Reaction of Nitrosyl Chloride with Steroid 5-Enes.1 Nuclear Magnetic Resonance as a Stereochemical Tool in Steroids

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Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.02; H, 8.30.

Continued elution with benzene–ethyl acetate (9:1) yielded a crystalline material (3.9 g.) which after recrystallization from methanol proved to be identical with 17β-hydroxyandrosta-1,4-dien-3-one acetate (IV) by mixture melting point comparison with an authentic sample. The melting point was 152–153°, $[\alpha]_D$ +32°; $\lambda_{max}^{C_2H_5OH}$ 244 mμ (log ε 4.18); lit.[10] m.p. 151–152°, $[\alpha]_D$ +28°.

4-Hydroxytestosterone (Va).—A solution of 1 g. of 4α,17β-dihydroxy-5α-androst-1-en-3-one diacetate (II) in 50 ml. of methanol was treated with 5 ml. of a 20% sodium hydroxide solution. The mixture was heated under reflux for 1 hr. The slightly yellow solution was poured into water, acidified with hydrochloric acid, and extracted with ether. The ether solution, after drying, was concentrated to a small volume, whereby the 4-hydroxytestosterone (Va) crystallized. After recrystallization from methanol–water, 0.45 g. of pure product was obtained, m.p. 216.5–218°, $\lambda_{max}^{C_2H_5OH}$ 278 mμ (log ε 4.076), lit.[11] m.p. 222–223°.

In the same way, 4-hydroxytestosterone was obtained by saponification of 4β,17β-dihydroxy-5α-androst-1-en-3-one diacetate (III).

Diacetate (Vb).—The diacetate was obtained in the usual way by acetylation with acetic anhydride–pyridine at room temperature. It melted at 168.5–169.5°, $[\alpha]_D$ +96.5°, $\lambda_{max}^{C_2H_5OH}$ 246 mμ (log ε 4.135); lit.[11] m.p. 170–172°, $[\alpha]_D$ +105°, $\lambda_{max}^{C_2H_5OH}$ 246 mμ (log ε 4.19). There was no depression of melting point by admixture with an authentic sample of 4-hydroxytestosterone diacetate.

4β,17β-Dihydroxy-5α-androstan-3-one Diacetate (VII).—A solution of 1 g. of 4β,17β-dihydroxy-5α-androst-1-en-3-one diacetate (III) in 150 ml. of ethyl acetate was hydrogenated under 30-p.s.i. pressure with 0.1 g. of 5% palladized charcoal catalyst. After 1 hr. the catalyst was separated by filtration and the filtrate was concentrated to dryness. The crystalline residue was recrystallized from ether–hexane to give 0.85 g. of pure 4β,17β-dihydroxy-5α-androstan-3-one diacetate (VII), m.p. 166–169.5°, $[\alpha]_D$ +67°; $\lambda_{max}^{CCl_4}$ 3.63, 5.76, 7.29, and 8.20 μ.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.63; H, 8.70.

4α,17β-Dihydroxy-5α-androstan-3-one Diacetate (VI). A. From 4α,17β-Dihydroxy-5α-androst-1-en-3-one Diacetate (II).—Hydrogenation of 0.5 g. of compound II in the above-described manner and crystallization from ether–hexane gave 0.3 g. of pure 4α,17β-dihydroxy-5α-androstan-3-one diacetate (VI), m.p. 197.5–198°, $[\alpha]_D$ −26.2°; $\lambda_{max}^{CCl_4}$ 3.43, 5.74, 7.27, and 8.10 μ; lit.[7] m.p. 196.5–197.50, $[\alpha]_D$ −24°.

Anal. Calcd. for $C_{23}H_{34}O_5$: C, 70.73; H, 8.77. Found: C, 70.76; H, 8.68.

B. From 4β,17β-Dihydroxy-5α-androstan-3-one Diacetate (VII).—A solution of 1 g. of VII in 50 ml. of glacial acetic acid was treated with a saturated solution of 1 ml. of hydrobromic acid in glacial acetic acid. The mixture was left to stand overnight, after which it was poured into water and extracted with ether. The ether solution was washed to neutrality, dried, and concentrated to dryness. Recrystallization of the residue from ether–hexane afforded 0.82 g. of 4α,17β-dihydroxy-5α-androstan-3-one diacetate (VI), m.p. 197.5–198°, $[\alpha]_D$ −24.7°.

The products obtained by methods A and B were identical by infrared spectral comparison and no depression was observed in the mixture melting point.

(10) H. H. Inhoffen, G. Zühlsdorff, and Huang-Minlon, *Ber.*, **73**, 451 (1950).

(11) B. Camerino, B. Patelli, and A. Vercellone, *J. Am. Chem. Soc.*, **78**, 3541 (1956).

Reaction of Nitrosyl Chloride with Steroid 5-Enes.[1] Nuclear Magnetic Resonance as a Stereochemical Tool in Steroids

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Steroid 5-enes, on treatment with an excess of nitrosyl chloride, give 5α-chloro-6β-nitro steroids in good yield. These nitrochloro adducts are transformed by pyridine into the corresponding 6-nitro-5-enes. The latter are reduced stereospecifically by sodium borohydride to 6α-nitro 5α-steroids. 6β-Nitro-5α-chlorocholestan-3β-ol acetate reacts with chromous chloride in methanolic hydrochloric acid to give 6-oximino-5α-methoxycholestan-3β-ol acetate. It is shown that the half-width of a band in the n.m.r. may be correlated with the conformation of the proton giving rise to the band. Thus, equatorial protons give rise to a narrow band (5–12 c.p.s.), while axial protons give a broad band (15–30 c.p.s.).

It has been shown by Closs and Brois that olefins may be transformed *via* their nitrosyl chloride adducts into aziridines.[2] In connection with our interest in the preparation of steroidal aziridines,[3] we investigated the reaction of nitrosyl chloride with some steroid 5-enes. Although nitrosyl chloride has been widely used in the terpene field,[4] it had apparently found no application in steroids.[5]

Cholesteryl acetate (**1a**) reacts with excess nitrosyl chloride at 0° in methylene chloride or carbon tetrachloride to give in 85% yield a crystalline product, m.p. 142–143°, for which structure **2a** is suggested on the basis of elemental analysis and characteristic nitro absorption bands in the infrared (1559, 1370, 864, and 640 cm.$^{-1}$).[5,6] Furthermore, the ultraviolet spectrum of **2a** in neutral and basic medium is very similar to that of nitrocyclohexane. On treatment with pyridine at room temperature, **2a** is transformed into the known 6-nitrocholesteryl acetate (**4a**).[5,6] Methanolic hydrochloric acid converts the acetate **2a** into the corresponding alcohol **3a**. Similar transformations are observed with 5-androsten-3β-ol-17-one acetate (**1b**), methyl 3β-acetoxy-5-cholenate (**1c**), and 5-pregnen-3β-ol-20-one formate (**1d**). The 5α,6β-configuration in **2a** has been assigned largely because ready elimination of

(1)(a) Nitro Steroids. II. Paper I: A. Hassner and J. M. Larkin, *J. Am. Chem. Soc.*, **85**, 2181 (1963). (b) This investigation was supported in part by Public Health Service Grant CY-4474, from the National Cancer Institute. (c) Presented in part before the Division of Organic Chemistry at the 146th National Meeting of the American Chemical Society, Denver, Colo., Jan., 1964. (d) National Science Foundation Fellow, 1961–1963.

