NOTES.

731. *Cyclic Amidines. Part XIII.*[1] *2-Alkylamino-4-hydroxyquinolines.*

By W. R. Hallows and M. W. Partridge.

Sodium 2-amino-4-n-butoxyquinoline, formed in xylene, yielded with an alkyl halide the corresponding 2-alkylamino-derivative. Evidence for this structure was provided by the synthesis of the 2-n-butylamino-derivative from 4-n-butoxy-2-chloroquinoline and n-butylamine. Certain of these ethers were dealkylated with hydrogen bromide to yield 2-alkylamino-4-hydroxyquinolines as structural analogues of the antibiotics Pyo Ic and Pyo Ib, 4-hydroxy-2-nonyl- and 2-heptyl-4-hydroxy-quinoline respectively.[2] The 2-alkylamino-4-hydroxyquinolines were devoid of useful antibacterial activity.

Experimental.—*2-Alkylamino-4-butoxyquinolines.* (i) 2-Amino-4-n-butoxyquinoline[3] (2·16 g.) was refluxed in dry xylene (50 ml.) with sodamide (0·39 g.) for 12 hr.; the alkyl halide (0·01 mole) was added and heating was continued for 24 hr. The suspension was clarified (charcoal and kieselguhr) and concentrated to incipient crystallisation. Recrystallisation was effected from light petroleum, ethanol, or aqueous ethanol. The yields obtained were 46—52% (see Table 1).

(ii) 4-n-Butoxy-2-chloroquinoline[3] (0·8 g.) and n-butylamine (0·35 g.) in ethanol (5 ml.) were heated in a sealed tube at 180° for 5 hr. The 2-butylaminoquinoline (0·6 g.) which separated when the solution was poured into water had m. p. and mixed m. p. 102—103° and afforded a picrate, m. p. and mixed m. p. 164—165°. This reaction could not be carried out in boiling ethanol. Attempted alkylation of sodium 2-acetamido-4-n-butoxyquinoline[3] in ethanol produced only 2-amino-4-n-butoxyquinoline.

2-Alkylamino-4-hydroxyquinolines. The 2-alkylamino-4-butoxyquinoline (0·02 mole) was refluxed for 5 hr. in a mixture of acetic acid (50 ml.) and 48% aqueous hydrogen bromide

[1] Part XII, Grout and Partridge, *J.*, 1960, 3551.
[2] Wells, *J. Biol. Chem.*, 1952, **196**, 331.
[3] Hardman and Partridge, *J.*, 1955, 510.

(30 ml.). Most of the solvent was evaporated and the resulting gum was crystallised from aqueous pyridine and, if necessary, from aqueous methanol (see Table 2).

TABLE 1. *2-Alkylamino-4-n-butoxyquinolines.*

			Found (%)			Required (%)		
Substituent	M. p.	Formula	C	H	N	C	H	N
Ethyl	145—146°	$C_{15}H_{20}N_2O$	74·0	8·4	11·2	73·7	8·3	11·5
picrate	184—185	$C_{21}H_{23}N_5O_8$	53·1	5·1	14·8	53·3	4·9	14·8
n-Propyl	129—130	$C_{16}H_{22}N_2O$	74·3	8·7	11·0	74·4	8·6	10·8
picrate	160—161	$C_{22}H_{25}N_5O_8$	54·5	5·1	14·3	54·2	5·2	14·4
n-Butyl	103—104	$C_{17}H_{24}N_2O$	74·6	8·6	10·4	75·0	8·9	10·3
picrate	165—166	$C_{23}H_{27}N_5O_8$	55·0	5·7	14·0	55·1	5·4	14·0
n-Pentyl	106—107	$C_{18}H_{26}N_2O$	75·1	8·9	9·8	75·5	9·2	9·8
n-Hexyl	91—92	$C_{19}H_{28}N_2O$	75·9	8·8	9·3	75·9	9·4	9·3
picrate	116—117	$C_{25}H_{31}N_5O_8$	56·6	5·9	13·0	56·7	5·9	13·2
n-Heptyl	85—87	$C_{20}H_{30}N_2O$	76·2	9·2	8·8	76·4	9·6	8·9
picrate	105—106	$C_{26}H_{33}N_5O_8$	57·1	5·7	12·6	57·5	6·1	12·9
n-Octyl	96—97	$C_{21}H_{32}N_2O$	77·1	9·7	8·7	76·8	9·8	8·5
n-Hexadecyl	102—103	$C_{29}H_{48}N_2O$	78·9	11·2	6·0	79·0	11·0	6·4

TABLE 2. *2-Alkylamino-4-hydroxyquinolines.*

			Found (%)			Required (%)		
Substituent	M. p.	Formula	C	H	N	C	H	N
n Butyl	188—189°	$C_{13}H_{16}N_2O$			13·1			13·0
n-Pentyl	185—186	$C_{14}H_{18}N_2O$	73·2	8·0	11·9	73·0	7·9	12·2
n-Hexyl	157—158	$C_{15}H_{20}N_2O$			11·4			11·5
n-Octyl	141—142	$C_{17}H_{24}N_2O$	74·7	8·8	10·3	75·0	8·9	10·3

The authors gratefully acknowledge their indebtedness to Miss G. L. M. Harmer for the antibacterial tests.

THE UNIVERSITY, NOTTINGHAM. [*Received, February 25th,* 1960.]

