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# 6β- AND 6α-NITROCHOLEST-4-ENE AND 5α-CYANO-6α-NITROCHOLESTANE

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**Abstract**—The direct isomerization of 6β- to 6α-nitrocholest-4-ene is described. Evidence is presented that the adduct of 6-nitrocholest-5-ene with hydrocyanic acid is 5α-cyano-6α-nitrocholestane, and the derivation of several other compounds from reactions of these nitro-steroids is discussed.

CONSIDERABLE interest has recently been shown in the chemistry of nitro-steroids (e.g. relevant Refs quoted below.) In this laboratory, increasing use is made of these compounds (particularly nitro-olefins) as synthetical intermediates, and some aspects of the chemistry of the derivatives of the readily accessible 6-nitrocholest-5-ene (I; R = H) are described in this paper.

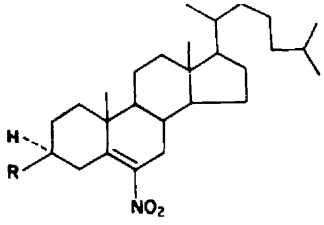
Treatment of 6-nitrocholest-5-ene with alcoholic alkali, followed by acidification of the resulting solution, was shown by Mitui[1] to yield an isomer which he did not correctly formulate, but which we showed[2] some years ago to be 6β-nitrocholest-4-ene (II) from its spectroscopic properties and from analogy to related work;[3] a similar conclusion has also been reached recently by other workers.[4] In principle, it seemed that isomerization of the 6β to the thermodynamically more stable 6α-isomer should be possible by suitable alkaline treatment (since both isomers are acidic) although experimental conditions for this and similar isomerizations are less easily established than is the case for analogous 3-keto-steroids[3,5] or for alicyclic nitro-compounds lacking a β,γ olefinic bond, probably for the reasons suggested by Bowers *et al.*[3] After trying various procedures, it was found that 6α-nitrocholest-4-ene (III) could be obtained in nearly 30% yield (about half this yield of 6β-isomer was recovered) by refluxing the 6β-isomer in methanol for long periods (upwards of one week) with a trace of sodium methoxide. The equilibrium-concentration of the equatorial 6α-isomer would undoubtedly be much higher* than that corresponding to the quoted yields, but we could not investigate this point accurately in the face of evidence that attrition was taking place, other compounds being produced, two of which we identified as 4β-methoxy-cholest-5-ene (IV)[7,8] and 6β-methoxy-cholest-4-ene (V).[7,8]

* Presumably 6-nitrocholest-5-ene is not reformed in this process, conjugation between nitro- and olefinic groups notwithstanding, because this conjugation results in the nitro group becoming coplanar with $C_4$, $C_5$, and $C_6$, with consequent steric interaction between oxygen and $C_4$—H.

[1] P. Mitui, *Bull. Agric. Chem. Soc. Japan*, **16**, 144 (1940).
[2a] P. B. Smith, Ph.D. Thesis, Sheffield (1963); cf. [2b] R. A. Y. Jones, *Science Progress* 198 (1963).
[3] A. Bowers, M. B. Sanchez, and H. J. Ringold, *J. Amer. Chem. Soc.* **81**, 3702 (1959).
[4] J. R. Bull, Sir Ewart R. H. Jones, and G. D. Meakins, *J. Chem. Soc.* 2601 (1965).
[5] M. Davis, *J. Chem. Soc.* 2830 (1964).
[6a] H. E. Zimmerman and T. E. Nevins, *J. Amer. Chem. Soc.* **79**, 6559 (1957); [6b] A. T. Nielson, *J. Org. Chem.* **27**, 1998 (1962).
[7] E. J. Becker and E. S. Wallis, *J. Org. Chem.* **20**, 353 (1955).
[8] H. Schmid and K. Kägi *Helv. Chim. Acta* **35**, 2194 (1952).

Formation of these isomers may be represented, without detailed mechanistic implications, by the arrows in formulae II and III: the nitro group is presumably displaced as nitrite. Analogous work (cf. Ref. 4) on compounds derived from 4-nitrocholest-4-ene will be described later.