(2) G. Closs and S. J. Brois, *J. Am. Chem. Soc.*, **82**, 6068 (1960).

(3) A. Hassner and C. Heathcock, *Tetrahedron Letters*, 393 (1963).

(4) For a review of nitrosyl chloride chemistry, see L. J. Beckham, W. A. Fessler, and M. A. Kise, *Chem. Rev.*, **48**, 319 (1951).

(5) After the present work was essentially complete, however, the work of Tanabe and Hayashi appeared in print.[6] These workers describe the preparation of compounds **2a**, **2b**, **3a**, **4a**, and **4b** in the same manner as that described here.

(6) K. Tanabe and R. Hayashi, *Chem. Pharm. Bull.* (Tokyo), **10**, 1177 (1962).

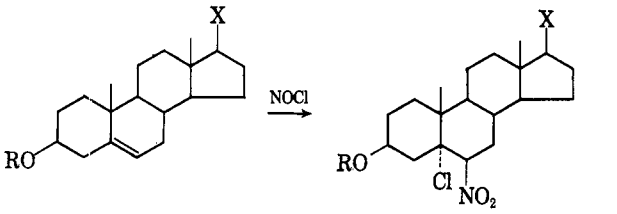
NO_2Cl from **2a** by zinc dust is consistent with diaxially disposed groups.[6] This assignment is now corroborated for compounds **2a–d** and **3a–d** by means of n.m.r. spectra (see below).

Ogloblin has recorded examples of isolation in low yield of nitro compounds in nitrosyl chloride additions to olefins,[7,8] but there seems to be no previously reported case in which a nitro compound is the only product observed in such a reaction. When cholesteryl acetate (**1a**) was treated with one molar equivalent of nitrosyl chloride, a mixture of starting olefin and nitrochloro compound **2a** was obtained. Exclusion of oxygen did not alter the results of the addition reaction. Nitryl chloride reacts with cholesteryl acetate to yield a mixture of products which is difficult to separate and which consists only in part of nitro steroids. Since it is known that nitroso alkanes readily are oxidized to nitro compounds,[4,9] products **2** most likely arise by oxidation of the initially formed nitroso chloride by nitrosyl chloride.[10]

With regard to the mode of addition of nitrosyl chloride to steroid 5-enes, one expects attack at the 6-position by NO^+ or $NO\cdot$ to give an intermediate tertiary carbonium ion or free radical, respectively. Whereas ionic additions to steroid 5-enes generally proceed by attack of the electrophile from the α-side,[11] the products from the NOCl addition contain the nitro group in the less stable axial 6β-configuration. This is compatible with a stereoelectronically controlled axial approach of NO^+. The fact, however, that free-radical addition of hydrogen bromide[12] to cholesterol yields 6β-bromocholestan-3β-ol[13] suggests that the addition of nitrosyl chloride might proceed by a free-radical *trans* addition.[14] The determination of the precise mechanism involved is still under investigation.

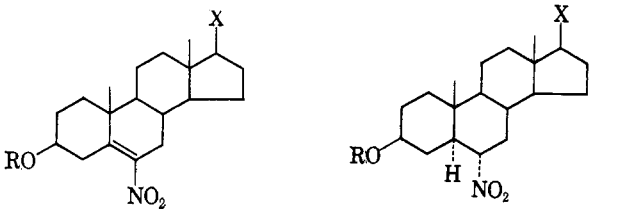
Several attempts (*i.e.*, catalytic reductions with palladium or platinum, stannous chloride, or ferrous sulfate) to reduce the nitrochloro adduct **2a** to the corresponding chloro amine were unsuccessful. Zinc dust or iron dust in refluxing glacial acetic acid regenerated cholesteryl acetate (**1a**). The reluctance of the nitro group to be reduced is in accord with the assignment to it of an axial configuration.

On treatment of **2a** with chromous chloride in methanolic hydrochloric acid, there is obtained a substance, $C_{30}H_{51}NO_4$, which was assigned structure **5**. In the infrared, **5** shows absorption characteristic of an oxime (3450 and 1655 cm.$^{-1}$); its diacetate shows bands for an oxime acetate[15] (1785 and 1640 cm.$^{-1}$). The n.m.r. spectrum shows a sharp singlet at τ 6.90 (OCH_3). Therefore, the nitro group in **2a** has been reduced to the oxime stage, while the chlorine has been solvolyzed by



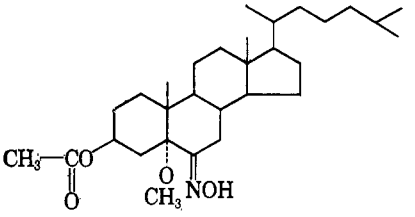
1a, R = $COCH_3$; X = C_8H_{17}
b, R = $COCH_3$; X = O
c, R = $COCH_3$; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H_5$
d, R = CHO; X = $COCH_3$

2a, R = $COCH_3$; X = C_8H_{17}
b, R = $COCH_3$; X = O
c, R = $COCH_3$; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H_5$
d, R = $COCH_3$; X = $COCH_3$
3a, R = H; X = C_8H_{17}
c, R = H; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H_5$
d, R = H; X = $COCH_3$



4a, R = $COCH_3$; X = C_8H_{17}
b, R = $COCH_3$; X = O
c, R = $COCH_3$; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H$

6a, R = $COCH_3$; X = C_8H_{17}
b, R = $COCH_3$; X = $OCOCH_3$
c, R = $COCH_3$; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H_5$
d, R = $COCH_3$; X = $CH(OCOCH_3)CH_3$
7a, R = H; X = C_8H_{17}
b, R = H; X = OH
c, R = H; X = $CH(CH_3)$-$CH_2CH_2CO_2C_2H_5$
d, R = H; X = $CH(OH)CH_3$



5

methanol. Since the 3α-proton appears as a band at τ 5.17 with a band width at half-height of 24 c.p.s. (see discussion below), it is axial and the A–B ring junction is *trans*. It follows that the methoxy group is 5α.

