SIMPLIFIED ANALOGUES OF LYSERGIC ACID

IV. SYNTHESIS OF 1-METHYL-1,2,3,7,8,9-HEXAHYDRO-5,6-BENZQUINOLINE

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Summary

The lysergic acid analogue 1-methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (III; R=H) was prepared from 2-bromo-α-tetralone by two parallel routes. The first, a seven-stage sequence, involved conversion of the starting material into 2-[*N*-methyl-*N*-(2′-oxo-n-propyl)]-amino-α-tetralone (IX) via its ethylene ketal, followed by ring closure to the tricyclic 1-methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (V). This was transformed into its ethylene dithioketal (XXIX) and thence by desulphurization into (III; R=H).

The second pathway, a five-step synthesis, utilized dimethylaminoacetone to obtain directly the quaternary diketone (XXI), which was cyclized to 1,1-dimethyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinolinium bromide (XXV), identical with that obtained by the alternative route.

I. INTRODUCTION

The marked pharmacological activity found in *N*-alkylated derivatives of 1,2,3,4-tetrahydro-2-naphthylamine (I), particularly in the *N*-methyl-*N*-n-propyl compound (II) (Cymerman Craig, Moore, and Ritchie 1959) which exhibited high and specific anti-serotonin activity (Pennefather and Thorp 1958) and hypotensive action (Pennefather and Thorp 1959), makes of considerable interest the preparation of 1-methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline-3-carboxylic acid (III; R=COOH) and of the corresponding base (III; R=H) constituting the structure of rings A, C, and D of the lysergic acid molecule (IV), but lacking ring B. These syntheses have been examined, and considerable progress made. In view of a recent publication (Leemann and Fabbri 1959), our results leading to the preparation of 1-methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (III; R=H) are now reported.

The synthesis of the tricyclic conjugated ketone 1-methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (V) was carried out by two pathways. Bromination of α-tetralone by a modification of the method of Wilds (1942) and Wilds and Johnson (1946) gave 2-bromo-α-tetralone (VI; $R_1=R_2=H$) showing ultraviolet absorption similar to that of α-tetralone (Table 1). Hassner and Cromwell (1958*a*) have shown that the bromine in 2-bromo-4,4-dimethyl-α-tetralone (VI; $R_1=R_2=Me$) occupies the equatorial position ($\nu_{max.}$ 1705 cm^{-1}), while it is axial in both 2-benzyl-2-bromo- and 2-bromo-2-(α-bromobenzyl)-4,4-dimethyl-α-tetralone ($\nu_{max.}$ 1692 and 1690 cm^{-1} respectively).

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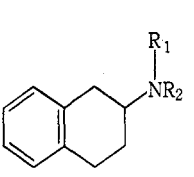
It is known that an equatorial bromine adjacent to the C=O of cyclohexanones effects a displacement of +16 to +22 cm^{-1} in the carbonyl frequency (Jones *et al.* 1952), while an axial bromine, which causes only a slight shift in the C=O region, will result in a bathochromic displacement of 10 to 15 mμ in the high-intensity (K) band of the ultraviolet spectrum (Cookson 1954). Moreover, equatorial carbon-bromine linkages in steroids have been shown to absorb at 703–772 cm^{-1}, and the corresponding axial linkages at 591–692 cm^{-1} (Barton, Page, and Shoppee 1956).



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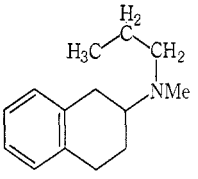

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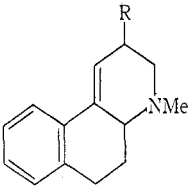

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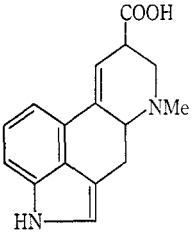

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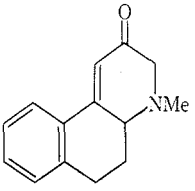

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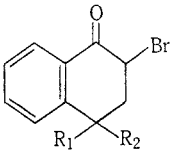

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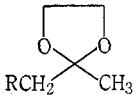

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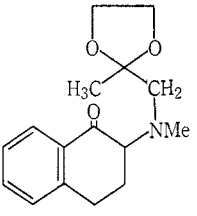

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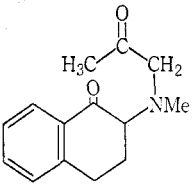


(IX)

Since the infrared absorption of 2-bromo-α-tetralone ($\nu_{max.}$ 1685, 756, 730, and 642 cm^{-1}) was identical with that of α-tetralone ($\nu_{max.}$ 1685, 761, and 731 cm^{-1}), the bromine in the former compound appears to be in the axial position, as confirmed by the bathochromic shift (+7 mμ) in the ultraviolet. The absorption band at 642 cm^{-1}, in a region characteristic of an axial carbon-bromine bond, is further evidence for the axial conformation of the halogen atom in 2-bromo-α-tetralone.

TABLE 1

ULTRAVIOLET LIGHT ABSORPTION IN 95% ETHANOL

Compound	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
α-Tetralone	249 294	11800 1800
2-Bromo α-tetralone (VI; $R_1=R_2=H$)	256 297	10400 3000
4,4-Dimethyl-α-tetralone*	246 289	10900 1500
2-Bromo-4,4-dimethyl-α-tetralone (VI; $R_1=R_2=Me$)*	251 294	11200 1800
2-Benzyl-4,4-dimethyl-α-tetralone*	248 300	12600 1700
2-Benzyl-2-bromo-4,4-dimethyl-α-tetralone*	258 292	10600 2500
2-Benzyl-α-tetralone†	247 292	12600 1700
2-[*N*-Methyl-*N*-(2′-oxo-n-propyl)]amino-α-tetralone 2′-ethylene ketal (VIII)	247 295	14000 2400
2-[*N*-Methyl-*N*-(2′-oxo-n-propyl)]amino-α-tetralone (IX)	250 298	15000 1800
1-Methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (V)	228 233‡ 298	8600 7800 14200
1-Oxo-1,2,3,4,9,10-hexahydrophenanthrene (XII)‖	230 236 298	13000 13000 17500
3,3a,4,5-Tetrahydrobenz[e]inden-2-one (XIII)‖	223·5 287	12000 24000
Benzalacetone (XIV)‖	220·5 286	12000 23500
Hydrobromide of (V)	228 235‡ 295	10800 9500 20300
3-Hydroxy-1-methyl-7,8-dihydro-5,6-benzquinolinium hydroxide betaine (XVIII)	251 355	13900 5300

TABLE 1 (*Continued*)

Compound	$\lambda_{max.}$ (mμ)	$\varepsilon_{max.}$
4-Acetyl-4,5,5a,6-tetrahydro-9-hydroxy-7-methylindolo(4,3,-fg)-quinolinium hydroxide betaine (XX)§	246 351	29000 6900
NN-Dimethyl-*N*-(α-oxo-2-tetralyl)-*N*-(2′-oxo-n-propyl)ammonium bromide (XXI ; X=Br)	234 255 295	14800 7050 5050
1,1-Dimethyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinolinium bromide (XXV ; X=Br)	231 265 310	8600 9600 19300
1,3-Dimethyl-3-hydroxy-5,6-(1′,2′-naphtho)-2,3-dihydro-1,4-oxazine (XV)	248 340	13600 6100
1,1-Dimethyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinolinium bromide ethylene dithioketal (XXVIII ; X=Br)	281 305	8500 4100
1-Methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline picrate (III ; picrate)	250 304 360	24600 12400 20700

* Hassner and Cromwell (1958*a*).
† Hassner, Cromwell, and Davis (1957).
‡ Inflexion.
|| Wilds *et al.* (1947).
§ Kornfeld *et al.* (1956).