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732. 5α,17β-*Dihydroxy*-6α,17α-*dimethylandrostan*-3-*one.*

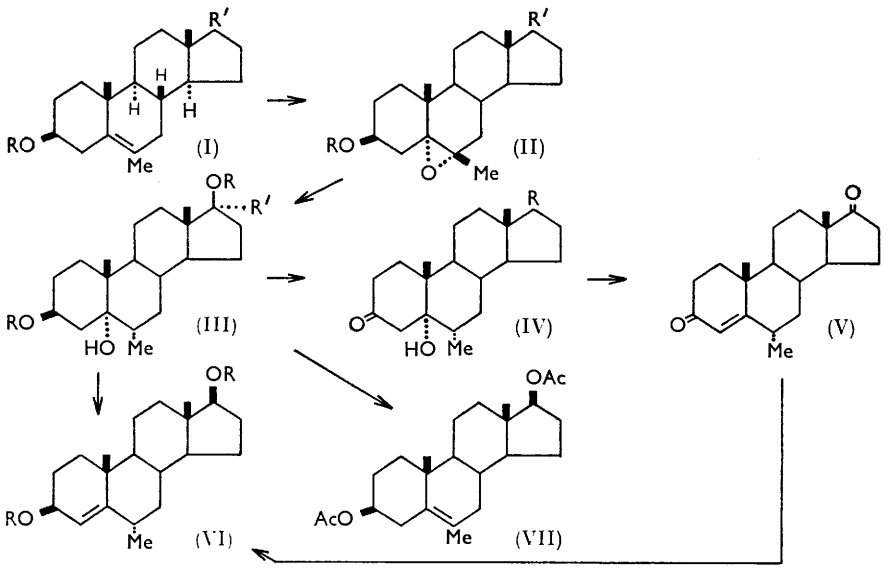
By G. COOLEY, B. ELLIS, and V. PETROW.

TREATMENT of 3β-acetoxy-6-methylandrost-5-en-17-one [1] (I; R = Ac, R′ = :O) with monoperphthalic acid gave, in high yield, a single crystalline compound regarded as 3β-acetoxy-5α,6α-epoxy-6β-methylandrostan-17-one (II; R = Ac, R′ = :O). Reductive fission of the epoxide ring with lithium aluminium hydride in hot dioxan–tetrahydrofuran led to 6α-methylandrostane-3β,5α,17β-triol (III; R = R′ = H), which formed a diacetate (III; R = Ac, R′ = H), and which was oxidised with chromium trioxide–pyridine to 5α-hydroxy-6α-methylandrostane-3,17-dione (IV; R = :O). Treatment of the last compound with thionyl chloride–pyridine converted it into the known 6α-methylandrost-4-ene-3,17-dione [2] (V). Similar dehydration of 3β,17β-diacetoxy-6α-methylandrostan-5α-ol (III; R = Ac, R′ = H) furnished an apparently homogeneous product $C_{24}H_{36}O_4$, m. p. 110—114°, which was shown to be an approximately 1 : 1 molecular complex of 3β,17β-diacetoxy-6-methylandrost-5-ene [1] (VII) and 3β,17β-diacetoxy-6α-methylandrost-4-ene (VI; R = Ac) by its preparation from its component parts. The unsaturated diacetate (VI; R = Ac) required for this purpose was conveniently obtained by reduction of the diketone (V) with lithium aluminium hydride followed by acetylation of the resulting 3β,17β-diol (VI; R = H). Its formation from the saturated compound (III; R = Ac, R′ = H) establishes in the latter both the position of the hydroxyl substituent and the configuration of the 6-methyl group.

6,17α-Dimethylandrost-5-ene-3β,17β-diol [1] (I; R = H, R′ = –OH, ···Me) was similarly converted into the epoxide (II; R = H, R′ = –OH, ···Me) and thence, by

[1] Grenville, Patel, Petrow, Stuart-Webb, and Williamson, *J.*, 1957, 4105.
[2] See Ackroyd, Adams, Ellis, Petrow, and Stuart-Webb, *J.*, 1957, 4099.

reduction followed by oxidation of the triol (III; R = H, R′ = Me), into 5α,17β-dihydroxy-6α,17α-dimethylandrostan-3-one (IV; R = –OH, ••• Me) required for biological study. This ketone afforded an optical rotatory dispersion curve showing a single positive Cotton effect above 250 mμ, consistent with a *trans*-fusion of rings A and B.[3] These transformations bear a formal resemblance to certain experiments reported[4] in the cholestane series.



Experimental.—Optical rotations were measured for chloroform solutions in a 1 dm. tube unless otherwise stated. The optical rotatory dispersion curve was kindly determined by Mr. M. T. Davies, B.Sc., and Miss D. F. Dobson, B.Sc.

3β-*Acetoxy*-5α,6α-*epoxy*-6β-*methylandrostan*-17-*one* (II; R = Ac, R′ = :O) (with Dr. D. N. Kirk). 3β-Acetoxy-6-methylandrost-5-en-17-one[1] (5 g.) in chloroform (50 ml.) was treated with monoperphthalic acid (4·5 g.) in ether (70 ml.) and set aside at 0° for 18 hr. After removal of acidic materials, the *epoxide* was isolated with ether and purified from acetone–hexane. It separated in flakes, m. p. 187—189°, $[\alpha]_D^{24}$ +12° (*c* 0·34) (Found: C, 73·1; H, 9·0. $C_{22}H_{32}O_4$ requires C, 73·3; H, 8·95%).

