TABLE I

PROPERTIES AND HERBICIDAL ACTIVITY OF VARIOUS NEW ESTERS OF 2,4-DICHLOROPHENOXYACETIC ACID

Ester	M.p., °C.	Formula	Chlorine, % Calcd.	Chlorine, % Found	Herbicidal activity[a]
Methyl (control)[b]					+++++
4-Acetophenyl	120.5–121.5	$C_{16}H_{12}Cl_2O_4$	20.9	21.0	++
2-Methyl-4,6-dibromophenyl	174.5–175.5	$C_{15}H_{10}Cl_2Br_2O_3$	44.2[c]	44.3[c]	+
Carvacryl	144–146	$C_{18}H_{18}Cl_2O_3$	19.5	19.7	+
4-Nitrophenyl	119–120	$C_{14}H_9NCl_2O_5$	18.7	18.5	+++
Cetyl	41–42	$C_{24}H_{38}Cl_2O_3$	15.4	15.4	+
Guaiacyl	96–98	$C_{15}H_{12}Cl_2O_4$	21.7	21.5	+++
Eugenyl	54–55.5	$C_{18}H_{16}Cl_2O_4$	19.3	19.7	++++
Bornyl	178–180	$C_{18}H_{22}Cl_2O_3$	19.9	20.0	++++
p-Cresyl	94–95	$C_{15}H_{12}Cl_2O_3$	22.3	22.3	+++++
Benzyl	156	$C_{15}H_{12}Cl_2O_3$	24.1	23.6	+
4-Chloro-*o*-cresyl	103–104	$C_{15}H_{11}Cl_3O_3$	30.8	31.1	+++++
3-Methyl-4-chlorophenyl	125–130.5	$C_{15}H_{11}Cl_3O_3$	30.8	31.4	+
3-Methyl-4-chloro-2-nitrophenyl	104–106	$C_{15}H_{10}NCl_3O_5$	27.2	27.6	+++++
4-Methylphenylthio	83–84	$C_{15}H_{11}SCl_2O_2$	21.7	21.6	+++
2-Methylphenylthio	79–80	$C_{15}H_{11}SCl_2O_2$	21.7	21.2	++++
Phenylthio	74.5–75.5	$C_{14}H_{10}SCl_2O_2$	22.6	22.4	+++++

[a] The number of plus signs indicate the relative magnitude of activity of each substance. [b] Previously synthesized, M. S. Newman, Wm. Jones and M. Renoll, THIS JOURNAL, **69**, 718 (1947). The methyl ester has considerable herbicidal action on plants and was used to compare the activity of the other esters. [c] Expressed as total per cent. halide.

dichlorophenoxyacetyl chloride[2] with the appropriate hydroxyl compound.

The herbicidal activity of these substances was determined by preparing solutions of each of the esters having concentrations of 1, 10 and 100 p.p.m. by diluting a 1% stock solution with water. A variety of seeds of field and vegetable crops were soaked in these solutions for 4 and 12 hours, respectively. They were removed, dried on filter to remove excess moisture, planted in flats containing sand and after 2 weeks in the greenhouse were harvested. The herbicidal activity was evaluated by comparing the number of germinated seeds, total fresh weight and height of the treated seedlings with that of the non-treated plants (control) and also with plants treated with methyl 2,4-dichlorophenoxyacetate.

p-Cresyl 2,4-dichlorophenoxyacetate, 4-chloro-*o*-cresyl 2,4-dichlorophenoxyacetate, 3-methyl-4-chloro-2-nitro 2,4-dichlorophenoxyacetate and phenyl 2,4-dichlorophenoxythioacetate at the same concentrations had herbicidal activity equivalent to methyl 2,4-dichlorophenoxyacetate. Eugenyl 2,4-dichlorophenoxyacetate, bornyl 2,4-dichlorophenoxyacetate and 2-methyl-2,4-dichlorophenoxythioacetic acid had slightly less activity than the former substances. The remainder of the esters were much lower in activity and appear to have little potential value.

The chemical and physical properties and herbicidal activity of the new compounds are summarized in Table I.

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[2] V. H. Freed, THIS JOURNAL, **68**, 2112 (1946).

