mosphere was added dropwise over 30 min "solution A". After the feed, the cooling bath was removed and the mixture was stirred for 1 h. At the end of the reaction period the layers were separated (pH of water ~7) after which the organic layer was washed once with water (50 mL), dried over Na_2SO_4, and concentrated to give 14.75 g (70%) of yellow liquid **11**: NMR (CCl_3D) δ 0.80–2.00 (m, 28), 2.95 (t, 8, NCH_2).

Anal. Calcd for $C_{16}H_{36}N_2S_3$: C, 54.59; H, 10.29; N, 7.94; S, 27.27. Found: C, 53.78; H, 9.52; N, 7.70; S, 28.35.

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Registry No.—**3**, 51229-17-5; **4a**, 111-92-2; **4b**, 110-91-8; **4c**, 142-84-7; **4d**, 103-67-3; **4e**, 14321-27-8; **4f**, 110-89-4; **4g**, 109-89-7; **5a**, 67271-09-4; **5b**, 103-34-4; **5c**, 38126-23-7; **5d**, 62158-05-8; **5e**, 67271-10-7; **5f**, 10220-20-9; **5g**, 15575-30-1; **6a**, 6541-82-8; **6b**, 2958-89-6; **6c**, 34695-15-3; **6d**, 53370-27-7; **6e**, 55285-27-3; **6f**, 16005-90-6; **6g**, 14274-26-1; **9x**, 67271-11-8; **10**, 67271-12-9; **11**, 67271-13-0; HF, 7664-39-3; S_2Cl_2, 10025-67-9; SO_2Cl_2, 7791-25-5; methyl isocyanate, 624-83-9; methyl *N*-methylcarbamate, 6642-30-4.

References and Notes

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(3) For example, see: (a) E. Kuehle and I. Hammann, German Patent 2 106 300 (August 1972); (b) E. Kuehle, E. Klauke, W. Behren, P. Frahberger, and E. Paul, German Patent 2 041 322 (February 1972); (c) E. Kuehle, E. Klauke, B. Hamburger, and H. Scheinpflug, German Patent 2 243 626 (March 1974).
(4) Shortly after completion of our investigation, Belgian patent applications 843 415 and 843 416 were published which parallel portions of this work.
(5) It is interesting to note that we were unable to carry out the corresponding carbamoyl chloride chemistry. In our hands, *N*-methylcarbamoyl chloride decomposed upon the slightest provocation.
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(7) (a) D. Armitage and C. Tso, *J. Chem. Soc., Chem. Commun.*, 1413 (1971); (b) M. Raban, D. Noyd, and L. Bermann, *J. Org. Chem.*, **40**, 752 (1975).

Notes

Heterocycles in Organic Synthesis. 11.[1] Reactions of Heteroaromatic *N*-Oxides with Pyridine and Diazoles

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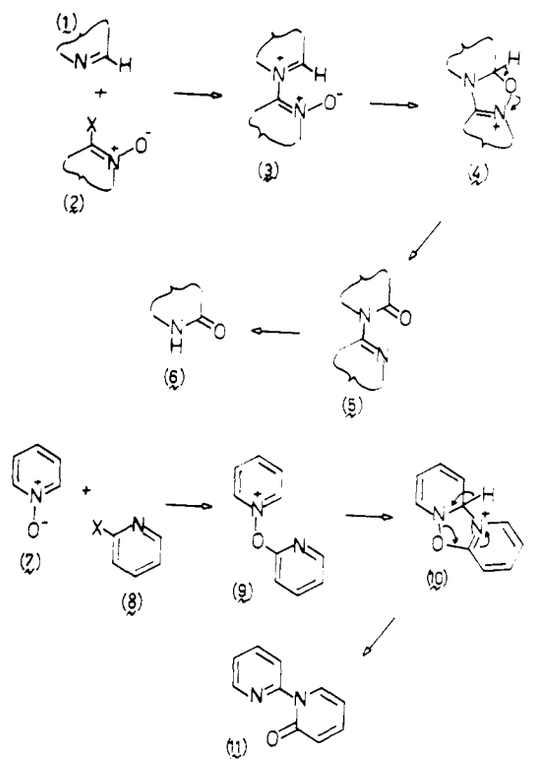
The aim of the present work was to develop a synthetic sequence for the oxidation of heterocyclic nitrogen compounds **1** to the corresponding α-oxo derivatives **6**. Previous methods are inconvenient and/or not general. Direct conversion of pyridine to 2-pyridone requires extreme conditions[2] or conversion to *N*-oxide.[3] Benzimidazole is attacked by most oxidizing agents at the benzene ring,[4] although imidazole itself slowly gives 2-imidazolone with singlet oxygen.[5] Pyrazole is resistant to oxidation.[6]

The reported[7] conversion of pyridine 1-oxide (**7**) to the pyridylpyridone **11** by condensation with a suitably 2-substituted pyridine **8** and intermediates **9** and **10**, led us to consider the reaction sequence **1** + **2** → **6** via intermediates **3**, **4**, and **5** (Scheme I).

