4-Androsten-14α-ol-3,17-dione (I) and 4-Androsten-14β-ol-3,17-dione (XII) from 14α,15α-Oxido-4-androstene-3,17-dione (V) and 14β,15β-Oxido-4-androstene-3,17-dione (IV).—To a slurry of 7.5 g. of lithium aluminum hydride in 1200 ml. of tetrahydrofuran under a nitrogen atmosphere was added dropwise a solution of 4.5 g. of a mixture of the oxides IV and V (1:1) in 300 ml. of tetrahydrofuran. The mixture was refluxed for 2 hr. and cooled to room temperature and the excess lithium aluminum hydride was decomposed by dropwise addition of a saturated sodium sulfate solution. The solids were filtered and the solvent was removed at reduced pressure leaving 4.5 g. of residue. An infrared spectrum of the residue showed no carbonyl absorption.

To 1 g. of this residue dissolved in 100 ml. of acetone Jones reagent was added dropwise until a slight excess was present. Filtration through Celite, addition of water and chloroform extraction afforded 800 mg. of an oil. The oil was dissolved in benzene and chromatographed on silica gel. Elution with benzene–ether gave 300 mg. of recovered oxides IV and V and further elution with ether gave 350 mg. of an equal mixture of 14α- and 14β-ols I and XII. Separation of this alcohol mixture on an 8 × 8 in. × 2 mm. alumina G t.l.c. plate using a chloroform–ethyl acetate solvent system gave samples of the pure alcohols. One of the alcohols had a t.l.c. mobility and infrared spectrum identical with that of an authentic sample of 4-androsten-14α-ol-3,17-dione (I) and the other was identical with 4-androsten-14β-ol-3,17-dione (XII) obtained from the oxidation of 4-androstene-14β,17-diol-3-one (IXa).

17α-Tosyloxy-4-androsten-14β-ol-3-one (IXb).—To a solution of 0.26 g. of IXa in 6 ml. of pyridine under a nitrogen atmosphere at 0° was added 0.3 g. of *p*-toluenesulfonyl chloride. After 5 min. at 0° the solution was allowed to warm to room temperature. After 16 hr. a slurry of 25 ml. of ice–water was added to the reaction mixture and the product precipitated. The precipitate was extracted into 50 ml. of chloroform and the aqueous phase was extracted two more times with 50-ml. portions of chloroform. The chloroform washings were combined, washed with 75 ml. of 2 *N* hydrochloric acid, 75 ml. of 5% sodium bicarbonate, and two times with 75-ml. portions of water, and dried over sodium sulfate. The solvent was removed at reduced pressure leaving 377 mg. of residue: $\lambda_{\max}^{\text{Nujol}}$ 2.85, 6.0, 6.2, 6.23, 8.4, and 8.5 μ. This material was used without further purification.

13,14-Seco-4-*cis*-13(17)-androstadiene-3,14-dione (X).—To a slurry of 0.43 g. of sodium hydride in 20 ml. of dry tetrahydrofuran under a nitrogen atmosphere was added dropwise a solution of 0.35 g. of IXb in 20 ml. of dry tetrahydrofuran. The reaction mixture was refluxed for 28 hr. and cooled to room temperature and the excess sodium hydride was decomposed by dropwise addition of 2 ml. of water. An additional 50 ml. of water was added and the solution was extracted with 50 ml. of ethyl ether–20% chloroform and two times with chloroform–ether. The combined extracts were washed with 50 ml. of 5% sodium bicarbonate and three times with 75-ml. portions of water and dried over sodium sulfate. The solvent was removed at reduced pressure leaving 190 mg. of semisolid residue. An analytical sample was prepared by sublimation at 80° (10^{-5} mm.): m.p. 150–151; $\lambda_{\max}^{\text{Nujol}}$ 5.92, 6.0, and 6.2 μ; $\lambda_{\max}^{\text{MeOH}}$ 238 mμ (ϵ 14,900); n.m.r. τ 4.27 (C-4 H), 4.5 (C-17 H), 8.41 (C-18 3H), and 8.86 (C-19 3H).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 80.03; H, 9.33.