COMMUNICATIONS TO THE EDITOR

PARTIAL SYNTHESIS OF 16α,21-DIACETOXYPROGESTERONE

Sir:

The isolation[1] of a 16-hydroxylated steroid, Δ^5-pregnene-$3\beta,16\alpha,20\alpha$-triol from the urine of a boy with an adrenal tumor prompted us to synthesize[2] suitably substituted 16-oxygenated steroids with the object of determining their biological properties and of facilitating a search for their presence in adrenal secretions. The simplest compound of this type which could be expected to possess adrenocortical activity is 16α,21-dihydroxyprogesterone which we have now prepared in the form of its diacetate (I). During the course of this synthesis Simpson and Tait[3] reported on the properties of electrocortin, the most active hormone of the adrenal cortex concerned with

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[1] H. Hirschmann and F. B. Hirschmann, *J. Biol. Chem.*, **184**, 259 (1950).

[2] H. Hirschmann, F. B. Hirschmann and M. A. Daus, THIS JOURNAL, **74**, 539 (1952); H. Hirschmann, F. B. Hirschmann and J. W. Corcoran, *Federation Proc.*, **12**, 218 (1953).

[3] A paper presented by S. A. Simpson and J. F. Tait to the Society for Endocrinology, a copy of which was very kindly sent to us by the authors.

mineral metabolism and suggested that it may be a desoxycorticosterone with one extra hydroxyl group in close proximity to the side chain. Since Professor Reichstein and his collaborators have just announced the isolation of crystalline electrocortin, we are presenting our findings so that the physical properties of I can be compared with those of acetylated electrocortin.

3β-Formyloxy-16α-benzyloxy-Δ^5-pregnen-20-one[2] (m.p. 130.5–131°, $[\alpha]_D$ −44°, chf. *Anal.* Calcd. for $C_{29}H_{38}O_4$: C, 77.30; H, 8.50. Found: C, 77.46; H, 8.63) in 95% ethanol on hydrogenation with palladium on charcoal and acetylation gave 3β-formyloxy-16α-acetoxy-Δ^1-pregnen-20-one (m.p. 195–197.5 ± 2°, $[\alpha]_D$ −45°, chf. *Anal.* Calcd. for $C_{24}H_{34}O_5$: C, 71.61; H, 8.51. Found: C, 71.77; H, 8.54; infrared (all measurements in carbon disulfide) maxima at ~ 8.48, 5.79 (formate), 8.03, 5.74 (acetate), 5.84 (ketone) (the carbonyl peaks were not fully resolved), 12.45, 12.22 μ (Δ^5). Treatment with lead tetracetate in acetic acid containing acetic anhydride introduced one acetoxy group into the 21-position as deduced from the composition (*Anal.* Calcd. for $C_{26}H_{36}O_7$: C, 67.80; H, 7.88. Found: C, 67.98; H, 7.98), the change in molecular rotation (+75°) and the infrared spectrum (two acetate peaks[4] at 8.04 and 8.12 μ, a very intense unresolved peak at 5.78 μ (16-acetate, formate and 20-ketone[4]) with shoulder at 5.71 μ (21-acetate)). Moreover, 3β-formyloxy, 16α,21-diacetoxy-Δ^5-pregnen-20-one (m.p. 180.5–182.5°, $[\alpha]_D$ −23°, chf.) reduced 2,3,5-triphenyl-2H-tetrazolium chloride. The newly introduced acetoxy group was hydrolyzed by dilute potassium bicarbonate at 22° at a rate comparable to that of desoxycorticosterone acetate. Brief exposure, however, gave as the main product 16α,21-diacetoxy-Δ^5-pregnen-3β-ol-20-one (m.p. 158–160°; infrared, no formate peak near 8.48 μ, maxima at 8.05, 8.12, 5.76, 5.71 (shoulder), 2.78 μ (unassociated hydroxy). Treatment with bromine, chromium trioxide and chromous chloride gave I (m.p. 150.5–153°, $[\alpha]_D$ +110° alc. (*c*, 0.3). *Anal.* Calcd. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96. Found: C, 69.65; H, 7.93. Absorption maxima: 8.12, 8.05, 5.95 (Δ^4-3-ketone), 5.70 μ (shoulder) and 240 mμ (ϵ = 16400 alc.).