6α-*Methylandrostane*-3β,5α,17β-*triol* (III; R = R′ = H). The foregoing epoxide (4 g.) in tetrahydrofuran (100 ml.) and dioxan (200 ml.) was added to lithium aluminium hydride (8 g.) in dioxan (400 ml.). The mixture was heated at 100° for 6½ hr., then cooled, and excess of reagent was decomposed with ethyl acetate. The *triol* was isolated with ethyl acetate and crystallised from aqueous methanol as needles, m. p. 213—215°, $[\alpha]_D^{23}$ −6° (*c* 1·07 in $CHCl_3$ containing 5% of EtOH) (Found: C, 74·8; H, 10·7. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·6%). The 3β,17β-*diacetate* crystallised from aqueous methanol in needles, m. p. 183—184°, $[\alpha]_D^{23}$ −16° (*c* 1·02) (Found: C, 70·8; H, 9·4. $C_{24}H_{38}O_5$ requires C, 70·9; H, 9·4%).

5α-*Hydroxy*-6α-*methylandrostane*-3,17-*dione* (IV; R = :O). 6α-Methylandrostane-3β,5α,17β-triol (0·76 g.) in pyridine (7·5 ml.) was added to chromium trioxide (1·5 g.) in pyridine (15 ml.), and the mixture was set aside overnight. The product was isolated with ether and purified from acetone–hexane. The *dione* formed prisms, m. p. 187—189°, $[\alpha]_D^{23}$ +40° (*c* 0·9) (Found: C, 75·3; H, 9·8. $C_{20}H_{30}O_3$ requires C, 75·4; H, 9·5%).

6α-*Methylandrost*-4-*ene*-3,17-*dione* (V). The foregoing compound (0·27 g.) in pyridine (2·5 ml.) was treated at 0° with thionyl chloride (0·2 ml.), dropwise during 5 min. After a further 10 min. the mixture was poured into water. The product crystallised from acetone–hexane to give 6α-methylandrost-4-ene-3,17-dione, prisms, m. p. 167—168°, identified by mixed m. p. determination and by its infrared spectrum.

[3] See Djerassi and Closson, *J. Amer. Chem. Soc.*, 1956, **78**, 3761 and references cited therein.
[4] Shiota, *J. Chem. Soc. Japan*, 1956, **77**, 1116; *Chem. Abs.*, 1959, **53**, 5338.

Dehydration of 3β,17β-*diacetoxy*-5α-*hydroxy*-6α-*methylandrostane* (III; R = Ac, R′ = H). Thionyl chloride (0·3 ml.) was added dropwise to a solution of the diacetate (0·5 g.) in pyridine (3 ml.) at 0°. After 10 min., the mixture was poured into water, and the product crystallised from aqueous methanol. The 1 : 1 molecular *complex* of 3β,17β-diacetoxy-6-methylandrost-5-ene [1] and 3β,17β-diacetoxy-6α-methylandrost-4-ene (see below) separated in flat needles, m. p. 110—114°, $[\alpha]_D^{20}$ −43° (*c* 1·0) (Found: C, 73·95; H, 9·1. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·3%).

When a mixture of equal weights of authentic 3β,17β-diacetoxy-6-methylandrost-5-ene ($[\alpha]_D$ −82°) and 3β,17β-diacetoxy-6α-methylandrost-4-ene ($[\alpha]_D$ −4°) (see below) crystallised from aqueous methanol, there was obtained a complex identical with the foregoing dehydration product in m. p., mixed m. p., optical rotation, and infrared spectrum.

6α-*Methylandrost*-4-*ene*-3β,17β-*diol* (VI; R = H). 6α-Methylandrost-4-ene-3,17-dione (5 g.) in tetrahydrofuran (70 ml.) was added during 30 min. to a stirred solution of lithium aluminium hydride (1·5 g.) in tetrahydrofuran (150 ml.) at 0°. Thereafter, the mixture was heated under reflux for 1 hr., cooled, and treated cautiously with ethyl acetate (100 ml.). After addition of water (40 ml.) and sodium sulphate (14 g.), the whole was vigorously shaken and then filtered. The dried filtrate was evaporated *in vacuo*, and the residue purified from acetone–hexane, to give the *diol*, needles, m. p. 139—141°, $[\alpha]_D^{23}$ +39·5° (*c* 0·84) (Found: C, 78·85; H, 10·9. $C_{20}H_{32}O_2$ requires C, 78·9; H, 10·6%).

3β,17β-*Diacetoxy*-6α-*methylandrost*-4-*ene* (VI; R = Ac), obtained by acetylation of the foregoing diol, crystallised from aqueous methanol in plates, m. p. 157—158°, $[\alpha]_D^{20}$ −4° (*c* 0·92) (Found: C, 73·85; H, 9·4. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·3%).

6β,17α-*Dimethyl*-5α,6α-*epoxyandrostane*-3β,17β-*diol* (II; R = H, R′ = −OH, ···Me). 6,17α-Dimethylandrost-5-ene-3β,17β-diol [1] (24·7 g.) in chloroform (900 ml.) was treated with monoperphthalic acid (16·8 g.) in ether (300 ml.) and set aside at 0° overnight. The *epoxide*, isolated in the usual way, crystallised from acetone–hexane, giving needles, m. p. 210—212° (decomp.), $[\alpha]_D^{21}$ −75° (*c* 0·66) (Found: C, 75·6; H, 10·6. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·25%).

