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Phosphafluoainic Acid

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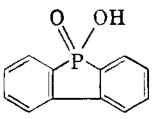
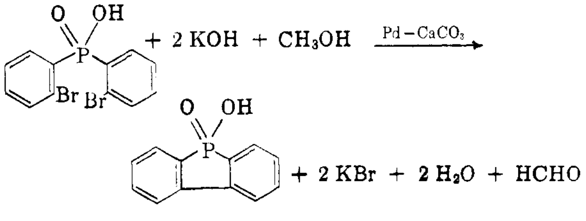
In contrast to the considerable number of heterocyclic derivatives of arsenic which have been described, only a few similar derivatives of phosphorus are known.[1] One reason for the difference is that it is much more difficult to prepare organophosphorus compounds. In the last few years, however, several convenient new methods of preparing such compounds have been reported.[2] These methods make readily available a wide variety of organophosphorus compounds which hitherto have been difficult if not impossible to prepare. It now seems feasible to attempt the synthesis of many heterocyclic derivatives of phosphorus by reactions similar to those previously employed for the arsenic analogues. The present paper describes the preparation of phosphafluorinic acid (I).



I

Arsafluorinic acid can be readily prepared by heating 2-biphenylarsonic acid with concentrated sulfuric acid for ten minutes at 100°.[3] We were unable, however, to obtain phosphafluorinic acid from 2-biphenylylphosphonic acid[4] by this procedure. Similarly, the method used by Morgan and Davies[5] for converting diphenylmethane-2-stibonic acid to stibacridinic acid failed to cyclize 2-biphenylylphosphonic acid. We finally succeeded in preparing phosphafluorinic acid by making use of a method developed by Busch[6] for the catalytic reduction of halobenzene derivatives to biphenyl derivatives The following reaction was employed.



Phosphafluorinic acid was characterized by analysis and ultraviolet absorption. As indicated in Table I the spectra of arsafluorinic and phosphafluorinic acids are remarkably similar. The spectrum of diphenylphosphinic acid (which is formed as a by-product in the above reaction) is included for comparison.

TABLE I
ULTRAVIOLET ABSORPTION MAXIMA

Compound	λ_{max}, mμ	ϵ_{max}
Arsafluorinic acid[a]	226	25,700
	232.5	29,600
	240	28,000
	276.5	8,210
	287.5	6,870
Phosphafluorinic acid	226	26,200
	232.5	30,200
	239.5	27,500
	278	10,100
	289.5	8,370
Diphenylphosphinic acid[b]	224	13,100
	259.5	956
	265	1,200
	271.5	917

[a] Taken from Freedman, *J. Am. Chem. Soc.*, **77**, 6223 (1955). [b] Taken from Jaffé and Freedman, *J. Am. Chem. Soc.*, **74**, 1069 (1952).

EXPERIMENTAL

Phosphafluorinic acid. Bis(*o*-bromophenyl)phosphinic acid[7] (9.40 g.) and 6.0 g. of 1% palladium-on-calcium carbonate[6b] were added to a mixture of 80 ml. of 1.25 *N* aqueous potassium hydroxide and 90 ml. of methanol in a 2-necked flask equipped with a sealed stirrer and a reflux condenser. The mixture was stirred and refluxed for 48 hours. The catalyst, which was now completely black, was removed by filtration.[8] The filtrate was evaporated on a steam-bath to approximately 80 ml., and then acidified with 10 ml. of conc'd. hydrochloric acid whereupon a white solid separated from solution. The mixture was cooled, and the solid was removed by filtration and then was dissolved in 25 ml. of hot 10% sodium hydroxide solution. When this solution was cooled,

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(1) Mann, *The Heterocyclic Derivatives of Phosphorus, Arsenic, Antimony, Bismuth, and Silicon*, Interscience Publishers, Inc., New York, N. Y., 1950, p. 4.