Use of the long-known[9] adduct of hydrocyanic acid and 6-nitrocholest-5-ene as a synthetical intermediate requires knowledge of the configurations of the $C_5$-cyano

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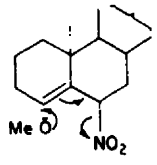


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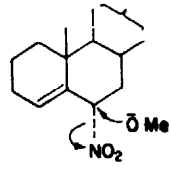


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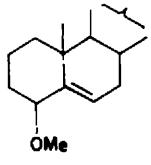


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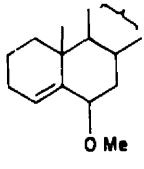


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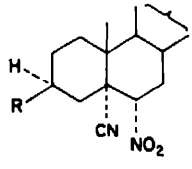


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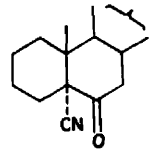


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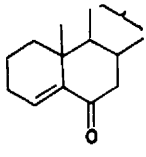
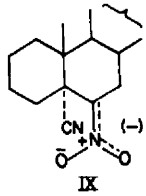
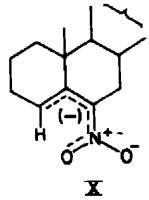



VIII




IX




X

and the $C_6$-nitro group, and we have investigated each point. The half-intensity width (18 c/s) of the multiplet (not fully resolved) corresponding to the 6-proton in the NMR spectrum of the adduct indicates[10] that this proton is axial, and therefore that the nitro-group is equatorial (6α, as in formula VI; R = H). A decision about the stereochemistry of the cyano group was less straightforward. Only one stereochemical form of the adduct was obtained either in methanol or in dimethylformamide.[11] If the reaction conditions permitted thermodynamic equilibration at $C_5$, the adduct could confidently be written with a 5α-cyano group (as in VI), the steric demands of this group, axially oriented in formula VI being quite small.[12] Reversal of the addition of hydrocyanic acid to α,β-unsaturated ketones, with the attendant possibility of equilibration of the relevant adducts, can apparently[11a,13] take place in hot alkaline

[9] A. Windaus, *Ber. Dtsch. Chem. Ges.* **53**, 488 (1920).

[10] *Inter alia*, A. Hassner and C. Heathcock, *J. Org. Chem.* **29**, 1350 (1964); cf. Ref. 2*b*.

[11a] cf. W. L. Meyer and J. F. Wolfe, *J. Org. Chem.* **29**, 170 (1964); [b] A. D. Cross and I. T. Harrison, *J. Amer. Chem. Soc.* **85**, 3223 (1963).

[12] N. L. Allinger and W. Szkrybalo. *J. Org. Chem.* **27**, 4601 (1962); B. Rickborn and F. R. Jensen *Ibid.* 4606 (1962).

[13] A. Bowers, *J. Org. Chem.* **26**, 2043 (1961).

alcoholic solvents, but we have demonstrated by exchange experiments using $^{14}C$-labelled cyanide that no such process takes place during formation of the adduct from the nitro-olefin in methanol: the addition is therefore kinetically controlled.

To investigate orientation at $C_5$ we studied the adduct VI (R = OMe) from 3β-methoxy-6-nitrocholest-5-ene, (I; R = OMe) in the NMR spectrum of which the 3-proton appeared as a broad, not fully resolved, multiplet (half-intensity with ca. 20 c/s) corresponding to a proton with axial conformation; since this proton must be 3α (as in the $\Delta_5$-unsaturated reactant) the A/B ring fusion is therefore *trans* and the cyano-group is therefore α-oriented (VI; R = OMe). By analogy, the unmethoxylated parent also has the 5-cyano group in the α-orientation, as in formula VI (R = H).