6α,17α-*Dimethylandrostane*-3β,5α,17β-*triol* (III; R = H, R′ = Me). The foregoing compound (10 g.) in tetrahydrofuran (350 ml.) and dioxan (1 l.) was added to lithium aluminium hydride (10 g.) in dioxan (1 l.). The stirred mixture was heated at 100° for 8 hr., cooled, and treated with ethyl acetate. Crystallisation of the product from aqueous methanol gave the *triol*, needles, m. p. 230—233°, $[\alpha]_D^{25}$ −23° (*c* 0·92 in $CHCl_3$ containing 5% of EtOH) (Found: C, 74·8; H, 10·7. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%).

5α,17β-*Dihydroxy*-6α,17α-*dimethylandrostan*-3-*one* (IV; R = −OH, ···Me). The foregoing triol (1·5 g.) in pyridine (15 ml.) was added to chromium trioxide (1·5 g.) in pyridine (15 ml.). The mixture was set aside for 3 days. After isolation with ether, the *ketone* crystallised from acetone–hexane as rods, m. p. 230—233°, $[\alpha]_D^{24}$ −20° (*c* 0·45 in $CHCl_3$ containing 1% of EtOH) (Found: C, 75·2; H, 10·1. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·25%). The optical rotatory dispersion curve in methanol (*c* 0·51) showed a single positive Cotton effect with peak at 310 mμ, $[\alpha]^{25}$ +1400°.

The authors thank the Directors of The British Drug Houses, Ltd., for permission to publish this work.

CHEMICAL RESEARCH LABORATORIES,
THE BRITISH DRUG HOUSES, LTD., LONDON, N.1. [*Received, February 26th*, 1960.]

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733. *The Heterogeneous Catalysis by Metals of Electron-transfer Reactions in Solution.*

By M. SPIRO.

METALS catalyse many reactions in solution which involve gases, such as the decomposition of hydrogen peroxide and of formic acid. It might be expected that metal surfaces would accelerate other kinds of process in solution, such as oxidation–reduction. Several instances of this have now been recorded,[1,2] and Waind [1] has suggested that here the

[1] Waind, *Chem. and Ind.*, 1955, 1388; Gilks and Waind, *Discuss. Faraday Soc.*, in the press.
[2] Lewis, Coryell, and Irvine, *J.*, 1949, S386.

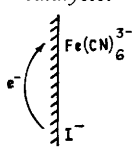
catalyst could act as a conductor. It is the purpose of this Note to report further qualitative experiments, and to show that the results can be explained by an extension of Waind's suggestion.

Just [3] discovered that platinum increased the rate of the reaction $2Fe(CN)_6^{3-} + 3I^- \longrightarrow 2Fe(CN)_6^{4-} + I_3^-$, and quantitative confirmation was obtained in this laboratory by e.m.f. measurements.[4] With Just's technique of observing the metal when it was suspended in the mixed solution alone or with added thiosulphate and starch, it was found that ruthenium, rhodium, iridium, palladium, and gold were also catalysts. The gold foil looked tarnished after immersion. On mercury, a thin green film formed in the mixture was identified chemically and by *X*-rays as mercurous iodide. No perceptible reaction occurred when the metals were in contact for short periods with appropriate solutions containing only ferricyanide and ferrocyanide or iodide and iodine, although mercury was slowly attacked by ferricyanide.

When exposed to the reaction $2Fe^{3+} + 3I^- \longrightarrow 2Fe^{2+} + I_3^-$, platinum was again surrounded by iodine, and mercury by mercurous iodide. No appreciable interaction took place with platinum or mercury in the process $S_2O_8^{2-} + 3I^- \longrightarrow 2SO_4^{2-} + I_3^-$.

These results can be explained on the simple hypothesis that iodide ions and oxidant ions are adsorbed on the metal surface, and that electrons may be transferred between them through the metal (see Figure). Little catalysis can occur when the oxidant ion withdraws electrons very slowly, and this is the case with persulphate as is shown by the electrochemical irreversibility of the $S_2O_8^{2-}$–SO_4^{2-} couple; nor, presumably, would there be any catalysis were iodide replaced by a reductant reluctant to supply electrons. But if electrons are transferred rapidly then the same products are formed as on electrolysis. Anodes of platinum, gold, and other noble metals oxidise iodide to iodine whereas mercury becomes coated with a skin of mercurous iodide.[5]

Model of metal catalysis.



If this mechanism is correct it should be possible to predict the extent and kind of interaction between metals and electron-transfer reactions from a knowledge of electrode behaviour.

My thanks are offered to the Mond Nickel Co. for samples of pure ruthenium, rhodium, iridium, and palladium.

UNIVERSITY OF MELBOURNE, AUSTRALIA. [*Received, February 29th,* 1960.]

[3] Just, *Z. phys. Chem.*, 1908, **63**, 513.
[4] Spiro, Johnston, and Wagner, *Electrochim. Acta*, in the press.
[5] Kolthoff and Miller, *J. Amer. Chem. Soc.*, 1941, **63**, 1405.