We found that reduction of 5α-chloro-6β-nitro steroids, *i.e.*, **2a**, or of 6-nitro steroid 5-enes with sodium borohydride in ethanol leads in a stereospecific manner to 6α-nitro 5α-steroids. Thus, 6-nitrocholesteryl acetate (**4a**) is converted in 85% yield to 6α-nitrocholestan-3β-ol (**7a**). No detectable amount of any other diastereomer is produced in this reaction. Oxidation of **7a** by the Jones reagent[16] leads to 6α-nitrocholestan-3-one (**8a**). Nitro alcohol **7a** is also produced by base-catalyzed hydrolysis of 6α-nitrocholestan-3β-ol acetate[17] (**6a**), which is formed in 49% yield in the reaction of 6β-nitro-5α-chlorocholestan-3β-ol acetate (**7**) with sodium

(7) K. A. Ogloblin, *Zh. Obshch. Khim.*, **27**, 2541 (1957); **28**, 3245 (1958).
(8) K. A. Ogloblin and A. A. Potekhin, *ibid.*, **31**, 2438 (1961).
(9) W. E. Noland and R. Libers, *Tetrahedron*, **19**, 23 (1963).
(10) That the 6-nitroso steroid would have to be oxidized to the 6-nitro compound before it is able to tautomerize to an oxime is indicated by the well-known[4] fact that oximes are oxidized by NOCl not to nitro but to α-chloronitroso or α-chloronitro compounds.
(11) For instance in the hypobromous acid addition to steroid 5-enes [M. Akhtar and D. H. R. Barton, *J. Am. Chem. Soc.*, **84**, 1496 (1962)].
(12) In contrast with ionic addition of DCl which leads to 6α-deuterio-5α-chloro steroids (C. W. Shoppee, private communication).
(13) C. W. Shoppee and R. Lack, *J. Chem. Soc.*, 4864 (1960).
(14) A recent postulate of *cis* addition of NOCl to norbornene [J. Meinwald, Y. C. Meinwald, and T. N. Baker, *J. Am. Chem. Soc.*, **85**, 2513 (1963)] is based on the assumption that NO^+ or NOCl would approach from the least hindered side which does not seem to be the case with steroid 5-enes.
(15) A. Hassner and I. H. Pomerantz, *J. Org. Chem.*, **27**, 1760 (1962).
(16) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(17) This compound is practically identical by infrared with 6α-nitrocholestan-3β-ol acetate synthesized independently from the 6-ketoxime by G. D. Meakins and E. R. H. Jones. We are grateful to these authors for informing us of their results prior to publication.

borohydride in ethanol. This latter reaction probably proceeds *via* the initial formation of nitro olefin **4a**, which is reduced in the normal manner to give nitro acetate **6a**.[18]

In a similar manner, 6-nitro-5-androsten-3β-ol-17-one acetate (**4b**) is reduced by sodium borohydride to 6α-nitroandrostane-3β,17β-diol (**7b**) in 64% yield. Nitrodiol **7b** was characterized as diacetate **6b** and by oxidation to 6α-nitroandrostane-3,17-dione (**8b**). Methyl 6-nitro-5-cholenate (**4c**) is likewise reduced by sodium borohydride in ethanol, with concomittant ester interchange in the side chain, to give a mixture of ethyl 6α-nitro-3β-acetoxy-5α-cholanate (**6c**) and ethyl 6α-nitro-3β-hydroxy-5α-cholanate (**7c**) in 76% yield. Alcohol **7c** is converted by acetic anhydride in pyridine to the acetate **6c**. 6-Nitro-5-pregnen-3β-ol-20-one formate (**4d**), on borohydride reduction, gives in 92% yield crude nitrodiol (**7d**) as a mixture of the C-20 epimers. Crystallization of this mixture from methanol–water gave one of the pure epimers, m.p. 247–248.5°, which was also characterized as its diacetate derivative (**6d**).

Since hydride reduction of nitro compounds to amides sometimes proceeds with inversion,[19] we chose n.m.r. spectra instead of reduction to amines for the assignment of stereochemistry at C-5 and C-6 on compounds **6–7**. These are assigned the 5α- and 6α-configuration because the half-width (20–25 c.p.s.) of the bands for the C-3 and C-6 protons in the n.m.r. indicate them to be axial protons (see discussion below).

The reduction of 6-nitro steroid 5-enes probably occurs by a Michael addition of hydride to the α,β-unsaturated nitro system with formation of the anion of the *aci*-nitro compounds. Protonation and equilibration then gives the thermodynamically more stable equatorial epimer (6α).[20] The initial stereospecificity of the reaction at C-5 indicates that the hydride prefers to attack from the α-side, giving the more stable *trans* A–B ring junction. This is in accord with results obtained in the sodium borohydride reduction of 3-keto-4-androstenes where 5α-androstan-3-ols are the products.[21] Reductions of nitro olefins and even of nitro benzenes with sodium borohydride have been reported.[22,23] Schechter and co-workers have shown that nitro olefins may be reduced by metal hydrides to give the corresponding nitro alkanes.[22] They found, however, that a major product, and indeed sometimes the only product, was the dimer or higher polymer formed by Michael addition of the initially formed *aci*-nitro anion to the nitro olefin. In the case of 6-nitro steroid 5-enes, this competing dimerization reaction evidently does not take place, probably for steric reasons.

Nuclear magnetic resonance has recently been successfully employed in differentiation of isomers in steroids.[24–26] Chemical shift differences between epimers are generally not great and in many cases both isomers are required for conclusive assignments to be made. The fact, that diaxial vicinal coupling constants are much greater than diequatorial or axial–equatorial ones,[25] also can be used to assign configurations to steroidal epimers. In general, when an electronegative substituent is attached to the steroid framework, the geminal proton is found downfield in the unobscured region of the spectrum. However, such a proton will usually be adjacent to several others and will give rise to a broad band in which the number of closely spaced lines due to spin–spin coupling are not readily discernible. The width of such a band, measured at one-half its height (referred to as the half-width and symbolized by $W^{1/2}$), will reflect the magnitude of the vicinal coupling constants. Thus, an axial proton, split by adjacent axial ($J \sim 9$ c.p.s.) and equatorial protons ($J \sim 2$ c.p.s.), should give rise to a much wider band than an equatorial proton split by adjacent axial ($J \sim 2$ c.p.s.) and equatorial protons ($J \sim 2$ c.p.s.). The utility of half-widths in assignment of stereochemistry has been pointed out recently in a number of cases, mainly in hydroxy and acetoxy cyclohexanes with a rigid skeleton.[24–27] Anomalies have also been reported.[27]

