ether. After drying overnight at 60° under vacuum the yield was 2.4 g. (28% of the theoretical amount).

**7-Hydroxy-5-methylmercapto-2-phenyl-v-triazolo(d)pyrimidine.**—A weight of 7 g. (0.027 mole) of 4-amino-6-hydroxy-2-methylmercapto-5-phenylazopyrimidine together with 25 ml. of pyridine was added to a hot mixture of 20 g. of copper sulfate pentahydrate, 40 ml. of pyridine and 40 ml. of water. The mixture was refluxed 3 hours with stirring, then poured into 400 ml. of water and acidified with hydrochloric acid. The precipitate which separated was filtered, dissolved in 1% sodium hydroxide solution, and reprecipitated with hydrochloric acid. The solid was separated by centrifuging, then dissolved in dilute ammonium hydroxide solution, treated with charcoal, and filtered. The crude product was precipitated by the addition of acetic acid and separated from the supernatant liquid by centrifuging. After recrystallization from hot dioxane the white solid was washed with ether and dried overnight at 60° under vacuum. The yield was 1.6 g. (23%).

**2-*p*-Carboxyphenyl-5,7-diamino-v-triazolo(d)pyrimidine.**—To a mixture of 13.3 g. of copper sulfate pentahydrate, 27 ml. of water and 27 ml. of pyridine were added 5.5 g. (0.018 mole) of 2,4,6-triamino-5-*p*-carboxyphenylazopyrimidine monohydrate and 17 ml. of pyridine. The mixture, which did not give a homogeneous solution, was refluxed with stirring for 2.5 hours, then cooled, diluted with 300 ml. of water, the precipitate filtered and washed with water. The precipitate was returned to the original reaction vessel and treated with copper sulfate and aqueous pyridine as before. The mixture was cooled, poured into water, and the precipitate filtered and washed with water until free of blue coloration. The precipitate was slurried with two portions of hot 10% acetic acid, filtered and washed with water, alcohol, and ether. The light yellow product which was dried under vacuum at 60° overnight weighed 4.7 g. (95%).

LABORATORY OF ADVANCED RESEARCH
REMINGTON RAND, INC.
SOUTH NORWALK, CONNECTICUT

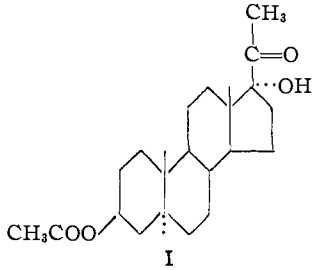
## Perbenzoic Acid Oxidation of Reichstein's "L" Acetate[1]

BY NORMA S. LEEDS, DAVID K. FUKUSHIMA AND T. F. GALLAGHER

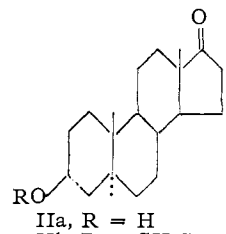
RECEIVED JANUARY 8, 1954

The oxidation of 20-ketosteroids to 17-acetoxy derivatives of steroids by perbenzoic acid is a generally known reaction.[2-4]

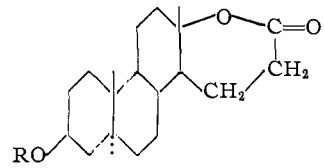
In accordance with the mechanism proposed for this reaction,[5,6] the oxidation of 3β-acetoxy-17α-hydroxyallopregnane-20-one (Reichstein's Substance "L" acetate (I)) with perbenzoic acid should yield isoandrosterone acetate (IIb).




