Arylazo-steroids. Part IV.† The Reaction of Phenylhydrazine and 1-Methyl-1-phenylhydrazine with Bromo- and Dibromo-5α-cholestanones; Osazone Formation from α-Halogeno-ketones

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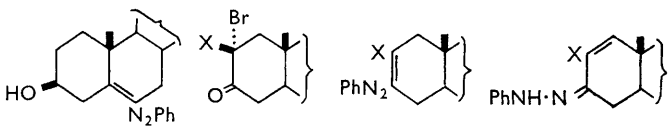
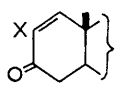
The reaction of phenylhydrazine with 2α-bromo- and 2,2-dibromo-5α-cholestan-3-ones affords initially isolable arylazo-alkenes, followed by the bisphenylhydrazone of 5α-cholestane-2,3-dione. The osazone is thought to arise by a 1,4-addition of arylhydrazine to the arylazo-alkene. Phenylhydrazine and 1α,2β-dibromo-5α-cholestan-3-one gave the phenylhydrazone of 2-bromo-5α-cholest-1-en-3-one, while from 5α,6β-dibromocholestan-3-one was obtained an arylazo-alkadiene, 3-phenylazocholesta-3,5-diene. These products are thought to arise through the ene-hydrazine form of the intermediate phenylhydrazones. Reaction of 2α-bromo- and 2,2-dibromo-cholestan-3-ones with 1-methyl-1-phenylhydrazine yielded a heterocyclic steroid which probably arose from cyclization of an intermediate osazone.

In Part I [1] we showed that the orange product obtained from the reaction of phenylhydrazine with 3β,5α-dihydroxycholestan-6-one and the corresponding 5α-bromo-ketone was the arylazo-alkene (1), which resulted from the initially formed phenylhydrazones. At that time there were relatively few known members of the class of arylazo-alkenes,[2-4] and we therefore undertook a study of the reaction of phenylhydrazine with some of the readily available steroidal ring A ketones, in order to find out whether this formation of azo-alkenes was a general reaction or whether the case of 5α-bromo-3β-hydroxycholestan-6-one was a special one because of the tertiary bromo-substituent. A preliminary account of some of this work has appeared;[5] concurrent studies by Caglioti and his co-workers [6] and Hassner and Catsoulacos [7] have also dealt with the formation of osazones from α-halogeno-ketones.

The reaction of 2,4-dinitrophenylhydrazine with steroidal α-halogeno-ketones is well known to lead usually to the corresponding αβ-unsaturated ketone dinitrophenylhydrazone (the Mattox–Kendall reaction [8,9]), but in no case concerning 2,4-dinitrophenylhydrazine has it been suggested that the product has the azo-alkene structure; if such a product was formed initially, it must have isomerised very rapidly to the isomeric hydrazone.



(1) (2a,b) (3a,b) (4a,b)



(5a,b)

a; X = H
b; X = Br

The first ketone investigated was 2α-bromo-5α-cholestan-3-one (2a).‡ Reaction with phenylhydrazine in hot ethanol containing a trace of acetic acid gave an almost immediate bright yellow crystalline precipitate of 3-phenylazo-5α-cholest-2-ene (3a). This structural

† Part III, J. Buckingham and R. D. Guthrie, *J. Chem. Soc.* (*C*), 1968, 1445.

‡ The reaction of this ketone with phenylhydrazine in acetic acid was studied cursorily by Djerassi,[8] who reported that although the product had lost hydrogen bromide, it crystallised poorly, and he did not attempt to identify it.

[1] J. Buckingham and R. D. Guthrie, *J. Chem. Soc.* (*C*), 1967, 1700.

[2] J. van Alphen, *Rec. Trav. chim.*, 1945, **64**, 109, 305.

[3] S. Veibel and T. Vrang, *Dansk. Tidsskr. Farm.*, 1943, **17**, 112 (*Chem. Abs.*, 1945, **39**, 67).

[4] M. L. Wolfrom, A. Thompson, and D. R. Lineback, *J. Org. Chem.*, 1962, **27**, 2563; M. L. Wolfrom, G. Fraenkel, D. R. Lineback, and F. Komitsky, jun., *ibid.*, 1964, **29**, 457.

[5] J. Buckingham and R. D. Guthrie, *Chem. Comm.*, 1966, 781.

