Oxidation of Indoles with Lead Tetra-acetate and Hydrolysis of 1,2-Disubstituted Indol-3-yl Acetates

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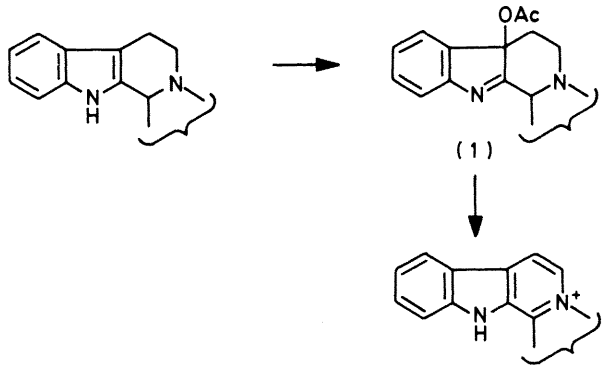
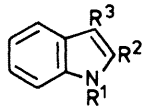
Oxidation of some 1,2-disubstituted indoles with lead tetra-acetate gives the corresponding 3-acetoxy derivatives. Similar oxidation of ethyl indole-2-carboxylate affords an acetoxylated 3,3'-bi-indolyl product; methyl 1-methylindol-3-ylacetate is acetoxylated at the benzylic position of the side-chain. Alkaline hydrolysis of 1,2-disubstituted indol-3-yl acetates is accompanied by autoxidation and rearrangement to give dioxindoles, but hydrolysis of 2-ethoxycarbonyl-1-methylindol-3-yl acetate gives *NN'*-dimethyl derivatives of indigo and indirubin.

In spite of the versatility of lead tetra-acetate (LTA) for the oxidation of aromatic and nitrogen-containing organic compounds,[1,2] there are very few reports of the oxidation of indoles by this reagent.[3-5] Yohimbine alkaloids are aromatised by treatment with LTA in acetic acid,[3] and intermediate 3*H*-indol-3-yl acetates (1) are isolable with LTA in dichloromethane (Scheme 1).[4] Oxidation at the α-carbon of the 2-substituent occurs for 2,3-dimethylindole and 2-benzyl-3-phenylindole to give the products (2) and (3), respectively;[5] in both cases mechanisms can be written involving 3*H*-indol-3-yl acetates as intermediates. The indole-ester (4) with LTA in refluxing dichloromethane gave a 5- or 6-acetoxy derivative in low yield.[6] Our previous work on the LTA oxidation of enamine-esters[6,7] and the similarity between indoles and enamines led us to undertake a more systematic study of the oxidation of indoles by LTA.



Scheme 1.



(2) R^1 = H, R^2 = $CH(OAc)_2$, R^3 = Me
(3) R^1 = Ac, R^2 = COPh, R^3 = Ph
(4) R^1 = Me, R^2 = R^3 = CO_2Me
(5) R^1 = R^3 = H, R^2 = CO_2Et

Results and Discussion

From a series of 1,2-disubstituted indoles (6a—e) we were able to obtain the corresponding indol-3-yl acetates (7a—e) using LTA in dichloromethane; the products (7d and e) containing a 2-acyl group were obtained less readily and in lower yield than compounds (7a—c) (Table). The mass spectra of (7a—e) included strong fragment ions due to the loss of CH_2CO from the acetoxy group. The resonance due to 3-H in the ^1H n.m.r. spectra of the indoles (6a—e) was replaced by one due to the OAc group in the spectra of (7a—e). The resonance assigned to C-3 in the ^{13}C n.m.r. spectra of the indoles (6) [*e.g.*, δ_C 102.0 p.p.m. in (6b)] was shifted to lower field in the spectra of the products (7) [δ_C 117.4 p.p.m. in (7b)] and no longer coupled to ^1H in the off-resonance spectra.

Alkaline hydrolysis of the indol-3-yl acetates (7a—c) was accompanied by autoxidation and rearrangement to give the dioxindoles (9a—c). This unexpected result was confirmed by formation of the known compound (9d) from 1,2-dimethylindol-3-yl benzoate (8) under the same hydrolysis conditions and by independent syntheses of (9a and b) from *N*-methylisatin and the appropriate aryl Grignard reagent.