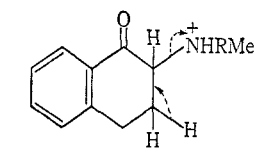
The first route for the preparation of the tricyclic ketone (V) was similar to that used by Kornfeld *et al.* (1956) for the synthesis of lysergic acid. The method of Kornfeld *et al.* (1956) for the reaction of bromoacetone ethylene ketal (Kuhn 1940) (VII ; R=Br) with anhydrous methylamine gave low yields in small-scale preparations, but alcoholic methylamine afforded good conversion to the desired methylaminoacetone ethylene ketal (VII ; R=CH_3NH). Reaction of this with 2-bromo-α-tetralone was complete after 6·5 hr and gave the ketal-ketone (VIII), showing infrared absorption at 1687 cm^{-1} as in 2-benzyl-α-tetralone ($\nu_{max.}$ 1686 cm^{-1}) (Hassner, Cromwell, and Davis 1957) and ultraviolet absorption similar to this compound (Table 1).

No ketonic derivatives of the ketal-ketone (VIII) could be prepared ; the substance was characterized as the picrate and hydrobromide. Leemann and Fabbri (1959) obtained this base from the same reactants after refluxing for 20 hr.

Removal of the protecting ketal group was effected by 3N hydrochloric acid, to give the unstable diketone (IX) as a yellow solid which rapidly darkened on exposure to air. To obtain this compound, it was found essential to conduct all operations under nitrogen and at the lowest possible temperatures, and to use peroxide-free solvents. It is noteworthy that Kornfeld *et al.* (1956) refer to the

corresponding diketone obtained in their lysergic acid synthesis, as " very susceptible to aerial oxidation ".

In presence of air, the hydrolysis of the ketal-ketone (VIII) led only to α-naphthol, probably arising by an intramolecular elimination of tertiary amine from the protonated 2-amino-α-tetralone (X) to give the dienone (XI) which would undergo a facile rearrangement to the resonance-stabilized α-naphthol.



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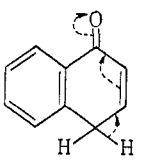

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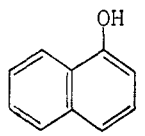

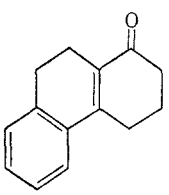

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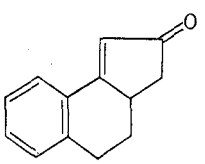

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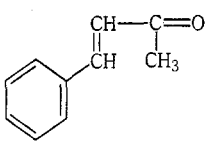

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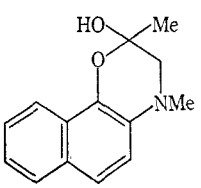

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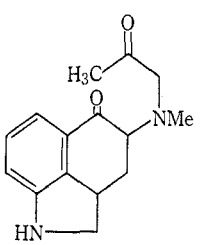

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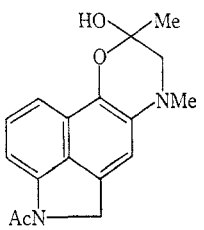
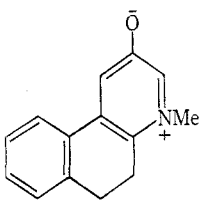


(XVII)

Again, no carbonyl derivatives could be prepared from (VIII), but a hydrobromide and a methiodide were obtained. The infrared absorption maxima of (IX) confirmed the presence of aliphatic (1710 cm^{-1}) and aromatic (1690 cm^{-1}) carbonyl functions, and its ultraviolet spectrum (Table 1) resembled that of its ketal-ketone precursor (VIII).

Cyclization of the diketone (IX) was achieved using sodium methoxide or potassium t-butoxide at low temperatures, affording the unstable tricyclic ketone (V). This showed ultraviolet absorption at 228, 233 (inflex.), and 298 mμ (Table 1), resembling that of the similar chromophoric systems in the phenanthrene derivative (XII) and the benzindene (XIII), and also in the open-chain analogue benzalacetone (XIV) (Table 1).

Cyclization of (IX) with 50% sulphuric acid at 0 °C (Adamson *et al.* 1937 ; Hills and McQuillin 1953) also resulted in a product identical with (V) in its light absorption properties. Its infrared spectrum demonstrated the disappearance of the aliphatic carbonyl group at 1710 cm^{-1}, and the shift of the aromatic carbonyl absorption from 1690 to 1665 cm^{-1} indicated the introduction of a conjugated double bond between the carbonyl group and the benzene ring



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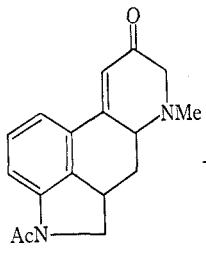

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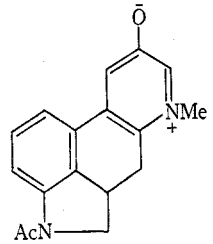

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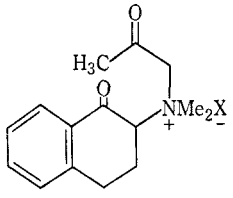
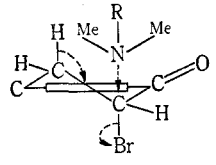


(XXI)



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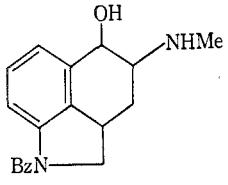

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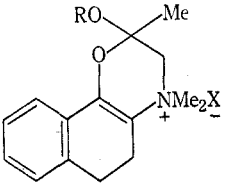


(XXIV)

in (V). The base was characterized as its hydrobromide and methiodide. Leemann and Fabbri (1959) were able to obtain the ketone (V) only by direct action of polyphosphoric acid on the ketal-ketone (VIII), and failed to achieve ring-closure under alkaline conditions.