[6] L. Caglioti, G. Rosini, and F. Rossi, *J. Amer. Chem. Soc.*, 1966, **88**, 3865.

[7] A. Hassner and P. Catsoulacos, *Chem. Comm.*, 1967, 121.

[8] C. Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003.

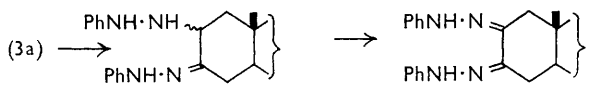
[9] V. R. Mattox and E. C. Kendall, *J. Amer. Chem. Soc.*, 1948, **70**, 882.

assignment was supported by the spectroscopic properties of the product and by the fact that it was distinct from the colourless phenylhydrazone (4a) of 5α-cholest-1-en-3-one, which could be prepared by treating the parent ketone (5a) with phenylhydrazine. As pointed out by Hassner and Catsoulacos,[7] isomerisation of the azo-alkene (3a) to the hydrazone (4a) requires combined acid–base catalysis and does not take place with acid or base alone.

The arylazo-alkene (3a) was also the isolated product when the reaction was carried out in cold pyridine; when it was carried out in cold neutral dioxan, colourless solutions were obtained which were presumed to contain the unstable intermediate α-bromo-ketone phenylhydrazone, but on further manipulation these invariably turned spontaneously yellow within a few seconds, and it was not therefore possible to isolate this compound in the solid state.

The reaction between 2,2-dibromo-5α-cholestan-3-one (2b) and phenylhydrazine proceeded similarly, to yield as the initial product the orange 2-bromo-3-phenylazo-5α-cholest-2-ene (3b), which could be isomerised to the almost colourless hydrazone (4b), also obtained from the parent ketone (5b). An attempt to remove the hydrazone residue from (4b) by an exchange reaction with pyruvic acid, a method which in the dinitrophenylhydrazone series has afforded the ketone (5b) in 30% yield,[8] was unsuccessful.

When the suspension of the phenylazo-cholestone (3a), containing an excess of phenylhydrazine, which had been obtained in the earlier experiment, was boiled for 1 hour,

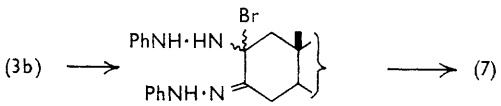


(6) (7)

the initial crystalline precipitate redissolved, and on cooling, the osazone (7) of cholestane-2,3-dione was obtained, identical with that prepared from cholestane-2,3-dione and phenylhydrazine.

Although many cases of the formation of osazones from α-halogeno-, α-acetoxy-, and other negatively α-substituted aldehydes and ketones, including many sugars, have been described, virtually no attention seemed to have been paid until recently to the mechanism of this reaction. In only one case had azo-alkenes been isolated as intermediates;[10] these workers apparently did not consider the azo-alkenes to be true intermediates, but only by-products in equilibrium with the α-halogeno-ketone phenylhydrazones. Osazone formation was considered[10] to take place by reaction of the arylhydrazine with the α-halogeno-ketone phenylhydrazone, although no mechanism was suggested.

That this is incorrect, and that the azo-alkene is a true intermediate, was shown by heating the pure arylazoalkene (3a) with phenylhydrazine and acetic acid in ethanol, when a quantitative yield of the osazone (7) was obtained. Aniline was detected in the mother-liquors. It is thus evident that osazone formation from this α-halogeno-ketone was taking place by 1,4-addition of phenylhydrazine to the initially formed 3-phenylazo-5α-cholest-2-ene, followed by Weygand-B type oxidation of the hydrazino-hydrazone (6) thus produced, as has been discussed elsewhere.[6,11] It is not yet clear to what extent this process is important in the case of α-ketols, where it may be taking place simultaneously with the Weygand A and B mechanisms. In the steroid series,

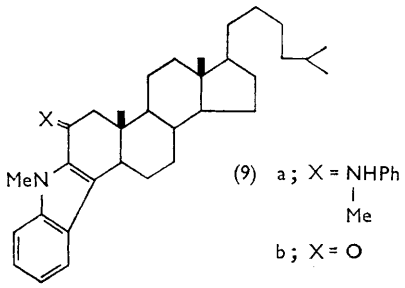


(8)

the isolation of the arylazo-alkenes is made easy by the large non-polar hydrocarbon residue, which lowers their solubility in ethanol. In other structural classes of compounds, they could easily be undetected intermediates.