Enzymatic hydrolysis with cholinesterase from red cells yielded a product which migrated in a paper chromatogram (propylene glycol–toluene) at a rate very close to that of a highly potent sodium retaining factor from canine adrenal venous blood.[5] Further characterization of the hydrolyzed product awaits the preparation of additional material.[6]

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[4] For spectra of 21-acetoxy-20-ketones see R. N. Jones, V. Z. Williams, M. J. Whalen and K. Dobriner, THIS JOURNAL, **70**, 2024 (1948).

[5] G. L. Farrell and J. B. Richards, *Proc. Soc. Exp. Biol. and Med.*, **83**, 628 (1953).

[6] Addendum September 19, 1953.—The hydrolytic product has been assayed by Dr. John Luetscher, Jr., Stanford University, and Dr. Paul Royce. The tests have failed to demonstrate the high salt retaining activity of electrocortin.

1,3-DIMETHYL-5-IMINOTETRAZOLE, A NEW CYCLIC "MESO-IONIC" COMPOUND

Sir:

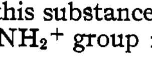
2-Methyl-5-aminotetrazole (m.p. 104.5–105.5°; C, 24.60; H, 5.04; N, 71.33) is obtained in 25–35% yield, together with 35–50% of the 1-isomer,[1] when an aqueous solution of sodium 5-aminotetrazole (1 mole) is heated with dimethyl sulfate (0.5 mole). When the 2-isomer is alkylated with methyl benzenesulfonate according to the procedure of Herbst, Roberts and Harvill,[2] there is recovered in 85% yield a basic, hygroscopic dimethyl derivative which melts at 88–90° after several recystallizations, first from benzene and finally from methylene chloride–petroleum ether (C, 32.07; H, 6.00; N, 61.92). This compound is different than *2-methyl-5-methylaminotetrazole* (m.p. 48–49°; N, 62.04). The *hydrochloride* (C, 24.16; H, 5.24; N, 47.08; Cl, 23.90) melts at 203–205° after recrystallization from 90% isopropyl alcohol.

The structure of this compound was established as *1,3-dimethyl-5-iminotetrazole,* instead of the anticipated 1,2-dimethyl derivative, by analysis of the X-ray data obtained on crystals of the hydrochloride and hydrobromide. These salts are orthorhombic and have the following cell constants:

	a_0, Å.	b_0, Å.	c_0, Å.
HCl salt	10.90	9.60	6.58
HBr salt	11.21	9.82	6.71

There are four molecules per unit cell, and the space group is Pbnm. The symmetry of the rotation photograph obtained about the *c*-axis shows that the molecules lie in mirror planes and hence are completely planar. The layer nature of the crystal is also shown by the great intensity of all orders of (001). Since the two crystals are isomorphous, it is possible to obtain the structure without any prior assumptions, by first using crystal data from the hydrobromide, and then applying the results to the data from the hydrochloride. Figure 1 shows the structure of the crystal as obtained by this procedure. The imino nitrogen was identified primarily by its being at distances of 3.15 Å. and 3.18 Å. from two chloride ions. This is the usual N-H · · · Cl bond length that has been found in a number of hydrochloride salts.[3]

This tetrazole derivative appears to belong to a class of compounds which have been called "cyclic meso-ionic" compounds,[4] and which have been given the general formula



The syndones were the first group of this type to be well characterized.[4] In our case, X is N, Y–Z is NRC(:NH), and R is CH_3; this is one of the predicted types.[4]

A large number of possible resonance structures can be written for this substance. In addition, the existence of the $=NH_2^+$ group increases the num-

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[1] R. Stolle, *et al.*, *J. prakt. Chem.*, **134**, 282 (1932).

[2] R. Herbst, C. Roberts and E. Harvill, *J. Org. Chem.*, **16**, 139 (1951).

[3] J. Donohue, *J. Phys. Chem.*, **56**, 502 (1952).

[4] W. Baker, W. D. Ollis and V. D. Poole, *J. Chem. Soc.*, 307 (1949); R. A. W. Hill and L. E. Sutton, *ibid.*, 746 (1949).