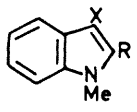
Alkaline hydrolysis of indol-3-yl acetate gives indoxyl, which is readily autoxidised *via* leucoindigo (12a) to indigo;[8] hydrolysis of 1-methyl- and 1-ethyl-indol-3-yl acetates in air similarly gives *NN'*-dialkylindigo derivatives.[9,10] Other indolin-3-ones are also readily oxidised to dimeric products *e.g.* (12b—d).[11,12] However, we obtained the dioxindoles (9b and c) in very high yield, and no dimeric products analogous to (12b and c) were detected, in spite of the expected formation of indolin-3-ones (11) on hydrolysis of indol-3-yl esters (Scheme 2).

Solvolysis of 3*H*-indol-3-yl acetates (1) in methanol–acetic acid is accompanied by rearrangement to give the oxindoles (13).[4] There are also precedents for the autoxidative hydroxylation of oxindoles under basic conditions,[13,14] including formation of the dioxindole (9a) from 1-methyl-3-phenyloxindole on treatment with sodium hydride in *NN*-dimethylformamide and exposure to air.[15] However, the formation of dioxindoles (9a—d) from indol-3-yl esters (7a—c) and (8) is best accounted for by hydrolysis, hydroxylation at the 2-position, and rearrangement occurring in that order (Scheme 2). The last two steps also explain how the dioxindole (9d) was obtained instead of the expected product (11; R = Me) from Dieckmann cyclisation of the diester (14).[16] The final step of Scheme 2 resembles the benzilic acid rearrangement of 1,2-diketones, and more particularly the formation of dioxindoles (10a and b) *via* 2-hydroxyindolin-3-ones from 3*H*-indol-3-ones (15a and b).[17,18]

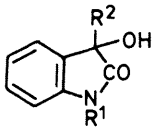
Alkaline hydrolysis of the indol-3-yl acetate (7e) under mild conditions afforded the indoxyl derivative (16) (44%), together with *NN'*-dimethylindigo (17) (4%) and other intensely coloured by-products. Compound (16) gave a dark green colour with iron(III) chloride and its i.r. spectrum showed an absorption for the hydroxy group. ^1H and ^{13}C N.m.r. spectra

Table. Characterisation of 1-methylindol-3-yl acetates (7)

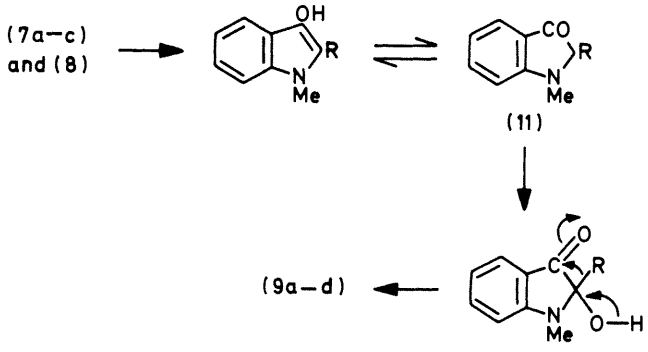
Compound	R	Yield (%)	M.p. (°C)	Found (%) (Required) C	H	N	δ_H (OAc)	M^+
(7a) ($C_{17}H_{15}NO_2$)	Ph	30	101—103	77.0 (77.0	5.9 5.7	5.3 5.3)	2.20	265
(7b) ($C_{17}H_{14}ClNO_2$)	C_6H_4Cl-*p*	44	167—168	68.1 (68.1	4.9 4.7	4.6 4.7)	2.15	299/301
(7c) ($C_{15}H_{19}NO_2$)	Bu^t	35	95—96	73.2 (73.4	7.9 7.8	5.7 5.7)	2.28	245
(7d) ($C_{18}H_{15}NO_3$)	COPh	13	128—129	73.5 (73.7	5.3 5.2	4.7 4.8)	1.72	293
(7e) ($C_{14}H_{15}NO_4$)	CO_2Et	25	93—95	64.4 (64.4	5.7 5.8	5.4 5.4)	2.38	261