Various by-products were obtained (in comparatively small yields) from the methanol residues after separation of the hydrocyanic acid adduct of 6-nitrocholest-5-ene. Two of these have been well characterized—one is provisionally formulated from its properties (Experimental Section) and origin as 5α-cyanocholestan-6-one (VII) and the other has been more positively identified as cholest-4-en-6-one[14] (VIII), evidently derived by elimination of hydrocyanic acid. The cyano-ketone could also be directly prepared in moderate yields from the hydrocyanic acid adduct by two processes, described in detail in the Experimental, which are interpretable as oxidation (possibly aerial oxidation) or as a Nef reaction respectively. Precedents[15] are available in the literature for the oxidation of nitro compounds to ketones by various methods, the nitro group presumably being removed as nitrite or nitrate. Further work on the constitution of our cyano-ketone and on the mode of its formation will be described in due course.

Reduction of conjugated steroidal nitro-olefins such as 6-nitrocholest-5-ene by a variety of procedures is described in the literature: e.g. by catalytic hydrogenation,[4,16a] sodium borohydride,[10] or LAH[16b,c]—reduction of 6-nitrocholest-5-ene by the last reagent is in our laboratory the preferred preparative procedure for 6β-aminocholestane, which is formed exclusively in this reaction. We find that reduction of the same nitro-steroid, or (curiously) of its adduct with hydrocyanic acid, or of 6β-nitrocholest-4-ene, with sodium and amyl alcohol gives mixtures of 6α- and 6β-aminocholestanes in all three cases (each isomer being formed in substantial proportion). The amines (particularly the β-isomer) are less readily isolated and purified from the reduction mixture from the adduct, which in this case contains moderately large proportions of other unidentified products, but reduction of 6-nitrocholest-5-ene with sodium and amyl alcohol, followed by isolation of the ether-insoluble hydrochloride of 6α-aminocholestane, is in our opinion the most convenient preparative route to this base.

Some comments may finally be made on the observed interesting stereospecificities of three reaction-steps which take place during two of the reactions described above. The kinetically controlled α-cyanation at $C_5$ during addition to 6-nitrocholest-5-ene

[14] H. Reich, F. E. Walker and R. W. Collins, *J. Org. Chem.* **16**, 1753 (1951).

[15] *Inter alia* G. A. Russell, *J. Amer. Chem. Soc.* **76**, 1595 (1954); K. Tanabe and R. Hayashi, *Chem. and Pharm. Bull. Japan* **10**, 1177 (1962).

[16] [a] B. G. Ketcheson and A. Taurins, *Canad. J. Chem.* 981 (1960); [b] B. B. Gent and J. McKenna, *J. Chem. Soc.* 137 (1959); [c] C. W. Shoppee, D. E. Evans and G. H. R. Summers, *J. Chem. Soc.* 97 (1957).

unfortunately gives us no real information about transition-state geometry, as transition states corresponding to the observed product orientation would be preferred for either extreme type of transition-state geometry—that is, either near-tetrahedral or near-trigonal at $C_6$: *if* we knew that the latter type of transition state were preferred then we could meaningfully[17] use the concept of reagent approach from the less hindered ($\alpha$-) side. We cannot be quite sure from the available experimental evidence whether the 6$\beta$-protonation of the intermediate ion (IX) during formation of the hydrocyanic acid adduct is thermodynamically or kinetically controlled, but it is probably the former, as the careful and detailed work of Zimmerman and Nevins[6a] indicates that kinetically controlled protonation of such an anion involves near-trigonal valencies at the carbon atom being attacked in the relevant transition states, with consequent development of an axial orientation for the nitro group, which does not compete sterically in such a transition state. The recent results of Jones *et al.*[4] who observed apparently kinetically controlled axial protonation on acidification of alkaline solutions of saturated nitro-steroids under nearly the same experimental conditions as those used by Zimmermann and Nevins, indicate that we must carefully consider what particular species is being protonated in a particular experiment, but it is doubtless the anion in alkaline methanol. The observed equatorial (6$\alpha$) protonation on acidification of an alkaline solution of 6-nitrocholest-5-ene is obviously kinetically controlled, and equally obviously involves a transition state with near-trigonal geometry at $C_6$: more-tetrahedral geometry would of course yield the 6$\alpha$-nitro compound in kinetic control, the nitro group successfully competing sterically with the partly attached proton (or, more broadly, with the fairly remotely positioned proton donor) for the less hindered equatorial position. Trigonality at $C_6$ in the relevant transition state is probably favoured because of the increased potential energy demand which would be associated with a twisting of the long $\pi$-system in either the anion (X) or in the derived aci-nitro compound, and one can meaningfully with such transition states speak of base attack from the less hindered $\alpha$-side of the steroid molecule (cf. Refs 17, 5).