Experiments with 2-Chloro-5-nitropyridine 1-Oxide (12) as Compound 2. This oxide possesses a reactive chlorine atom and readily formed substitution products with aniline (**13**, R = NHPh) and piperidine [**13**, R = $N(CH_2)_5$] (Scheme II). Pyrazole also gave the expected product **14**, but this was stable to heat and sublimed unchanged: with acetic anhydride an acetoxy group was introduced into the 6 position of the pyridine ring to give **15** by a known[8] reaction, leaving the pyrazole ring unaffected.

Imidazole readily formed **16**, which was again stable to heat and also sublimed unchanged. It was converted by acetic anhydride to **17**, which was also obtained directly from **12** by Ac_2O treatment. The structure of **17** was confirmed by hydrolysis to the known[9] 1-hydroxy-2-pyridone **18**. Methyl tosylate with **16** gave **19** (X = OTs), whereas **19** (X = Cl) was

Scheme I



obtained by direct reaction of **12** and methylimidazole. The salts **19** (X = Cl or OTs) gave an inseparable mixture after prolonged heating in the presence of a hindered base.

Attempted reaction of **12** with pyridine did not succeed. With pyridine 1-oxide, the product was **20** (Scheme II), apparently formed by the reaction of **12** with itself followed by reduction and hydrolysis. This structure of **20** was based on analytical, mass spectral, IR, and NMR data; attempts to synthesize **20** by reaction of 2-chloro-5-nitropyridine with **18**, or the sodium salt of **18**, failed.

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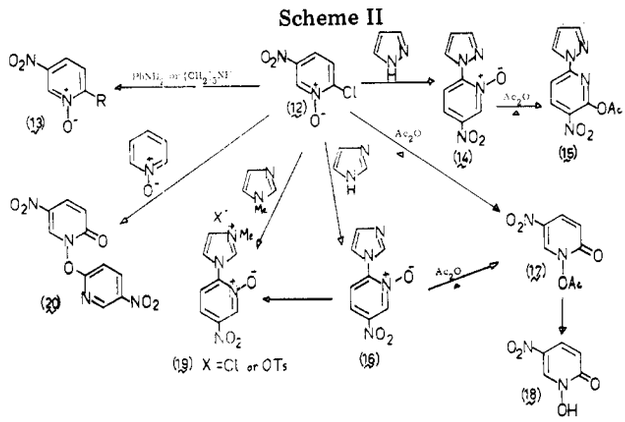
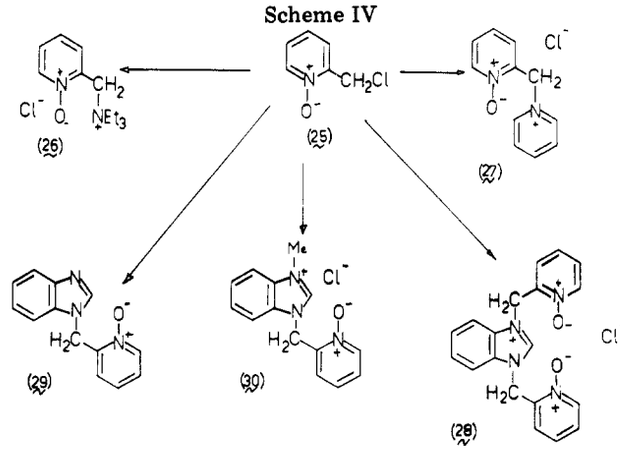
Scheme II



Scheme IV



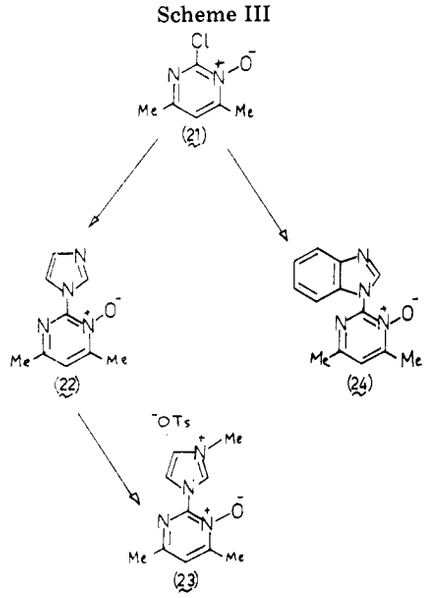
Experiments with 2-Chloro-4,6-dimethylpyrimidine 1-Oxide (21) as Compound 2. Imidazole reacted with the oxide **21** to form the expected product **22** (Scheme III), which was recovered unchanged after sublimation or after prolonged heating in the presence of a hindered base. With benzimidazole, the oxide **21** gave **24,** which also sublimed unchanged. Methylation of the imidazole **22** gave **23,** but the methyl derivative did not react smoothly with bases under various conditions.[10]