The osazone (7) of 5α-cholestane-2,3-dione was also isolated when 2,2-dibromo-5α-cholestan-3-one (2b) was treated with phenylhydrazine over an extended period. The formation of an osazone from this compound was thought to follow the same general pathway as that from 2α-bromo-5α-cholestan-3-one except that the intermediate (8) would be capable of direct elimination of hydrogen bromide instead of Weygand-type oxidation. That the formation of arylazo-alkenes from steroidal α-bromo-ketones is a fairly general reaction was shown further by the reaction of 4β-bromo-5β-cholestan-3-one with phenylhydrazine, which gave a product considered to be 3-phenylazo-5β-cholest-3-ene.

It was of interest to investigate the reaction of these bromo-ketones with 1-methyl-1-phenylhydrazine, in order to determine whether osazone formation still took place when azo-alkene formation was blocked. Surprisingly, the results obtained indicate that it did. From the reaction of both 2α-bromo-5α-cholestan-3-one

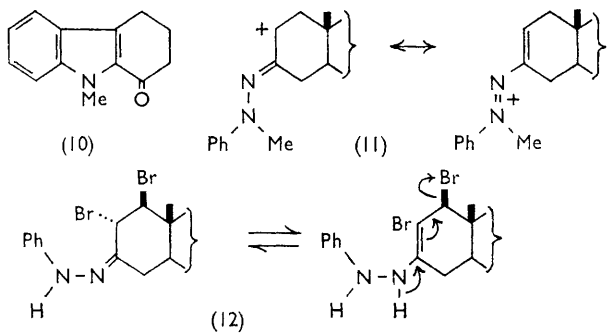


and 2,2-dibromo-5α-cholestan-3-one with this arylhydrazine was isolated a bright yellow substance, which contained no bromine or oxygen, of formula $C_{41}H_{57}N_3$.

[10] F. G. Chattaway and co-workers, *J. Amer. Chem. Soc.*, 1932, **54**, 263, and earlier papers.

[11] H. Simon, G. Heubach, and H. Wacker, *Chem. Ber.*, 1967, **100**, 3101, 3106.

The ultraviolet and visible spectrum did not correspond to any well known chromophore; the n.m.r. spectrum showed the presence of what appeared to be two *N*-methyl groups (sharp singlets at τ 5·81 and 6·90) and nine aromatic protons. The presence of three nitrogen atoms in the molecule can only be explained on the assumption that a Fischer indole or other cyclization has taken place from an initially N_4 structure. The formula (9a) is thought to represent the structure of the yellow compound; it is preferred to the possible alternative structure in which cyclization occurred on to C-1 because of the unlikelihood of cyclization to such a hindered position. An attempt was made to verify this assignment by the preparation of a phenylhydrazone or *N*-methylphenylhydrazone of the known 9-methyl-3,4-dihydrocarbazol-1(2*H*)-one (10), for comparison of ultraviolet spectra, but no reaction could be induced except in boiling dimethylformamide, when unidentified tars were obtained. This lack of reaction with the carbazole (10) shows that the ketone (9b) was probably

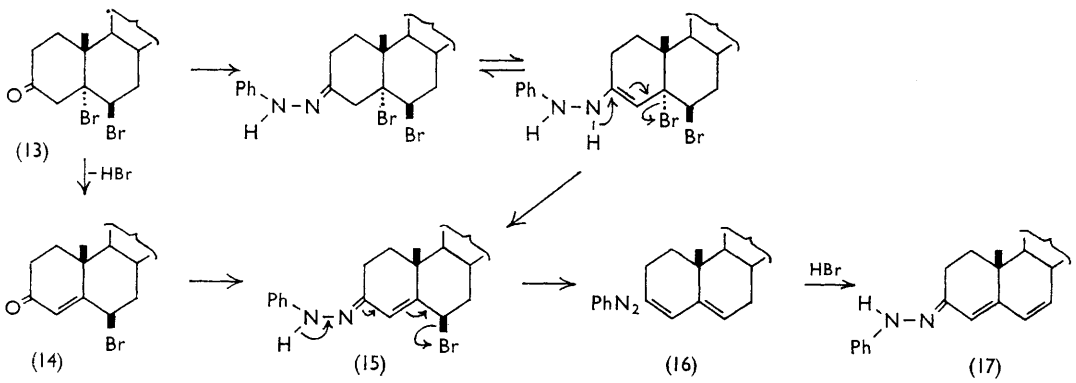


not an intermediate in the formation of the hydrazone (9a), which presumably arose by cyclization of cholestane-2,3-dione bis-1-methyl-1-phenylhydrazone. This osazone cannot arise through an azo-alkene but the cation (11) may be the intermediate, or alternatively, a direct nucleophilic displacement of bromine by the arylhydrazine may take place.