## EXPERIMENTAL

NMR spectra were run in $CHCl_3$ containing tetramethylsilane ($\tau$ = 10·00) on A.E.I. R.S.2. or Varian A 60 spectrometers. IR spectra were run in "Nujol" and UV spectra in EtOH on Perkin–Elmer "Infracord" and "Uvicord" instruments respectively. Only those spectroscopic signals significant in the relevant contexts are quoted. Optical rotations were measured in either alcohol or $CHCl_3$ (as indicated) at concentrations of 0·5–2% on an ETL–NPL automatic polarimeter, type 143 A, with a 0·2 dm cell. Mol. wts quoted were determined on an A.E.I. M.S. 9 mass-spectrometer; the limits quoted refer to standard deviations. $^{14}C$ counts were measured on a Packard "Tricarb" scintillation spectrometer. Petroleum refers to the fraction of b.p. 40–60°.

*6-Nitrocholest-5-ene.* Nitration of cholest-5-ene with fuming $HNO_3$ proving in practice to be a rather uncertain process. (Jones *et al.* recently reported[4] a 60% success rate) we developed after initial unsatisfactory experience the following procedure which works consistently giving yields of >50%. A suspension of finely ground cholest-5-ene (10 g) in glacial acetic acid (60 ml) contained in an open conical flask is stirred on a hot-plate stirrer behind a suitable shield and treated slowly with yellow fuming $HNO_3$ (16 ml) and then with finely ground $NaNO_2$ (5 g) added portionwise over 1 hr. For the first 20 min the temp is kept in the range 40–50° and for the last 40 min in the range 50–60°. After cooling in the refrigerator, the solid is filtered off, washed with a little cold glacial acetic acid and then with water, and finally recrystallized from alcohol (m.p. 116–118°; lit.,[9] m.p. 117–118°).

*6$\beta$-Nitrocholest-4-ene.* 6-Nitrocholest-5-ene (1 g) was shaken at room temp with 5% MeONa in MeOH (30 ml) for 96 hr, during which time the solid slowly dissolved. The solution was acidified

[17] cf. J. McKenna, J. M. McKenna and A. Tulley, *J. Chem. Soc.* in press (1965).

with glacial acetic acid, diluted with water, and the precipitated isomer filtered off (yield, 90%) and recrystallized from EtOH. The product had m.p. 113–114·5° (lit.,[1,4] m.p. 113·5–115°) $[\alpha]_D$ −68° (EtOH) $\nu_{max}$ 1540 cm$^{-1}$, NMR: vinyl hydrogen at 4·09τ, H—C—$NO_2$ unresolved multiplet centred on 5·35τ with half intensity width ca. 7 c/s (equatorial H). (Found: C, 78·4; H, 11·0; N, 3·4. Calc. for $C_{27}H_{45}NO_2$: C, 78·0; H, 10·9; N, 3·4%.) The UV spectrum had $\lambda_{max}$ 288 mμ, ε = 108 (*cf.* $\lambda_{max}$ 268 mμ, ε = 4,500 for 6-nitrocholest-5-ene).

6α-*Nitrocholest-4-ene*. The 6β-isomer (370 mg) was refluxed for 6 days in MeOH (25 ml) containing MeONa (1·5 mg)* and the solution was evaporated *in vacuo*. The residue was extracted with petroleum and the extract chromatographed on a silica-gel column, which removed a number of unidentified strongly adsorbed compounds. The eluted (benzene–ether) mixture was then separated by thin layer chromatography (Merck's "Kieselgel G"; benzene–petroleum, 1:2) into the 6β-isomer (60 mg) the 6α-isomer (105 mg) and a fraction believed to be 4β-methoxycholest-5-ene (10 mg). Chromatography of the extract on neutral alumina was less successful in separating these compounds, but in one such chromatogram a minor fraction was isolated which is believed to be 6β-methoxycholest-4-ene.