(2) (a) Mikhailov and Kucherova, *Doklady Akad. Nauk SSSR*, **74**, 501 (1950); (b) Burger and Dawson, *J. Org. Chem.*, **16**, 1250 (1951); (c) Doak and Freedman, *J. Am. Chem. Soc.*, **73**, 5658 (1951).

(3) Aeschlimann, Lees, McCleland, and Nicklin, *J. Chem. Soc.*, **127**, 66 (1925).

(4) Jaffé, Freedman, and Doak, *J. Am. Chem Soc.*, **76**, 1548 (1954).

(5) Morgan and Davies, *Proc. Roy. Soc. London*, **A143**, 38 (1933).

(6) (a) Busch and Weber, *J. prakt. Chem.*, **146**, 1 (1936); (b) See also Mayo and Hurwitz, *J. Am. Chem. Soc.*, **71**, 776 (1949).

(7) Doak and Freedman, *J. Am. Chem. Soc.*, **75**, 683 (1953).

(8) Bromide ion analyses on aliquots from the filtrate showed that all of the bromine had been split from the ring.

the sodium salt of phosphafluorinic acid crystallized.[9] The salt was removed by filtration and washed with 10 ml. of 10% sodium hydroxide solution. A second crop of the sodium salt could be obtained by evaporating the combined filtrate and washings to 15 ml. In order to isolate the free phosphinic acid, both crops of sodium salt were combined and dissolved in 35 ml. of water, and the solution was filtered from a trace of undissolved material; phosphafluorinic acid separated when the solution was acidified to Congo Red and cooled. The yield was 2.2 g., 41%, m.p. 239–248°. After the acid was twice recrystallized from 95% ethanol, the m.p. was 253–257° and was not changed by further recrystallization. The ultraviolet absorption of the acid was not affected by recrystallization.

Anal. Calc'd for $C_{12}H_9O_2P$: P, 14.33; Neut. equiv., 216.2. Found: P, 14.03; Neut. equiv., 215.5.

Absorption spectra measurements. The ultraviolet absorption spectra were determined in 95% ethyl alcohol by the procedure previously used [*cf.* footnote (b) of Table I].

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(9) The sodium salt of diphenylphosphinic acid does not crystallize from solution under these conditions.

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Steroids. LXXV.[1] Dehydrogenation of Testosterone to $\Delta^{1,4}$-Androstadien-17β-ol-3-one with Selenium Dioxide

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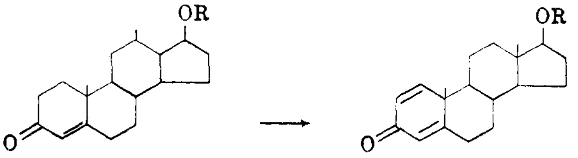
Steroidal $\Delta^{1,4}$-dien-3-ones of type II are of interest since on pyrolysis they yield 19-nor-$\Delta^{1,3,5}$-trien-3-ols of the estrone type[2,3] and they have taken on increased importance within the last year with the discovery that the $\Delta^{1,4}$-dien-3-ones corresponding to cortisone,[4a] hydrocortisone,[4a] and 9-fluoro-hydrocortisone[4b] are considerably more active than the parent hormones. The only known chemical route to such $\Delta^{1,4}$-dienones, until recently, has been one involving the 2,4-dibromination and subsequent dehydrobromination of saturated 3-ketosteroids of the 5α or 5β-configuration.[4b,5] It would be advantageous to prepare the dienones from the corresponding Δ^4-en-3-ones of type I,[6] in view of the ready availability of the latter in most series. Although it is known that the action of manganese dioxide[7] or of *N*-bromosuccinimide followed by collidine dehydrobromination[8] introduces a Δ^6-double bond into Δ^4-3-ones, it has been shown that the desired Δ^1-dehydrogenation may be effected by means of lead tetra-acetate in acetic acid;[9] in this way testosterone acetate (Ib) was converted to $\Delta^{1,4}$-androstadien-17β-ol-3-one acetate (IIb) and progesterone to $\Delta^{1,4}$-pregnadien-21-ol-3,20-dione acetate. Unfortunately the dienones were only by-products, being obtained in yields of 1.5–8%.[9,9a]