Other dibromo-cholestanones were then investigated. 2α,4α-Dibromo-5a-cholestan-3-one gave a very complex mixture of products, some of which were highly coloured, so it is evident that some elimination of bromine must have taken place. The reaction of 2,4-dinitrophenylhydrazone with this ketone similarly gives a complex mixture.[9]

Reaction of 1α,2β-dibromo-5α-cholestanone with phenylhydrazine in hot ethanol gave a good yield of 2-bromocholest-1-en-3-one phenylhydrazone (4b), *i.e.* the β-bromo-substituent was eliminated in preference to the α. The simplest explanation of this finding is that the elimination takes place through the ene-hydrazine form of the initially formed phenylhydrazone (12). Although the ene-hydrazine form of arylhydrazones is thought to be an intermediate in the Fischer indole synthesis, it does not seem to have been suggested as an intermediate in the β-elimination reactions of arylhydrazones, many of which occur readily.[12]

The reaction of 5α,6β-dibromocholestan-3-one (13) with phenylhydrazine in the usual way led to the rapid decomposition of the ketone, but in cold pyridine a bright orange, bromine-free compound was obtained in good yield. Its analytical and spectroscopic properties, its ready isomerisation to the colourless, unstable phenylhydrazone (17) of cholesta-4,6-dien-3-one, and its alternative preparation from 6β-bromocholest-4-en-3-one show that it is 3-phenylazocholesta-3,5-diene (16), the first representative of the class of azo-alkadienes. Based on the phenomena already observed with the other bromo-ketones, a mechanism for the formation of this product can be suggested, based on an ene-hydrazine elimination to give 6β-bromocholest-4-en-3-one phenylhydrazone (15), followed by a vinylogue of the α-bromo-ketone ⟶ azoalkene elimination reaction. Since the dibromo-ketone (13) is dehydrobrominated by cold pyridine to 6β-bromocholest-4-en-3-one (14), some of the azo-alkadiene (16) must also arise by this route, but the rate of formation of the azo-compound (16) is much faster than dehydrobromination of the dibromo-ketone (13) in the absence of phenylhydrazine.



The u.v.-visible spectrum of this product (and of its

[12] For example, M. G. Blair, D. Lipkin, J. C. Sowden, and D. R. Strobach, *J. Org. Chem.*, 1960, **25**, 1679; M. Miyamoto, Y. Kawamatsu, M. Shinohara, Y. Nakadaira, and K. Nakanishi, *Tetrahedron*, 1966, **22**, 2785.

p-tolyl analogue) appears to be anomalous. In the arylazo-alkenes there is a bathochromic shift of both the $\pi \longrightarrow \pi^*$ and $n \longrightarrow \pi^*$ bands with respect to the position which they occupy in arylazo-alkanes.[13,14] In the arylazo-alkadienes, one would expect, *a priori*, a further red shift and increase of intensity of both bands. This is indeed true of the $\pi \longrightarrow \pi^*$ band, but the $n \longrightarrow \pi^*$ band shows no further shift and becomes partially obscured by the intense $\pi \longrightarrow \pi^*$ band. The assignment of the semi-obscured maximum in the visible spectra of these compounds as an $n \longrightarrow \pi^*$ transition is supported by the fact that it is c.d. active, one extremum of a Cotton effect being discernable in the o.r.d. spectrum.

During the course of this work, the incidental observation was made that the phenylhydrazones of 5α-cholest-1-en-3-one and 5α-cholest-4-en-3-one form fairly stable, bright yellow compounds with halogen acids. These are evidently salts of the arylhydrazone [15] ($\nu_{max.}$ *ca.* 270 mμ, broad), but whereas the compounds from cholest-4-en-3-one phenylhydrazone contain the expected 1 mol. of hydrogen halide, that from cholest-1-en-3-one contains 2 mol.; the mode of bonding, if any, of the second hydrogen bromide could not be determined.