After recrystallization from MeOH, 6α-*nitrocholest-4-ene* had m.p. 92–93°, $[\alpha]_D$ +76° ($CHCl_3$), $\nu_{max}$ 1555 cm$^{-1}$, NMR: vinyl H at 4·82τ H—C—$NO_2$ not clearly seen. (Found: C, 78·0; H, 10·9; N, 3·7. $C_{27}H_{45}NO_2$ requires: C, 78·0; H, 10·9; N, 3·4%.) No clearly defined maximum in the region >250 mμ was seen in the UV spectrum.

The presumed isomeric ethers isolated from this reaction, 4β-methoxycholest-5-ene (Found: M.W., 400·367 ± 0·003) and 6β-methoxycholest-4-ene. (Found: M.W., 400·364 + 0·003. Calc. for $C_{28}H_{48}O$: 400·370) had m.p. 68–70° (lit, 65·5–66·5°;[7] 67·5–68·5°[8]) and m.p. 95–97° (lit., 96–97°;[7] 99°,[8]) respectively. The IR spectra corresponded closely with the published spectra for these compounds, most significantly in the region near 1100 cm$^{-1}$, where methyl ethers have strong C—O—C stretching vibrations, and in the olefinic C—H deformation region (bands at 815 cm$^{-1}$, appropriate for a cholest-4-ene, and at 805, 820 cm$^{-1}$ appropriate for a-5-ene, seen in the relevant spectra).

*Conversion of* 6α- *into* 6β-*nitrocholest-4-ene*. The 6α-isomer was dissolved in a hot 5% solution of MeONa in MeOH and the solution refluxed for 3 hr and then cooled. Acidification with glacial acetic acid, dilution with water, and extraction with ether yielded the 6β-isomer identified by its IR spectrum, m.p. (111°) and mixed m.p. (111°) with an authentic specimen.

*Reduction of* 6-*nitrocholest-5-ene*, 6β-*nitrocholest-4-ene*, *and* 5α-*cyano-6α-nitrocholestane with sodium in isoamyl alcohol*. A solution of 6-nitrocholest-5-ene (200 mg) in refluxing isoamyl alcohol (50 ml) was saturated with Na during 2 hr and the resultant mixture of bases, isolated with ether was treated with HCl aq yielding a mixture of 6α (120 mg; ether-insoluble) and 6β-aminocholestane hydrochloride (80 mg; ether soluble). The IR spectra of the hydrochlorides corresponded to the spectra of authentic specimens, and they were converted for further characterization into the free amines[14b] (6α, m.p. 125°; 6β, m.p. 105°) and N-acetyl derivatives[14a] (6α, m.p. 118–120°; 6β, m.p. 188–190°). Shoppee *et al.*[14] record a double m.p. 117–118° and 185–187° for 6α-acetylaminocholestane but except on one occasion we have observed only the lower value.

The ratio of 6α- to 6β-bases obtained in this reduction varied a little between experiments.

Similar reduction of 6β-nitrocholest-4-ene and 5α-cyano-6α-nitrocholestane (see below) also gave the 6α- and the 6β-amines in each case. The product ratio from 6β-nitrocholest-4-ene was similar to that quoted above. Substantial proportions of other unidentified ether-soluble products were obtained in the reduction of the cyano-nitro compound, which made isolation of the pure 6β-amine difficult. Each saturated base was obtained in about 25% yield.