4-Androsten-14α-ol-3,17-dione (I) from 3-Keto-14α-hydroxy-17α-acetoxy-4-etiocholenic Acid (XI).—To a solution of 0.390 g. of XI in 0.125 ml. of pyridine and 4 ml. of benzene was added 0.40 g. of lead tetraacetate. The reaction mixture was refluxed for 4 hr. under a nitrogen atmosphere and then cooled to room temperature. An additional 10 ml. of benzene was added and the solid that had precipitated was filtered. The filter cake was washed with 10 ml. of benzene and 10 ml. of ethyl ether. The organic solution was washed with 25-ml. portions of 1 *N* sodium hydroxide, 1 *N* hydrochloric acid, saturated sodium chloride, and water and dried over sodium sulfate. The solvent was removed at reduced pressure leaving 0.2 g. of residue. Crystallization from methylene chloride afforded 50 mg. of a sample that had an infrared spectrum and thin layer chromatographic mobility identical with those of 4-androsten-14α-ol-3,17-dione (I).

The Reaction of 1,3-Disubstituted Ureas with Phosphorus Pentachloride[1]

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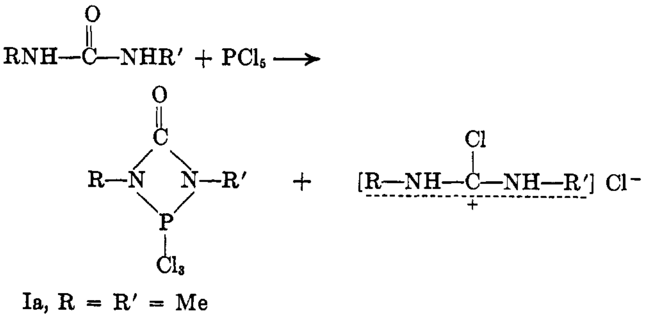
Nitrogen attack was observed in the reaction of phosphorus pentachloride with 1,3-disubstituted ureas in which at least one N-substituent was a primary alkyl group. Thus, 1,3-dialkyl- and 1-phenyl-3-alkylureas gave rise to the novel 2,4-disubstituted 1,1,1-trichloro-1,2,4-phosphadiazetidin-3-ones; 1-*p*-toluenesulfonyl-3-*n*-butylurea yielded *p*-toluenesulfonyltrichlorophosphazene and *n*-butyl isocyanate; and 1-benzoyl-3-*n*-butylurea gave benzonitrile, *n*-butyl isocyanate, and phosphorus oxychloride.

Earlier studies have shown that the reaction of 1,3-dialkylureas with either carbonyl[2] or oxalyl[3] chlorides gives rise to products formed *via* nitrogen attack. Recent studies show that the reaction of phosphorus pentachloride with 1,3-disubstituted ureas, in which at least one N-substituent is a primary alkyl group, gives rise to analogous products, *i.e.*, 1,1,1-trichloro-1,2,4-phosphadiazetidin-3-ones (I).

N,N′-Dialkylchloroformamidine hydrochlorides (II), formed in small amounts from the primary alkyl cases, are the main products obtained from the reaction of phosphorus pentachloride with 1,3-dialkylureas having secondary alkyl N substituents.[4]



Ia, R = R′ = Me
b, R = R′ = *n*-Bu
c, R = *n*-Bu; R′ = phenyl

Structural assignments for the trichloro-1,2,4-phosphadiazetidin-3-ones (I) were made on the basis of elementary analysis and infrared and n.m.r. spectroscopy. Absorption of the carbonyl group at 5.6 μ is in accord with the postulated four-membered ring. The H^1 n.m.r. spectra (Varian A-60) of compounds Ib and Ic showed the CH_2 groups adjacent to nitrogen to

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[1] Part of this work was presented as a communication: H. Ulrich and A. A. R. Sayigh, *Angew. Chem.*, **76**, 647 (1964); *Angew. Chem. Intern. Ed. Engl.*, **3**, 585 (1964).