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734. *The Conversion of Theobromine into 2,3-Dihydro-3,7-dimethyl-2-oxopurine.*

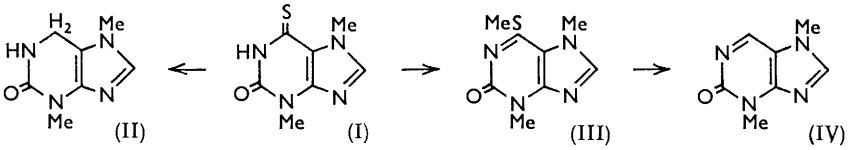
By ABRAHAM KALMUS and FELIX BERGMANN.

REPLACEMENT of the 6-hydroxy-group in theobromine by hydrogen was achieved by Tafel [1] in a two-step process: electrolytic reduction on a lead cathode in 50% sulphuric acid yielded first a dihydro-derivative (" desoxytheobromine ") of the probable structure (II), derived from 2,3-dihydro-3,7-dimethyl-2-oxopurine (IV) by saturation of the 1,6-double bond; then dehydrogenation by bromine or silver acetate. Fichter and Kern [2] reduced theobromine to the dihydro-compound (II) with zinc and hydrochloric acid.

It is known [3] that xanthine reacts with phosphorus pentasulphide selectively at position 6. This has been found to apply also to methylxanthines, such as theophylline and theobromine, the latter giving 6-thiotheobromine (I). Desulphuration of this yielded

[1] Tafel, *Ber.*, 1899, **32**, 3194.
[2] Fichter and Kern, *Helv. Chim. Acta*, 1926, **9**, 380.
[3] Beaman, *J. Amer. Chem. Soc.*, 1954, **76**, 5633.

Tafel's " desoxytheobromine; " the absence of an ultraviolet absorption maximum above 220 mμ supports the formulation (II).



Different results were obtained with the 6-methylthio-derivative (III). This, on treatment with Raney nickel in water at 80°, gave satisfactory yields of the purine derivative (IV) which is now thus easily available.

The tendency of compound (I) to exchange its sulphur atom for *two* hydrogen atoms may be ascribed to its reluctance to pass into the mercapto-form. Such an explanation is, however, at variance with the observation that with Raney nickel at 100° the compound (IV) is slowly reduced (to II). The reason for the different behaviour of compounds (I) and (III) is therefore that the 6-methylthio-derivative reacts with Raney nickel at a temperature (80°) at which compound (I) is not attacked at all. It appears probable that compound (IV) is also the intermediate in the conversion of (I) into (II). Similar observations have recently been reported by Fox and van Praag in the desulphuration of 4-thiouracil.[4]

Experimental.—6-*Thiotheobromine* (I). A solution of theobromine (4 g.) and phosphorus pentasulphide (10 g., 2 equiv.) in pyridine (200 ml.) was refluxed for 6 hr. The solvent was removed *in vacuo* and the residue boiled with water (200 ml.). The aqueous extract, when filtered and cooled, deposited a yellow-brown material (4 g., 92%), which was dissolved in hot N-sodium hydroxide. This solution was decolorised with charcoal and acidified with glacial acetic acid. Recrystallisation from 95% ethanol gave yellow needles, m. p. 270—275° (decomp.) (Found: C, 43·1; H, 4·0. Calc. for $C_7H_8N_4OS$: C, 42·9; H, 4·1%).

1,2,3,6-*Tetrahydro*-3,7-*dimethyl*-2-*oxopurine* (II). Raney nickel (3 g.) was added to a solution of 6-thiotheobromine (1 g.) in 5% aqueous ammonia (15 ml.), and the mixture stirred under reflux for 1 hr. The catalyst was removed and the filtrate concentrated *in vacuo*. After 3 days at 0°, white needles (0·3 g., 33%) appeared, which melted at 210—215°, as reported by Tafel.[1] The picrate, which crystallised from water in yellow rods, had m. p. 205° (decomp.), as reported by Fichter and Kern.[2]

2,3-*Dihydro*-3,7-*dimethyl*-6-*methylthio*-2-*oxopurine* (III). A mixture of 6-thiotheobromine (1 g.), 2·5% aqueous sodium hydroxide (10 ml.), and methyl iodide (0·5 ml.) was stirred at room temperature for 1 hr. The white precipitate was filtered off and recrystallised from water, to give a 56% yield of needles, m. p. 260—262° (decomp.) (Found: C, 45·9; H, 4·6; N, 26·3. Calc. for $C_8H_{10}N_4OS$: C, 45·7; H, 4·8; N, 26·7%).

2,3-*Dihydro*-3,7-*dimethyl*-2-*oxopurine* (IV). Raney nickel (4 g.) was added to a stirred solution of the preceding compound (0·8 g.) in water (40 ml.), and the mixture kept at 80—90° for 1 hr. The catalyst was removed and the filtrate concentrated *in vacuo*. After 24 hr., a white precipitate (0·4 g., 58%) was obtained, which crystallised from ethanol in plates, m. p. 255—256° (decomp.). Above 100° the substance changes to a grey powder (Tafel [1] reports the same m. p. for the substance, after it had lost its water of crystallisation at 100°) (Found: C, 46·4; H, 5·1. Calc. for $C_7H_8N_4O,H_2O$: C, 46·2; H, 5·5%).

The absorption maxima (see Table) were measured in 0·01N-phosphate buffer of pH 8·0. The R_F values (see Table) were determined on Whatman paper No. 1 by the descending method;

Ultraviolet absorption spectra and R_F values.