In order to further test the general applicability of this simple technique in assigning stereochemistry in steroids, the spectra of over forty steroids with various functional groups (equatorial and axial) have been obtained. The steroids tested had the cholestane, coprostane, androstane, cholanic acid, or pregnane skeleton. The following functional groups were present at C-2: OH, OAc, NH_2, NHAc, NCO, $NHCO_2CH_3$, and I; at C-3: OH, OAc, $OCOC_6H_5$, OCHO, NH_2, NHAc, I, Cl, and NO_2; at C-4: OH; at C-5: OH, OCH_3, and Cl; at C-6: OH, OAc, and NO_2; at C-7: OAc; at C-12: OAc. Fig. 1A–F shows partial spectra of some compounds examined. Inspection of the results reveals that *the half-width of the bands due to equatorial protons is 5–10 c.p.s., while that for axial protons is 15–30 c.p.s.* Often it is not necessary to measure the exact band width, since a visual inspection reveals the configuration (see Fig. 1). It should be pointed out that the equatorial hydrogen geminal to the axial NH–$COCH_3$ or $NHCO_2CH_3$, in 2β-acetamido-3α-acetoxy- and 3α-acetamido-2β-acetoxycholestanes or in 3β-(N-carbomethoxy)-

(18) These results suggest that the sodium borohydride reduction of 17-bromo-17-nitro steroids to 17-nitro steroids reported recently [A. A. Pachett, F. Hoffmann, F. F. Giarrusso, H. Schwam, and G. E. Arth, *J. Org. Chem.*, **27**, 3823 (1962)] also proceeds by elimination of H–Br followed by hydride reduction of the 17-nitro 16-olefin.

(19) H. Shechter, N. Kornblum, and L. Fishbein, *J. Am. Chem. Soc.*, **77**, 6266 (1955); S. J. Cristol, Abstract of the XVIIIth National Organic Chemistry Symposium, Columbus, Ohio, June 1963, p. 21.

(20) Although protonation of the anion of *aci*-nitro groups generally leads to axial nitro compounds, equilibration in base gives the more stable equatorial isomer [*cf.* A. Bowers, M. B. Sanchez, and H. J. Ringold, *J. Am. Chem. Soc.*, **81**, 3702 (1959); H. E. Zimmerman and T. E. Nevins, *ibid.*, **79**, 6559 (1957)].

(21) F. Sondheimer, M. Velasco, E. Batres, and G. Rosenkranz, *Chem. Ind.* (London), 1482 (1954).

(22) H. Shechter, D. E. Lev, and E. B. Roberson, *J. Am. Chem. Soc.*, **78**, 4984 (1956).

(23) T. Severin and M. Adam, *Ber.*, **96**, 448 (1963).

(24) (a) G. Slomp and B. R. McGarvey, *J. Am. Chem. Soc.*, **81**, 2200 (1959); (b) J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4610 (1962); (c) A. D. Cross, *J. Am. Chem. Soc.*, **84**, 3206 (1962); (d) K. L. Williamson and W. J. Johnson, *ibid.*, **83**, 4623 (1961).

(25) R. U. Lemieux, R. K. Kulling, H. J. Bernstein, and W. G. Schneider, *ibid.*, **79**, 1005 (1957); **80**, 6098 (1958).

(26) R. C. Tweit, A. H. Goldkamp, and R. M. Dodson, *J. Org. Chem.*, **26**, 2856 (1961); R. C. Tweit, R. M. Dodson, and R. D. Muir, *ibid.*, **27**, 3654 (1962); R. C. Tweit, *ibid.*, **27**, 2693 (1962); K. Kawazoe, *Chem. Pharm. Bull.* (Tokyo), **11**, 328 (1963); S. G. Levine, N. H. Endy, and E. C. Farthing, *Tetrahedron Letters*, 1517 (1963).

(27) J. I. Musher, *J. Am. Chem. Soc.*, **83**, 1146 (1961).

amino-3α-iodocholestane, gives rise to broader bands (13–17 c.p.s.) than expected. That this is due to additional coupling with the N–H can be shown by the fact that the signal for the N–H appears as a doublet (J = 6–7 c.p.s.).

Whereas the chemical shift, *e.g.*, for the axial hydrogen geminal to a hydroxy or an acetoxy group at C-3, varies considerably with the structure of the rest of the steroid molecule[28] and is of use only if both epimers are available, the half-width of such a proton (15–25 c.p.s.) allows a clear distinction between an axial and an equatorial configuration in all cases studied.

The use of this technique for assigning stereochemistry to a number of 6-nitro steroids is illustrated. The spectra of the 6-nitro-5-chloro 3β-alcohols (**3**) and their acetates (**2**) all show a band in the region from τ 5.22 to 5.37, with a half-width of 5–7 c.p.s. In each case this narrow band is accompanied by a broad band ($W^{1/2}$ 21–24 c.p.s.) which appears in the region τ 4.5–4.7 in the acetates and τ 5.6–5.8 in the free alcohols. These spectra are similar to that of 3β,6β-diacetoxycholestan-5α-ol. It is readily apparent that the compounds have one axial and one equatorial functional group. The narrow band in the τ 5.3 region may be assigned to the C-6 proton, geminal to the nitro group, since it is not shifted appreciably in going from the alcohol to its acetate. The broad band in each spectrum is then assigned to the 3α-hydrogen. The shift in this band of *ca.* 1 p.p.m. between the alcohols and their acetates is of the expected order of magnitude. Therefore, the correct configuration for these compounds is the one which has the nitro group axial (6β) and the oxygen function equatorial and β, thus fixing the A–B ring junction as *trans*. This case is especially interesting, since it enables us to use the band-width of the C-3 proton resonance to establish the configuration at C-5.