EXPERIMENTAL

The identity of compounds was proved where necessary by mixed m.p., infrared spectroscopy, and t.l.c. Rotations and u.v. spectra were determined for chloroform solutions, the latter at 23°.

Reaction of Ketones with Arylhydrazines.—1. *2α-Bromocholestan-3-one.* (*a*) The ketone (2a) (5·4 g.) in hot ethanol (500 ml.) containing acetic acid (1 drop) was treated with phenylhydrazine (2·5 ml.). Yellow-orange plates crystallized out almost immediately. Cooling the solution and recrystallization of the product from ethyl acetate afforded *3-phenylazo-5α-cholest-2-ene* (3a) (3·25 g., 70%), m.p. 178—179°, $[\alpha]_D$ +94·0° (*c* 0·42), $\lambda_{max.}$ 311 and 434 mμ (ε 21,400 and 400) (Found: C, 83·7; H, 10·4; N, 6·3, 6·4. $C_{33}H_{50}N_2$ requires C, 83·5; H, 10·6; N, 5·9%).

The product was recovered unchanged (82%), m.p. and mixed m.p. 175—177°, when boiled for 1·75 hr. in 2·5% ethanolic acetic acid. It was similarly recovered (91%), m.p. and mixed m.p. 175—177°, after being boiled for 3 hr. with sodium methoxide in methanol (1N).

(*b*) The bromo-ketone (2a) (55 mg.) in warm pyridine (2 ml.), treated with phenylhydrazine (2 drops), gave, after addition of water and recrystallization of the product from ethyl acetate, the same product (37 mg., 66%), m.p. 176—177°.

(*c*) The bromo-ketone (2a) (300 mg.) was treated with phenylhydrazine (0·07 ml.) in cold dioxan (5 ml.) during 2 min. The colourless solution obtained was partitioned between light petroleum and water, and the light petroleum solution washed with water. A colourless solution was obtained which after a brief interval turned suddenly yellow, and on evaporation 3-phenylazocholest-2-ene was obtained.

(*d*) The bromo-ketone (2a) (100 mg.), in boiling ethanol (20 ml.), was treated with phenylhydrazine (0·2 ml.) and acetic acid (0·5 ml.) during 1 hr. Cooling the concentrated solution resulted in the precipitation of a gelatinous yellow precipitate. This was collected and water was added to the mother liquors to precipitate a further quantity of 5α-cholestane-2,3-dione bisphenylhydrazone (7) (total yield 10 mg., 91%), m.p. 205—209° (decomp.), which was purified by passing a light petroleum solution of the product down a column of silica gel, to give an analytical sample, m.p. 206—209° (decomp.), $[\alpha]_D$ +132° (*c* 0·36) (Found: C, 80·6; H, 9·9; N, 9·35. $C_{39}H_{56}N_4$ requires C, 80·6; H, 9·9; N, 9·65%).

The same product was obtained when 3-phenylazo-5α-cholest-2-ene (3a) was treated with phenylhydrazine and acetic acid in hot ethanol. Addition of 2,4-dinitrofluorobenzene and solid sodium carbonate to the mother liquors gave, after 2 hr., a solution containing 2,4-dinitrodiphenylamine (t.l.c.), by comparison with an authentic sample.

2. *5α-Cholest-1-en-3-one* (5a). The *phenylhydrazone* (4a), prepared in the usual way, crystallized from ethyl acetate–light petroleum as colourless plates (45%), m.p. approx. 205° (decomp., rapid heating), $[\alpha]_D$ +88·5° (*c* 0·24), $\lambda_{max.}$ 246, 303, and 322·5 mμ (ε 10,000, 27,800, and 34,600) (Found: N, 5·65. $C_{33}H_{50}N_2$ requires N, 5·9%). The substance began to decompose in air after 1—2 hr. The *bis-hydrogen bromide* compound was obtained in quantitative yield by treating a solution of the phenylhydrazone in ether with an excess of a solution of hydrogen bromide in acetic acid (4·5%). It crystallized from light petroleum as bright yellow needles, m.p. 187·5—188° (decomp., rapid heating), $[\alpha]_D$ −113° (*c* 0·31), $\lambda_{max.}$ 303 and 321 mμ (ε 16,600 and 18,250) (Found: C, 62·2; H, 8·1; Br, 25·6; N, 4·4. $C_{33}H_{52}Br_2N_2$ requires C, 62·3; H, 8·2; Br, 25·1; N, 4·4%). The product decomposed with evolution of fumes of hydrogen bromide on prolonged boiling in solution.