Compound	$\lambda_{max.}$ (mμ)	log ε	R_F A	R_F B	Fluorescence
(I)	255, 346	2·93, 3·61	0·65	0·8	Yellow
(III)	270, 317	3·95, 4·09	0·6	0·65	Blue
(IV)	272, 318	4·00, 4·12	0·7	0·75	White

A: 95% ethanol–acetic acid–water (17 : 1 : 2). B: 95% ethanol–pyridine–water (7 : 2 : 1).

[4] Fox and van Praag, *J. Amer. Chem. Soc.*, 1960, **82**, 486.

spots were located by their fluorescence under a Mineralight ultraviolet lamp, emitting light of about 255 mμ.

This study was supported by grant No. RG-6631 from the United States National Institutes of Health.

DEPARTMENT OF PHARMACOLOGY, THE HEBREW UNIVERSITY-HADASSAH MEDICAL SCHOOL, JERUSALEM, ISRAEL. [*Received, March 17th*, 1960.]

735. *Infrared Spectra of Deuterium Compounds. Part II.* The Methyl Crotonates.*

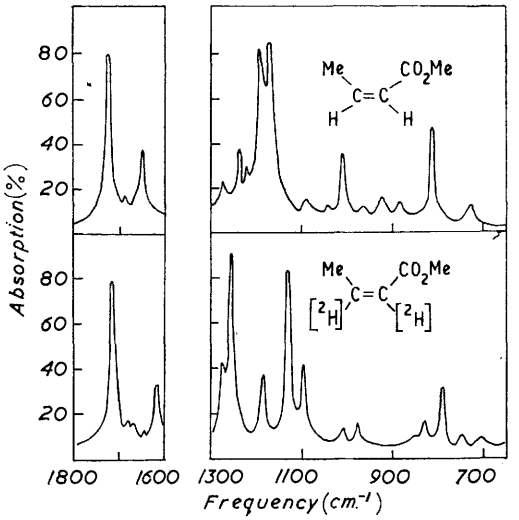
By F. DALTON, P. S. ELLINGTON, and G. D. MEAKINS.

WHILE conjugation of a 1,2-disubstituted ethylenic centre with carbon–carbon multiple bonds has been shown to cause regular shifts in the olefinic C–H out-of-plane bending vibrations, the effect of conjugation with C=O groups has not been systematically studied.[1] In this connection an important result is the correlation of the olefinic hydrogen bending

Infrared frequencies (cm.$^{-1}$) of methyl crotonates, RMeC=C·RCO$_2$Me.

The compounds were examined in carbon disulphide on a Perkin–Elmer model 21 spectrometer. Figures in parentheses are apparent molecular extinction coefficients (mole^{-1} l. cm.$^{-1}$).

	Ester	C=O stretching	C=C stretching	Prominent bands between 1350 and 650 cm.$^{-1}$				
trans	R = H	1726(~800)	1657(180)	1311(300)	1290(170)	1193(~400)		969(220)
					1263(250)	1176(~450)		
	R = [^{2}H]	1720(~800)	1623(110)		1260(~500)		1080(240)	718(120)
					1244(~450)			
cis	R = H	1723(~800)	1646(120)		1241(100)	1192(~400)	1012(90)	812(150)
						1172(~500)		
	R = [^{2}H]	1718(~800)	1620(80)		1277(100)	1130(350)	1089(90)	791(70)
					1256(~550)			



in *trans*- and *cis*-CH=CH·CO·X (X = OH, OR, NHR) with bands near 980 and 820 cm.$^{-1}$, respectively.[2] The shift ascribed to conjugation is exceptionally large in the second case (cf. the isolated *cis*-CH=CH– group with olefinic bending near 700 cm.$^{-1}$), and an alternative assignment of the 820 cm.$^{-1}$ band is possible.[3] The purpose of the present work was to

* Part I, *J.*, 1960, 2927.

[1] Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, p. 40.
[2] For references see Allan, Meakins, and Whiting, *J.*, 1955, 1874.
[3] Walton and Hughes, *Analyt. Chem.*, 1956, **28**, 1388; *J. Amer. Chem. Soc.*, 1957, **79**, 3985.

locate the ethylenic hydrogen bending bands in the methyl crotonates by comparing their spectra with those of the corresponding αβ-dideutero-derivatives.

Deuteration of methyl tetrolate afforded methyl *cis*-[αβ-$^2H_2$]crotonate which was isomerised to the *trans*-[αβ-$^2H_2$]crotonate without change in deuterium content (see Experimental). The Figure and Table show that the 968 cm.$^{-1}$ band of the normal *trans*-crotonate and the 820 cm.$^{-1}$ band of the normal *cis*-ester are missing from the spectra of the deuterium compounds, in agreement with the assignment of these bands to the –CH=CH– groupings in the normal series. The 718 cm.$^{-1}$ band of the *trans*-[αβ-$^2H_2$]crotonate may correspond to the 968 cm.$^{-1}$ band of the normal compound, but no such correlation could be made in the *cis*-compounds.* It is possible that the 820 cm.$^{-1}$ band of the normal *cis*-ester represents two superimposed absorptions, the main one being the olefinic CH deformation, and the weaker one a skeletal vibration which appears at 791 cm.$^{-1}$ in the deutero-derivative.

