oxo group.[10] Consequently, the order of substituent effects of the oxo groups is as follows: H > 17-oxo > 20-oxo > 11-oxo.

Finally, concerning the acetoxyl groups, the 11α-acetoxyl group gives a slightly more positive effect than the 11α-hydroxyl groups, and 5β-ketone formation in an 11α-acetoxyl derivative increases in comparison with that from the corresponding parent compound (compare **14b** with **13**). The 11β- and 17β-acetoxyl groups have certainly less negative effects than those of the corresponding β-hydroxyl groups, the 17β-acetoxy compound giving the 5β ketone in even greater yield than the parent compound (compare **7b** and **15b** with **4** and **13**, respectively; **3b** with **1**). The 17α-acetoxyl group provides a strongly positive effect except when hydrochloric acid in acetic acid is added, although the effect is somewhat smaller than that of the hydroxyl group (compare **2b** and **2a** with **1**). The effects of 20α- and 20β-acetoxyl groups are similar to those of the corresponding hydroxyl groups and more negative than that of 11β-acetoxyl group (compare **11b** and **12b** with **10**; **7b** and **15b** with **4** and **13**, respectively). The order of substituent effects of the acetoxyl groups is therefore as follows: 17α-OAc > 17β-OAc ≅ 11α-OAc > H > 11β-OAc > 20α-OAc ≅ 20β-OAc.

The fact that the equatorial 11α-acetoxyl group has a slightly more positive effect than an equatorial 11α-hydroxyl group which shows nearly the same effect as that of 11α hydrogen, does not contradict the concept of steric effect. On the other hand, the 11β-hydroxyl (axial) group has a more negative effect than the corresponding acetoxyl group, while the 17α-hydroxyl (quasiaxial) group has definitely a more positive effect than the 17α-acetoxyl group. These result cannot be interpreted in steric terms. The negative effect of the quasiequatorial 17β-hydroxyl group is as great as that of the axial 11β-hydroxyl group, but such an effect is scarcely noticeable when a 17β-acetoxyl group is present. These facts suggest that the effect of hydroxyl groups is electronic rather than steric. The large negative effect of the oxo group is also considered as arising from electronic factors.[11]

Experimental Section

Materials.—4-Androsten-3-one (**1**) was supplied from Teikoku Hormone Manufacturing Company, Ltd. Testosterone (**3a**), testosterone acetate (**3b**), and 4-cholesten-3-one (**9**) were described in a previous paper.[4] Epitestosterone (**2a**), progesterone (**13**), 11α-hydroxyprogesterone (**14a**), and 11-oxoprogesterone (**16**) were obtained commercially and recrystallized. 17β-Acetoxy-11β-hydroxy-4-androsten-3-one (**5**),[12] 11β-hydroxy-4-androstene-3,17-dione (**7a**),[13] 11β-acetoxy-4-androstene-3,17-dione (**7b**),[14] 4-androstene-3,11,17-trione (**8**),[13] 4-pregnene-3-one (**10**),[15] 20α-hydroxy-4-pregnen-3-one (**11a**),[16] 20β-hydroxy-4-pregnen-3-one (**12a**),[17] 11β-hydroxyprogesterone (**15a**),[18] and 11β-acetoxyprogesterone (**15b**)[14] were prepared by published procedures. Epitestosterone acetate (**2b**), 20α-acetoxy-4-pregnen-3-one (**11b**), 20β-acetoxy-4-pregnen-3-one (**12b**), 11α-acetoxyprogesterone (**14b**), epitestosterone benzoate (**2c**), testosterone benzoate (**3c**), 4-androstene-3,17-dione (**4**), and 17β-acetoxy-4-androstene-3,11-dione (**6**) were prepared from the corresponding hydroxy steroids by acetylation, benzoylation, or oxidation in the usual way. Purity of these compounds was checked by gas–liquid partition chromatography (glpc). Palladium hydroxide was prepared as previously described.[4,19]