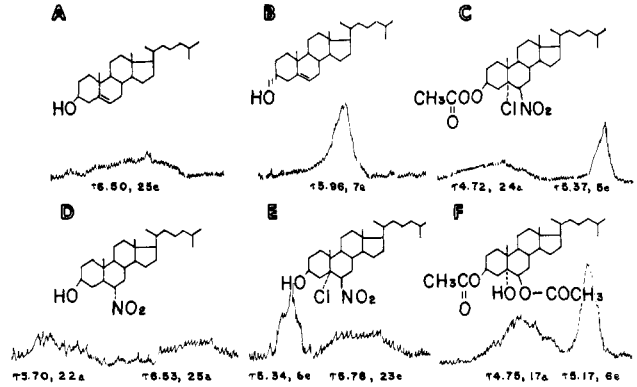


Fig. 1.—Determination of configuration in steroids by means of nuclear magnetic resonance. The first number below each peak is the chemical shift in τ units. The second number is the width of the band at half-height ($W^{1/2}$) in c.p.s., and the letter a (axial) or e (equatorial) denotes the configuration of the proton responsible for the band. There are two errors in this figure: A should read τ 6.50, 25a; E should read τ 5.34, 6e, and τ 5.78, 23a.

Experimental[29]

Nitrosyl Chloride Addition to Steroid 5-Enes. General Procedure.—Nitrosyl chloride (from a cylinder of the compressed gas, or freshly prepared) was passed into methylene chloride or carbon tetrachloride (25–100 ml.) at 0° until the solution had a deep burgundy color. This gave a 10–15% solution. The steroid olefin (5–10 g.) or a solution of the olefin in carbon tetrachloride was added. The solution was kept for 2–24 hr. at 0 to −16° in the dark. The excess of nitrosyl chloride and the solvent were removed *in vacuo* and the product was crystallized.

6β-Nitro-5α-chlorocholestan-3β-ol Acetate (2a).—From 4.93 g. of cholesteryl acetate (**1a**) there was obtained 5.1 g. of product, m.p. 132–136°. Crystallizations from ether–methanol and from methanol brought the melting point to 142–143°, lit.[8] m.p. 141–142°; ν_{max} 1750 (C=O), 1559 and 1370 (NO_2), 1240 and 1036 cm.$^{-1}$ (acetate). The n.m.r. spectrum, in carbon tetrachloride, has a broad band ($W^{1/2}$ 24 c.p.s.) at τ 4.72 (C-3 H, axial), a narrow band ($W^{1/2}$ 5 c.p.s.) at 5.37 (C-6 H, equatorial), and methyl peaks at 8.97 (C-19, singlet), 9.14 (C-26 and C-27, doublet, J = 6.5 c.p.s.), and 9.28 (C-18, singlet). **2a** had λ_{max} 283 mμ (ε 50) and λ_{min} 264 mμ (ε 39). In 0.1 N methanolic potassium hydroxide, λ_{max} changed to 265 mμ (ε 1440) immediately and to 275 mμ (ε 3320) after 24 hr.

Anal. Calcd. for $C_{29}H_{48}ClNO_4$: C, 68.26; H, 9.50; Cl, 6.95; N, 2.75. Found: C, 68.35, 68.12, 68.23, 68.13; H, 9.39, 9.64, 9.67, 9.41; Cl, 7.16; N, 2.67.

6β-Nitro-5α-chloroandrostan-3β-ol-17-one Acetate (2b).—From 7.23 g. of **1b** there was obtained 7.41 g. of white prisms, m.p. 220–225° dec., and 1.44 g., m.p. 209–221° dec. Crystallizations from benzene–hexane raised the melting point to 227–230° dec., lit.[6] m.p. 209–210°; ν_{max} 1740, 1548, 1360, 1240, and 1023 cm.$^{-1}$.

Anal. Calcd. for $C_{21}H_{30}ClNO_5$: C, 61.23; H, 7.34; Cl, 8.61. Found: C, 61.12; H, 7.58; Cl, 8.67.

Methyl 6β-Nitro-5α-chloro-3β-acetoxycholenate (2c).—From 5.0 g. of methyl 3β-acetoxy-5-cholenate (**1c**) 4.45 g. (75%) of **2c** was obtained, m.p. 160–161.5°, which on further recrystallization from acetone–hexane melted at 165–167°; ν_{max} 1738, 1550, 1362, 1250, 1163, and 1036 cm.$^{-1}$.

Anal. Calcd. for $C_{27}H_{42}ClNO_6$: C, 63.32; H, 8.27; Cl, 6.92. Found: C, 63.52; H, 8.35; Cl, 6.88.

6β-Nitro-5α-chloropregnan-3β-ol-20-one Formate (2d).—5-Pregnen-3β-ol-20-one formate (**1d**, 20.0 g.) was converted to 15.95 g. of product, m.p. 155–158°, which on crystallization from acetone–hexane melted at 160–161°; ν_{max} 1723 (C-17, =O), 1700 (formate C=O), 1552 and 1353 (NO_2), and 1170 cm.$^{-1}$ (ester).

Anal. Calcd. for $C_{22}H_{32}ClNO_5$: C, 62.03; H, 7.57; Cl, 8.32. Found: C, 62.08; H, 7.65; Cl, 8.54.

6β-Nitro-5α-chlorocholestan-3β-ol (3a).—A solution containing 1.22 g. of nitrocholoro acetate **2a** and 10 ml. of 4.8 N hydrochloric acid in 100 ml. of methanol was refluxed for 2 hr. and then allowed to stand overnight at room temperature. The resulting precipitate was filtered off and air-dried. The product weighed 930 mg. and melted at 95–101°, lit.[6] m.p. 98–104° (the melting point was not improved by repeated recrystallization from methanol); ν_{max} 3400 (O–H), 1552 and 1362 cm.$^{-1}$ (NO_2). The n.m.r. spectrum in CCl_4–$CDCl_3$ has bands at τ 5.33 (C-6 H, $W^{1/2}$ = 7 c.p.s., equatorial), 5.78 (C-3 H, $W^{1/2}$ = 20 c.p.s., axial), and methyl peaks at 8.98 (C-19, singlet), 9.12 (C-26 and C-27, doublet, J = 6.5 c.p.s.), and 9.27 (C-18, singlet).

Methyl 6β-nitro-5α-chloro-3β-hydroxycholanate (3c) was prepared in a similar manner from nitrochloro acetate **2c**. The yield of crude alcohol, m.p. 109–112°, was 87%. After recrystallization from methanol–water, the substance melted at 113–115°; ν_{max} 3500 (OH), 1725 (C=O), 1550 and 1360 (NO_2), 1162 (ester), 1062 and 1035 cm.$^{-1}$ (C–O).

Anal. Calcd. for $C_{25}H_{42}ClNO_5$: C, 63.90; H, 8.58. Found: C, 63.90, 63.82; H, 8.56, 8.62.