Experiments with 2-(Chloromethyl)pyridine 1-Oxide (25) as Compound 2. This benzylic type chlorine of **25** is known to be displaced by various nucleophiles[11] and **25** has been used to introduce the 2-picolyl 1-oxide group into substrates,[12] where it has been used to protect amino functions.[13] Removal should also be easy.[14] As expected, the *N*-oxide **25** readily reacted with triethylamine to give **26** (Scheme IV). With pyridine, **25** gave **27,** 1-methylbenzimidazole similarly formed **30,** and isoquinoline formed the corresponding quaternary salt, whereas benzimidazole itself, although yielding some of the monoadduct **29,** mainly underwent a double reaction to yield **28.** Salt **28** is very hygroscopic and normal samples display ν(OH) at 3380 cm^{-1}; and proton NMR signal for the 2CH at δ 10.3 is rapidly exchanged for deuterium by shaking with D_2O (cf. ref 15, 16). 1-Benzyl-3-methylbenzimidazolinium cation (but not 2-benzylisoquinolinium cation) also underwent rapid hydrogen exchange under similar conditions.

All attempts to transfer the *N*-oxide oxygen atoms of species **27–30,** and the analogous cation formed from isoquinoline, to the other heterocyclic ring failed.[17]

Conclusions. We believe that the failure to achieve reaction sequences of type **3** → **6** is due to difficulty with the proton abstraction step **4** → **5** and are therefore now exploring reagents in which such proton transfer can be achieved intramolecularly.

Scheme III



Experimental Section

^{1}H NMR spectra were recorded with Varian HA-100 and Perkin-Elmer R 12 spectrometers (Me_4Si as internal standard), IR spectra with a Perkin-Elmer 257 spectrometer, and mass spectra with a Hitachi Perkin-Elmer spectrometer.

The following compounds were prepared by literature methods. 2-Chloro-5-nitropyridine: needles, 88.5%, mp 107 °C (MeOH; lit.[18] mp 106 °C). 2-Chloro-5-nitropyridine 1-oxide: needles, 54%, mp 137 °C (CH_2Cl_2–Et_2O; lit.[19] mp 137–139 °C). 1-Methylbenzimidazole: plates, 61%, mp 60 °C, bp 168 °C (20 mm) [lit.[20] bp 183–185 °C (37 mm)]. 1-Methylimidazole, 51%, bp 99 °C (18 mm) [lit.[21] bp 97 °C (18 mm)]. 2-Chloro-4,6-dimethylpyrimidine: 74%, bp 64–66 °C (2 mm), mp 38 °C (lit.[22] mp 38 °C). 2-Chloromethylpyridine: 45%, bp 45–47 °C (1.5 mm) [lit.[23] bp 45–47 °C (1.5 mm)]. 2-Chloromethylpyridine 1-oxide (**26**): 98%, needles from benzene, mp 74–75 °C (lit.[12] mp 75 °C).

2-Anilino-5-nitropyridine 1-Oxide (13, R = NHPh). Aniline (0.213 g), 2-chloro-5-nitropyridine 1-oxide (**12**) (0.20 g), and CH_2Cl_2 (3 mL) were stirred for 12 h at 20 °C. The solvent was evaporated under reduced pressure and the residue crystallized from EtOH to give the 1-oxide **13** (R = NHPh) as needles (0.160 g, 60%): mp 186 °C.

Anal. Calcd for $C_{11}H_9N_3O_3$: C, 57.1; H, 3.9; N, 18.3; M, 241. Found: C, 57.0; H, 4.0; N, 18.2; M^+·, 241.

5-Nitro-2-piperidiniopyridine 1-Oxide [13, R = N(CH$_2$)$_5$]. Piperidine (0.195 g) in CH_2Cl_2 (5 mL) was added to 2-chloro-5-nitropyridine 1-oxide (0.2 g) in CH_2Cl_2 (5 mL) and stirred at 20 °C for 1 h. The solvent was evaporated to give the 1-oxide **13** [R = NH(CH$_2$)$_5$] as needles (0.152 g, 60%): mp 149 °C (from light petroleum bp 80–100 °C).

Anal. Calcd for $C_{10}H_{13}N_3O_3$: C, 53.8; H, 5.9; N, 18.8; M, 223. Found: C, 53.7; H, 5.8; N, 18.5; M^+·, 223.