An unsuccessful attempted cyclization of the diketone (IX) gave, on treatment with dry hydrogen chloride, a product which showed absorption at 3300 cm^{-1} (OH) but none in the 1650–1750 cm^{-1} region, and must therefore be the hydrochloride of the cyclic hemiketal (XV) formed by air oxidation of (IX) under acidic conditions. Its analysis and ultraviolet spectrum are in agreement with this aromatic structure. Kornfeld *et al.* (1956) obtained the closely related hemiketal (XVII) by treatment of (XVI) with acetic anhydride in methanol.

A water-soluble by-product obtained from the alkaline cyclization of (IX) showed ultraviolet absorption ($\lambda_{max.}$ 251 and 355 mμ) resembling that of a benzquinoline, and on the basis of its analysis, solubility, and light absorption must be the stable 3-hydroxy-1-methyl-7,8-dihydro-5,6-benzquinolinium hydroxide betaine (XVIII) formed by air oxidation of (V) in alkaline solution. The closely related betaine (XX) obtained by Kornfeld *et al.* (1956) from the tetracyclic ketone (XIX), absorbed at 246 and 351 mμ (Table 1).

The second synthetic pathway leading to the tricyclic ketone (V) involved the formation of the intermediate quaternary ammonium salt (XXI), prepared by reaction of dimethylaminoacetone with 2-bromo-α-tetralone.

A synthesis of dimethylaminoacetone from chloroacetone and aqueous dimethylamine (Stoermer and Dzimski 1895) gave low yields. However, the reaction of liquid dimethylamine and bromoacetone ethylene ketal proceeded smoothly in an autoclave to give the tertiary dimethylaminoacetone ethylene ketal (VII; R=NMe_2), and dimethylaminoacetone was prepared by the hydrolysis of this ketal, or more simply by direct interaction of bromoacetone with aqueous dimethylamine.

Dimethylaminoacetone was quaternized with methyl iodide to observe the effect of the quaternary ammonium group on the infrared spectrum. The carbonyl frequency in (2-oxo-n-propyl)trimethylammonium iodide was located at 1728 cm^{-1} both in a Nujol mull or in chloroform solution, compared with that of acetone at 1710 cm^{-1} (as a liquid film or in chloroform solution), while dimethylaminoacetone absorbed at 1705 cm^{-1}.

These variations may be explained by the opposing effects on the carbonyl frequency of the neighbouring groups. The powerfully electron-attracting quaternary ammonium group reduces the tendency of the keto-group to enolize, and thus effectively shortens or strengthens the carbonyl double bond, causing an increase in the frequency of the infrared absorption similar to that observed with an α-halogen substituent.

Conversely, the dimethylamino group reduces the frequency of the infrared carbonyl absorption in a manner similar to that in *NN*-dialkylsubstituted amides. This may arise either from hydrogen-bonding in the enolic form, or possibly by the dimethylamino group acting as an electron source, increasing the contribution of the enolic form to the keto-enol tautomerism. Both effects will make the C=O double bond longer and weaker thereby reducing its absorption frequency. A similar shift to a lower frequency was observed in pinacolone, in which the strongly electron-repelling t-butyl group reduces the carbonyl frequency to 1705 cm^{-1}.

In agreement with the generalizations made by Bergmann and Pinchas (1952) and Lagrange and Mastagli (1955) regarding ethyleneglycol cyclic ketals, the several dioxolanes examined all exhibited characteristic infrared absorption in the 1000–1200 cm^{-1} region, with bands at about 1050, 1080, 1130, and 1200 cm^{-1}, of which the first was the most intense. Attempted reaction of dimethylaminoacetone ethylene ketal with 2-bromo-α-tetralone in acetone, benzene, or xylene solution to give the quaternary salt was unsuccessful, resulting

solely in dehydrobromination with the formation of α-naphthol and the tertiary amine hydrobromide.

In the case of the unprotected dimethylaminoacetone, it was possible to isolate the desired quaternary ammonium bromide, but again an appreciable amount of elimination occurred simultaneously.

Reactions of amines with 2-halo-α-tetralones and cyclohexanones to give substitution products are known (Hassner, Cromwell, and Davis 1957), but the corresponding elimination reaction often occurs also and the dehydrohalogenated compound may be the major or sole product when tertiary bases are used (Hassner, Cromwell, and Davis 1957). Thus 2-bromo-6-methyl-α-tetralone gave 6-methyl-1-naphthol when heated with diethylaniline (Fieser and Dunn 1936), 2-bromocyclohexanone and aniline gave cyclohexene (Koetz 1907), and 2-bromo-4,4-dimethyl-α-tetralone underwent both dehydrobromination and substitution by morpholine (Hassner and Cromwell 1958*b*).

In the non-polar solvents used, nucleophilic attack by the tertiary nitrogen may be expected to occur on the halogen-bearing carbon atom of the 2-bromo-α-tetralone, known from its ultraviolet and infrared absorption to possess the halogen in the axial conformation, as shown in (XXII).

The transition state formed on the approach of the tertiary nitrogen may then react in two ways: (i) by an S_N2 mechanism, to yield the quaternary ammonium salt, e.g. (XXI), or (ii) by the collapse of the transition state, to give a facile *trans*-diaxial elimination of hydrogen bromide resulting in the dienone (XI) which rearranges to 1-naphthol.

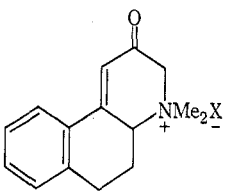
Steric hindrance due to the increased spatial requirements of the tertiary amines, compared with those of the corresponding secondary bases, particularly in the transition state formed from (XXII) and possibly also in the quaternary salt (XXI), will lead to an attack on the axial hydrogen atom in (XXII), and may be readily held to account for the high proportion of elimination observed in the reactions employing dimethylaminoacetone. This conclusion is supported by the facts that (i) the secondary base, methylaminoacetone ethylene ketal (VII; R=NHMe) reacted normally with 2-bromo-α-tetralone to give (46%) the substitution product (VIII); (ii) the tertiary base (VII; R=NMe_2) gave none of the substitution product, only elimination (43%) occurring; (iii) the spatially less-demanding dimethylaminoacetone gave both substitution (16·5%) and elimination (33%) products.

When the functional groups were reversed, and 2-dimethylamino-α-tetralone treated with bromoacetone, only dehydrobromination (29%) occurred. Steric considerations must again be operative in this instance, as the related secondary amine (XXIII) was reported to condense with bromoacetone by a substitution reaction in 40% yield (Kornfeld *et al.* 1956).