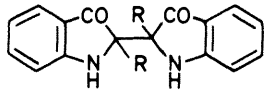
(6) a; X = H, R = Ph
b; X = H, R = C_6H_4Cl-*p*
c; X = H, R = Bu^t
d; X = H, R = COPh
e; X = H, R = CO_2Et
(7) a; X = OAc, R = Ph
b; X = OAc, R = C_6H_4Cl-*p*
c; X = OAc, R = Bu^t
d; X = OAc, R = COPh
e; X = OAc, R = CO_2Et
(8) X = OCOPh, R = Me



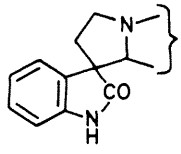
(9) a; R^1 = Me, R^2 = Ph
b; R^1 = Me, R^2 = C_6H_4Cl-*p*
c; R^1 = Me, R^2 = Bu^t
d; R^1 = R^2 = Me
(10) a; R^1 = H, R^2 = Ph
b; R^1 = H, R^2 = Bu^t



Scheme 2.



(12) a; R = H
b; R = Me
c; R = Ph
d; R = CO_2Et



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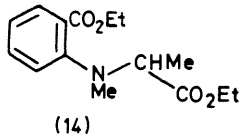

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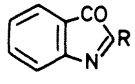


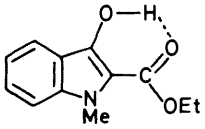
(15) a; R = Ph
b; R = Bu^t

confirmed the correctness of the 3-hydroxyindole structure (16), which is preferred to that of an indolin-3-one tautomer, as is the case for some hydroxypyrrole-esters.[6,19]

A third product, which formed dark red-violet crystals, was obtained (26%) by hydrolysis of (7e) with more concentrated alkali. Elemental analysis and mass spectrometry showed this product to be isomeric with (17), but its ^{1}H n.m.r. spectrum showed two resonances for NMe groups. Accordingly, this compound was identified as *NN'*-dimethylindirubin (18). The formation of indigoid products (17) and (18) is understandable, since hydrolysis of the ester group in (16) would be followed by decarboxylation (β-keto acid) to give 1-methylindolin-3-one (11; R = H), autoxidative dimerisation of which would follow the known precedent of the behaviour of indoxyl.[8,20]

Oxidation of ethyl indole-2-carboxylate (5) with LTA in refluxing benzene afforded a dimeric product, $C_{24}H_{22}N_2O_6$. I.r. and ^{1}H n.m.r. spectra indicated the presence of one NH, one OAc, and two non-equivalent OEt groups. All the evidence is consistent with the assignment of the 3,3'-bisindolyl structure (19), which is presumably formed by acetoxylation of the intermediate (20). Treatment of acyclic enamine-esters and of ethyl 4-ethoxypyrrole-2-carboxylate with LTA also results in oxidative dimerisation.[7,21]

Methyl 1-methylindol-3-ylacetate (21a) was oxidised by LTA, which attacked the side-chain in preference to the vacant 2-position of the ring. The primary product, the benzylic acetate (21b), afforded the α-methoxy derivative (21c) from hot methanol. On analogy with related side-chain-substitution reactions in the indole series,[22] the lability of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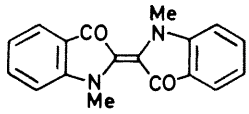
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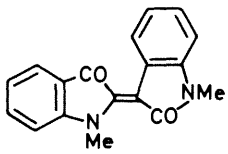
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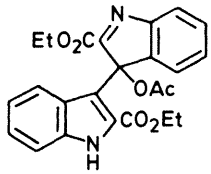
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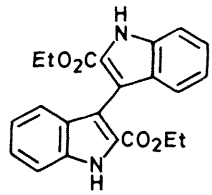
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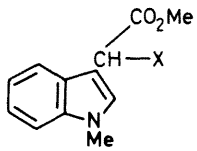
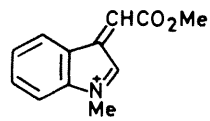

(21) a; X = H
b; X = OAc
c; X = OMe


(22)

compound (21b) is attributable to formation of the 3*H*-indolium intermediate (22).