5-Nitro-2-(1-pyrazolyl)pyridine 1-Oxide (14). 2-Chloro-5-nitropyridine 1-oxide (0.2 g), pyrazole (0.156 g), and toluene (15 mL) were heated under reflux for 4 h and then left for 12 h. The 1-oxide crystallized as needles (0.18 g, 76%): mp 174 °C (from CH_2Cl_2–Et_2O); IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^{1}H NMR [100 MHz, $(CD_3)_2SO$] δ 9.35 (d, 1 H, J = 1 Hz), 9.24 (m, 1 H), 8.27 (m, 2 H), 8.03 (d, 1 H, J = 1 Hz), 6.68 (m, 1 H).

Anal. Calcd for $C_8H_6N_4O_3$: C, 46.6; H, 2.9; N, 27.2; M, 206. Found: C, 46.4; H, 3.2; N, 26.6; M^+·, 206.

6-Acetoxy-5-nitro-2-(1-pyrazolyl)pyridine (15). 5-Nitro-2-(1-pyrazolyl)pyridine 1-oxide (0.206 g) and Ac_2O (25 mL) were heated under reflux for 3 h. The solvent was removed under reduced pressure and the residue crystallized from MeOH to give needles of the 6-acetoxypyridine (0.17 g, 58%): mp 140 °C; IR (Nujol) 1775 (C=O), 1200 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 8.65 (d, 1 H, J = 6 Hz), 8.5 (d, 1 H, J = 2 Hz), 8.05 (d, 1 H, J = 6 Hz), 7.82 (s, 1 H), 6.52 (m, 1 H), 2.45 (s, 3 H).

Anal. Calcd for $C_{10}H_8N_4O_4$: C, 48.4; H, 3.3; N, 22.6. Found: C, 48.1; H, 3.4; N, 22.9.

2-(1-Imidazolyl)-5-nitropyridine 1-Oxide (16). 2-Chloro-5-nitropyridine 1-oxide (0.2 g), imidazole (0.156 g), and MeCN (15 mL) were heated under reflux for 4 h and kept for 12 h. The 1-oxide separated from MeCN as needles (0.24 g, 93%): mp 215 °C; IR (Nujol)

1260 cm^{-1} (N^+–O^-); ^1H NMR [100 MHz, $(CD_3)_2SO$] δ 9.26 (d, 1 H, J = 1 Hz), 8.60 (s, 1 H), 8.26 (dd, 1 H, J = 1.5, J_o = 5 Hz), 8.04 (d, 1 H, J = 5 Hz), 7.90 (s, 1 H), 7.18 (s, 1 H).

Anal. Calcd for $C_8H_6N_4O_3$: C, 46.6; H, 2.9; N, 27.2; M, 206. Found: C, 46.0; H, 2.9; N, 26.6; M^+·, 206.

1-Acetoxy-5-nitro-2-pyridone (17). Method a. 2-Chloro-5-nitropyridine 1-oxide (0.349 g) was heated in Ac_2O (3 mL) at 140 °C for 1.5 h. Solvent was removed under reduced pressure and the residue crystallized from MeOH to give the 2-pyridone as needles (0.265 g, 67%): mp 161–163 °C; IR (Nujol) 1817, 1692 cm^{-1} (C=O); ^1H NMR [100 MHz, $(CD_3)_2SO$] δ 9.58 (d, 1 H, J = 1.5 Hz), 8.24 (dd, 1 H, J_m = 1.5, J_o = 5.5 Hz), 6.76 (d, 1 H, J = 5.5 Hz), 2.38 (s, 3 H).

Anal. Calcd for $C_7H_6N_2O_5$: C, 42.4; H, 3.1; N, 14.2. Found: C, 42.1; H, 3.2; N, 14.1.

Method b. 2-(1-Imidazolyl)-5-nitropyridine 1-oxide (0.1 g) was heated under reflux in Ac_2O (5 mL) for 1 h and cooled. Ice water (15 ml) was added and the product extracted with $CHCl_3$ (3 × 10 mL). The $CHCl_3$ extracts were washed with H_2O (10 mL), dried (K_2CO_3), and evaporated. Crystallization of the residue from MeOH gave the pyridone as needles (0.031 g, 30%): mp 162 °C; IR (Nujol) 1817, 1692 cm^{-1} (C=O).

1-Hydroxy-5-nitro-2-pyridone (18). 1-Acetoxy-5-nitro-2-pyridone (0.198 g), NaOH (0.04 g), and H_2O (10 mL) were stirred at 20 °C for 2 h and then acidified with HCl. The product was extracted with $CHCl_3$ (3 × 10 mL) and the extracts were dried ($MgSO_4$) and evaporated to give the hydroxypyridone (0.125 g, 80%): mp 180°C (lit.[9] mp 188 °C); IR (Nujol) 3200–3060 (OH), 1670 cm^{-1} (C=O); ^1H NMR [100 MHz, $(CD_3)_2SO$] δ 9.21 (d, 1 H, J = 1.5 Hz), 8.14 (dd, 1 H, J_m = 1.5, J_o = 5.5 Hz), 6.60 (d, 1 H, J = 5.5 Hz).