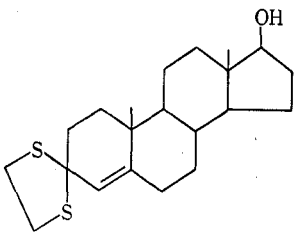
The quaternary diketone (XXI) showed infrared absorption at 3220 cm^{-1} (OH) suggesting that this material existed partially in the tricyclic hemiketal form (XXIV; R=H). Absorption bands were also present at 1675 cm^{-1} (aromatic C=O) and 1710 cm^{-1} (aliphatic C=O). The existence of the hemiketal (XXIV; R=H) was shown by its ready conversion to a methyl ether (XXIV;

R=Me) with methanolic hydrogen chloride. Similar hemiketals were reported by Kornfeld *et al.* (1956) in the indoloquinoline series.

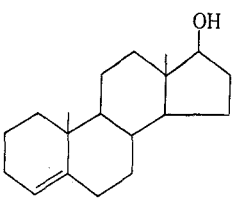
Cyclization of the quaternary diketone (XXI) was carried out by means of sodium methoxide in methanol or ethanol at −15 to −20 °C to give the tricyclic quaternary ketone (XXV; X=Br) which had infrared absorption identical with that of the methiodide obtained from (V), to which it was converted by means of sodium or potassium iodide in acetone. Mixed melting points established the identity of the two substances (XXV; X=I) and thus confirmed that the stereochemistry of the tricyclic ketone (V) and its quaternary salts (XXV) was the same by both methods of synthesis employed.



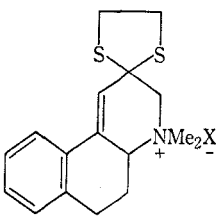
(XXV)



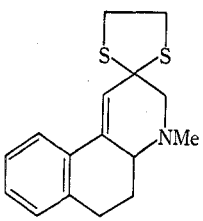
(XXVI)



(XXVII)



(XXVIII)



(XXIX)

The quaternary series, (XXI) and (XXV), were found to exhibit stability far superior to their tertiary analogues (IX) and (V). This was due not only to the greater ease of handling of crystalline solids rather than high-boiling liquids, but also to the electronic influence of the nitrogen substituent. Whereas the electron-attracting quaternary ammonium grouping $-\overset{+}{N}R_3$ stabilizes the neighbouring carbonyl system in the α-tetralone structure by resisting its enolization, the corresponding tertiary amine is able, by the use of its free electron pair, to weaken the carbonyl linkage and encourage enol formation, leading to ready aerial oxidation of the resulting dihydronaphthalene structure at neutral or alkaline pH values.

Attempts to form the dibenzyl mercaptal of the tricyclic quaternary ketone (XXV; X=Br) by reaction with benzyl thiol in presence of zinc chloride (Hauptmann 1947), dry hydrogen chloride or perchloric acid (d'Ouville, Myers, and Connor 1939; Hauptmann and Campos 1950), or boron trifluoride-etherate (Fieser 1954) were unsuccessful.

Using testosterone as a model for the αβ-unsaturated cyclic carbonyl system, reaction with ethanedithiol catalysed by boron trifluoride-etherate, gave a quantitative yield of the ethylene dithioketal (XXVI) which was satisfactorily desulphurized by means of Raney nickel to give the known Δ^4-androsten-17-ol (XXVII).

Using this method, the tricyclic quaternary ketone (XXV; X=Br) was converted to its ethylene dithioketal (XXVIII), characterized as the methopicrate.

Demethobromination of the quaternary dithioketal *in vacuo* was carried out by the method of Murphy and May (1954), May and Murphy (1955), and May and Fry (1957), and led to the amorphous tertiary dithioketal (XXIX). Evidence that the double bond in (XXIX) had not undergone isomerization into ring C to give a 3,4-dihydronaphthalene derivative was provided (i) by the fact that both the tertiary dithioketal and its hydrochloride showed an absorption maximum at 1630 cm^{-1}. The absence of a shift in the frequency of the C=C absorption on salt formation demonstrates that the double bond is in the βγ-position (Leonard and Gash 1954) whereas in αβ-unsaturated amines, salt formation is accompanied by a shift of *c.* 25 cm^{-1} due to the transformation $>C=C-N<$ to $>CH-C=\overset{+}{N}<$; (ii) by the presence in (XXIX) of an absorption band at 805 cm^{-1}, characteristic of a trisubstituted ethylene, but absent in tetrasubstituted olefins.

Desulphurization of (XXIX) with Raney nickel gave the amorphous 1-methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline (III; R=H), characterized as the picrate and (via the methiodide) as the methopicrate. Again both the tertiary base and its hydrobromide showed absorption maxima at 1605 cm^{-1}, demonstrating that the position of the βγ-double bond had not changed on desulphurization.

Further work in this field is in progress.

II. Experimental

Ultraviolet absorption spectra were determined in 95% ethanol on a Hilger "Uvispek" instrument. Infrared spectra were measured as capillary films or Nujol mulls unless otherwise indicated, on a Perkin-Elmer "Infracord" or Model 21 spectrophotometer, and melting points were taken on a Kofler block.

(*a*) *2-Bromo-α-tetralone.*—A stream of nitrogen was bubbled through a solution of α-tetralone (146 g; 1 mole) in carbon tetrachloride (500 ml) and a solution of bromine (160 g; 1 mole) in carbon tetrachloride was added dropwise. When the exothermic reaction had subsided, the mixture was warmed on the steam-bath for 1 hr and then distilled *in vacuo*, affording 2-bromo-α-tetralone (130·2 g, 59% yield) as a lachrymatory oil, b.p. 149–152 °C/2 mm, n_D^{22} 1·6135, which solidified to needles, m.p. 37–39 °C. Light absorption: $\nu_{max.}$ 1685 (aromatic C=O) and 642 cm^{-1} (axial C-Br).

(*b*) *Methylaminoacetone Ethylene Ketal.*—(i) A mixture of bromoacetone ethylene ketal (30 g; 0·165 mole) (b.p. 160 °C/710 mm, n_D^{23} 1·4752; Kuhn 1940) and liquid methylamine (80 g; 2·5 moles) was sealed in a 400 ml capacity autoclave and heated at 130 °C for 36 hr. The cooled mixture was stirred with ether and concentrated KOH soln., and the dried (sodium sulphate) ethereal extracts afforded on distillation methylaminoacetone ethylene ketal (2 g, 10% yield), b.p. 93 °C/70 mm, n_D^{23} 1·4340. Light absorption: $\nu_{max.}$ 1208, 1130, 1078, 1048 cm^{-1} (ketal).