6β-Nitro-5α-chloropregnan-3β-ol-20-one (3d) was prepared in the same manner from the nitrochloro acetate **2d**. This material was also obtained, in 65% yield, when compound **2d** (5.0 g.), ethylene glycol (5 ml.), *p*-toluenesulfonic acid (100 mg.), and benzene (110 ml.) were refluxed under a water separator for 22 hr. in an attempt to prepare the 17-ethylenedioxy derivative. The crude material melted at 184–189°. The infrared spectrum has

(28) For instance the axial 3α-H appears at τ 6.33 in cholestan-3β ol, 5.58 in cholestan-3β,6β-diol, 5.27 in 7-cholesten-3β-ol, and 6.60 in 5-androsten-3β-ol-17-one.

(29) All melting points are uncorrected and were determined on a Fisher-Johns melting block. Infrared spectra were determined in potassium bromide pellets on a Perkin-Elmer 21 infrared spectrometer and nuclear magnetic resonance spectra were obtained on a Varian A-60 spectrometer on dilute solutions (*ca.* 10% by weight) in carbon tetrachloride or deuteriochloroform with tetramethylsilane as an internal standard. Chemica shifts were taken as the geometrical center of the band concerned and are expressed on the τ scale. Microanalyses were performed by A. Bernhardt, Muelheim, Germany.

peaks at 3500 (OH), 1697 (C=O), 1542 and 1360 (NO_2), 1086, 1060, and 1040 cm.$^{-1}$ (C–O).

Anal. Calcd. for $C_{21}H_{32}ClNO_4$: C, 64.45; H, 7.87. Found: C, 64.37; H, 8.03.

Methyl 6-Nitro-3β-acetoxy-5-cholenate (4c).—A solution of 1.0 g. of the nitrochloro acetate **2c** in 10 ml. of anhydrous pyridine was kept at room temperature for 6 hr. The solvent was removed under reduced pressure at 50°, leaving a semisolid. This material was partitioned between 20 ml. of water and 20 ml. of ether. The aqueous layer was extracted with another 20 ml. of ether, and the combined ether extracts were washed with 5% sulfuric acid (20 ml.) and water (20 ml.). From the dried ethereal solution there was obtained white prisms, m.p. 151–153°, in 67% yield. Recrystallization from methanol raised the melting point to 154–155°; ν_{max} 1745 (C=O), 1520 and 1360 (NO_2), 1235 and 1160 (ester bands), and 1036 cm.$^{-1}$ (C–O).

Anal. Calcd. for $C_{27}H_{41}NO_6$: C, 68.18; H, 8.69; N, 2.95. Found: C, 68.05; H, 8.66; N, 2.92.

6-Nitrocholesteryl acetate (4a) [m.p. 103–105°, lit.[30] m.p. 104°; ν_{max} 1518 cm.$^{-1}$, lit.[30] 1518 cm.$^{-1}$; λ_{max} 262 mμ (ε 1920), lit.[30] 258 mμ (ε 1940)] was obtained from **2a** in the same manner.

6-Nitro-5-androsten-3β-ol-17-one acetate (4b) was prepared as described for **4c**. The product recrystallized from ethanol melted at 221–223°, lit.[8] m.p. 215–216°; ν_{max} 1743 (C=O), 1527, 1518, and 1362 (NO_2), 1240 (ester), and 1028 cm.$^{-1}$ (C–O).

6-Nitro-5-pregnen-3β-ol-20-one Formate (4d).—From 5.0 g. of compound **2d** in 40 ml. of anhydrous pyridine there was obtained 4.39 g. (96%) of **4d**, m.p. 213–214°. Crystallization from methanol furnished an analytical sample, m.p. 216–218°; ν_{max} 1730 (C-17, =O), 1698 (formate C=O), 1515 and 1353 (NO_2), and 1168 cm.$^{-1}$ (ester band).

Anal. Calcd. for $C_{22}H_{31}NO_5$: C, 67.84; H, 8.02; N, 3.60. Found: C, 67.97; H, 7.97; N, 3.55.

6-Oximino-5α-methoxycholestan-3β-ol 3-Acetate (5).—Sodium dichromate dihydrate (5.96 g.) was dissolved in 100 ml. of 6 *N* hydrochloric acid. Zinc dust (10 g.) was added and allowed to react under a blanket of nitrogen. This chromous chloride solution was added in one portion to a refluxing solution of 2.0 g. of compound **2a** in 100 ml. of methanol. The reaction mixture turned green immediately, and a white solid separated. After refluxing under nitrogen for 5 min., the slurry was cooled and then filtered. The air-dried product weighed 1.80 g. and melted at 185–197°. Upon crystallization from methanol–water, there was obtained 875 mg. of the oxime, m.p. 222–224°. Two additional crystallizations, from methanol–water and acetone–water, raised the melting point to 231–234°; ν_{max} 3450 (OH), 1720 (C=O), 1655 (C=N), 1270 (ester band), and 1060 cm.$^{-1}$ (C–O). The n.m.r. spectrum, in CCl_4, had peaks at τ 1.12 (OH), 5.17 (C-3 H, $W^{1/2}$ = 24 c.p.s., axial), 6.90 (OCH_3), 8.01 (acetate CH_3), 9.13 (C-19, singlet), 9.13 (C-26 and C-27, doublet, J = 6.5 c.p.s.), and 9.36 (C-18, singlet).

Anal. Calcd. for $C_{30}H_{51}NO_4$: C, 73.57; H, 10.50. Found: C, 73.70; H, 10.33.

Oxime **5** (170 mg.) was converted to its acetate by treatment with acetic anhydride and pyridine at room temperature for 18 hr. Work-up from ether and crystallization from methanol–water gave 80 mg. of 6-oximino-5α-methoxycholestan-3β-ol diacetate, m.p. 130.5–132°; ν_{max} 1785 (C=O of acetoxime), 1735 (C=O of 3-acetate), 1640 (C=N), 1260 and 1235 cm.$^{-1}$ (ester bands).

Sodium Borohydride Reduction of Nitro Steroids. General Procedure.—To a solution of nitro olefin **4** or of nitrochloro steroid **2** or **3** in absolute ethanol there was added sodium borohydride (*ca.* one-fifth the weight of the nitro compound). The solution was kept at room temperature for *ca.* 24 hr. and then was poured into water. The resulting suspension was extracted with ether. The oil, obtained from the washed ether extracts on evaporation, was chromatographed on Woelm neutral alumina activity grade I.

6α-Nitrocholestan-3β-ol Acetate (6a).—From 4.0 g. of 6β-nitro-5α-chlorocholestan-3β-ol acetate (**2a**) was obtained 3.57 g. of an oil which on chromatography gave 1.84 g. of **6a** eluted with 50:1 hexane–ether to pure ether. Crystallization from methanol gave 1.6 g. of product, m.p. 132–134°. The analytical sample melted at 134–136°; ν_{max} 1750 (C=O), 1553, and 1372 (NO_2), 1243 (ester), 1028 cm.$^{-1}$ (C–O).