Three patterns of reaction are now established for differently substituted indoles with LTA. Their usefulness will be developed in future work.

Experimental

I.r. spectra were recorded for Nujol mulls (unless otherwise stated), and absorptions are quoted only for the regions 1 600—1 800 and 3 000—3 500 cm^{-1}. ^1H N.m.r. spectra were obtained at 60 or 100 MHz (Varian EM-360A or JEOL MH-100 instruments) and ^{13}C n.m.r. spectra at 15 MHz (JEOL FX60) for solutions in deuteriochloroform; chemical shifts are quoted in p.p.m. downfield from internal tetramethylsilane. Mass spectra were obtained by electron impact at 70 eV (Kratos MS30); only the more important fragment ions (>20% relative intensity) are reported. Ether refers to diethyl ether. Light petroleum refers to that fraction boiling in the range 80—100 °C.

N-Methylindoles.—With the exception of 2-benzoylindole, all the required *N*-unsubstituted indoles were prepared by Fischer's synthesis, cyclisation of the appropriate phenylhydrazone by heating in polyphosphoric acid. 2-Benzoylindole was prepared from indole-2-carboxylic acid and phenyllithium,[23] but we found neither this nor a more recent method [24] to be as good as claimed.

2-t-Butylindole (3.5 g) was added to a stirred suspension of sodium hydride (1.2 g) in dry dimethyl sulphoxide (35 ml) under nitrogen. After 1 h this was followed by addition of methyl iodide (10 g) and the mixture was stirred overnight and then poured into water and extracted with ether; the extract was separated, washed with water, dried ($MgSO_4$), and the ether was evaporated off. Two short-path distillations of the residue *in vacuo* at 120 °C (bath) afforded *2-t-butyl-1-methylindole* (6c) (2.8 g, 74%) as an oil (Found: C, 83.6; H, 9.2; N, 7.5. $C_{13}H_{17}N$ requires C, 83.4; H, 9.2; N, 7.5%); δ_H 7.0—7.6 (4 H, m, ArH), 6.30 (1 H, s, 3-H), 3.72 (3 H, s, NMe), and 1.40 (9 H, s, Bu^t); *m/z* 187 (M^+, 88%), 173 (27), 172 ([M − Me]$^+$, 100), and 157 (27).

2-Benzoylindole was methylated by the same procedure to give 2-benzoyl-1-methylindole (6d) as an oil, b.p. 140—144 °C at 0.08 mmHg, which solidified after distillation, m.p. 53—54 °C (from light petroleum, b.p. 40—60 °C) (lit.,[23] b.p. 180 °C at 1 mmHg) (Found: C, 81.6; H, 5.5; N, 5.8. Calc. for $C_{16}H_{13}NO$: C, 81.7; H, 5.6; N, 5.95%); δ_H 7.0—7.9 (9 H, m, ArH), 6.92 (1 H, s, 3-H), and 4.03 (3 H, s, NMe); *m/z* 235 (M^+, 96%), 234 (100), 105 ($PhCO^+$, 36), 89 (50), 78 (97), and 77 (69).

N-Methylation of other indoles by the same procedure gave the known compounds (6a and b) and (21a), all having m.p.s in agreement with reported values.[25-27] The indole (5) with methyl iodide and potassium carbonate in refluxing acetone afforded ethyl 1-methylindole-2-carboxylate (6e), m.p. 59—60.5 °C (lit.,[28] 63—64 °C).

Oxidations with LTA.—LTA (4.43 g, 10 mmol) was added to a solution of 1-methyl-2-phenylindole (6a) (2.1 g, 10 mmol) in dry dichloromethane (25 ml) and the mixture was kept at ambient temperature for 5 h. After being tested for the absence of unchanged lead(IV), the solution was filtered from lead diacetate; the filtrate was washed in turn with water and aqueous sodium hydrogen carbonate, and was dried. After removal of dichloromethane, the oily residue was chromatographed on silica gel, from which light petroleum eluted *1-methyl-2-phenylindol-3-yl acetate* (7a), which was recrystallised from ethanol. Data are given in the Table.