(ii) A mixture of bromoacetone ethylene ketal (20 g; 0·11 mole) and ethanolic methylamine (100 ml, 30% v/v; 1 mole) was sealed in a 650 ml capacity autoclave and heated at 100 °C for

64 hr. Addition of 4 volumes of ether to the cooled solution precipitated methylamine hydrochloride (11·8 g, 95% yield). The filtrate was heated on the steam-bath to remove ethanol, and the residue taken up in ether, washed with conc. KOH, and dried over KOH. Distillation gave the ketal (9·06 g, 62% yield), b.p. 140–146 °C/735 mm, n_D^{21} 1·4321. Its hydrochloride had m.p. 166–167 °C; Kornfeld *et al.* (1956) give m.p. 165–167 °C.

(*c*) *Dimethylaminoacetone Ethylene Ketal.*—A mixture of bromoacetone ethylene ketal (30 g; 0·165 mole) and liquid dimethylamine (70 g; 100 ml; 1·55 moles) was sealed in a 650 ml capacity autoclave and heated at 170 °C for 26 hr. It was cooled, excess dimethylamine allowed to evaporate, and the contents diluted with ether and stirred with conc. KOH soln. The ether layer was combined with a subsequent ether-extract of the alkaline solution, dried over sodium sulphate, and distilled to give the ketal (13·0 g, 54% yield) as an oil, b.p. 83 °C/50 mm, n_D^{27} 1·4290. Light absorption: $\nu_{max.}$ 1208, 1165, 1130, 1095, and 1050 cm^{-1} (ketal).

The *hydrochloride* crystallized from ethanol–ether as needles of a hydrate, m.p. 161–162 °C (Found (after drying at 100 °C/2 mm): C, 45·4, 45·3; H, 8·8, 8·7; N, 7·6%. Calc. for $C_7H_{16}ClNO_2.0.25H_2O$: C, 45·3; H, 8·9; N, 7·5%).

The *hydrobromide* had m.p. 172–174 °C from ethanol–ether (Found: C, 36·8; H, 7·0; N, 6·0%. Calc. for $C_7H_{16}BrNO_2$: C, 37·2; H, 7·1; N, 6·2%).

(*d*) *Dimethylaminoacetone.*—(i) Dimethylaminoacetone ethylene ketal hydrochloride (1 g) was dissolved in 3N HCl (30 ml) and heated on a steam-bath for 8 hr. The solution was cooled, neutralized with dil. NaOH, and extracted with ether. The extract was dried over sodium sulphate and distilled, giving the base (0·42 g, 75% yield), b.p. 114 °C, n_D^{26} 1·4151.

(ii) Bromoacetone (70 g; 0·52 mole) was added dropwise with stirring and ice-cooling to a 26% w/v aqueous solution of dimethylamine (200 ml; 1·10 moles) during 1 hr. The dark solution was stirred overnight, then acidified with conc. HCl and non-basic material extracted with ether. (The ether solution yielded, on drying and evaporating, a trace of unchanged bromoacetone.) The acid solution was basified with sodium hydroxide and extracted with ether and chloroform. The combined extracts were dried over calcium chloride and distilled, affording the base (28·2 g, 54% yield), b.p. 65–75 °C/190 mm, n_D^{25} 1·4172. Light absorption: $\nu_{max.}$ 1705 cm^{-1} (C=O).

(iii) Chloroacetone (18·5 g; 0·20 mole) was added dropwise with stirring and cooling to a 10% excess of 33% w/v ethanolic dimethylamine (60 ml). The mixture was allowed to stand for 24 hr in a stoppered flask and evaporated to half its volume to remove dimethylamine. On cooling a precipitate of amine hydrochloride was deposited. The solution was basified and extracted with ether; distillation of the dried ether-extracts gave the amine (1·6 g, 8% yield), b.p. 124–125 °C, n_D^{31} 1·4080.

(*e*) (*2-Oxo-n-propyl*)*trimethylammonium Iodide.*—A mixture of dimethylaminoacetone (0·1 g), dry ethanol (10 ml), and methyl iodide in excess was refluxed for 3 hr. Cooling and addition of ether gave the *methiodide* (0·17 g, 68% yield), crystallizing from ethanol–ether as needles, m.p. 171–172 °C (Found: C, 29·5; H, 5·7%. Calc. for $C_6H_{14}INO$: C, 29·6; H, 5·8%). Light absorption: $\nu_{max.}$ 1728 cm^{-1} (C=O) (Nujol mull and $CHCl_3$ soln.).

(*f*) *2-[N-Methyl-N-(2'-oxo-n-propyl)]amino-α-tetralone 2'-Ethylene Ketal* (*VIII*).—A solution of methylaminoacetone ethylene ketal (9·0 g; 0·069 mole) and 2-bromo-α-tetralone (6·3 g; 0·028 mole) in benzene (50 ml) was refluxed on a steam-bath for 6·5 hr in a stream of nitrogen. The stoppered flask was kept at 0 °C overnight, the precipitated amino-ketal hydrobromide filtered, washed with benzene, and dried (6 g, 75% yield). The benzene filtrate on further heating deposited no more solid. It was cooled and washed with a little ice-water, then three times with cold 0·5N hydrochloric acid. The combined chilled acid extracts were immediately basified in a stream of nitrogen and the free base extracted into cold peroxide-free ether. The combined ether layers were dried at 0 °C over sodium sulphate and distilled, giving the tertiary amine (2·52 g, 46% yield), b.p. 125–135 °C/0·01 mm, n_D^{25} 1·5441 (Found: C, 69·5; H, 7·7; N, 4·8%. Calc. for $C_{16}H_{21}NO_3$: C, 69·8; H, 7·7; N, 5·1%). Light absorption: $\nu_{max.}$ 1687 (aromatic C=O), 1205, 1150, 1110, 1085, 1047 cm^{-1} (ketal).

Leemann and Fabbri (1959) report this compound but give no b.p. or refractive index.

The *picrate* crystallized from ethanol as yellow prisms, m.p. 145–147 °C (decomp.) (Found: C, 52·4; H, 4·7%; mol. wt. (method of Cunningham, Dawson, and Spring 1951), 500. Calc. for $C_{22}H_{24}N_4O_{10}$: C, 52·4; H, 4·8%; mol. wt., 504).

Treatment with alcoholic hydrogen bromide followed by dry ether gave the *hydrobromide* crystallizing from ethanol–ether as needles, m.p. 153–155 °C, of the hemihydrate (Found: C, 53·0; H, 6·3; N, 3·9%. Calc. for $C_{16}H_{22}BrNO_3.\frac{1}{2}H_2O$: C, 52·6; H, 6·3; N, 3·8%).