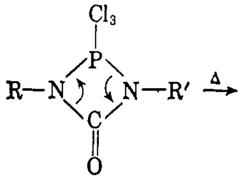
[2] H. Ulrich, J. N. Tilley, and A. A. R. Sayigh, *J. Org. Chem.*, **29**, 2401 (1964).

[3] H. Ulrich and A. A. R. Sayigh, in press.

[4] H. Eilingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960).

be coupled both with the neighboring methylene group and with the phosphorus nucleus. The chemical shifts (in CCl_4) for the triplet pairs of equal intensity are 192 c.p.s. (3.2 p.p.m., $J_{PH} = 20$ c.p.s.) for Ib and 215 c.p.s. (3.6 p.p.m., $J_{PH} = 34$ c.p.s.) for Ic, both relative to tetramethylsilane. For Ia, two pairs of doublets at 198 (3.3 p.p.m., $J_{PH} = 20$ c.p.s.) and 173 c.p.s. (2.9 p.p.m., $J_{PH} = 21$ c.p.s.) were observed, probably owing to geometrical isomerization as the methyl groups may be either both above or alternately above and below the plane of the four-membered ring. Geometrically isomeric phosphazene dimers were observed by Trippett.[5]

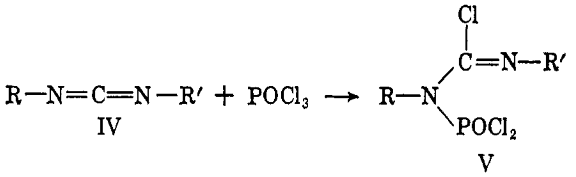
The pyrolysis products of I were interpreted as additional evidence for the proposed four-membered ring structure. On heating I above 100° in an inert solvent, carbodiimide (IV) and phosphorus oxychloride formation were observed. As earlier studies showed that the reaction of trichlorophosphazenes (III) with isocyanates gives rise to carbodiimides,[6] the initial formation of these compounds (III) was postulated.



I

$$R{-}N{=}P{-}Cl_3 + R'{-}N{=}C{=}O \longrightarrow$$

III

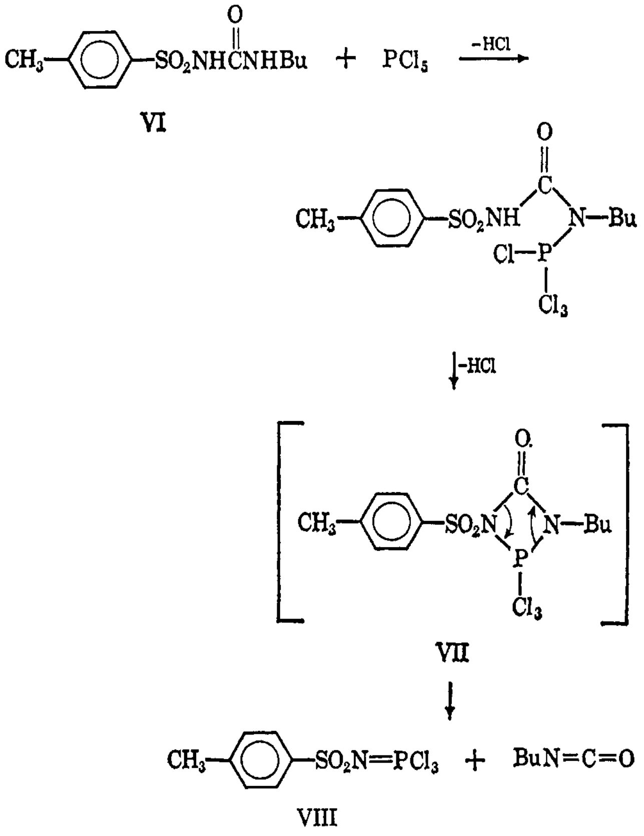


IV V

The thermal decomposition was followed in the infrared spectrometer by observation of the —N=C=O and —N=C=N— absorption at 4.42 and 4.7 μ, respectively. The generated carbodiimides (IV) were detectable in the infrared spectra, since condensation of phosphorus oxychloride with IV to afford V occurs at a low rate in a nonpolar solvent.[6,7]