Anal. Calcd for $C_5H_4N_2O_4$: C, 38.4; H, 2.6. Found: C, 38.2; H, 2.9.

1-Methyl-3-(5-nitro-1-oxido-2-pyridyl)imidazolium *p*-Toluenesulfonate (19, X = OTs). 2-(1-Imidazolyl)-5-nitropyridine 1-oxide (0.432 g), methyl *p*-toluenesulfonate (0.744 g), and MeCN (50 mL) were heated under reflux for 30 h. The *p*-toluenesulfonate (0.595 g, 74%) crystallized from MeCN as plates: mp 212 °C; IR (Nujol) 1265 cm^{-1} (N^+–O^-); ^1H NMR (60 MHz, CF_3CO_2H) δ 9.8 (s, 1 H), 9.62 (s, 1 H), 8.65 (s, 1 H), 8.45 (s, 1 H), 8.1 (s, 1 H), 7.88 (s, 1 H), 7.82 (d, 2 H, J = 6 Hz), 7.38 (d, 2 H, J = 6 Hz), 4.2 (s, 3 H), 2.45 (s, 3 H).

Anal. Calcd for $C_{16}H_{16}N_4O_6S$: C, 49.0; H, 4.1; N, 14.3. Found: C, 48.9; H, 4.3; N, 14.3.

1-Methyl-3-(5-nitro-1-oxido-2-pyridyl)imidazolium Chloride (19). 2-Chloro-5-nitropyridine 1-oxide (**12**, 0.175 g) and *N*-methylimidazole (0.082 g) were kept at 20 °C for 48 h. The solid obtained was washed with $(CH_2)_4O$ (2 × 20 mL) and recrystallized from MeOH–Et_2O to give the chloride **19** as plates (0.120 g, 53%): mp 228–230 °C; IR (Nujol) 1265 cm^{-1} (N^+–O^-); ^1H NMR (CF_3CO_2H) δ 9.75 (s, 1 H), 9.65 (s, 1 H), 8.78 (d, 1 H), 8.35 (d, 1 H), 8.1 (s, 1 H), 7.75 (s, 1 H), 4.25 (s, 3 H).

Anal. Calcd for $C_9H_9ClN_4O_3$: C, 42.1; H, 3.6; N, 21.9. Found: C, 42.4; H, 3.7; N, 21.8.

5-Nitro-1-(5-nitro-2-pyridyloxy)-2-pyridone (20). 2-Chloro-5-nitropyridine 1-oxide (0.349 g) in toluene (25 mL) was added to pyridine 1-oxide (0.190 g) in toluene (10 mL), heated under reflux for 3 h, and then set aside for 12 h. A dark oil which deposited was removed and the solution concentrated to give the pyridone (0.043 g, 6%) as needles from toluene: mp 247 °C; IR (Nujol) 1680 (C=O), 1560, 1350 cm^{-1} (NO_2); ^1H NMR [100 MHz, $(CD_3)_2SO$] δ 9.25 (dd, 2 H, J_m = 1.5, J_o 5.5 Hz), 8.1–8.3 (m, 3 H), 6.7 (d, 1 H, J = 5.5 Hz).

Anal. Calcd for $C_{10}H_6N_4O_6$: C, 43.2; H, 2.2; N, 20.1; M, 270. Found: C, 43.3; H, 2.0; N, 19.6; M^+·, 270.

2-Chloro-4,6-dimethylpyrimidine 1-Oxide (21). Maleic anhydride (24 g) in $CHCl_3$ (80 mL) was treated with 30% H_2O_2 (3.4 g) at 0–5 °C, and the mixture was stirred for 2 h at 0–5 °C. 2-Chloro-4,6-dimethylpyrimidine (1.43 g) was added and set aside for 5 days at 10 °C. Maleic acid (17 g) was filtered off. The $CHCl_3$ solution was washed with aqueous K_2CO_3 (10%, 4 × 20 mL), dried (K_2CO_3), and evaporated at 30 °C (20 mm Hg). The semisolid residue was extracted with boiling light petroleum (bp 60–80 °C, 3 × 40 mL). Extracts were evaporated to 80 mL and the *N*-oxide separated from light petroleum as needles (0.53 g, 34%): mp 97 °C; IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^1H NMR ($CDCl_3$) δ 7.15 (s, 1 H), 2.60 (s, 3 H), 2.50 (s, 3 H).

Anal. Calcd for $C_6H_7ClN_2O$: C, 45.4; H, 4.5; N, 17.7. Found: C, 45.7; H, 4.5; N, 17.4.