*Addition of cyanide to* 6-*nitrocholest-5-ene*

(a) *In dimethylformamide*. A mixture of the unsaturated nitro-compound (2 g), dimethylformamide (75 ml), KCN (0·75 g in 5 ml $H_2O$) and $NH_4Cl$ (0·45 g in 5 ml $H_2O$) was refluxed for 1 hr, cooled, diluted with water, and extracted with ethyl acetate, which was then washed again with water. Concentration of the ethyl acetate and dilution with MeOH gave 5α-cyano-6α-nitrocholestane (1·5 g), m.p. 161–163° (lit.,[9] m.p. 162°), $[\alpha]_D$ −0·7° ($CHCl_3$) $\nu_{max}$ 2262 cm$^{-1}$ (—C≡N), 1574 cm$^{-1}$ (C—$NO_2$), NMR: H—C—$NO_2$, multiplet (three peaks resolved) centred on 5·43τ with half-intensity

* Milder isomerization conditions were inadequate: e.g., the 6β-isomer was recovered after mixing a suspension (part solution) in 95% EtOH (100 mg in 1 ml) with 0·5 ml of 95% EtOH saturated with $NaHCO_3$, and refluxing the mixture for 5 hr.

band width ca. 18 c/s (axial H). More of the adduct was obtained (total yield, 85%) by thin-layer chromatography of the residue from the mother liquors, together with unidentified products and traces of 6β-nitrocholest-4-ene.

(b) *In methanol.* A mixture of 6-nitrocholest-5-ene (5 g), KCN (1·25 g) and MeOH (150 ml) was refluxed for 4 hr and cooled. The cyano-adduct (3·5 g), identical with that described above, crystallized out on cooling. The mother liquor was concentrated to ca. 50 ml, diluted with water, and extracted with ether. The ether extract was evaporated and the residue (0·9 g) shown both by analytical thin-layer chromatography and large-scale chromatography on alumina to contain roughly comparable quantities of 6β-nitrocholest-4-ene, the above cyanide adduct, and an unidentified more strongly adsorbed product. The aqueous solution from the above ether extraction was acidified with acetic acid and extracted again with ether, which on concentration gave a residue (0·75 g) shown by alumina- or thin layer-chromatography to contain a complex mixture of unidentified compounds (at least one with an intense IR peak at 1780 $cm^{-1}$) together with a further quantity of 6β-nitrocholest-4-ene.

In other experiments, run on the same scale as that described above, the MeOH mother liquors from filtration of the cyano-adduct were evaporated to dryness (rather than concentrated, as in the procedure described in the last paragraph) *in vacuo* on the steam bath, and the dry residue thoroughly triturated with ether; initially most of the residue appeared to dissolve in the ether, but a solid residue appeared on standing during 24 hr after which time the ether was filtered. The solid was treated with more ether and dil. acetic acid; this ether extract was then evaporated and the residue (0·8 g) examined by thin-layer-and alimina-chromatography: it was mostly 6β-nitrocholest-4-ene. The ether filtrate from the trituration was evaporated, and the residue (1 g) shown by chromatography to consist mainly again of 6β-nitrocholest-4-ene, but we also obtained 150 mg of a compound of m.p. 118°, $[\alpha]_D$ −120° (EtOH), $\nu_{max}$ 2225 $cm^{-1}$ (—C≡N), 1720 $cm^{-1}$ (>C=O) $\lambda_{max}$ 297 mμ (ε = 70) NMR; multiplet (2H on integration) in the area 7·25–7·6τ (—$CH_2$·CO—), provisionally formulated as *5α-cyanocholestan-6-one.* (Found: C, 81·9; H, 10·6; N, 3·9. $C_{28}H_{45}ON$ requires: C, 81·7; H, 11·0; N, 3·4%). Elution with benzene yielded 100 mg of a compound, m.p. 103–105°, $[\alpha]_D$ +30° (EtOH), $\lambda_{max}$ 243 mμ (log ε, 4·2), $\nu_{max}$ 1625 $cm^{-1}$, 1695 $cm^{-1}$ (α,β-unsaturated ketone), NMR; vinyl hydrogen multiplet centred on 3·55τ, —$CH_2$—CO— too diffuse for characterization. These physical data on the whole correspond fairly well with published data[14] for cholest-4-en-6-one (m.p. 109°, $[\alpha]_D$ +36° (EtOH) $\lambda_{max}$ 243 mμ, (log ε = 3·8), $\nu_{max}$ corresponding to 5·89 mμ i.e. ca. 1700 $cm^{-1}$). (Found: M.W., 384·337 ± 0·002 Calc. for $C_{27}H_{44}O$; 384·339).