The same general procedure was employed for oxidation of other indoles, with the following modifications. Compound (6b) was allowed to react for 22 h with LTA before work-up, and the product afforded the acetate (7b) on trituration with methanol. Compound (6c) was mixed with LTA at 0 °C, then kept for 18 h at room temperature before work-up; the crude product was chromatographed on alumina, from which the acetate (7c) was eluted with benzene and then recrystallised from light petroleum. Compounds (6d and e) were heated with LTA in dichloromethane under reflux for 22 and 16 h, respectively, before work-up, and the crude products afforded the acetates (7d and e) on trituration with methanol. The indol-3-yl acetates (7a—e) were characterised by the data presented in the Table.

The indole (5) (1.9 g) and LTA (4.43 g) in benzene (40 ml) were heated under reflux for 6 h; the mixture was cooled and worked up by the standard procedure. The crude product was chromatographed on silica gel, from which ether–dichloromethane (9 : 1 v/v) eluted the *3-acetoxy-3,3′-bi-indolyl derivative* (19) (0.3 g, 13%), m.p. 160—162 °C (from methanol) (Found: C, 66.3; H, 5.2; N, 6.5. $C_{24}H_{22}N_2O_6$ requires C, 66.35; H, 5.1; N, 6.45%); $\nu_{max.}$ ($CHCl_3$) 1 730 (C=O) and 3 460 (N–H) cm^{-1}; δ_H 9.08 (1 H, br, NH), 7.78 (1 H, d, *J* 8 Hz, 7-H) 7.1—7.6 (7 H, m, other ArH), 4.28 (4 H, two overlapping q, 2 × OCH_2), 2.12 (3 H, s, COMe), and 1.25 (6 H, two overlapping t, 2 × CH_2Me); δ_C 168.4, 161.1, and 160.6 (C=O), 153.0 (C=N), 139.1, 135.5, 130.3, 129.1, 125.5, 123.6, 123.3, 121.2, 114.4, and 112.2 (benzene ring carbons and C-2′ and C-3′), 61.8 and 61.5 (OCH_2), 21.2 (COMe), and 14.3 and 14.1 p.p.m. (CH_2Me); *m/z* 434 (M^+, 3%), 392 ([M − CH_2CO]$^+$, 5), 377 (27), 376 ([M − OAc]$^+$, 100), 284 (24), 258 (39), and 257 (48).

The indole (21a) (2.0 g) and LTA (4.4 g) were mixed in

dichloromethane (25 ml) at 0 °C, then left for 6 h at room temperature before work-up. The crude product was a yellow oil which contained the acetate (21b) [δ_H 2.15 (OAc)]; on one occasion trituration with methanol induced crystallisation of a solid (1.3 g), m.p. 94—100 °C, but attempted recrystallisation of this from hot methanol gave *methyl α-methoxy-1-methylindol-3-ylacetate* (21c) (0.76 g, 33%) as an oil, which was purified by short-path distillation *in vacuo* (Found: C, 67.0; H, 6.45; N, 5.6. $C_{13}H_{15}NO_3$ requires C, 66.9; H, 6.5; N, 6.0%); $\nu_{max.}$ 1 620 and 1 750 cm^{-1}; δ_H 7.0—7.9 (4 H, m, ArH), 7.08 (1 H, s, 2-H), 5.08 (1 H, s, α-CH), and 3.63, 3.57, and 3.37 (each 3 H, s, together 2 × OMe and NMe); δ_C 171.3 (C=O), 136.8, 128.3, 126.0, 121.7, 119.4, and 109.2 (benzene ring carbons, C-2, and C-3), 75.9 (tertiary carbon), 56.4 and 51.8 (OMe), and 32.4 p.p.m. (NMe); *m/z* 233 (M^+, 17%), 174 ($[M - CO_2Me]^+$, 100), 158 (47), 119 (46), 117 (46), and 84 (30).