(*g*) *2-[N-Methyl-N-(2'-oxo-n-propyl)]amino-α-tetralone* (*IX*).—A solution of the preceding ethylene ketal (4·9 g; 0·018 mole) in ice-cold, nitrogen-saturated 3N HCl (90 ml) was sealed in a 100 ml flask and heated at 65±2 °C for 7 hr. The flask was chilled in ice, opened, and the contents basified in a stream of nitrogen with $NaHCO_3$. The free base was extracted four times as rapidly as possible with ice-cold peroxide-free ether, and the extracts dried over sodium sulphate at 0 °C. Distillation gave the amorphous *diketone* (2·81 g, 68% yield), b.p. 135–140 °C/10^{-5} mm, n_D^{19} 1·5845 (Found: C, 72·8; H, 7·3; N, 5·6%. Calc. for $C_{14}H_{17}NO_2$: C, 72·7; H, 7·4; N, 6·1%).

On standing, the liquid solidified to yellow crystals, m.p. 65–67 °C, which rapidly darkened on exposure to air. Light absorption: $\nu_{max.}$ 1710 (liq. film) or 1715 ($CHCl_3$) (aliphatic C=O) and 1690 cm^{-1} (aromatic C=O).

Alcoholic hydrogen bromide and ether gave the *hydrobromide*, crystallizing from ethanol–ether as a hemihydrate, m.p. 164–165 °C, even after drying *in vacuo* over P_2O_5 (Found: C, 52·3; H, 5·7%. Calc. for $C_{14}H_{18}BrNO_2.\frac{1}{2}H_2O$: C, 52·3; H, 6·0%).

The *methiodide* was deposited on refluxing an acetone solution of the amino-diketone under nitrogen with methyl iodide in excess for 2 hr. It crystallized from ethanol–ether as needles of a hemihydrate, m.p. 168–168·5 °C (Found: C, 47·2; H, 5·3; N, 4·2%. Calc. for $C_{15}H_{20}INO_2.\frac{1}{2}H_2O$: C, 47·1; H, 5·5; N, 3·7%).

(*h*) *1-Methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline* (*V*).—Sodium methoxide (prepared from 0·60 g (0·026 mole) of sodium) was dissolved in dry methanol (7 ml) and the solution was added dropwise to a stirred solution of the preceding diketone (1·55 g; 0·0067 mole) in dry ethanol (25 ml) in an atmosphere of nitrogen at —20 °C. The temperature was kept at —10 °C for 15 min, then lowered to —25 °C while the sodium methoxide was decomposed by the addition of ice-water. The mixture was extracted three times with ether and chloroform, and the extracts washed with water to remove NaOH, dried over sodium sulphate at 0 °C, and evaporated. The residual amorphous cyclic ketone (0·525 g, 37% yield) had n_D^{22} 1·5950. Light absorption: $\nu_{max.}$ 1665 cm^{-1} (conjugated C=O). Leemann and Fabbri (1959) report $\nu_{max.}$ 1665 cm^{-1}.

The crude cyclization product (275 mg) was dissolved in absolute ethanol (4 ml) and treated with alcoholic hydrogen bromide until just acid. Addition of ether and crystallization from methanol–ether gave the *hydrobromide* as needles, m.p. 158–159 °C, of a hemihydrate even after drying at 60 °C/2 mm (Found: C, 55·7; H, 5·6; N, 4·7%. Calc. for $C_{14}H_{16}BrNO.\frac{1}{2}H_2O$: C, 55·5; H, 5·7; N, 4·6%). Light absorption: $\nu_{max.}$ 1650 cm^{-1} (conjugated C=O).

The crude cyclization product (70 mg) in absolute ethanol (5 ml) was refluxed with excess of methyl iodide for 1·5 hr. The mixture was chilled overnight and the solid filtered and recrystallized from ethanol, giving the *methiodide* as pale yellow needles, m.p. 198 °C (Found: C, 50·9; H, 5·3; N, 4·0%. Calc. for $C_{15}H_{18}INO$: C, 50·7; H, 5·1; N, 3·9%). Light absorption: $\nu_{max.}$ 1650 cm^{-1} (conjugated C=O).

(*i*) *2,3-Dihydro-1,3-dimethyl-3-hydroxy-5,6-(1'-2'-naphtho)-1,4-oxazine* (*XV*).—When the crude product obtained from an unsuccessful attempted cyclization of the diketone (IX) was kept at 0 °C overnight in the presence of dry HCl, crystallization of the product from methanol–ether gave the cyclic *hemiketal hydrochloride* as needles, m.p. 217–219 °C (Found: C, 63·3; H, 6·1; N, 5·8%. Calc. for $C_{14}H_{16}ClNO_2$: C, 63·3; H, 6·1; N, 5·3%). The compound was water soluble and gave an orange colour with ferric chloride solution. Light absorption: $\nu_{max.}$ 3300 (OH), 1600, 1230, 990, 930, 850, and 780 cm^{-1}.

(*j*) *3-Hydroxy-1-methyl-7,8-dihydro-5,6-benzquinolinium Hydroxide Betaine* (*XVIII*).—When the aqueous mother liquors from (*h*) above were made strongly alkaline with NaOH and extracted with chloroform, distillation of the extracts gave a solid residue (0·537 g) crystallizing from benzene–hexane as yellow needles, m.p. 129–130 °C, of the hydrated *betaine* (Found: C, 71·3;

H, 6·9%. Calc. for $C_{14}H_{18}NO.1·5H_2O$: C, 70·6 ; H, 6·8%). It was soluble in water and gave an orange colour with ferric chloride. Light absorption : $\nu_{max.}$ 3300 (OH), 1580, 1560, 1355, 1230, 1115, 1055, 890, 760, and 750 cm^{-1}.

(*k*) *Reaction of 2-Bromo-α-tetralone with Dimethylaminoacetone Ethylene Ketal.*—(i) Dimethylaminoacetone ethylene ketal (0·80 g ; 0·0055 mole) and 2-bromo-α-tetralone (1·25 g ; 0·0055 mole) in dry acetone (20 ml) were refluxed in a stream of nitrogen for 8 hr. On cooling, a solid (0·13 g) was deposited, filtered, and washed with ether. A further 0·11 g was obtained when the mother liquors were evaporated and the residue treated with ether. Recrystallization from ethanol–ether gave needles, m.p. 169–170 °C, of *dimethylaminoacetone ethylene ketal hydrobromide* (19% yield) (Found : C, 36·8 ; H, 7·0 ; N, 6·0%. Calc. for $C_7H_{16}BrNO_2$: C, 37·2 ; H, 7·1 ; N, 6·2%). Light absorption : $\nu_{max.}$ 1130, 1095, 1040 cm^{-1} (ketal) ; no absorption in the 1600–1700 cm^{-1} region.

(ii) Dimethylaminoacetone ethylene ketal (1·45 g ; 0·01 mole) and 2-bromo-α-tetralone (2·25 g ; 0·01 mole) in xylene (25 ml) were refluxed in nitrogen for 18 hr. On cooling, a solid was deposited, which was filtered, and washed with ether. It crystallized from ethanol–ether as needles (0·89 g, 40% yield), m.p. 169–170·5 °C, undepressed on admixture with the amino-ketal hydrobromide from (*i*) above.