Hydrogenation and Analysis.—The steroid (10 mg) was hydrogenated in the solvent (10 ml) with prereduced palladium hydroxide (5 mg) at 25° and under atmospheric pressure. After hydrogenation of the catalyst in isopropyl alcohol or acetic acid, 3 *N* hydrochloric acid (0.05 ml), if necessary, was added to the suspension. After the steroid had been hydrogenated for 0.5 hr, the reaction was stopped to analyze the products by glpc. A Shimazu Seisakusho Model GC-4APF gas chromatograph equipped with dual flame detectors was employed. The glass columns (2 m × 4 mm inside diameter) contained 1.5% OV-17 on 80–100 mesh Shimalite W (Shimazu Co.) washed with acid and silanized with dichlorodimethylsilane. The carrier gas was nitrogen at a flow rate of 70 ml/min and the column tempearature was suitably selected for each product between 205 and 260°. Quantitative estimation of the products was carried out by multiplying the height of the peak by the width at half-height.

Acknowledgment.—The authors are grateful to Teikoku Hormone Manufacturing Company, Ltd., for providing 4-androsten-3-one.

(10) Since the negative effects of the oxo groups are great, **8** with an 11,17-dioxo group and especially **16** with an 11,20-dioxo group mainly lead to the formation of the 5α ketones.

(11) *Cf.* D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier, Amsterdam, London, New York, N. Y., 1968, p 16.

(12) O. Mancera, G. Rosenkranz, and F. Sondheimer, *J. Chem. Soc.*, 2189 (1953).

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(18) B. J. Magerlein and R. H. Levin, *ibid.*, **75**, 3654 (1953).

(19) The ratio of 5β to 5α ketone is somewhat changed using different batches of catalyst, particularly in isopropyl alcohol.

An Improved Synthesis of Phenyl Benzohydroxamate and Its Conversion to Phenyl *O*-Phenyl- and *O*-Ethylbenzohydroxamate

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Although alkyl benzohydroxamates may be prepared by simple alkylation,[2] aryl benzohydroxamates are not readily accessible and, in fact, only two representatives of this class of derivatives have been previously reported. Thus, arylation of potassium benzohydroxamate with diphenyliodonium bromide gave phenyl benzohydroxamate in 24% yield,[3] while treatment of the same salt with 2,4-dinitrofluorobenzene gave 2,4-dinitrophenyl benzohydroxamate in 20% yield.[4]

We have recently reported[5] the formation of an unstable *N*-chlorosulfite by reaction of thionyl chloride with 1-hydroxy-2(1*H*)-pyridone; subsequent treatment with thallium(I) carboxylates gave 1-acyloxy-2(1*H*)-pyridones. Extension of this reaction to open-chain hydroxamic acids would have provided simple access to aryl hydroxamate derivatives. In order to explore this possibility, we treated an ethereal solution of benzo-

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(1) NRCC Postdoctoral Fellow, 1968–1970.

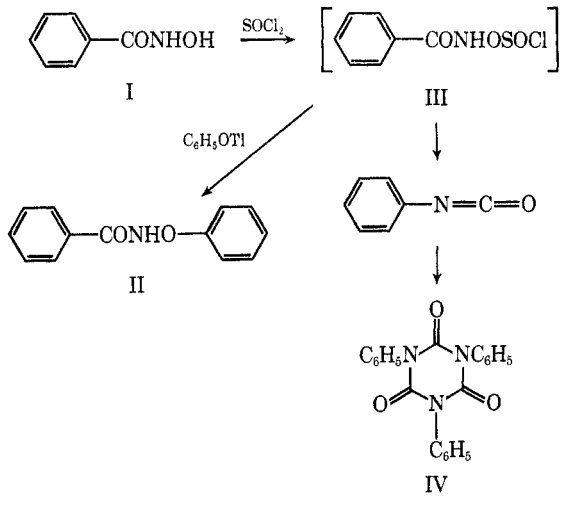
(2) P. A. S. Smith, "The Chemistry of Open-chain Nitrogen Compounds," Vol. II, W. A. Benjamin, New York, N. Y., 1966.