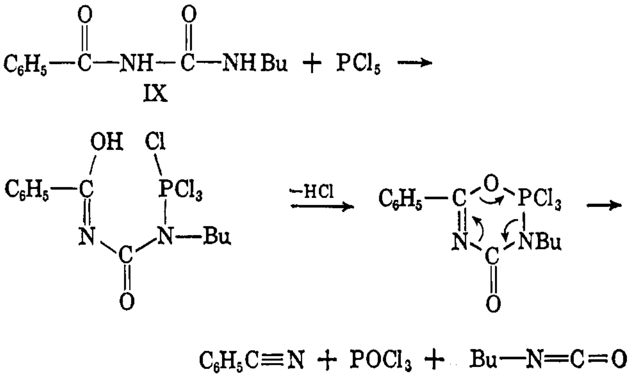
Compound V, isomeric to I, was prepared from the direct reaction of IV and $POCl_3$ and exhibited —C=N absorption at 6.0 μ. Distilled I, on long standing, exhibited a viscosity increase and C=N absorption at 6.0 μ.

1-*p*-Toluenesulfonyl-3-*n*-butylurea (VI) underwent a similar reaction to yield *n*-butyl isocyanate and *p*-toluenesulfonyltrichlorophosphazene (VIII). The proposed 1,1,1-trichloro-1,2,4-phosphadiazetidin-3-one intermediate (VII) was not isolable. The generated phosphazene (VIII) and *n*-butyl isocyanate did not react to form the corresponding sulfonylcarbodiimide, as evidenced by the absence of the characteristic infrared absorption at 4.6 μ.[8]



VI VII VIII

The reaction of phosphorus pentachloride with 1-benzoyl-3-*n*-butylurea (IX) at room temperature yielded benzonitrile, phosphorus oxychloride, and *n*-butyl isocyanate. As the expected benzoyltrichlorophosphazene is stable under the reaction conditions,[9] a different mechanism may be operative, *i.e.*, initial alkyl-substituted nitrogen attack followed by a cyclic concerted mechanism similar to the Chugaev elimination.



IX

If initial oxygen attack occurred, an alternate six-membered cyclic elimination could be visualized, but such a reaction course would require the energetically less favorable P–O bond cleavage.

Experimental

2,4-Dimethyl-1,1,1-trichloro-1,2,4-phosphadiazetidin-3-one (Ia).—Phosphorus pentachloride (33.3 g., 0.16 mole) was added to a solution of 1,3-dimethylurea (13.2 g., 0.15 mole) in carbon tetrachloride (150 ml.), the mixture was refluxed at 79–80° for 1 hr. and then purged with nitrogen for 20 min., the solvent was

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[5] S. Trippett, *J. Chem. Soc.*, 4731 (1962).

[6] H. Ulrich and A. A. R. Sayigh, *Angew. Chem.*, **74**, 900 (1962); *Angew. Chem. Intern. Ed. Engl.*, **1**, 595 (1962); *J. Chem. Soc.*, 5558 (1963).

[7] P. Fischer, German Patent 1,131,661 (1962); *Chem. Abstr.*, **58**, 1401 (1963).

[8] H. Ulrich and A. A. R. Sayigh, *Angew. Chem.*, **76**, 78 (1964); *Angew. Chem. Intern. Ed. Engl.*, **3**, 639 (1964).