The mother liquor from this amine hydrobromide was diluted with ether and extracted twice with dil. NaOH solution. The alkaline extract was acidified with HCl and the acid extracted with chloroform. Removal of solvent gave a crystalline residue (0·62 g, 43% yield), m.p. 85–91 °C, identified as α-naphthol by giving a characteristic blue colour when warmed in sodium hydroxide solution with chloroform and copper bronze, and by the formation of the picrate (orange needles from ethanol), m.p. and mixed m.p. 189–189·5 °C.

(*l*) *NN-Dimethyl-N-(α-oxo-2-tetralyl)-N-(2′-oxo-n-propyl)ammonium Bromide* (*XXI*).—(i) A solution of dimethylaminoacetone (7·0 g ; 0·069 mole) and 2-bromo-α-tetralone (15·5 g ; 0·069 mole) in dry acetone (70 ml) was refluxed in nitrogen for 17 hr. A solid began to precipitate during this period. After cooling, the solid (2·5 g) (m.p. 194–195 °C) was filtered and washed with acetone. The acetone mother liquors on standing for several days at room temperature deposited a further 1·18 g (m.p. 194 °C). Crystallization from ethanol–ether gave the *quaternary bromide* (16·3% yield), m.p. 197 °C (Found : C, 55·1, 55·0 ; H, 6·3, 6·0 ; N, 4·1%. Calc. for $C_{15}H_{20}BrNO_2$: C, 55·2 ; H, 6·2 ; N, 4·3%. Calc. for $C_{15}H_{18}BrNO_2$: C, 55·9 ; H, 5·6%). Light absorption : $\nu_{max.}$ 3220 (OH), 1710 (aliphatic C=O), 1675 cm^{-1} (conjugated C=O).

(ii) After an identical experiment using 2·85 g of dimethylaminoacetone, the mother liquor from the quaternary bromide was concentrated and the residue chilled in an attempt to increase the yield. The solid, m.p. 81–85 °C, produced (1·7 g, 33% yield) was filtered and washed with acetone. It was water-soluble, contained ionic halide, and was *dimethylaminoacetone hydrobromide* (Found : C, 32·6 ; H, 6·8%. Calc. for $C_5H_{12}BrNO$: C, 33·0 ; H, 6·7%).

(*m*) *Reaction of 2-Dimethylamino-α-tetralone with Bromoacetone.*—2-Dimethylamino-α-tetralone (0·80 g ; 0·0042 mole) and bromoacetone (0·58 g ; 0·0042 mole) in dry acetone (50 ml) were refluxed in nitrogen for 3 hr. There was no precipitate on cooling. The solution was evaporated to dryness, and the residue recrystallized from acetone–ether, giving *2-dimethylamino-α-tetralone hydrobromide* (0·35 g, 29% yield), m.p. 81–84 °C as a hydrate (Found : C, 49·6 ; H, 6·3 ; N, 4·3 ; Br, 27·9%, equiv. wt., 287. Calc. for $C_{12}H_{20}BrNO.H_2O$: C, 50·0 ; H, 6·3 ; N, 4·8 ; Br, 27·7% ; equiv. wt., 288).

(*n*) *2,3-Dihydro-1,3-dimethyl-3-methoxy-5,6-(1′,2′-naphtho)-1,4-oxazine Methobromide* (*XXIV* ; *R*=*Me*).—A solution of the quaternary ammonium compound, m.p. 194 °C (100 mg), obtained in (*l*) above in dry methanol (6 ml) was saturated with dry hydrogen chloride, and kept at room temperature for 19 hr. Removal of solvent and crystallization of the residue from methanol–ether gave needles (61 mg, 59% yield), m.p. 154–155 °C, of the hydrated *methyl ether*, not dehydrated on drying *in vacuo* over P_2O_5 (Found : C, 54·1, 54·4 ; H, 6·7, 7·0%. Calc. for $C_{16}H_{22}BrNO_2.H_2O$: C, 53·6 ; H, 6·8%. Calc. for $C_{16}H_{22}BrNO_2.0·75H_2O$: C, 54·3 ; H, 6·7%). The analysis was unchanged after drying at 80 °C/3 mm (Found : C, 54·3 ; H, 6·8%). After recrystallization from isopropanol–ether, and drying at 75 °C/3 mm for 3 hr it had m.p. 160–161 °C (Found : C, 56·5 ; H, 6·7 ; N, 3·9%. Calc. for $C_{16}H_{22}BrNO_2$: C, 56·5 ; H, 6·5 N, 4·1%).

(*o*) *Cyclization of Quaternary Diketone.*—The quaternary diketone (2·28 g; 0·007 mole) obtained in (*k*) above was dissolved in dry methanol (200 ml) and the solution stirred in a current of nitrogen at —15 °C. A solution of sodium methoxide (prepared from 0·48 g (0·021 mole) of Na) in methanol (50 ml) was added to the diketone solution and the mixture stirred at —15 °C for 0·5 hr. Sodium methoxide in excess was neutralized by addition of ethanolic hydrogen bromide to pH 6 and the solution evaporated to dryness at reduced pressure. The dry residue was extracted three times with boiling anhydrous ethanol. The ethanol extracts when diluted with ether deposited the tricyclic *quaternary ketone* (XXV; X=Br) (1·27 g, 59% yield), m.p. 198–200 °C, from methanol (Found: C, 58·0; H, 6·1; N, 4·5; Br, 29·4%. Calc. for $C_{15}H_{18}BrNO$: C, 58·4; H, 5·9; N, 4·6; Br, 29·9%). Its infrared spectrum, $\nu_{max.}$ 1650 cm^{-1} (conjugated C=O), was practically identical with that of the methiodide, m.p. 198 °C, obtained in (*h*) above.

Extraction of the ethanol-insoluble residue with boiling anhydrous methanol afforded a further crop (0·3 g) of the product, m.p. and mixed m.p. 198 °C, with identical infrared absorption, a total of 1·57 g (73% yield). Recrystallization of this material from methanol–ether gave needles of a hemihydrate, m.p. 189–190 °C (Found: C, 57·0; H, 6·2%. Calc. for $C_{15}H_{18}BrNO.\frac{1}{2}H_2O$: C, 56·8; H, 6·0%).

(*p*) *Conversion of the Tricyclic Ketone Methobromide to the Methiodide.*—(i) A dry acetone extract (50 ml) of the crude cyclization product obtained in (*o*) above was refluxed for 1 hr with KI (100 mg). A white solid was deposited almost immediately and shown to be KBr (m.p. above 250 °C). The mother liquor was evaporated to dryness, and the residue recrystallized from ethanol to give needles, m.p. 198–199 °C, undepressed on admixture with the methiodide (m.p. 198 °C) of 1-methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline obtained in (*h*) above.

