and heating carefully in an oil bath.

(1) J. A. Miller, E. C. Miller, and G. C. Finger, *Cancer Res.*, **13**, 93 (1953).

(2) J. A. Miller, E. C. Miller, and G. C. Finger, *ibid.*, **17**, 387 (1957).

(3) Melting points are corrected and were determined in a capillary tube; boiling points are uncorrected. Analyses were performed by the CSIRO Australian Microanalytical Service.

(4) K. H. Pausacker and J. G. Scroggie, *J. Chem. Soc.*, 1897 (1955).