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SYNTHETIC STUDIES ON SUBSTITUTED 9H-PYRROLO[1,2-a]INDOLES AND 2,3-DIHYDRO-1H-PYRROLO[1,2-a]INDOLES

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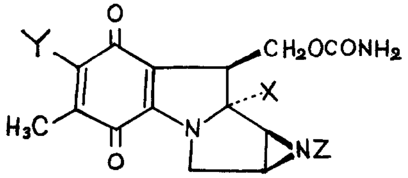
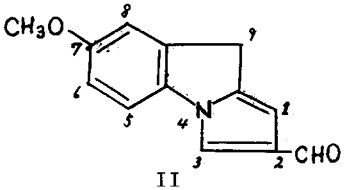
Mitomycin antibiotics (I) have a novel ring system that is aziridinopyrrolo [1,2-a]indoloquinone(1). In synthetic studies on mitomycin analogs Lederle group synthesised 7-benzyloxy-9H-pyrrolo[1,2-a]indole(2) and substituted 2,3-dihydro-1H-pyrrolo[1,2-a]indoles(3)(2a). In this paper we wish to discribe a new method for synthesis of substituted 9H-pyrrolo[1,2-a]indoles(IV) and 2,3-dihydro-1H-pyrrolo[1,2-a]indoles(V).

2-Formyl-5-alkoxyindoles(III) were converted to 2-acetyl-7-alkoxy-9H-pyrrolo [1,2-a]indoles(IV) by treatment with methylvinylketone in the presence of trimethylbenzylammonium hydroxide in dioxane in 25% yield. IVa: m.p. 115°, UV λ_{max}^{EtOH} (mμ) 241(ε 8,000),289(ε 20,100),311(ε 19,600) IR(nujol) $\nu_{c=o}$1640cm^{-1}, nmr (CDCl$_3$) δ 2.38(3H s),3.75(5H s),6.47(1H s),6.80(1H q),6.93(1H d),7.54(1H s). IVb: m.p. 150°,UV λ_{max}^{EtOH} (mμ) 202(ε 37,800),243(ε 9,400),292(ε 21,900),312(ε 21,600). IR (nujol) $\nu_{c=o}$ 1645 cm^{-1}, nmr (CDCl$_3$) δ 2.49(3H s),3.71(2H s),5.01(2H s),6.49 (1H s),6.89(1H q),7.10(1H d),7.15(1H d),7.28-7.94(5H),7.55(1H s). IVc: m.p. 168°, UV λ_{max}^{EtOH} (mμ) 207(ε 37,900), 244(ε 8,300),293(ε 20,300), IR (nujol) $\nu_{c=o}$ 1650 cm-1, nmr (CDCl$_3$) δ 2.32(3H s), 2.41(3H s),3.72(2H s),5.06(2H s),6.51(1H s),6.96(1H s),7.24(1H s), 7.32-7.46(5H),7.55(1H s).

2-Formyl-7-methoxy-9H-pyrrlo[1,2-a]indole(II) was also obtained by treating 2-formyl-5-methoxyindole with acrolein and trimethylbenzylammonum hyroxide. II: m.p. 134.5°, UV λ_{max}^{EtOH} (mμ) 242(ε 9,000),289(ε 20,900),311(ε 20,700), IR $\nu_{c=o}$ 1645 cm^{-1}, nmr(CDCl$_3$) δ 3.79(5H s),6.54(1H s),6.85(1H q) 6.97(1H d),7.59(1H s). By reducing (IVa) with metalic lithium in liquid ammonia 2-acetyl-2,3-dihydro-1H-pyrrolo[1,2-a]indole(Va) was obtained. By the same procedure to IVb and IVc debenzylation occurred and 2-acetyl-7-hydroxy-2,3-dihydro-1H-pyrrolo[1,2-a]