4,6-Dimethyl-2-(1-imidazolyl)pyrimidine 1-Oxide (22). Imidazole (0.294 g) and 2-chloro-4,6-dimethylpyrimidine 1-oxide (0.343 g) in MeCN (15 mL) were heated under reflux for 6 h. The solvent was evaporated under reduced pressure and the residue extracted with boiling benzene (2 × 20 mL). The extracts on evaporation gave the 1-oxide as a residue (0.293 g, 71%) which formed needles from light petroleum (bp 80–100 °C); mp 154 °C; IR (Nujol) 1260 cm^{-1} N^+–O^-); ^1H NMR (60 MHz, $CDCl_3$) δ 9.35 (s, 1 H), 8.25 (s, 1 H), 7.17 (d, 2 H, J = 3 Hz), 2.16 (s, 3 H), 2.58 (s, 3 H).

Anal. Calcd for $C_9H_{10}N_4O$: C, 56.8; H, 5.3; N, 29.5; M, 190. Found: C, 56.8; H, 5.4; N, 29.1; M^+·, 190.

1-Methyl-3-(4,6-dimethyl-1-oxidopyrimidin-2-yl)imidazolium *p*-Toluenesulfonate (23). 4,6-Dimethyl-2-(1-imidazolyl)pyrimidine 1-oxide (**22**, 0.575 g), methyl *p*-toluenesulfonate (0.570 g), and MeCN (40 mL) were heated under reflux for 30 h. The solvent was evaporated under reduced pressure and the residue washed with hot $(CH_2)_4O$ (3 × 10 mL) giving the *p*-toluenesulfonate **23** as rods (0.981 g, 82%): mp 170 °C (from MeOH–Et_2O); IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^1H NMR ($CDCl_3$) δ 10.31 (s, 1 H), 8.29 (s, 1 H), 7.96 (s, 1 H), 7.65 (d, 2 H), 7.31 (s, 1 H), 7.01 (d, 2 H), 4.11 (s, 3 H), 2.47 (s, 6 H), 2.34 (s, 3 H).

Anal. Calcd for $C_{17}H_{20}N_4O_4S$: C, 54.2; H, 5.4; N, 14.9. Found: C, 54.0; H, 5.1; N, 15.0.

2-(1-Benzimidazolyl)-4,6-dimethylpyrimidine 1-Oxide (24). 2-Chloro-4,6-dimethylpyrimidine 1-oxide (0.23 g) and benzimidazole (0.18 g) were heated under reflux in $(CH_2)_4O$ (10 mL) for 6 h. Benzimidazole hydrochloride was filtered off and the filtrate was evaporated. The residue was extracted with benzene (3 × 10 mL) and the extracts concentrated to give the *N*-oxide (0.16 g, 46%) which separated from benzene as plates: mp 174 °C; IR (Nujol) 1250 cm^{-1} (N^+–O^-); ^1H NMR (60 MHz) ($CDCl_3$) δ 9.81 (s, 1 H), 8.01 (m, 2 H), 7.22 (m, 2 H), 2.60 (s, 3 H), 2.58 (s, 3 H).

Anal. Calcd for $C_{13}H_{12}N_4O$: C, 65.0; H, 5.0; N, 22.3; M, 240. Found: C, 64.7; H, 5.1; N, 22.6; M^+·, 240.

1-(1-Oxido-2-pyridylmethyl)pyridinium Chloride (27). 2-Chloromethylpyridine 1-oxide **25** (1.15 g) and pyridine (1.30 g) were heated under reflux in MeCN (80 mL) for 24 h. The solvent was removed at 80 °C (15 mm Hg) and the residue washed with hot Et_2O (2 × 50 mL) leaving the solid highly hygroscopic chloride **27** (1.77 g, 98%), mp 215–220 °C, which crystallized as needles (from EtOH–Et_2O): mp 220–222 °C; IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^1H NMR [$(CD_3)_2SO$] δ 6.1 (s, 2 H), 7.4 (m, 2 H), 8.0–8.3 (m, 4 H), 8.6 (m, 1 H), 9.3 (d, 2 H, finely split, J = 6, J = 1 Hz); *m/e* 187 (M^+ − Cl). The compound was characterized as the dipicrate as yellow needles: mp 142–143 °C (from EtOH) (lit.[24] 142–143 °C).

Anal. Calcd for $C_{11}H_{12}N_2O\cdot[(NO_2)_3C_6H_2O]_2$: C, 42.9; H, 2.5; N, 17.4. Found: C, 42.8; H, 2.6; N, 17.4.