Ia, R = H
b, R = Ac

IIa, R = H
b, R = Ac

We have now investigated the action of a number of different dehydrogenating agents on steroidal Δ^4-3-ones, especially on testosterone, (Ia), with the aim of discovering a superior reagent to lead tetra-acetate. Selenium dioxide proved to be such a one and when testosterone was treated with this substance in boiling benzene containing a little water[10]

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(1) Paper LXXIV, Ringold, Rosenkranz, and Sondheimer, *J. Am. Chem. Soc.*, **78**, in press (1956).

(2) *Inter al.* (a) Inhoffen and Zühlsdorff, *Ber.*, **74**, 1911 (1941); (b) Inhoffen, *Angew. Chem.*, **59**, 207 (1947); (c) Wilds and Djerassi, *J. Am. Chem. Soc.*, **68**, 2125 (1946); (d) Hershberg, Rubin, and Schwenk, *J. Org. Chem.*, **15**, 292 (1950).

(3) Such aromatic compounds are of use not only as such as estrogenic hormones but also as starting materials for the highly active 19-nor hormone analogs [Birch, *J. Chem. Soc.*, 367 (1950); Wilds and Nelson, *J. Am. Chem. Soc.*, **75**, 5366 (1953); Djerassi, Rosenkranz, Sondheimer, *et al.*, *J. Am. Chem. Soc.*, **75**, 4440 (1953); **76**, 4092, 6210 (1954); **77**, 148 (1955)].

(4) Bunim, Pechet, and Bollet, *J. Am. Med. Assoc.*, **157**, 311 (1955); Herzog, Nobile, Tolksdorf, Charney, Hershberg, Perlman, and Pechet, *Science*, **121**, 176 (1955); (b) Hirshmann, Miller, Beyler, Sarett and Tishler, *J. Am. Chem. Soc.*, **77**, 3166 (1955); Fried, Florey, Sabo, Herz, Restivo, Borman, and Singer, *J. Am. Chem. Soc.*, **77**, 4181 (1955).

(5)*Cf.* footnote 2b for leading references. See also Djerassi and Scholz, *J. Am. Chem. Soc.*, **69**, 2404 (1947); Djerassi and Rosenkranz, *Experientia*, **7**, 93 (1951).

(6) This type of transformation has been carried out microbiologically [Vischer and Wettstein, *Experientia*, **9**, 371 (1953); Fried, Thoma, and Klingsberg, *J. Am. Chem. Soc.*, **75**, 5764 (1953); Vischer, Meystre, and Wettstein, *Helv. Chim. Acta*, **38**, 835 (1955); Nobile, Charney, Perlman, Herzog, Payne, Tully, Jevnik, and Hershberg, *J. Am. Chem. Soc.*, **77**, 4184 (1955)].

(7) Sondheimer, Amendolla, and Rosenkranz, *J. Am. Chem. Soc.*, **75**, 5932 (1953).

(8) Meystre and Wettstein, *Experientia*, **2**, 408 (1946); Djerassi, Rosenkranz, Romo, Kaufmann, and Pataki, *J. Am. Chem. Soc.*, **72**, 4534 (1950).

(9) Clarke, Dobriner, Mooradian, and Martini, *J. Am. Chem. Soc.*, **77**, 661 (1955).

(9a) Since this manuscript was prepared, another conversion of Δ^4-en-3-ones to $\Delta^{1,4}$-dien-3-ones by a three step process has been described [Hogg, Lincoln, Nathan, Hanze, Schneider, Beal, and Korman, *J. Am. Chem. Soc.*, **77**, 4438 (1955).]

(10) The fact that the presence of water was necessary indicates that the dehydrogenating agent is selenious acid rather than selenium dioxide.