I




IIa, R = H
IIb, R = $CH_3CO$




IIIa, R = H
IIIb, R = $CH_3CO$

When this reaction was carried out in the usual way in the presence of *p*-toluenesulfonic acid for 7 days at room temperature, the principal product obtained was isoandrololactone acetate (IIIb), a substance previously prepared by the action of peracetic acid on isoandrosterone.[7] The expected isoandrosterone acetate was obtained in only small yield. However, in the absence of the acid catalyst and with the time of reaction lessened to two days, isoandrosterone acetate was the principal product; isoandrololactone acetate was obtained only in small amounts. It appears, therefore, that the 17-ketosteroid is an intermediate in the peracid oxidation of a 17α-hydroxy-20-ketosteroid and that further reaction with the oxidant leads to the lactone III by the rupture of the $C_{13}$–$C_{17}$ bond.[8]

### Experimental[9]

**Isoandrololactone Acetate (IIIb).**—To 5 ml. of a benzene solution containing 275 mg. of 3β-acetoxy-17α-hydroxyallopregnane-20-one (I) was added 2.2 ml. of 0.65 *M* perbenzoic acid and 19 mg. of *p*-toluenesulfonic acid monohydrate in 0.025 ml. of acetic anhydride and 0.3 ml. of acetic acid. The solution was allowed to stand in the dark for 7 days at room temperature and was then diluted with ether, washed with sodium carbonate solution and with water. The solution was dried over sodium sulfate and the solvent removed under reduced pressure. The 223 mg. of product so obtained was chromatographed on 45 g. of silica gel and eluted with increasing concentration of ether–petroleum ether. Crystalline eluates were obtained with anhydrous ether and together weighed 114 mg. (43%) with melting points ranging from 145 to 155°. Recrystallization from ether–petroleum ether afforded pure isoandrololactone acetate (IIIb), m.p. 159–160°, $[\alpha]^{23}D$ −42° (dioxane), reported[7] m.p. 158.5–159.9°. The m.p. of a mixture with an authentic sample of isoandrololactone acetate[10] showed no depression. The infrared spectrum of the reaction product and the authentic sample was identical.

*Anal.* Calcd. for $C_{21}H_{32}O_4$: C, 72.41; H, 9.19. Found: C, 72.50; H, 8.83.

The early fractions of the chromatogram eluted with 40 to 50% ether–petroleum ether were combined and 36 mg. of isoandrosterone acetate identified by infrared spectrum was obtained.

**Isoandrosterone (IIa).**—A solution of 305 mg. of 3β-acetoxy-17α-hydroxyallopregnane-20-one (I) in 2.8 ml. of 0.35 *M* perbenzoic acid in benzene was stored for 2 days. After dilution with ether, the solution was washed with sodium carbonate and with water. The ether solution was dried over sodium sulfate and the solvent was removed under diminished pressure, leaving a residue of 213 mg. The reaction product was saponified with 3.2 ml. of 1.25 *N* sodium hydroxide in 8 ml. of methanol at room temperature overnight. Ether was added to the saponification mixture which was then washed free of base and dried over sodium sulfate. Upon evaporation of the solvent, 145 mg. of product was obtained and was chromatographed on 25 g. of silica gel. From the earlier eluates of the chromatogram, 102 mg.

(1) This investigation was supported by grants from the Anna Fuller Fund, the Lillia Babbitt Hyde Foundation, the Teagle Foundation, and the National Cancer Institute, United States Public Health Service (C-440).

(2) V. Burckhardt and T. Reichstein, *Helv. Chim. Acta*, **25**, 1434 (1942).

(3) L. H. Sarett, THIS JOURNAL, **69**, 2899 (1947).

(4) T. F. Gallagher and T. H. Kritchevsky, *ibid.*, **72**, 882 (1950).

(5) R. B. Turner, *ibid.*, **72**, 878 (1950).

(6) W. von E. Doering and L. Speers, *ibid.*, **72**, 5515 (1950).

(7) H. Levy and R. P. Jacobsen, *J. Biol. Chem.*, **171**, 71 (1947).

(8) The structure of isoandrololactone acetate (IIIb) has been inferred from the results of studies by D. Prins (unpublished findings) and C. von Seemann and G. A. Grant (THIS JOURNAL, **72**, 4073 (1950)). The tertiary oxygen adjacent to the bridgehead is consistent with their findings (see also G. M. Picha, *ibid.*, **74**, 703 (1952)).

(9) All m.p.'s are corrected.

(10) We wish to thank Dr. D. Prins for supplying a sample of isoandrololactone acetate for comparison studies.

of crystalline product was obtained and was characterized as isoandrosterone by infrared spectrometry. A portion, m.p. 175–176°, when admixed with an authentic sample of isoandrosterone, m.p. 175–178°, showed no depression of the m.p.