1-(1-Oxido-2-pyridylmethyl)-3-methylbenzimidazolium Chloride (30). 1-Methylbenzimidazole (1.32 g) and the 1-oxide **25** (0.72 g) were heated under reflux in MeCN (50 mL) for 24 hr. MeCN was removed at 80 °C (15 mm Hg) to give the chloride **30** (1.02 g, 74%) which separated from EtOH–Et_2O as prisms: mp 217–221 °C; IR ($CHBr_3$) 1255 cm^{-1} (N^+–O^-); ^1H NMR [$(CD_3)_2SO$] δ 4.2 (s, 3 H), 6.0 (s, 2 H), 7.4–7.8 (m, 4 H), 7.9–8.5 (m, 4 H), 10.2 (s, 1 H); *m/e* 240 (M^+ − Cl).

The salt was characterized as the perchlorate which crystallized as flakes (from EtOH); mp 212.5–214 °C.

Anal. Calcd for $C_{14}H_{14}ClN_3O_5$: C, 49.5; H, 4.2; N, 12.4. Found: C, 49.1; H, 4.2; N, 12.6.

2-(1-Oxido-2-pyridylmethyl)isoquinolinium Chloride. Isoquinoline (2.10 g) and the 1-oxide **25** (1.15 g) were heated under reflux in MeCN (80 mL) for 24 h. Solvent was removed at 80 °C (15 mmHg) and the residue washed with hot EtOAc (2 × 25 mL); the residual chloride (2.10 g, 95%), crystallized from EtOH–Et_2O as greenish needles: mp 183–185 °C; IR ($CHBr_3$) 1650 (C=N), 1265 cm^{-1} (N^+–O^-); ^1H NMR [$(CD_3)_2SO$] δ 6.1 (s, 2 H), 7.5 (m, 2 H), 7.9–8.6 (m, 7 H), 8.9 (d, 1 H, finely split, J = 7, J = 1 Hz), 10.3 (s, 1 H, finely split, J = 1 Hz); *m/e* 237 (M^+ − Cl).

The salt was characterized as the perchlorate, which crystallized as fine needles (from EtOH): mp 157–158 °C; IR ($CHBr_3$) 1650 (C=N), 1260 (N^+–O^-), 1080 cm^{-1} (ClO).

Anal. Calcd for $C_{15}H_{13}N_2O\cdot ClO_4$: C, 53.5; H, 3.9; N, 8.3. Found: C, 53.8; H, 4.1; N, 8.1.

1,3-Di(1-oxido-2-pyridylmethyl)benzimidazolium Chloride (28). Benzimidazole (0.236 g) and the 1-oxide **25** (0.585 g) were heated under reflux in MeCN (40 mL) for 40 h. Volatiles were removed at 80 °C (15 mmHg) and the residual oil washed with hot Et_2O (2 × 50 mL), leaving the solid chloride **28** (0.783 g, 94%), which crystallized as flakes: mp 250–252 °C (from EtOH–Et_2O); IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^1H (NMR) [$(CD_3)_2SO$] δ 6.2 (s, 2 H), 7.5–8.6 (m, 12 H), 10.3 (s, 1 H); *m/e* 333 (M^+ − Cl).

Anal. Calcd for $C_{19}H_{17}ClN_4O_2$: C, 61.7; H, 4.9; N, 15.2; Cl, 9.6. Found: C, 61.4; H, 4.8; N, 14.6; Cl, 9.8.

1-(1-Oxido-2-pyridylmethyl)benzimidazole (29). The 1-oxide **25** (0.90 g) in EtOH (10 mL) was added dropwise during 1 h with stirring to benzimidazole (1.50 g) and K_2CO_3 (2.0 g) in EtOH (10 mL) at 0 °C. The solution was stirred for 72 h at 20 °C. Potassium chloride was filtered off and the solvent removed at 80 °C (15 mm). The oily residue was dissolved in hot EtOAc (20 mL); on cooling, the *N*-oxide **29** (1.13 g, 81%) separated and was recrystallized from EtOAc to give

needles: mp 166–167 °C; IR ($CHBr_3$) 1250 cm^{-1} (N^+–O^-); ^1H NMR ($CDCl_3$) δ 5.8 (s, 2 H), 6.8 (d, 1 H, J = 2 Hz), 7.2–7.4 (m, 5 H), 8.1 (m, 1 H), 8.2 (s, 1 H), 8.5 (dd, 1 H, J = 6, J = 1 Hz); m/e 225 (M^+).

Anal. Calcd for $C_{13}H_{11}N_3O$: C, 69.3; H, 4.9; N, 18.7. Found: C, 69.1; H, 4.9; N, 18.9.

The *N*-oxide **29** gave the corresponding 3-methylperchlorate **30** by methylation and conversion to the perchlorate, which crystallized as flakes (from EtOH): mp 212–214 °C.