3. *2,2-Dibromo-5α-cholestan-3-one* (2b). (*a*) The dibromoketone [16] (0·5 g.), in the minimum volume of boiling ethanol was treated with phenylhydrazine (0·5 ml.). On cooling the solution after 2 min. an orange precipitate was obtained, which was collected, washed with saturated sodium hydrogen carbonate solution, and recrystallized from acetone, affording orange rods (305 mg., 60%) of *2-bromo-3-phenylazo-5α-cholest-2-ene* (3b), m.p. 164—165°, $[\alpha]_D$ +103° (*c* 0·30), $\lambda_{max.}$ 335 and 455 mμ (ε 54,600 and 710) (Found: C, 71·7; H, 8·8; Br, 14·55; N, 5·2. $C_{33}H_{49}BrN_2$ requires C, 71·6; H, 8·9; Br, 14·4; N, 5·1%).

The product (143 mg.) suspended in ethanol (15 ml.) containing pyruvic acid (1 ml.), was boiled under reflux for 5 hr., during which period it dissolved to give a pale yellow solution. Addition of water and cooling yielded 2-bromo-5α-cholest-1-en-3-one phenylhydrazone (4b) (see below) (115 mg., 81%), m.p. 180—183° (decomp., rapid heating).

(*b*) When the crude product as obtained in (*a*) above was boiled with acetone without prior washing, the solution rapidly turned pale yellow, and on concentration and cooling, pale yellow crystals (65%) of 2-bromo-cholest-1-en-3-one phenylhydrazone, identical with the samples obtained below, were deposited.

(*c*) Further action of phenylhydrazine in boiling ethanol on the ketone (103 mg.) produced cholestane-2,3-dione bisphenylhydrazone (7) (44 mg., 40%) (from acetone–

[13] J. Buckingham and R. D. Guthrie, unpublished work.
[14] A. J. Bellamy and R. D. Guthrie, *J. Chem. Soc.*, 1965, 2788.
[15] F. Schmidt, *Annalen*, 1889, **252**, 300.
[16] C. W. P. Crowne, R. M. Evans, G. F. H. Green, and A. G. Long, *J. Chem. Soc.*, 1956, 4351.

ethanol) (charcoal), identical with the previously obtained sample.

4. 2-*Bromocholest*-1-*en*-3-*one* (5b). The ketone [17] (160 mg.) on treatment with phenylhydrazine (0·15 ml.) and acetic acid (0·05 ml.) in hot ethanol (10 ml.) gave after 3 min. pale yellow needles (120 mg., 63%) of the *phenylhydrazone* (4b), m.p. 180—182° (decomp., rapid heating), $[\alpha]_D$ +57·3° (*c* 0·34), $\lambda_{max.}$ 328 mμ (ε 30,500) (Found: C, 71·8; H, 8·7; Br, 14·3; N, 4·8. $C_{33}H_{49}BrN_2$ requires C, 71·6; H, 8·9; Br, 14·4; N, 5·1%).

5. 5α-*Cholestane*-2,3-*dione*. The crude dione [18] (50 mg.), on treatment with phenylhydrazine in acid ethanol afforded a sample of the osazone (7) (55 mg., 77%), identical with previously obtained specimens.

6. 4β-*Bromo*-5β-*cholestan*-3-*one*. The bromo-steroid (crude product [19]) (0·5 g.) was dissolved in hot ethanol (40 ml.) and the filtered solution was concentrated by boiling to about 15 ml., and cooled to 40—50°. Phenylhydrazine (0·15 ml.) was added, followed by acetic acid (1 drop). After development of the orange colour (*ca.* 20 sec.) the solution was chilled in acetone–Drikold, the precipitated solid collected, and a little water added to the mother-liquors to precipitate a further quantity of crude material. The combined air-dried product was recrystallized from chloroform–methanol and then from acetone, affording orange feathery needles of 3-*phenylazo*-5β-*cholest*-3-*ene* (90 mg., 18%), m.p. 122°, $[\alpha]_D$ +30·0° (*c* 0·62), $\lambda_{max.}$ 311 and 431 mμ (ε 29,300 and 394) (Found: C, 83·25; H, 10·7; N, 5·8. $C_{33}H_{50}N_2$ requires C, 83·5; H, 10·6; N, 5·9%).