[9] A. V. Kirsanov, *Chem. Abstr.*, **49**, 13162 (1955); *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 646 (1954).

evaporated, and the residue was distilled *in vacuo* to give compound Ia (24.1 g., 71.9%), b.p. 78–79° (1.5 mm.). The infrared spectrum in CCl_4 exhibited a carbonyl peak at 5.6 μ.

Anal. Calcd. for $C_3H_6Cl_3N_2OP$: C, 16.15; H, 2.70; Cl, 47.61; N, 12.53; P, 13.86. Found: C, 13.66; H, 2.65; Cl, 47.75; N, 12.00; P, 14.29.

2,4-Di-*n*-Butyl-1,1,1-trichloro-1,2,4-phosphadiazetidin-3-one (Ib).—Phosphorus pentachloride (23 g., 0.11 mole) was added to a solution of 1,3-di-*n*-butylurea (17.2 g., 0.1 mole) in carbon tetrachloride (180 ml.), the mixture was refluxed for 90 min. at 79–80° and then purged 10 min. with nitrogen, the solvent was evaporated, and the residue was distilled *in vacuo* to give compound Ib (21.8 g., 71%), b.p. 105–108° (0.3 mm.). The infrared spectrum (in CCl_4) exhibited a carbonyl peak at 5.6 μ.

Anal. Calcd. for $C_9H_{18}Cl_3N_2OP$: C, 35.14; H, 5.89; Cl, 34.58; N, 9.10; P, 10.07. Found: C, 35.36; H, 6.15; Cl, 34.53; N, 9.42; P, 9.84.

2-*n*-Butyl-4-phenyl-1,1,1-trichloro-1,2,4-phosphadiazetidin-3-one (Ic).—Phosphorus pentachloride (20.8 g., 0.1 mole) was added to a solution of 1-*n*-butyl-3-phenylurea (19.2 g., 0.1 mole) in carbon tetrachloride (200 ml.). Slight warming caused a vigorous reaction with hydrogen chloride evolution. The reaction mixture was refluxed for 90 min. with constant nitrogen purgation and the solvent was evaporated to give Ic as a viscous oil (31.7 g., 96%). The infrared spectrum (in CCl_4) exhibited a carbonyl peak at 5.6 μ.

Anal. Calcd. for $C_{11}H_{14}Cl_3N_2OP$: N, 8.55. Found: N, 8.87.

Refluxing in chlorobenzene resulted in rapid isocyanate and carbodiimide formation as evidenced by infrared absorption at 4.42 (—NCO) and 4.7 μ (—N=C=N—).

Reaction of 1-*p*-Toluenesulfonyl-3-*n*-butylurea and PCl_5.—Phosphorus pentachloride (2.1 g., 0.01 mole) was added to a solution of 1-*p*-toluenesufonyl-3-*n*-butylurea (2.7 g., 0.01 mole) in carbon tetrachloride (40 ml.) and the mixture was refluxed for 1 hr., after which time the hydrogen chloride evolution virtually stopped. The *n*-butyl isocyanate generated (0.8 g., 80.8% by titration with excess di-*n*-butylamine) was removed with the solvent, and the residue (3.1 g.) was recrystallized from carbon tetrachloride to give *p*-toluenesulfonyltrichlorophosphazene (2.35 g., 77%), m.p. 88–90°.[10] The infrared spectrum (in CCl_4) exhibited two characteristic SO_2 peaks at 7.43 and 8.63 μ.

Reaction of 1-Benzoyl-3-*n*-butylurea and PCl_5.—1-Benzoyl-3-*n*-butylurea (11 g., 0.05 mole) was added with stirring at room temperature to a solution of phosphorus pentachloride (10.4 g., 0.05 mole) in carbon tetrachloride (150 ml.). A rapid reaction ensued. The mixture was stirred for 60 min., nitrogen purged for 75 min., and fractionally distilled to give phosphorus oxychloride, *n*-butyl isocyanate (3.3 g., 66.7%, b.p. 115°), and benzonitrile (4.1 g., 82%, b.p. 41–44° at 1 mm.). The infrared spectrum of the carbon tetrachloride solution before distillation showed strong absorption at 4.45 (-NCO) and 4.5 μ (-CN).