(3) J. S. Nicholson and D. A. Peak, *Chem. Ind. (London)*, 1244 (1962).

(4) P. M. Gallop, S. Seifter, M. Lukin, and E. Meilman, *J. Biol. Chem.*, **235**, 2619 (1960).

(5) E. C. Taylor, F. Kienzle, and A. McKillop, *J. Org. Chem.*, **35**, 1672 (1970).

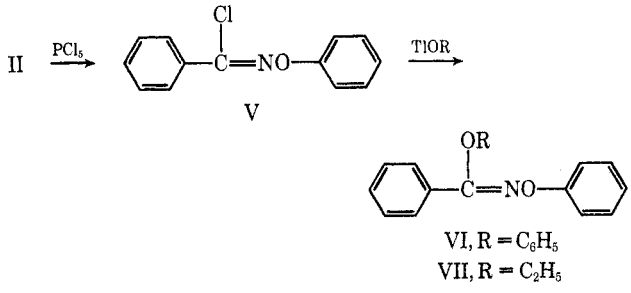
hydroxamic acid (I) at 0° with thionyl chloride. Evaporation of the ether followed by treatment of the residual syrup with thallium(I) phenoxide in benzene gave phenyl benzohydroxamate (II) in 6.2% yield, indicating the probable intermediacy of *N*-chlorosulfite III. The principle product (22.5%) isolated, however, was triphenyl isocyanurate (IV) which probably arose by trimerization of phenyl isocyanate, the product of a Lossen rearrangement of III.[6]



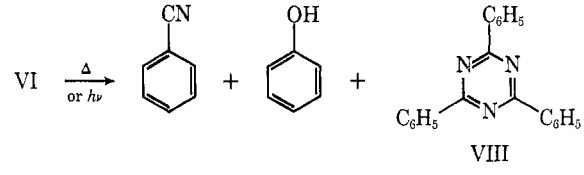
IV

Phenyl benzohydroxamate (II) could, however, be prepared in satisfactory yield (66%) by reaction of thallium(I) benzohydroxamate with diphenyliodonium chloride. This is a considerable improvement over the previously reported method[3] for the preparation of this compound.

Reaction of II with phosphorus pentachloride gave *O*-phenylbenzohydroximoyl chloride (V) in 77% yield. Subsequent nucleophilic displacement of chlorine was readily achieved by treatment of V with thallium(I) phenoxide[7] and thallium(I) ethoxide to give, respectively, phenyl *O*-phenylbenzohydroximate (VI)[8] and phenyl *O*-ethylbenzohydroximate (VII). Alkyl *O*-alkylbenzohydroximates have been synthesized previously,[2] but neither aryl *O*-aryl- nor aryl *O*-alkylbenzohydroximates are known. Compounds VI and VII, therefore, represent the first examples of these new classes of hydroximate derivatives.



The tendency of hydroxamic and imido acid derivatives to rearrange is well known,[2] and we therefore briefly examined the stability of VI. It was found that VI, when heated or irradiated with 3000-Å light, gave as major products benzonitrile and phenol; no rearrangement products were observed. Under both sets of conditions, 2,4,6-triphenyl-1,3,5-triazine (cyaphenine) (VIII) was isolated in small amounts.[9]



VIII

Experimental Section[10]

Phenyl Benzohydroxamate (II).—To a solution of 13.7 g (0.1 mol) of benzohydroxamic acid in 250 ml of ethanol was added, with vigorous stirring, 24.9 g (0.1 mol) of thallium(I) ethoxide. Thallium(I) benzohydroxamate immediately precipitated. After 10 min of continued stirring, diphenyliodonium chloride (31.7 g, 0.1 mol) was added, and the reaction mixture heated gently under reflux for 4 hr, and then cooled and filtered. Evaporation of the filtrate gave a liquid residue which was taken up in 150 ml of ether. The ether solution was extracted with four 50-ml portions of 1 *N* NaOH. Crude phenyl benzohydroxamate (14.1 g, 66%, mp 125–131°) was precipitated upon acidification of the combined alkaline extracts with dilute hydrochloric acid. Recrystallization from absolute alcohol raised the melting point to 136–137° (lit.[3] mp 137.5–139°).