The n.m.r. spectrum (in CCl_4) shows bands at τ 5.5 (C-6 H, $W^{1/2}$ 22 c.p.s., axial), 5.75 (C-3 H, $W^{1/2}$ 20 c.p.s., axial), 8.10 (acetate methyl singlet), 9.10 (C-19, singlet), 9.14 (C-26 and C-27, doublet, J = 6 c.p.s.), and 9.35 (C-18, singlet).

Anal. Calcd. for $C_{29}H_{49}NO_4$: C, 73.22; H, 10.38. Found: C, 72.82; H, 10.43.

6α-Nitrocholestan-3β-ol (7a).—From 3.0 g. of nitro olefin **4a** and 450 mg. of sodium borohydride there was obtained 2.33 of alcohol **7a** eluted with 19:1 ether–methanol, crystallizing as white needles, m.p. 76–82°. The analytical sample, prepared by two recrystallizations from methanol, melted at 76–82°; ν_{max} 3430 (O–H), 1545 and 1370 (NO_2), 1057, and 962 cm.$^{-1}$.

Anal. Calcd. for $C_{27}H_{47}NO_3$: C, 74.78; H, 10.92; N, 3.23. Found: C, 74.94; H, 10.76; N, 3.14.

The n.m.r. spectrum in CCl_4 has bands at τ 5.70 (C-6 H, $W^{1/2}$ 22 c.p.s., axial), 6.53 (C-3 H, $W^{1/2}$ 25 c.p.s., axial), 9.12 (C-19, singlet), 9.14 (C-26 and C-27, doublet, J = 6.5 c.p.s.), and 9.34 (C-18, singlet). The infrared spectrum of this material was identical with that of a sample obtained on mild basic hydrolysis of 6α-nitro-3β-cholestanyl acetate (**6a**).

6α-Nitroandrostane-3β,17β-diol (7b) was obtained in 64% yield, melting at 115–125°, by reduction of 6-nitro-5-androsten-3β-ol-17-one acetate (**4b**). Recrystallizations from methanol–water, acetone–hexane, and benzene gave long white needles, m.p. 105–113°; ν_{max} 3300 (OH), 1540 and 1370 (NO_2), 1060, 960, and 935 cm.$^{-1}$.

The n.m.r. spectrum in CCl_4 or $CHCl_3$ shows absorption bands at τ 2.68 (benzene of solvation, six protons by integration), 5.56 (C-6 H, $W^{1/2}$ 25 c.p.s., axial), 6.41 (C-3 H and C-17 H, $W^{1/2}$ 25 c.p.s., axial), 9.11 (C-19), and 9.27 (C-18).

Anal. Calcd. for $C_{19}H_{31}NO_4 \cdot C_6H_6$: C, 72.25; H, 8.98; N, 3.37. Found: C, 71.88; H, 8.97; N, 3.66.

Ethyl 3β-Acetoxy-6α-nitro-5α-cholanate (7c).—Sodium borohydride reduction of methyl 3β-acetoxy-6-nitro-5-cholenate (**4c**, 975 mg.) gave 915 mg. of clear oil which was chromatographed on 20 g. of alumina. Fractions 3 and 4 (9:1 benzene–ether to 4:1 benzene–ether) gave 99 mg. (10%) of ethyl 3β-acetoxy-6α-nitro-5α-cholanate (**7c**), m.p. 114–117°. Fractions 8 and 9 (49:1 ether–methanol) gave 592 mg. (66%) of oily ethyl 3β-hydroxy-6α-nitro-5α-cholanate (**6c**) which could not be induced to crystallize. Its infrared spectrum had bands at 3400 (OH), 1730 (C=O), 1548 and 1370 (NO_2), 1240, 1030, and 965 cm.$^{-1}$.

The crude alcohol **6c** was acetylated by heating on a steam bath for 20 min. with acetic anhydride and pyridine. The product weighed 585 mg. (60%) and melted at 107–109°. Recrystallization from methanol–water gave pure **7c**, m.p. 116–117°; ν_{max} 1740 and 1728 (C=O), 1543 and 1370 (NO_2), 1240, 1023, and 960 cm.$^{-1}$. The n.m.r. spectrum has bands at τ 5.4 (C-3 H and C-6 H, $W^{1/2}$ 35 c.p.s., axial), 5.81 (CH_2 of ethyl group, quartet, J = 7 c.p.s.), 7.96 (acetate methyl), 8.73 (CH_3 of ethyl group, triplet, J = 7 c.p.s.), 9.08 (C-19), and 9.31 (C-19).

Anal. Calcd. for $C_{27}H_{43}NO_6$: C, 68.40; H, 9.23. Found: C, 68.89; H, 9.40.

6α-Nitro-5α-pregnane-3β,20-diol (7d).—Reduction of 2.75 g. of nitro olefin **4d** gave a mixture of epimeric diols weighing 2.37 g. (96%) that melted at 198–215°. Recrystallization of 510 mg. of this crude material from methanol–water gave one of the epimers, 318 mg., m.p. 247–248.5°. The analytical sample melted at 246–247.5°; ν_{max} 3300 (OH), 1545 and 1373 (NO_2), 1051, 1032, and 968 cm.$^{-1}$.

Anal. Calcd. for $C_{21}H_{35}NO_4$: C, 69.00; H, 9.65; N, 3.83. Found: C, 68.92; H, 9.73; N, 3.93.

6α-Nitro-5α-pregnane-3β,20-diol Diacetate (6d).—Crude diol **7d** (1.3 g., m.p. 198–215°) was acetylated with acetic anhydride in pyridine at room temperature to yield 515 mg. of material which crystallized from methanol, m.p. 168–175°. Two recrystallizations from acetone–hexane provided an analytical sample of **6d**, m.p. 177–179°; ν_{max} 1735 (C=O of acetate), 1548 and 1371 (NO_2), 1240, 1075, 1026, 970, and 768 cm.$^{-1}$.

Anal. Calcd. for $C_{25}H_{39}NO_6$: C, 66.79; H, 8.75; N, 3.12. Found: C, 66.92; H, 8.93; N, 3.30.

On acid-catalyzed hydrolysis, in 2.4 *N* methanolic hydrochloric acid at reflux for 30 min. diacetate **13**, m.p. 177–179°, gave in 90% yield the diol **7d**, m.p. 240–247°, identified by its infrared spectrum.