Acknowledgment.—We are indebted to Benjamin Tucker for his assistance in the experimental aspects of this work.

[10] A. V. Kirsanov, *Chem. Abstr.*, **46**, 11135 (1952); *Zh. Obshch. Khim.*, **22**, 269 (1952).

The Reaction of Oxalyl Chloride with Substituted Ureas and Thioureas

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Oxalyl chloride reaction with mono- and 1,3-dialkylureas gave the corresponding substituted parabanic acids while reaction with mono- and 1,3-dialkylthioureas afforded the novel thiazolidine-4,5-dione derivatives. Oxalyl chloride reaction with *p*-chlorobenzenesulfonyl-3-*n*-propylthiourea yielded *p*-chlorobenzenesulfonyl chloride and 1-*n*-propylthioparabanic acid.

Earlier studies have shown that the reaction of carbonyl chloride,[2a] thionyl chloride,[2b] and phosphorus pentachloride[3] with 1,3-di(primary alkyl)ureas gives rise to products formed *via* nitrogen attack, while reaction with 1,3-di(secondary alkyl)ureas[2] results in products formed from initial oxygen attack. Oxalyl chloride is reported to react with disubstituted alkylureas to afford either chloroformamidine hydrochlorides[4] or the corresponding parabanic acid derivatives.[5] Mono- and 1,3-dialkylthioureas were reported to react with oxalyl chloride to form thioparabanic acid derivatives,[5] a surprising result in view of the thiourea—acid chloride reactions which occur exclusively at the sulfur atom. These anomalous results led to our present studies on the oxalyl chloride reaction with ureas and thioureas.

Oxalyl chloride reactions with 1,3-disubstituted ureas having primary, secondary, and tertiary alkyl substituents unfailingly gave the corresponding 1,3-dialkylparabanic acid (IV) in high yield (see Table I). Product identification was made on the basis of elemental analysis and infrared spectral evidence. In some cases the parabanic acid was independently synthesized from the corresponding carbodiimide and oxalyl chloride.

Although the reaction of carbodiimides with both acetyl[6] and carbonyl[7,8] chlorides is known to be general, the only carbodiimide reported to have reacted with oxalyl chloride is diisopropylcarbodiimide.[9] Our results indicate the existence of a general oxalyl chloride and alkyl- or arylcarbodiimide reaction which affords the corresponding 1,1-parabanyl dichloride III (see Scheme I). Evidence for structural assignment included C=O absorption at 1760 cm.$^{-1}$ and the absence of both -C=N and a second C=O group in the infrared spectra. The geminate dichlorides III were readily hydrolyzed to the corresponding parabanic acids (IV).

The mechanism for the oxalyl chloride–1,3-dialkylurea reaction may involve initial oxygen attack similar to that which occurs in both the carbonyl chloride–

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[1] To whom inquiries should be directed.

[2] (a) H. Ulrich, J. N. Tilley, and A. A. R. Sayigh, *J. Org. Chem.*, **29**, 2401 (1964); (b) unpublished results.

[3] H. Ulrich and A. A. R. Sayigh, *Angew. Chem.*, **76**, 647 (1964); *Angew. Chem., Intern. Ed. Engl.*, **3**, 585 (1964); in press.

[4] H. Eilingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960).

[5] H. Biltz and E. Topp, *Ber.*, **47**, 1387 (1913).

[6] K. Hartke and J. Bartulin, *Angew. Chem.*, **74**, 214 (1962).

[7] H. Ulrich and A. A. R. Sayigh, *J. Org. Chem.*, **28**, 1427 (1963).

[8] P. Fischer, German Patent, 1,131,661 (1962); *Chem. Abstr.*, **58**, 1401 (1963).

[9] H. D. Stachel, *Angew. Chem.*, **71**, 246 (1959).