(ii) In another experiment, the pure cyclization product obtained in (*o*) above (83 mg; 0·00027 mole) was dissolved in dry acetone and refluxed with NaI (38 mg; 0·00025 mole) for 1 hr. It was evaporated to 50 ml, cooled, and the trace of solid which separated was filtered. The filtrate was evaporated to dryness, leaving a residue (85 mg) which crystallized from ethanol–ether as needles, m.p. 196–197 °C, identical (mixed m.p. and infrared spectrum) (absorption bands at 2290, 1650, 1580, 1300, 1230, 1180, 760, and 720 cm^{-1}) with the methiodide (m.p. 198 °C) obtained in the above.

(*q*) *1,1-Dimethyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinolinium Bromide Ethylene Dithioketal* (*XXVIII*; *X=Br*).—(i) The tricyclic quaternary ketone (XXV; X=Br) (0·42 g; 0·0013 mole) was stirred with ethanedithiol (0·25 ml; 0·0026 mole) and boron trifluoride etherate (0·15 ml) The mixture, which became slightly warm, was stoppered and set aside for 2½ days at room temperature. It was diluted with ether and the grey solid filtered and washed with ether to give 496 mg (94% yield) of crude product (m.p. 218–220 °C). Recrystallization from ethanol gave white needles (0·322 g, 62% yield), m.p. 230–231 °C, of the *dithioketal* as a hemihydrate (Found: C, 52·1; H, 5·6; N, 3·6; S, 16·6%. Calc. for $C_{17}H_{22}BrNS_2.\frac{1}{2}H_2O$: C, 51·9; H, 5·9; N, 3·6; S, 16·3%). Light absorption: $\nu_{max.}$ 1620 cm^{-1}.

(ii) In an identical experiment, recrystallization of the product from methanol gave needles, m.p. 185 °C, of the monohydrate (Found: C, 50·4; H, 5·8; N, 3·3; Br, 20·1%. Calc. for $C_{17}H_{22}BrNS_2.H_2O$: C, 50·7; H, 6·0; N, 3·5; Br, 19·9%), showing infrared absorption identical with that of the compound obtained in (*q*) (i).

(iii) Treatment of an aqueous solution of the above methobromide with lithium picrate gave the *methopicrate* as needles from aqueous ethanol, m.p. 218–222 °C (Found: C, 51·4; H, 4·8%. Calc. for $C_{23}H_{24}N_4S_2O_7.\frac{1}{2}H_2O$: C, 51·0; H, 4·7%).

(*r*) *1-Methyl-3-oxo-1,2,3,7,8,9-hexahydro-5,6-benzquinoline Ethylene Dithioketal* (*XXIX*).—The quaternary dithioketal obtained above in (*q*) (215 mg; 0·00056 mole) was heated at 215 °C (bath temp.) *in vacuo* (0·7 mm) for 10 min. The yellowish amorphous residue of the tertiary amine (177 mg) showed light absorption ($\nu_{max.}$) at 1630 cm^{-1}.

The hydrochloride, prepared from an ethereal solution of the amine with dry ethereal hydrogen chloride, similarly had light absorption ($\nu_{max.}$) at 1630 cm^{-1}, demonstrating that the double bond was in the $\beta\gamma$-position.

The base was used without purification for the next step.

(*s*) *1-Methyl-1,2,3,7,8,9-hexahydro-5,6-benzquinoline* (*III*; *R=H*).—The tertiary dithioketal obtained above in (*r*) (177 mg) was refluxed for 16 hr with Raney nickel (1 g) in ethanol (25 ml).

The catalyst was removed, washed with hot ethanol and ether, and the filtrate and washings evaporated, affording the amorphous hexahydrobenzquinoline (92 mg, 76% yield). Light absorption : $\nu_{max.}$ 1605 cm^{-1}. The hydrobromide, prepared using dry ethereal hydrogen bromide, similarly showed light absorption ($\nu_{max.}$) at 1605 cm^{-1}, demonstrating that the double bond was in the $\beta\gamma$-position.

The *picrate* formed needles from aqueous methanol, m.p. 176–177 °C (Found : C, 55·9 ; H, 4·5% ; mol. wt. (method of Cunningham, Dawson, and Spring 1951), 449. Calc. for $C_{20}H_{20}N_4O_7$: C, 56·1 ; H, 4·7% ; mol. wt., 428). Light absorption : $\nu_{max.}$ ($CHCl_3$ solution) 1605 cm^{-1}. Treatment of the amorphous tertiary base with methyl iodide followed by double decomposition with aqueous lithium picrate gave the *methopicrate*, crystallizing from water as needles, m.p. 208–210 °C (Found : mol. wt. (method of Cunningham, Dawson, and Spring 1951), 460. Calc for $C_{21}H_{22}N_4O_7$: mol. wt., 442).

(*t*) *Testosterone Ethylene Dithioketal.*—Testosterone (203 mg) was stirred with ethanedithiol (0·15 ml) and boron trifluoride etherate (0·1 ml). The solution warmed spontaneously and soon solidified. After standing for 1 hr it was diluted with methanol (5 ml), filtered, and dried. The *dithioketal* (260 mg, 100% yield) crystallized from ethanol as needles of a hemihydrate which sintered at 100–105 °C and melted at 163–165 °C (Found : C, 67·9 ; H, 9·0%. Calc. for $C_{21}H_{32}OS_2.\frac{1}{2}H_2O$: C, 67·5 ; H, 8·9%), obtained anhydrous after drying at 100 °C/2 mm for 16 hr (Found : C, 68·9 ; H, 8·8%. Calc. for $C_{21}H_{32}OS_2$: C, 69·2 ; H, 8·8%). Light absorption : $\nu_{max.}$ 3350 (OH), 2350, 1650, 1270, 1225, 1070, 1050, 850, 835, 725, and 670 cm^{-1}.

(*u*) *Δ-4-Androsten-17-ol.*—Testosterone ethylene dithioketal (70 mg) in ethanol (20 ml) was refluxed for 2 hr with Raney nickel (2 g). The solution was filtered and the catalyst washed twice with boiling ethanol. The combined filtrate and washings were evaporated, leaving a white solid (70 mg), crystallizing from methanol or ethanol as needles, m.p. 147 °C (lit. m.p. 146–149 °C). With tetranitromethane the compound gave a positive test for unsaturation, and Lassaigné's test for sulphur was negative (Found (after drying at 60 °C/2 mm overnight) : C, 80·1 ; H, 10·7%. Calc. for $C_{19}H_{30}O.\frac{1}{4}H_2O$: C, 80·5 ; H, 11·0%). Light absorption : $\nu_{max.}$ 3350 (OH), 2350, 1115, 1070, 1050, 1000, 815, and 670 cm^{-1}.

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