The aqueous alkaline layer from the saponification of the oxidation product was acidified and extracted with ether. The ether layer was washed free of acid with sodium chloride solution and dried. Evaporation of the solvent yielded 48 mg. of product, m.p. 157–167°, which proved to be identical with isoandrololactone (IIIa), m.p. 169–170°, by its infrared spectrum. Upon acetylation and recrystallization from ether–petroleum ether, isoandrololactone acetate (IIIb), m.p. 155–157°, was obtained which did not depress the m.p. of an authentic sample of isoandrololactone acetate[10] and exhibited an identical infrared spectrum with the authentic product.

SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
NEW YORK 21, N. Y.

## Quinoxaline-2-thiol and Derivatives

BY F. J. WOLF, R. M. WILSON, JR., AND MAX TISHLER

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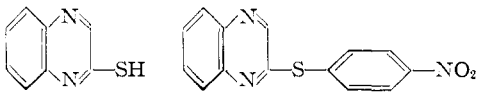
During a study of quinoxaline compounds of possible therapeutic value, the preparation of quinoxaline-2-thiol (I) and related compounds was under-



I II

taken. The parent thiol I was obtained readily by treating 2-chloroquinoxaline with thiourea followed by hydrolysis of the resulting S-2-quinoxalylisothiouronium chloride. 2-Quinoxalyl *p*-nitrophenyl sulfide (II) was prepared from 2-chloroquinoxaline and *p*-nitrothiophenol. In a similar manner, 2-chloro-6-(or 7)-nitroquinoxaline formed the expected sulfide when treated with *p*-nitrothiophenol. It is of interest that the sulfide II was not obtained from the thiol I and *p*-nitrochlorobenzene under the conditions studied. On the other hand, the thiol readily yielded di-2-quinoxalyl sulfide when heated with 2-chloroquinoxaline.

The sulfides were converted to the sulfones by oxidation with hydrogen peroxide.

### Experimental

**Quinoxaline-2-thiol.**—A solution of 22 g. of 2-chloroquinoxaline[1] and 20 g. of thiourea in 150 ml. of methanol was refluxed for ten minutes. After cooling to 5°, the crystalline crude isothiouronium hydrochloride was separated. The crude product, 31.5 g., 97.7% yield, melted at 150–155°; a sample recrystallized from methanol melted at 159–160°.

A mixture of 15 g. of the crude isothiouronium hydrochloride and 100 ml. of 2.5 *N* sodium hydroxide was heated on a steam-bath for 45 minutes. The orange solution was cooled, acidified with acetic acid and the product was separated by filtration. On recrystallization from 200 ml. of methanol, a bright orange crystalline product, m.p. 204–205°, 7.3 g., 73% yield, was obtained.

*Anal.*[2] Calcd. for $C_8H_6N_2S$: C, 59.3; H, 3.7; N, 17.3. Found: C, 59.2; H, 3.9; N, 17.3.

**2-Quinoxalyl *p*-Nitrophenyl Sulfide.**—A solution of 55 g. of *p,p'*-dinitrodiphenyl disulfide,[3] 26 g. of sodium sulfide nonahydrate and 14 g. of sodium hydroxide in 1500 ml. of 60% ethanol–water was refluxed for 20 minutes. The hot solution was added to a warm solution of 61 g. of 2-chloroquinoxaline in 1250 ml. of ethanol. The resulting dark red solution was refluxed 30 minutes and then refrigerated 18 hours at 5°. The crude product, 50 g., was filtered and recrystallized from 2 l. of methanol. The product, 19.5 g., 19.3% yield, was obtained as pale yellow needles having a silky appearance, m.p. 151–152°.

*Anal.* Calcd. for $C_{14}H_9N_3O_2S$: C, 59.4; H, 3.2; N, 14.8. Found: C, 59.0; H, 3.3; N, 15.2.