Hydrolysis of Indol-3-yl Esters.—1-Methyl-2-phenylindol-3-yl acetate (7a) (0.53 g, 2 mmol) was heated with potassium hydroxide (0.27 g) in aqueous ethanol (8 ml) under reflux for 4 h. The solution was cooled, neutralised by addition of dilute hydrochloric acid, and extracted with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated to give 1-methyl-3-phenyldioxindole (9a) (0.20 g, 42%), m.p. 142—144 °C (from ethanol) (lit.,[15] 139—141 °C), identical (mixed m.p. and i.r. spectrum) with a sample obtained by an independent synthesis from *N*-methylisatin and phenylmagnesium bromide.

The indol-3-yl acetate (7b) (0.56 g), heated with potassium hydroxide in aqueous ethanol for 18 h and worked up in the same way, afforded 3-p-*chlorophenyl*-1-*methyldioxindole* (9b) (0.47 g, 92%), m.p. 182—183 °C (from ethanol) (Found: C, 66.0; H, 4.4; N, 5.4. $C_{15}H_{12}ClNO_2$ requires C, 65.8; H, 4.4; N, 5.1%). The same product, (9b), was obtained independently from *N*-methylisatin and *p*-chlorophenylmagnesium bromide, m.p. and mixed m.p. 181—182.5 °C; identical i.r. spectrum: $\nu_{max.}$ 1 610, 1 710 (C=O), and 3 300 (O–H) cm^{-1}; δ_H 6.7—7.3 (8 H, m, ArH), 3.87 (1 H, br, OH, exchangeable), and 3.07 (3 H, s, NMe); δ_C 177.3 (C=O), 143.3, 138.7, 134.1, 131.4, 130.0, 128.6, 126.9, 124.8, 123.8, and 108.8 (benzene ring carbons), 77.6 (C-3), and 26.6 p.p.m. (NMe); *m/z* 275/273 (M^+, 33/100%), 259/258/257/256 (23/44/67/83), 247/246/245/244 (22/33/78/65), 231/230/229/228 (8/33/20/75), 222 (24), 221 (34), 193 (28), 165 (38), 152 (23), 139 (28), 134 (35), 111 (30), 77 (40), and 75 (30).

Alkaline hydrolysis of the indol-3-yl acetate (7c) (0.27 g) by the same procedure as described for (7a) similarly afforded 3-*t-butyl*-1-*methyldioxindole* (9c) (0.25 g, 99%), m.p. 127.5—128.5 °C (from light petroleum) (Found: C, 71.3; H, 7.8; N, 6.3. $C_{13}H_{17}NO_2$ requires C, 71.2; H, 7.8; N, 6.4%); $\nu_{max.}$ 1 615, 1 712 (C=O), and 3 430 (O–H) cm^{-1}; δ_H 7.5—6.7 (4 H, m, ArH), 3.13 (3 H, s, NMe), 2.87 (1 H, br, OH, exchangeable), and 1.04 (9 H, s, Bu^t); *m/z* 219 (M^+, 5%), 163 ($[M - C_4H_8]^+$, 100), and 58 (22).

1,2-Dimethylindol-3-yl benzoate (8) [29] (0.18 g) was hydrolysed by the same procedure. The crude product was chromatographed on alumina, from which dichloromethane eluted 1,3-dimethyldioxindole (9d) (35 mg, 29%), m.p. 151—152.5 °C (from benzene) (lit.,[16,30] m.p. 150—151, 157—159 °C).