***O*-Phenylbenzohydroximoyl Chloride (V).**—Crude phenyl benzohydroxamate (13.9 g, 0.065 mol) was suspended in cold carbon tetrachloride (500 ml) and phosphorus pentachloride (14.6 g, 0.07 mol) was added. The reaction mixture was stirred at 0° until most of the suspended solid had dissolved (6 hr). The resulting yellow solution was then evaporated, the residue dissolved in 200 ml of ether, and the ether solution washed once with 50 ml of water. Evaporation gave a syrup which crystallized on treatment with aqueous ethanol to give practically pure V, 11.6 g (76.5%), mp 34–35°. The analytical sample, mp 35–36°, was prepared by recrystallization from aqueous ethanol.

Anal. Calcd for $C_{13}H_{10}NOCl$: C, 67.40; H, 4.35; N, 6.05. Found: C, 67.20; H, 4.50; N, 6.18.

A mass spectrum showed a strong parent peak *m/e* 231 in addition to a medium intensity peak at *m/e* p + 2; ir 1592, 1260, 980, 948, 750, and 685 (strong), 1560, 1195, 1155, 1020, 1000, 825, and 705 cm^{-1} (medium).

Phenyl *O*-Phenylbenzohydroximate (VI).—*O*-Phenylbenzohydroximoyl chloride (5.78 g, 0.025 mol) was mixed well with thallium(I) phenoxide (7.44 g, 0.025 mol), 15 ml of dimethyl sulfoxide added, and the mixture heated on a steam bath for 5 hr. It was then cooled to room temperature and diluted with 150 ml of ether, and the insoluble thallium(I) chloride filtered off. The filtrate was extracted with four 20-ml portions of water and evaporated, and the residual brown syrup was taken up in 75 ml

(6) Treatment of hydroxamic acids with thionyl chloride has been reported to give isocyanates: R. Marquis, *C. R. Acad. Sci., Ser. C*, **143**, 1163 (1906); G. B. Bachman and J. E. Goldmacher, *J. Org. Chem.*, **29**, 2576 (1964).

(7) The advantages of thallium(I) *vs.* alkali metal salts of phenols in acylation, aroylation, and tosylation reactions have been stressed previously [E. C. Taylor, G. W. McLay, and A. McKillop, *J. Amer. Chem. Soc.*, **90**, 2422 (1968)]. In addition, thallium(I) phenoxide is a crystalline, stable solid which offers considerable manipulative advantages over deliquescent sodium phenoxide.

(8) Hydrolysis of this compound in alcoholic hydrochloric acid gave *O*-phenylhydroxylamine hydrochloride, mp 134° (lit.[3] mp 136°), thus confirming structure VI and excluding the possibility that a Chapman rearrangement (see ref 14) might have taken place under the reaction conditions.

(9) Benzonitrile is known to give rise to cyaphenine upon treatment with a variety of reagents, such as concentrated H_2SO_4, alcoholic HCl, Br_2 in a sealed tube, boiling sodium, etc. (Beilstein's "Handbuch der organischen Chemie," Vol. 26, Springer, Berlin, 1937, p 97). Since our reaction described above was carried out on pure VI, without the presence of catalysts, we favor a mechanism for the formation of VIII involving some activated nitrile species (*e.g.*, a triplet nitrile, R—C=N:).
↓ ↓

(10) Evaporations were carried out *in vacuo* (35–40° bath temperature). Melting points were determined on a Thomas–Hoover apparatus and are uncorrected. Infrared data refer to Nujol mull spectra taken on a Perkin-Elmer 237B grating infrared spectrometer.

of ethanol. Water was added to incipient turbidity. After 20 hr at 0°, 5.42 g of slightly colored but nearly pure VI, mp 50–51°, was collected by filtration. Addition of water to the mother liquor gave a second crop (0.25 g, mp 46–48°), total yield 79%. The combined material was dissolved in hexane and the solution passed through a short column of silica gel. Evaporation of the eluate and crystallization of the residue from aqueous ethanol gave 4.75 g of colorless prisms: mp 53–54°; ir 1585, 1322, 1195, 1160, 1070, 965, 755, and 685 (strong), 1625, 1300, 1025, 1000, 925, and 770 cm^{-1} (medium).