The overall differences between the spectra of the normal esters and the corresponding deutero-compounds are surprisingly large. As well as the lowering in the frequencies and intensities of the C=C stretching bands there are marked changes in the intense bands between 1300 and 1000 cm.$^{-1}$. (Somewhat similar, although less pronounced, differences between normal and deuterated esters have been observed previously.[4]) The occurrence of these changes in bands not primarily associated with the deformation of CH bonds is thought not to invalidate the above identifications of the olefinic CH out-of-plane bending bands, since these can reasonably be expected to appear below 1000 cm.$^{-1}$.

Experimental.—Methyl cis-[αβ-$^2H_2$]*crotonate.* A suspension of Lindlar catalyst (1 g.) [5] in 99·8% deuterium oxide (3 ml.) and dioxan (30 ml.) was shaken in deuterium for 16 hr. After evaporation of the mixture at 20 mm., the catalyst was dried at 60°/0·05 mm. for 6 hr. and added to a solution of methyl tetrolate (1·5 g.) [6] in dry ether (50 ml.). The mixture was shaken in deuterium until 353 ml. of gas had been adsorbed, and then filtered, and the solvent evaporated through a Vigreux column. Distillation of the residue afforded methyl *cis*-[αβ-$^2H_2$]crotonate (0·94 g.), b. p. 107—108° [1·90 atoms of deuterium per molecule (mass analysis); no impurities detectable by gas-phase chromatography].

Methyl trans-[αβ-$^2H_2$]*crotonate.* (The following procedure was developed after trial experiments with methyl *cis*-crotonate in carbon disulphide. The isomerisation was followed by infrared spectral examination of the solution, and the product was isolated and shown to be methyl *trans*-crotonate.) A solution of methyl *cis*-[αβ-$^2H_2$]crotonate (0·9 g.) and iodine (20 mg.) in dry ether (20 ml.), contained in a sealed Pyrex-glass tube, was warmed by irradiation with a 250w tungsten lamp for 28 days. Evaporation of the solution (fractionating column) and distillation of the residue gave methyl *trans*-[αβ-$^2H_2$]crotonate (0·55 g.), b. p. 118—119° [1·86 atoms of deuterium per molecule (mass analysis); no impurities detectable by gas-phase chromatography].

We are indebted to Dr. J. H. Baxendale for the mass analyses, to the Department of Scientific and Industrial Research for a grant (to F. D.), to the Ministry of Education for a research scholarship (to P. S. E.), and to Mrs. I. Croxon and Miss D. Trafford for technical assistance.

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* We are grateful to Dr. J. E. Page for examining the *cis*-compounds between 700 and 400 cm.$^{-1}$.

[4] Nolin and Jones, *Canad. J. Chem.*, 1956, **34**, 1382, 1392.
[5] Lindlar, *Helv. Chim. Acta*, 1952, **35**, 446.
[6] Henbest, Jones, and Walls, *J.*, 1950, 3646.

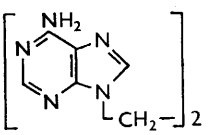
736. *Polypurines. Part II.*[1] *Occurrence of Isomers in the Preparation of* 1,2-*Di*-9′-*adeninylethane.*

By J. H. LISTER.

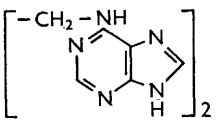
FROM the crude product obtained in the preparation of 1,2-di-9′-adeninylethane [1] (I), alkali removed a by-product which, although giving satisfactory analyses for the expected isomer (II), did not show ultraviolet absorption similar to that of simpler 6-(substituted

[1] Part I, Lister, *J.*, 1960, 3394.

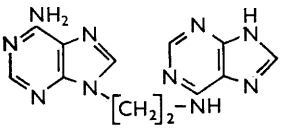
amino)purines, 6-methylaminopurine [2] being used for reference spectra. 1,2-Di-6′-purinylaminoethane (II) was prepared by condensing 6-chloropurine with ethylenediamine: its spectra were similar to those of 6-methylaminopurine but different from those of the by-product. However, the wavelength of the maximum absorption band of the by-product was intermediate between those of the isomers (I) and (II).



(I)



(II)



(III)

Therefore, the asymmetrically linked isomer (III) was prepared, by interaction of 9-2′-aminoethyladenine [3] and 6-chloropurine; both its ultraviolet and infrared spectra resembled those of the by-product but were not identical. The by-product was then found chromatographically to be inhomogeneous: the main spot was eluted and gave a spectrum identical with that of the asymmetric compound (III). Calculations from the ultraviolet data show that the by-product is mainly (III), with about 10% of (II). The crude product from the cyclisation is therefore a mixture of the three isomers with an approximate composition of (I) 80%, (III) 18%, and (II) 1—2%.

Absorption maximum (mμ) (*values in parentheses are for* 10^{-3} ε).

	pH 1		pH 13	
Subst.	$\lambda_{max.}$	$\lambda_{min.}$	$\lambda_{max.}$	$\lambda_{min.}$
(I)	258 (24·6)	232 (6·1)	258 (21·0)	230 (4·7)
(III)	266 (24·1)	233·5 (6·7)	263·5 (22·8)	237·5 (8·0)
(II)	277·5 (27·6)	234·5 (5·9)	276 (28·6)	241 (7·0)

Experimental.—Analyses are by Mr. P. R. W. Baker, Wellcome Research Laboratories, Beckenham. All compounds were dried at 140°.