The indol-3-yl acetate (7e) (1.2 g) was heated with potassium hydroxide (0.5 g) in refluxing aqueous ethanol (5 ml) for 3 h. The crude product obtained after the usual work-up was a dark green solid (0.83 g) which was recrystallised to give *ethyl 3-hydroxy-1-methylindole-2-carboxylate* (16) (0.44 g, 44%), m.p. 95—95.5 °C (from ethanol) (Found: C, 65.8; H, 5.95; N, 6.4. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4%); $\nu_{max.}$ 1 655 (C=O) and 3 320 (O–H) cm^{-1}; δ_H 8.70 (1 H, s, OH, exchangeable), 7.02—7.84 (4 H, m, ArH), 4.47 (2 H, q, OCH_2), 3.85 (3 H, s, NMe), and 1.43 (3 H, t, CH_2Me); δ_C 164.3 (C=O), 148.9, 137.5, 127.0, 120.1, 118.8, 116.3, 109.7, 109.3 (benzene ring carbons, C-2, and C-3), 60.6 (CH_2), 31.6 (NMe), and 14.4 p.p.m. (CH_2Me); *m/z* 219 (M^+, 49%), 173 (87), 145 (45), 117 (100), 104 (43), 77 (28), and 76 (35); *m** 136.7 (219 → 173), 121.5 (173 → 145), and 94.4 (145 → 117). Material recovered from the ethanolic mother liquor was a mixture of several coloured components, which was separated by preparative t.l.c. (p.l.c.) on silica gel to give *NN'*-dimethylindigo (17) (28 mg, 4%) as irridescent dark green crystals, m.p. 185—188 °C (from ethanol) (lit.,[9] m.p. 182 °C); $\lambda_{max.}$ (xylene) 303 and 642 nm, in agreement with reported values; [9] δ_H 7.49—6.73 (8 H, m, ArH) and 3.47 (6 H, s, 2 × NMe); *m/z* 290 (M^+, 100%).

Hydrolysis of compound (7e) (0.43 g) with potassium hydroxide (1.8 g) in refluxing aqueous ethanol (10 ml) for 4.5 h followed by the usual work-up procedure gave a dark blue crude product which contained several coloured components. P.l.c. separated *NN'-dimethylindirubin* (18) (63 mg, 26%) as dark red-violet crystals, m.p. 210.5—211.5 °C (from ethanol) (Found: C, 74.5; H, 4.9; N, 9.8. $C_{18}H_{14}N_2O_2$ requires C, 74.5; H, 4.9; N, 9.65%); $\lambda_{max.}$ ($CHCl_3$) 297, 369, and 579 nm; $\nu_{max.}$ ($CHCl_3$) 1 605 and 1 675 cm^{-1}; δ_H 8.7—6.8 (8 H, m, ArH) and 3.62 and 3.31 (each 3 H, s, NMe); *m/z* 291 (27%), 290 (M^+, 100), 289 (22), 261 (18), 105 (20), and 104 (21).

