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.

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Quinoxaline-2-thiol and Derivatives

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

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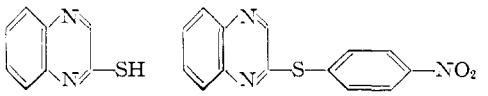
During a study of quinoxaline compounds of possible therapeutic value, the preparation of quinoxaline-2-thiol (I) and related compounds was under-



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. Gowenlock, 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. Elgersma, *Rec. trav. chim.*, **48**, 752 (1929).

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

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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).

TABLE I

Alkoxide, g.	Organic ester, g.	Time for exchange, min.	Yield of distilled alkoxide, %	B.p., °C.	B.p., Mm.	Metal, % Found	Metal, % Calcd.
$Ti(OEt)_4$ (5.7)	PrOAc (35)	30	92	130	0.2	16.87	16.85
$Ti(OEt)_4$ (6.2)	BuOAc (46)	45	90	160	0.8	14.08	14.07
$Ti(OPr^i)_4$ (11.8)	BuOAc (54)	40	94	162	1.0	14.10	14.07
$Ti(OPr^i)_4$ (8.4)	*s*-BuOAc (48)	60	90	124	4.0	14.11	14.07
$Ti(OPr^i)_4$ (8.6)	*t*-BuOAc (55)	60	90	81	2.0	14.09	14.07
$Zr(OEt)_4$ (4.4)	PrOAc (41)	90	82	215	0.2	27.91	27.85
$Zr(OPr^i)_4 \cdot Pr^iOH$ (7.2)	BuOAc (52)	75	93	253	0.3	23.83	23.78
$Zr(OPr^i)_4 \cdot Pr^iOH$ (7.0)	*s*-BuOAc (50)	90	85	170	0.2	23.80	23.78
$Zr(OPr^i)_4 \cdot Pr^iOH$ (12,4)	*t*-BuOAc (54)	120	80	81	3.0	23.85	23.78
$Hf(OPr^i)_4 \cdot Pr^iOH$ (6.1)	*t*-BuOAc (36)	120	84	88	6.0	38.02	37.93

shown that the alkoxides of titanium, zirconium and hafnium react with organic esters as

$$M(OR)_4 + 4R'OOCMe \rightleftarrows M(OR')_4 + 4ROOCMe$$

The reaction can be pushed to completion if the organic ester (ROOCMe) formed is more volatile and can be fractionated out of the system.

The following compounds were prepared by the above method in almost quantitative yields from their ethoxides or isopropoxides: *n*-propoxides and isomeric butoxides of titanium and zirconium and also hafnium *t*-butoxide. The technique may be of special advantage in the case of certain unstable alcohols and has proved of great practical utility in the preparation of the *t*-butoxides of zirconium and hafnium. The methods described in the literature[3-5] for the preparation of zirconium tetra-*t*-butoxide require a very long time and the yield in all the cases is poor. Similar remarks apply to the tetra-*t*-butoxide of hafnium.[6] The difference between the boiling points of *t*-butyl and isopropyl acetates is sufficiently large to enable a rapid fractionation of the isopropyl acetate. Moreover, the reaction between zirconium ethoxide and *t*-butyl alcohol appeared to be hindered beyond the formation of zirconium tri-*t*-butoxide monoethoxide, whereas the reaction between zirconium ethoxide and *t*-butyl acetate, though slow, goes to completion with the formation of zirconium tetra-*t*-butoxide. Hence the reaction of zirconium ethoxide appears to be less hindered with *t*-butyl acetate than with *t*-butyl alcohol. Similar observations have been made for aluminum alkoxides.[7]

Experimental

Materials.—Titanium, zirconium and hafnium alkoxides were prepared and purified as described in the literature.[2] The organic esters were commercial products of reagent grade and were dried carefully and purified by fractionation over a column (60 cm. long) filled with Fenske helices; *t*-butyl acetate was prepared by the action of acetic anhydride on *t*-butyl alcohol and, after purification, it was dried by refluxing and distilling over some titanium *t*-butoxide.

Apparatus.—All glass apparatus with interchangeable joints was used throughout and special precautions were taken to exclude moisture. In ester interchange experiments, fractionations were carried out in a 60-cm. long column packed with Fenske helices and fitted to a total condensation variable take-off stillhead.

General **Procedure.**—The method of ester interchange employed was similar in all cases and so for brevity, details would be given in the case of zirconium isopropoxide–*t*-butyl acetate reaction only.

Crystalline zirconium isopropoxide ($Zr(OPr^i)_4 \cdot Pr^iOH$, 12.4 g.) was refluxed in *t*-butyl acetate (54.0 g.) under the column at a bath temperature of 140–150°. About 2 cc. of the distillate was collected at 82° (isopropyl alcohol). Then the temperature of the distilling liquid rose to 89° and in the course of 45 minutes, about 8 g. of the distillate was collected at this temperature. The temperature then rose to about 93–94° and came down very slowly. Refluxing was continued and another 3 g. of the distillate was collected at 89° (isopropyl acetate) in the course of a half-hour. The remaining *t*-butyl acetate was then distilled at a high reflux ratio (1:25) at 97–97.5° to push the reaction to completion. Total time of refluxing was about two hours. Finally the product was allowed to cool; the remaining *t*-butyl acetate was removed under reduced pressure and the product, a pale yellow mobile liquid was analyzed (Zr, 23.96; Pr^iO, *ca.* 0.3%). Zirconium tetra-*t*-butoxide was distilled under reduced pressure and gave a colorless, mobile liquid (9.8 g., b.p. 81° (3.0 mm.), yield 80%).

Anal. Calcd. for $Zr(OC_4H_9)_4$: Zr, 23.78. Found: Zr, 23.85.

The reaction was much faster in the case of normal and secondary butyl acetates than in the case of *t*-butyl acetate both in the case of titanium and of zirconium. Also, in general the reaction was faster in the case of titanium alkoxides than in the case of corresponding zirconium alkoxides. The results are shown in Table I.

Reaction of Zirconium Isopropoxide with *t*-Butyl Chloride—Zirconium tetraisopropoxide (6.4 g.) was refluxed at 90–100° in *t*-butyl chloride (54 g.) under the column. The exchange reaction did not appear to proceed at all even after six hours of refluxing and the end product of the reaction was found to be unchanged isopropoxide. The failure of this reaction suggests that the exchange of the alkyl groups does not occur and the exchange reaction in the earlier experiments is probably due to the interchange of the alkoxy radicals.

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The Identification of Derivatives of Fluorene and Biphenyl by Filter Paper Electrophoresis[1]

BY JOHN H. PETERS AND HELMUT R. GUTMANN

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During the course of investigations on the tissue metabolism of the carcinogen 2-acetylaminofluorene filter paper electrophoresis has been applied to

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