***N*-(1-Oxido-2-pyridylmethyl)triethylammonium Chloride (26).** Et_3N (0.500 g) and the 1-oxide **25** (0.360 g) were heated under reflux in MeCN (40 mL) for 24 h. MeCN was evaporated 80 °C (15 mmHg) and the residue was washed with hot Et_2O (2 × 20 mL) leaving the chloride **27** (0.590 g, 96%), which separated from EtOH–Et_2O as prisms: mp 194–196 °C; IR (Nujol) 1260 cm^{-1} (N^+–O^-); ^1H NMR [$(CD_3)_2SO$] δ 1.1 (t, 9 H, J = 8 Hz), 3.2 (q, 9 H, J = 8 Hz), 4.6 (s, 2 H), 7.2–7.6 (m, 2 H), 7.8 (dd, 1 H, J = 8 Hz, J = 1 Hz), 8.3 (dd, 1 H, J = 6, J = 1 Hz).

The salt was characterized as the dipicrate, which crystallized from EtOH as yellow needles: mp 120.5–122 °C.

Anal. Calcd for $C_{12}H_{22}N_2O\cdot[(NO_2)_3C_6H_2O]_2$: C, 43.3; H, 3.9; N, 16.8. Found: C, 43.4; H, 4.0; N, 16.8.

1-Benzyl-3-methylbenzimidazolium Bromide. 1-Methylbenzimidazole (1.32 g) and benzyl bromide (1.71 g) were stirred in EtOAc (20 mL) for 24 h. The precipitated bromide (1.70 g, 56%) crystallized from EtOH–Et_2O as prisms: mp 78–80 °C; ^1H NMR [$(CD_3)_2SO$] δ 4.1 (s, 3 H), 5.8 (s, 2 H), 7.3–8.1 (m, 9 H), 10.3 (s, 1 H). The salt was characterized as the perchlorate rods (from EtOH): mp 146–147.5 °C; IR ($CHBr_3$) 1650 (C=N), 1080 cm^{-1} (ClO).

Anal. Calcd for $C_{15}H_{15}ClN_2O_4$: C, 55.8; H, 4.7; N, 8.7. Found: C, 55.9; H, 4.9; N, 8.3.

2-Benzylisoquinolinium Bromide. Isoquinoline (1.29 g) and benzyl bromide (1.71 g) were heated under reflux in MeCN (25 mL) for 3 h. Solvent was removed at 80 °C (15 mm), and the residual bromide (2.83 g, 94%) crystallized from EtOH–Et_2O as needles: mp 108–110 °C (lit.[25] mp 110–111.5 °C); ^1H NMR [$(CD_3)_2SO$] δ 6.1 (s, 2 H), 7.3–7.8 (m, 5 H), 7.9–8.4 (m, 4 H), 8.6 (d, 1 H), 9.0 (d, 1 H), 10.7 (s, 1 H, finely split, J = 1 Hz).

The corresponding perchlorate crystallized from EtOH as prisms: mp 170–172 °C (lit.[25] mp 167–168 °C).

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D-Homoandrostanes. 3. Incubation of Some *D*-Homo-5α-androstanes with *Aspergillus ochraceus*[1a]

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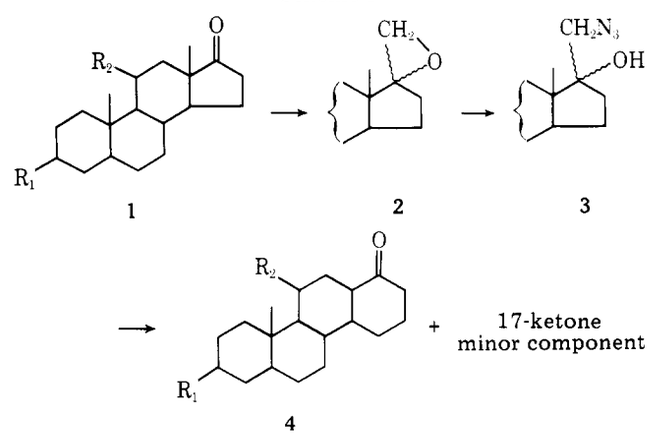
In preparing *D*-homo-5α-androstanes[2] our intention was to determine the effect of increase in terminal ring size on the course of microbiological hydroxylation as compared with that of normal steroids. For part of these studies we chose the microorganism *Aspergillus ochraceus,* which has been extensively documented[3] as an 11α-hydroxylator of steroids with very occasional transformations at C(1),[4] C(6),[5] and C(7).[5] Work with cell-free cultures of this microorganism has demonstrated[6] that two independently acting hydroxylase enzymes are responsible for the 11α- and 6β-hydroxylations.

Table I presents the times of incubation, the amount of starting material recovered, and the observed modifications of the steroid substrates, which have, with certain exceptions, been synthesized previously.[2]

3α-Hydroxy-*D*-homo-5α-andostan-17α-one[7] was prepared according to the established route (Scheme I, **1a** → **4a**). The two, 3,11-dioxygenated steroids were prepared from the

Scheme I



a, R_1 = α-OH, R_2 = H_2; b, R_1 = β-OH; R_2 = α-OH

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