By-product from the preparation of 1,2-*di*-9′-*adeninylethane*. The crude product [1] (60% yield) was digested with 2N-sodium hydroxide at 60° for 5 min. The suspension was filtered and the filtrate cooled and brought to pH 6 with acetic acid. The granular precipitate (0·15 g., 10% yield on starting material) was purified by further precipitations and washed with water and ethanol giving the *by-product*, m. p. >350° (Found: C, 46·8; H, 4·3; N, 45·4. $C_{12}H_{12}N_{10},\frac{1}{2}H_2O$ requires C, 47·2; H, 4·3; N, 45·9%). Chromatography on paper with 5% ammonia solution in 17 : 3 butanol–water gave a main spot, R_F 0·2, and a minor spot just above the origin.

1,2-*Di*-6′-*purinylaminoethane* (II).—A solution of 6-chloropurine (1 g.) in butan-1-ol (20 ml.) was heated under reflux with 70% aqueous ethylenediamine (0·3 g.) and triethylamine (3 ml.) for 3 hr. After cooling, the precipitate was filtered off, taken up in 2N-sodium hydroxide (charcoal), and reprecipitated with acetic acid, giving the *dipurine* (0·55 g., 57%), m. p. >350° (Found: C, 47·1; H, 4·3. $C_{12}H_{12}N_{10},\frac{1}{2}H_2O$ requires C, 47·2; H, 4·3%). From 2N-hydrochloric acid this gave a *dihydrochloride* (Found: C, 39·15; H, 3·8; N, 38·1. $C_{12}H_{12}N_{10},2HCl$ requires C, 39·0; H, 3·8; N, 37·9%).

9-(2-6′-*Purinylaminoethyl*)*adenine* (III).—To a solution of 9-2′-aminoethyladenine [3] (1·8 g.) in water (40 ml.) and triethylamine (8 ml.) was added 6-chloropurine (1·4 g.), and the mixture heated under reflux for 2 hr. The *product*, after cooling, was filtered off and washed with water and ethanol (1·2 g., 38%) and purified by dissolution in 50% acetic acid and precipitation at pH 6 with ammonia solution: it did not melt below 350° (Found: C, 45·7; H, 4·8; N, 44·3. $C_{12}H_{12}N_{10},H_2O$ requires C, 45·85; H, 4·5; N, 44·6%).

I thank Miss J. M. Wiseman and Dr. Lumley Jones for the ultraviolet and infrared absorption data respectively, and the Medical Research Council, the British Empire Cancer Campaign,

[2] Mason, *J.*, 1954, 2071.
[3] Lister and Timmis, *J.*, 1960, 327.

the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service for grants to this Institute.

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737. *The Solubilities of Some Alkali Bromides in Aqueous Bromine Solutions.*

By G. H. CHEESMAN and E. K. NUNN.

EARLIER work with which one of us has been associated has surveyed several systems of the type water–bromine–alkali bromide with the object of detecting polybromides as solid phases. The present report concerns three such systems that yielded no new compounds, but since the compositions of the invariant solutions give a useful indication of the general behaviour of each system, it is felt that the data are worth placing on record.

Ammonium Bromide.—In the system H_2O–Br_2–NH_4Br at 0° the compound NH_4Br_3 [1] has a long solubility arc terminated by two invariant solutions whose compositions are (all compositions are given as percentages by weight):

(1) NH_4Br, 35·04%; Br_2, 28·13%; in equilibrium with NH_4Br and NH_4Br_3
(2) NH_4Br, 9·39%; Br_2, 85·70%; in equilibrium with NH_4Br_3 and Br_2.

Sodium Bromide.—This system was examined by Harris [2] who reported that the highest invariant lay between hydrated sodium bromide, bromine, and solution; he gave no figures. We have determined that the invariant solution at 0° has the composition:

NaBr, 13·23%; Br_2, 73·86%; in equilibrium with $NaBr,2H_2O$ and Br_2.

Lithium Bromide.—In this system no polybromide is formed at 0° and the highest invariant solution has the composition:

LiBr, 6·12%; Br_2, 86·38%; in equilibrium with $LiBr,2H_2O$ and Br_2.

It is noteworthy that lithium bromide dihydrate appears as the stable phase at this invariant since Hüttig and Reuscher [3] showed that this hydrate only exists in stable equilibrium with aqueous solutions above 4°. We have confirmed (by using small concentrations of Xylene Cyanol FF, determined absorptiometrically) that at 0° and in the absence of bromine the trihydrate is the stable phase as stated by Hüttig and Reuscher, and find its solubility at this temperature to be 57·35% (by weight). However, the dihydrate is found (by seeding experiments) to be stable in contact with solutions containing as little as 0·76% of bromine; thus the invariant solution in equilibrium with the di- and tri-hydrates must contain less bromine than this.

In all the foregoing, the phase described as Br_2 is, of course, saturated with water and halide, but analysis showed the concentration of the latter to be negligible in all the three cases. This resembles the behaviour of potassium bromide [4] but contrasts markedly with cæsium bromide, which Harris [5] also studied; this dissolves to a considerable extent in the bromine-rich liquid. At lower bromide concentrations, in each case, bromine hydrate forms a solid phase at 0°.

THE UNIVERSITY OF TASMANIA, HOBART, TASMANIA. [*Received, April 20th,* 1960.]

[1] Roozeboom, *Ber.*, 1881, **14**, 2398.
[2] Harris, *J.*, 1932, 1697.
[3] *Z. anorg. Chem.*, 1924, **137**, 155.
[4] Harris, *J.*, 1932, 1694.
[5] Harris, *J.*, 1932, 2709.