7. 2α,4α-*Dibromo*-5α-*cholestan*-3-*one*. By reaction with phenylhydrazine as in 4, a dark red solution containing a large number of components (t.l.c.) was obtained. Evaporation of the solution gave an intractable oily product.

8. 1α,2β-*Dibromo*-5α-*cholestan*-3-*one*. The reaction, on 100 mg. of ketone,[17] was carried out as in 4. After 15 min. at room temperature the solution was cooled overnight, yielding pale yellow needles (76 mg., 74%) of 2-bromo-5α-cholest-1-en-3-one phenylhydrazone (4b), m.p. 182—184° (decomp., rapid heating).

9. 5α,6β-*Dibromo-cholestan*-3-*one* (13). The dibromo-ketone [20] (1 g.) was treated with phenylhydrazine (0·5 ml.) in cold pyridine (10 ml.). The solution rapidly turned orange and a crystalline precipitate appeared after a few min. After 1 hr. this was collected and a little water was added to the mother-liquors to precipitate a further quantity of solid. The combined product was washed with water and air-dried, affording 3-*phenylazocholesta*-3,5-*diene* (16) (0·62 g., 73%), m.p. 164—166°, $[\alpha]_D$ −73·8° (*c* 0·56), $\lambda_{max.}$ 359 and 436 mμ (ε 34,100 and 1000) (Found: C, 84·0; H, 10·35; N, 6·05. $C_{33}H_{48}N_2$ requires C, 83·8; H, 10·2; N, 5·9%). The product could be recrystallized (as orange rhombs) from ethyl acetate after first being freed of traces of base by crystallization from cold chloroform–methanol; the melting point did not change.

Reaction of the dibromo-ketone with *p*-tolylhydrazine in the same way gave orange blades (79%) of 3-p-*tolylazo-cholesta*-3,5-*diene*, m.p. 183—185° (from ethyl acetate), $[\alpha]_D$ −85·9° (*c* 0·54), $\lambda_{max.}$ 362 and 440 mμ (ε 50,700 and 1400) (Found: C, 84·2; H, 10·3; N, 5·8. $C_{34}H_{50}N_2$ requires C, 83·9; H, 10·35; N, 5·8%).

The azo-diene (16) (0·55 g.) in boiling ethyl acetate (25 ml.) was treated with a solution of hydrogen bromide in acetic acid (45%; 10 drops) during 2—3 min. Addition of methanol to the yellow solution and cooling, followed by recrystallization of the precipitated solid from light petroleum, gave off-white plates (0·42 g., 76%) of *cholesta*-4,6-*dien*-3-*one phenylhydrazone* (17), m.p. 135—152° (decomp.), $[\alpha]_D$ approx. −80° (solution decomposed rapidly) (*c* 0·56), $\lambda_{max.}$ 350 mμ (ε 48,700) (methanol + 0·2% dioxan) (Found: C, 83·65; H, 10·2; N, 6·2. $C_{33}H_{48}N_2$ requires C, 83·8; H, 10·2; N, 5·9%).

10. 6β-*Bromocholest*-4-*en*-3-*one* (14). The ketone [21] (0·5 g.) was treated with phenylhydrazine in pyridine as described in 9. After 10 min. the precipitate was collected and twice recrystallized from cold chloroform–methanol, affording 3-phenylazocholesta-3,5-diene (16) (0·39 g., 76%), m.p. 162—164°.

11. *Cholesta*-4,6-*dien*-3-*one*. The ketone (B.D.H. Ltd.) treated with phenylhydrazine in hot ethanol containing acetic acid during 1 min. and the product recrystallized from light petroleum, gave a sample of the phenylhydrazone (63%), having an identical infrared spectrum to that obtained in 9.