Anal. Calcd for $C_{19}H_{15}NO_2$: C, 78.87; H, 5.23; N, 4.84. Found: C, 78.75; H, 5.29; N, 5.02.

Phenyl *O*-Ethylbenzohydroximate (VII).—*O*-Phenylbenzohydroximoyl chloride (1.00 g, 4.3 mmol) was dissolved in 20 ml of ethanol and thallium(I) ethoxide (1.07 g, 4.3 mmol) was added. The mixture was heated under reflux for 4 hr, thallium(I) chloride filtered off, and the filtrate evaporated. The residue was dissolved in ethyl acetate–hexane (1:1) and the solution passed through a short column of silica gel. Evaporation of the eluate and crystallization of the residue from aqueous ethanol gave 550 mg (53%) of flat prisms: mp 43–44°; ir 1590, 1320, 1215, 755, and 695 (strong), 1625, 1575, 1300, 1155, 1105, 1075, 1025, 955, 930, and 770 cm^{-1} (medium).

Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.62; H, 6.27; N, 5.81. Found: C, 74.60; H, 6.24; N, 5.88.

Reaction of Benzohydroxamic Acid with Thionyl Chloride and Thallium(I) Phenoxide.—To a suspension of 1.37 g (0.01 mol) of benzohydroxamic acid in 150 ml of cold anhydrous ether was added 1.30 g (0.011 mol) of thionyl chloride. The resulting clear solution was stirred for 1 hr at 0° and evaporated (bath temperature 20°), and the residual syrup dissolved in 100 ml of dry, cold benzene. Thallium(I) phenoxide (2.97 g, 0.01 mol) was added (slight exothermic reaction) and the mixture stirred at room temperature for 2 hr. Filtration and evaporation of the filtrate gave a syrup which crystallized upon trituration with ethyl acetate–petroleum ether to give 250 mg (23%) of triphenyl isocyanurate, mp 275° (lit.[11] mp 275°).

Addition of more petroleum ether to the mother liquors gave 180 mg (6%) of impure phenyl benzohydroxamate, mp 120°, mmp (with pure II) 130°. The yield of this material was not increased when the reaction of benzohydroxamic acid with thionyl chloride and thallium(I) phenoxide was carried out at lower temperatures.

Thermolysis of Phenyl *O*-Phenylbenzohydroximate (VI).—Compound VI (1.00 g) was placed in a small round-bottom flask equipped with a condenser and immersed into a Wood's metal bath at 180°. The reaction mixture, which immediately started to boil violently, was maintained at 180° for 30 min and then cooled to room temperature. The partly crystalline product was dissolved in ethyl acetate–methanol (1:1) and the solution left at 0° for 20 hr. Filtration then gave 15 mg of 2,4,6-triphenyl-1,3,5-triazine (VIII), mp 231–232° (*m/e* 309) (lit.[12] mp 230°). Evaporation of the filtrate and chromatography of the residue on a silica gel column [eluent, hexane–ethyl acetate (5:1)] gave benzonitrile (250 mg) (containing a little VI and VIII), phenol (80 mg), and 170 mg of a mixture of at least three different, unidentified compounds.