*Direct conversion of 5α-cyano-6α-nitrocholestane into cyano-ketone.* Solutions of the cyano-nitro compound in methanolic MeONa were prepared by heating the compound in 400 mg lots under reflux for 2 hr in MeOH (80 ml) in which Na (0·25 g) had been dissolved and these solutions were treated by a variety of procedures. Best yields (25–60%) of cyano-ketone were obtained by evaporation to dryness under red. press. and shaking the residue with benzene or ether for 24 hr before addition of water and separation of the organic layer, from which the cyano-ketone (with physical properties identical with those described above) was obtained by evaporation and chromatography of the residue: small quantities of the starting compound and unidentified products were also obtained. Lower yields of the cyano-ketone were obtained by pouring the alkaline methanolic solution (prepared as above) into excess of dil. methanolic HCl aq (keeping all the organic material in solution) and letting the mixture stand for 4 days before precipitation of the organic compounds with water and chromatographic examination of the precipitate (Nef conditions?). Immediate treatment of the residue obtained by evaporation of an alkaline methanolic solution (prepared as above) with ether and water, or ether and dil. acetic acid, or keeping the residue in contact with water for 3 hr before acidification and ether-extraction, gave mainly starting cyano-nitro compound and little or no cyano-ketone.

*3β-Methoxy-5α-cyano-6α-nitrocholestane.* Nitrosyl chloride was passed through a solution of 3β-methoxycholest-5-ene (500 mg) in $CCl_4$ (2·5 ml) until the solution became burgundy-coloured; the solution was then left at ca. 10° in the dark for 24 hr before evaporation *in vacuo.* The residue was left under pyridine for 24 hr, the solvent removed at 50° *in vacuo*, and the residue shaken with a mixture of ether and water. Evaporation of the organic solvent gave a residue of crude 3β-methoxy-6-nitrocholest-5-ene, which, after purification by chromatography was converted into its cyano adduct with KCN in MeOH following the procedure described above. The *3β-methoxy-5α-cyano-6α-nitrocholestane* was recrystallized from MeOH–water, m.p. 166–167°, $[\alpha]_D$ −4° ($CHCl_3$). (Found:

C, 73·5; H, 10·1; N, 5·8. $C_{29}H_{48}N_2O_3$ requires: C, 73·7; H, 10·2; N, 5·9%.) The significant NMR signals were a broad multiplet (one proton) of half-intensity width ca. 20 c/s centered on 5·4τ (H—C—$NO_2$; axial H) and another broad multiplet (3 protons) partly overlapping the —OMe signal at 6·64τ and extending ca. 30 c/s downfield (H—C—OMe; axial H).

*Attempted exchange between 5α-cyano-6α-nitrocholestane and $^{14}$C-labelled cyanide anion in alkaline methanol.* A solution of 5α-cyano-6α-nitrocholestane (173 mg; 0·39 mmoles) and $^{14}$C-labelled KCN (33 mg; 0·51 milliequiv: estimated ca. 20 μC) in MeOH (15 ml) containing MeONa (54 mg; 1·0 milliequiv.) was refluxed for 24 hr and the total $^{14}$C activity of the solution then accurately determined (21·6 μC) by counting determinations on a diluted aliquot (1% of total). The remainder of the solution was concentrated to about ⅓ bulk, acidified with HCl aq, diluted with water, and extracted with $CHCl_3$; the extract was washed with water and evaporated, and the residue recrystallized from MeOH, yielding the adduct (116 mg) m.p. and mixed m.p. 161–163°. An attempt was made to estimate the total $^{14}$C activity in the adduct by counting determinations on aliquots, but the activity was too low (in relation to the solubility of the compound) for accurate results; it was, however, in the approximate range 0·01–0·02 μC for the 173 mg taken, or only 0·1–0·2% of the value (9·4 μC) corresponding to complete equilibration with the cyanide taken.

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