12. *Cholest*-4-*en*-3-*one*. The phenylhydrazone, prepared in the usual way, crystallized from chloroform–methanol as needles (50%), m.p. 151—152° (decomp.; rapid heating) (lit.,[22] 152°), $[\alpha]_D$ +208° ⟶ +186° (20 min., due to decomposition) (*c* 0·42), $\lambda_{max.}$ 320 mμ (ε 27,300) (Found: N, 6·15. $C_{33}H_{50}N_2$ requires N, 5·9%).

The phenylhydrazone formed a *mono-hydrogen bromide salt*, microscopic bright yellow rods from cold chloroform–light petroleum (79%), m.p. 169·5—171° (decomp.), $[\alpha]_D$ +318° (*c* 0·42), $\lambda_{max.}$ 321 mμ (ε 32,200) (Found: C, 71·6; H, 9·0; Br, 14·3; N, 5·1. $C_{33}H_{51}BrN_2$ requires C, 71·3; H, 9·25; Br, 14·4; N, 5·0%).

The *mono-hydrogen chloride salt* had m.p. 155—157° (decomp; with extensive prior decomposition), $[\alpha]_D$ +607° (*c* 0·59), $\lambda_{max.}$ 321 mμ (ε 28,300) (Found: Cl, 7·2; N, 5·7. $C_{33}H_{51}ClN_2$ requires Cl, 6·9; N, 5·5%).

The hydrogen bromide salt (107 mg.) in chloroform (2 ml.) was treated with ethanol (10 ml.), followed by water (5 ml.). The precipitate thus obtained was dried *in vacuo* to give a white solid (67 mg., 84%), m.p. 149—150° (decomp., rapid heating), having an identical infrared spectrum to the parent phenylhydrazone.

Reaction of Bromo-ketones with 1-*Methyl*-1-*phenylhydrazine*. —(*a*) 2α-Bromo-5α-cholestan-3-one (2a) (250 mg.) in boiling ethanol (25 ml.) was treated with 1-methyl-1-phenylhydrazine (0·5 ml.) and acetic acid (0·5 ml.). A deep orange colour soon developed. Addition of water to the solution precipitated a sticky yellow mass, which was twice recrystallized from ethyl acetate–light petroleum, giving bright yellow needles (92 mg., 29%) of what is considered to be the *hydrazone* (9a), m.p. 211·5—212·5° $[\alpha]_D$ −750° (*c* 0·40), $\lambda_{max.}$ 238·5, 305·5, 349, and 366 mμ (ε 23,000, 16,750, 10,900, and 10,200), $\lambda_{min.}$ 276·5 and 326 mμ (ε 6100 and 10,000) (hexane) (Found: C, 83·0; H, 9·5; N, 7·1. $C_{41}H_{57}N_3$ requires C, 83·2; H, 9·7; N, 7·1%).

(*b*) 2,2-Dibromo-5α-cholestanone (2b) (300 mg.), treated similarly, gave after 3 hr. a dark red solution which on cooling overnight deposited yellow needles of the same compound (103 mg., 33%), m.p. and mixed m.p. 210·5—212·5° (from ethyl acetate–ethanol).

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Action of Arylhydrazines on 9-*Methyl*-1(2H)-*one*-3,4-*dihydrocarbazole* (10).—(*a*) The carbazole (m.p. 98—99°; lit.,[23] 101°) (282 mg.) in boiling ethanol (25 ml.) was treated with 1-methyl-1-phenylhydrazine (0·2 ml.) and acetic acid (1 ml.) during 3 hr. Addition of water and cooling gave unchanged starting material (262 mg., 93%).

(*b*) To the carbazole (300 mg.) in boiling ethanol (25 ml.) and hydrochloric acid (12N; 5 ml.) containing sodium acetate (2 g.) and phenylhydrazine hydrochloride (0·5 g.) was added sufficient water to just dissolve the solids in the boiling solution. After being boiled for 4·5 hr. the solution was left to stand overnight, concentrated, cooled, and seeded to yield unchanged starting material (275 mg., 93%), m.p. and mixed m.p. 99—101°. (A similar result was obtained when the sodium acetate was omitted.)

(*c*) The carbazole (300 mg.) was treated with phenylhydrazine (0·3 ml.) in boiling dimethylformamide (15 ml.) for 30 min. The orange solution was worked up to give a dark red oil (0·7 g.) which could not be crystallized; t.l.c. indicated that it contained substantial amounts of unchanged starting material.

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