**6-(or 7)-Nitro-2-quinoxalyl *p*-Nitrophenyl Sulfide.**—The reaction was carried out as above with 10 g. of 6-(or 7)-nitro-2-chloroquinoxaline,[4] m.p. 184–186°. The crude product was recrystallized from glacial acetic acid yielding a pale orange micro-crystalline solid, m.p. 196°, 10.3 g., 65.5% yield.

*Anal.* Calcd. for $C_{14}H_8N_4O_4S$: C, 51.2; H, 2.4; N, 17.1. Found: C, 51.3; H, 2.5; N, 17.4.

**Di-2-quinoxalyl Sulfide.**—A solution of 16 g. of 2-chloroquinoxaline, 16 g. of quinoxaline-2-thiol and 5.35 g. of sodium methylate in 270 ml. of methanol was refluxed 16 hours. The mixture, containing some precipitated product, was cooled and filtered. The crude product was recrystallized from 1500 ml. of methanol, whereupon material, 16 g. melting at 159°, was obtained. A second crop (3 g., total yield 67.1%), m.p. 158–159°, was obtained by concentrating the recrystallization liquors.

*Anal.* Calcd. for $C_{16}H_{10}N_4S$: N, 19.4. Found: N, 19.4.

**2-Quinoxalyl *p*-Nitrophenyl Sulfone.**—A mixture of 11 g. of 2-quinoxyl *p*-nitrophenyl sulfide, 400 ml. of glacial acetic acid and 30 ml. of 30% hydrogen peroxide was shaken for four hours and the resultant solution allowed to stand four days at 30°. The crude product, precipitated by pouring the mixture into 1500 ml. of water, was recrystallized from 100 ml. of glacial acetic acid. The product, 5.6 g., 45% yield, was obtained as silky needles having a yellowish cast, m.p. 197–199°. A sample recrystallized for analysis from ethanol melted at 202–203°.

*Anal.* Calcd. for $C_{14}H_9N_3O_4S$: C, 53.4; H, 2.9; N, 13.3. Found: C, 53.3; H, 3.0; N, 13.5.

**Di-2-quinoxalyl Sulfone.**—The same method of preparation was used, the product, m.p. over 360°, was obtained as white needles in 32% yield.

*Anal.* Calcd. for $C_{16}H_{10}N_4O_2S$: C, 59.7; H, 3.1; N, 17.4. Found: C, 59.4; H, 3.5; N, 17.5.

**6-(or 7)-Nitro-2-quinoxalyl *p*-Nitrophenyl Sulfone.**—The same method of preparation was used, the product, m.p. over 240°, was obtained as white needles having a tan cast in 20% yield.

*Anal.* Calcd. for $C_{14}H_8N_4O_6S$: C, 46.8; H, 2.2; N, 15.5. Found: C, 46.8; H, 2.3; N, 15.4.

(1) A. H. Cowenlock, G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 622 (1945).

(2) Microanalyses were kindly performed by Messrs. R. Boos, E. Thornton, J. MacGregor, A. Rosalsky and Mrs. C. Miess.

(3) J. N. Elgerstma, *Rec. trav. chim.*, **48**, 752 (1929).

(4) F. J. Wolf, K. Pfister, R. H. Beutel, R. M. Wilson, C. A. Robinson and J. R. Stevens, THIS JOURNAL, **71**, 6 (1949).

RESEARCH LABORATORIES, CHEMICAL DIVISION
MERCK AND CO., INC.
RAHWAY, N. J.

## The Reaction of the Alkoxides of Titanium, Zirconium and Hafnium with Esters

BY R. C. MEHROTRA

RECEIVED DECEMBER 21, 1953

The reaction of aluminum isopropoxide with organic esters has been studied by Baker.[1] The preparation and properties of the alkoxides of titanium, zirconium and hafnium have been described in a number of recent communications[2] and it has been shown that in contrast with the tetraalkoxy silanes, the alkoxides of titanium, zirconium and hafnium readily exchange their alkoxy groups with other alcohols. In this communication, it has been

(1) R. H. Baker, THIS JOURNAL, **60**, 2673 (1938).

(2) D. C. Bradley, R. C. Mehrotra and W. Wardlaw, *J. Chem. Soc.*, 2027, 4204, 5020 (1952); 1634 (1953).