6α-Nitrocholestan-3-one (8a).—A solution of 817 mg. of the nitro alcohol **7a** and 300 mg. of sodium dichromate dihydrate in 20 ml. of glacial acetic acid was heated briefly to 60° and then allowed to stand at room temperature for 18 hr. Water was added and after 24 hr. a white solid was obtained by filtration.

(30) G. E. Anagnostopoulos and L. F. Fieser, *J. Am. Chem. Soc.*, **76**, 532 (1954).

It weighed 790 mg. (97%) and melted at 121–126°. Crystallization from ethanol raised the melting point to 138–140°; ν_{max} 1725 (C=O), 1550 and 1370 (NO_2), 1410, and 960 cm.$^{-1}$. The n.m.r. spectrum in CCl_4 shows bands at τ 5.65 (C-6 H, $W^{1/2}$ 25 c.p.s., axial), 8.94 (C-19, singlet), 9.14 (C-26 and C-27, doublet, J = 6.5 c.p.s.), and 9.32 (C-18, singlet).

Anal. Calcd. for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51; N, 3.25. Found: C, 75.33; H, 10.49; N, 3.42.

Nitro ketone **8a** was also obtained by oxidation of nitro alcohol **7** with 8 *N* chromic acid in acetone (Jones reagent); it gave a yellow 2,4-dinitrophenylhydrazone, m.p. 184–186° after recrystallization from methanol–acetone.

6α-Nitroandrostane-3β,17β-diol Diacetate (6b).—Acetylation of 140 mg. of diol **8** in 4 ml. of acetic anhydride and 1 ml. of pyridine at room temperature for 12 hr. gave 120 mg. (68%) of diacetate **6b**, m.p. 183–186°. Two crystallizations from methanol–water furnished the analytical sample, m.p. 187–189°; ν_{max} 1730 (acetate C=O), 1545 and 1370 (NO_2), 1238, 1025, and 900 cm.$^{-1}$.

Anal. Calcd. for $C_{23}H_{35}NO_6$: C, 65.53; H, 8.37; N, 3.32. Found: C, 65.43; H, 8.38; N, 3.51.

6α-Nitroandrostane-3,17-dione (8b).—A solution of 200 mg. of the nitrodiol **7b** in 5 ml. of glacial acetic acid was treated with 200 mg. of chromium trioxide in 5 ml. of 80% aqueous acetic acid. After 12 hr. at room temperature the solution was poured into ice water, made basic with sodium hydroxide, and then just neutralized with 10% hydrochloric acid. The crude dione which precipitated weighed 80 mg. and melted at 235–240°. Two crystallizations from aqueous methanol furnished **8b**, m.p. 244–246°. The infrared spectrum showed peaks at 1740 (C-17, =O), 1712 (C-3, =O), 1560, 1537, 1376, and 778 cm.$^{-1}$ (NO_2).

Anal. Calcd. for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.32; H, 8.29; N, 4.41.

The Preparation of Thiones in the Presence of Anhydrous Hydrogen Fluoride

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A rapid and facile preparation of aromatic and aliphatic thials and thiones or their polymeric forms is outlined. The method consists of the reaction of the corresponding aldehyde or ketone with hydrogen sulfide in the presence of anhydrous hydrogen fluoride. The scope and limitations of the reaction are described. The results are formulated on the basis of an optimum acid-catalyst concentration in accordance with that demonstrated for many other aldehyde and ketone reactions.

In the course of an electrochemical study on aromatic thiones in this laboratory it became necessary to prepare a number of thiones with a wide range of appended substituents. Thiones have previously been prepared in a number of ways depending on the availability and reactivity of the starting materials. *p,p'*-Dimethoxythiobenzophenone can be prepared from thiophosgene and anisole by the Friedel–Crafts reaction.[1] Michler's thione, $[(CH_3)_2NC_6H_4]_2C{=}S$, has been best prepared by treating auramine with hydrogen sulfide.[2] However, it can also be made by the reaction of Michler's ketone with P_2S_5.[3] *p*-Dimethylaminothiobenzophenone has been made by the action of hydrogen sulfide on the corresponding anil.[4] In a few cases sulfur changes a methylene group to a thiocarbonyl[5] as in the preparation of Michler's thione from *p,p'*-dimethylaminodiphenylmethane.

The most widely used method of preparation of thials and thiones depends upon the conversion of an aldehyde or ketone to the corresponding thio compound by hydrogen sulfide in the presence of alcoholic hydrogen chloride.[6] By this method all aliphatic ketones and all aldehydes can be converted to the corresponding thio derivatives which can only be isolated in the form of their dimeric, trimeric, or polymeric derivatives. Aromatic ketones are less reactive but this method has been successfully used to prepare thiobenzophenone, α-naphthylphenylthione, *p*-phenylthiobenzophenone, *p*-methylbenzothione,[7] and thiofluorenone.[8]

$$Ar_2CO + H_2S \underset{}{\overset{C_2H_5OH,\ HCl}{\rightleftharpoons}} Ar_2C{=}S + H_2O \qquad (1)$$

According to eq. 1 the reaction is reversible and considerable difficulty is encountered in preparing pure materials. In an attempt in this laboratory to force Michler's ketone to react directly with hydrogen sulfide, the ketone was dissolved in liquid anhydrous hydrogen fluoride and the cooled solution was treated with hydrogen sulfide. This resulted in an almost quantitative yield on Michler's thione. The scope and limitations of this reaction is the subject of this paper.

The original selection of liquid anhydrous hydrogen fluoride as a medium for the reaction was based on a number of considerations. This material is a good dehydrating agent, an acidic catalyst, and a good solvent for ketones, all of which would be favorable for thione formation. Unlike some other possible materials, such as sulfuric acid, hydrogen fluoride is neither an oxidizing nor a reducing reagent.

Experimental results with formaldehyde, benzaldehyde, acetone, Michler's ketone, and 3,3'-dinitrobenzophenone fully confirmed expectations. When hydrogen sulfide was passed into chilled solutions of the aldehydes or ketones in anhydrous hydrogen fluoride, quantitative yields of the trimeric thials and of the thiones were obtained.

When the reaction was attempted on benzophenone, much less satisfactory results were obtained. Initially, upon passing hydrogen sulfide into a solution of benzophenone in anhydrous hydrogen fluoride, very little thione was produced. However, if the temperature was allowed to rise and most of the hydrogen fluoride was allowed to evaporate, a blue solution was obtained which was shown by spectrophotometric analysis to contain about 60% thione and 40% ketone. Similar results were obtained with *p*-methylbenzophenone, but with α-naphthylphenyl ketone only about 10% conver-

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