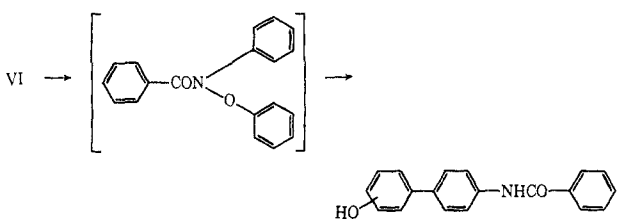
Photolysis of Phenyl *O*-Phenylbenzohydroximate (VI).—Compound VI (2.00 g) was dissolved in hexane (500 ml) and irradiated with 3000-Å light (Rayonet photochemical reactor) for 3 hr. Some insoluble brown material was filtered off and the filtrate irradiated for an additional 4 hr. Filtration gave a second crop of hexane-insoluble material, total yield 400 mg.[13] Evaporation of the filtrate gave a syrup which was separated on a silica gel column into VIII (12 mg), unreacted starting material (740 mg, containing a little benzonitrile), benzonitrile (50 mg), phenol (350 mg), 40 mg of a solid, recrystallized from water to give an amide (5 mg, mp 215–220°),[14] and 45 mg of an unidentified aromatic compound (no OH, NH, CO).

(11) A. W. Hofmann, *Ber.*, **18**, 3217 (1885).

(12) A. Pinner, *ibid.*, **22**, 1611 (1889).

(13) This material was insoluble in water, but it could be dissolved in hot benzene and precipitated again upon addition of petroleum ether to give a dark red powder, mp 140–150° dec. Its ir spectrum showed a medium strong absorption band at 1650 cm^{-1}. Its nmr spectrum (in DMSO-d_6) showed only one broad symmetrical peak at τ 3.05. The compound thus appears to be diphenoquinone, which is known to be unstable and to decompose at 165° [R. Willstätter and L. Kalb, *ibid.*, **38**, 1235 (1905)]. It also liberated iodine from an acidic potassium iodide solution, a characteristic reaction of diphenoquinone.

(14) Its ir spectrum showed NH absorption at 3340 cm^{-1}, strong bands at 1655 (amide I) and 1545 cm^{-1} (amide II), and additional bands at 1590, 1510, 825, and 725 cm^{-1}, suggesting the presence of phenyl groups. It has been shown [J. R. Cox, Jr., and M. F. Dunn, *Tetrahedron Lett.*, 985 (1963)] that *N*-acetyl-*O*,*N*-diphenylhydroxylamine rearranges spontaneously to 4- (and 2-) hydroxy-4′-acetylaminobiphenyl. It seems reasonable to suggest, therefore, that VI may have rearranged first by a Chapman-type rearrangement to phenyl *N*-phenylbenzohydroxamate, which subsequently underwent a further rearrangement to 4′-benzoylamino-hydroxybiphenyl according to the following scheme.



4′-Benzoylamino-4-hydroxybiphenyl melts at 284° [L. C. Raiford and E. P. Clark, *J. Amer. Chem. Soc.*, **48**, 483 (1926)]; our compound could be the unknown 2-hydroxy isomer.

Registry No.—II, 4380-77-2; V, 26630-25-1; VI, 26630-26-2; VII, 26630-27-3.

Tautomerism in 1,5-Dianilino-4,8-naphthoquinones

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While studying a number of 1,5-bis(alkylamino)-4,8-naphthoquinones,[1] we noted that the absorption spectra of the dianilide (1) was solvent dependent (Figure 1 and

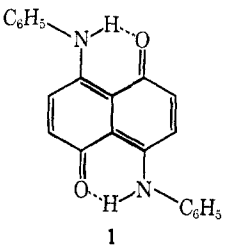

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Table I). In polar, associating solvents, the absorption at 661 nm of the dianilide is of maximum intensity and decreases with decreasing solvent associating ability. Conversely, the band at ~560 nm (broad) increases in intensity. The alkyl-substituted aminonaphthoquinones, however, have a limited dependence of the electronic spectrum upon solvent, the effects being in the range considered normal (for example, ϵ_0 shifting from 2.42 to 2.28 × 10^3 between ethanol and pyridine).[1]

Dähne and Paul discussed the strong solvent dependency of the electronic spectra of 1,8-diamino-2,7-naphthoquinones.[2] They attributed the solvent effect to mesomerism from the quadrapolar nature of the mole-

* To whom correspondence should be addressed, Harvard University.

(1) S. M. Bloom and G. Dudek, *Tetrahedron*, **26**, 1267 (1970).

(2) S. Dähne and H. Paul, *Chem. Ber.*, **97**, 1625 (1964).