References

1 R. Criegee in 'Oxidation in Organic Chemistry,' Part A, ed. K. B. Wiberg, Academic Press, New York, 1965, p. 227; D. R. Harvey and R. O. C. Norman, *J. Chem. Soc.*, 1964, 4860; R. O. C. Norman, C. B. Thomas, and J. S. Willson, *J. Chem. Soc. B*, 1971, 518; *J. Chem. Soc., Perkin Trans. 1*, 1973, 325.
2 R. N. Butler, *Chem. Ind. (London)*, 1968, 437; 1972, 523; J. Warkentin, *Synthesis*, 1970, 279; J. B. Aylward, *Quart. Rev.*, 1971, **25**, 407; R. N. Butler in 'Synthetic Reagents,' ed. J. S. Pizey, Ellis Horwood, Chichester, 1977, vol. 3, p. 277.
3 G. Hahn, E. Kappes, and H. Ludwig, *Ber.*, 1934, **67**, 686.
4 N. Finch, C. W. Gemenden, I. H.-C. Hsu, and W. I. Taylor, *J. Am. Chem. Soc.*, 1963, **85**, 1520.
5 F. Y. Chen and E. Leete, *Tetrahedron Lett.*, 1963, 2013.
6 J. M. Vernon, R. M. Carr, and M. A. Sukari, *J. Chem. Res.*, 1982, (*S*) 115; (*M*) 1310.
7 R. M. Carr, R. O. C. Norman, and J. M. Vernon, *J. Chem. Soc., Perkin Trans. 1*, 1980, 156; M. A. Sukari and J. M. Vernon, *Tetrahedron*, 1983, **39**, 793.
8 G. Spender, *J. Soc. Chem. Ind., London*, 1931, **50**, 63T; G. A. Russell and G. Kaupp, *J. Am. Chem. Soc.*, 1969, **91**, 3851.
9 L. Ettinger and P. Friedlaender, *Ber.*, 1912, **45**, 2074; J. Formanek, *Z. Angew. Chem.*, 1928, **41**, 1133.
10 J. van Alphen, *Recl. Trav. Chim. Pays-Bas*, 1942, **61**, 201.
11 E. Giovannini, F. Farkas, and J. Rosales, *Helv. Chim. Acta*, 1963, **46**, 1326; A. Hassner and M. J. Haddadin, *J. Org. Chem.*, 1963, **28**, 224.
12 *Cf.* L. Kalb, *Ber.*, 1911, **44**, 1455; R. M. Acheson and S. R. G. Booth, *J. Chem. Soc. C*, 1968, 30.
13 P. C. Julian and J. Pikl, *J. Am. Chem. Soc.*, 1935, **57**, 539; R. B. Longmore and B. Robinson, *Collect. Czech. Chem. Commun.*, 1967, **32**, 2184.
14 E. C. Kendall and A. Osterberg, *J. Am. Chem. Soc.*, 1927, **49**, 2047; K. Freter, H. Weissbach, B. Redfield, S. Udenfriend, and B. Witkop, *ibid.*, 1958, **80**, 983.
15 P. Aeberli and W. J. Houlihan, *J. Org. Chem.*, 1968, **33**, 1640.
16 E. Giovannini and J. Rosales, *Helv. Chim. Acta*, 1963, **46**, 1322.
17 L. Kalb and J. Bayer, *Ber.*, 1912, **45**, 2150; E. Pfeil, G. Geissler, W. Jacquemin, and F. Lömker, *Chem. Ber.*, 1956, **89**, 1210; C. W. Rees and C. R. Sabet, *J. Chem. Soc.*, 1965, 870.
18 M. A. Colle and S. David, *C.R. Hebd. Seances, Acad. Sci.*, 1960, **250**, 2226; *cf.* also ref. 12.
19 R. Chong and P. Clezy, *Aust. J. Chem.*, 1967, **20**, 935.

20 A. G. Perkin and F. Thomas, *J. Chem. Soc.*, 1909, **95**, 739; A. Wahl and P. Barnard, *Bull. Soc. Chim. Fr.*, [4], 1910, **7**, 1090.
21 H. Bauer, *Chem. Ber.*, 1968, **101**, 1286.
22 T. A. Geissman and A. Armen, *J. Am. Chem. Soc.*, 1952, **74**, 3916; E. Leete and L. Marion, *Can. J. Chem.*, 1953, **31**, 775; F. C. Uhle and L. S. Harris, *J. Am. Chem. Soc.*, 1957, **79**, 102; E. Leete, *ibid.*, 1959, **81**, 6023.
23 N. V. Koninklijke Pharmaceutische Fabrieken, Belg.P. 637 355/1964 (*Chem. Abstr.*, 1965, **62**, 7731).
24 D. St. C. Black and L. C. H. Wong, *J. Chem. Soc., Chem. Commun.*, 1980, 200.
25 M. I. Grineva, V. L. Sodovskaya, and N. V. Ufimtsev, *Zh. Obshch. Khim.*, 1963, **33**, 552.
26 C. E. Blades and W. L. Wilds, *J. Org. Chem.*, 1956, **21**, 1013.
27 A. R. Katritzky, *J. Chem. Soc.*, 1955, 2581.
28 J. R. Johnson, R. B. Hasbrouck, J. D. Dutcher, and W. F. Bruce, *J. Am. Chem. Soc.*, 1945, **67**, 423.
29 Y. Kanaoka, M. Aiura, and S. Hariya, *J. Org. Chem.*, 1971, **36**, 458.
30 A. S. Bailey, C. J. Barnes, and P. A. Wilkinson, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1321.

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