I



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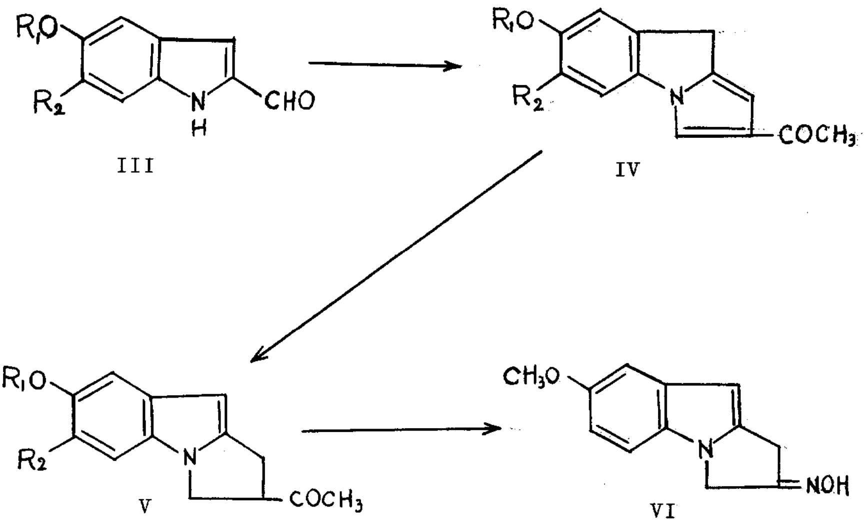
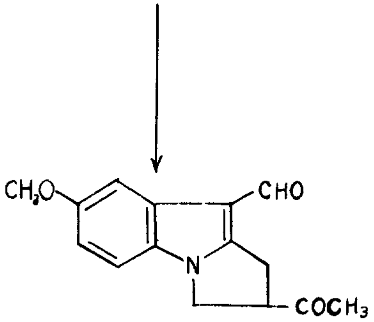




VIII

	R1	R2
a:	CH3	H
b:	PhCH2	H
c:	PhCH2	CH3
d:	H	H
e:	H	CH3

indole (Vd) and 2-acetyl-6-methyl-7-hydroxy-2,3-dihydro-1H-pyrrolo[1,2-a]indole(Ve) were obtained in poor yield. Va: m.p. 127°,UV λ_{max}^{EtOH} (mμ) 220(ε 33,400), 277 (ε 8,300), IR $\nu_{c=o}$ 1702 cm^{-1}, nmr ($CDCl_3$) δ 2.20(3H s),3.15(2H m),3.75(4H m), 4.15(2H d),6.02(1H s),6.73(1H q),6.96(1H d),7.05(1H d).

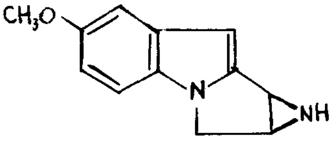
Vd: m.p. 141° ,UV λ_{max}^{EtOH} (mμ) 218(ε 36,700),277(ε 10,200), IR (nujol) ν_{O-H} 3330 cm^{-1} $\nu_{c=o}$ 1700 cm^{-1}, nmr($CDCl_3$) δ 2.22(3H s),3.18(2H m),3.80(1H m),4.16(2H m),4.68(1H), 5.98(1H s),6.64(1H q),6.89(1H d),7.20(1H d).

Ve: m.p. 137°, UV λ_{max}^{EtOH} (mμ) 213(ε 32,300),276(ε 8,400), IR $\nu_{c=o}$ 1695 cm^{-1}, νO-H 3440 cm^{-1}, nmr (DMSO) δ 2.20(6H), 3.12(2H m),3.80-4.15(3H m),5.85(1H s),6.80(1H s),6.98(1H s),8.55(1H s).

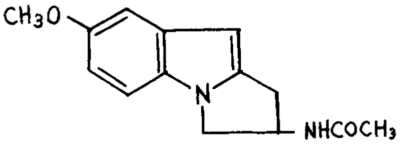
The oxime of Va (m.p.143°) would not undergo Beckmann Rearrangement to give 2-acetylamino-7-methoxy-2,3-dihydro-1H-pyrrolo[1,2-a]indole(IX). The methylketone (Va) was transformed to 2-oximio-7-methoxy-2,3-dihydro-1H-pyrrolo[1,2-a]indole (VI) by treatment with ethyl nitrite and sodium ethoxide in ethanol in good yield. VI: m.p.decomposed, UV λ_{max}^{EtOH} (mμ) 203(ε 31,200), 220(ε 30,800),276(ε 7,900), IR ν_{O-H} 3280 cm^{-1}, 1620 cm^{-1}, 1575 cm^{-1}, 1490 cm^{-1}(nujol), nmr (DMSO) δ 3.71(5H s), 4.70(2H d),6.15(1H s),6.70(1H q),6.98(1H d),7.15(1H q).

The attempt to transform (VI) to aziridinopyrrolo[1,2-a]indole(VII) by refluxing with $LiAlH_4$ in tetrahydrofuran (4) was unsuccessful. 2-Acetyl-7-methoxy-9-formyl -2,3-dihydro-1H-pyrrolo[1,2-a]indole(VIII) which obtained from (Va) by Vilsmeier -Haack reaction (3a) did not react with ethyl nitrite to give 2-oximo compound. VIII: m.p. 153°, IR (nujole) $\nu_{c=O}$ 1708 cm^{-1},1640 cm^{-1}.

All compounds synthesised gave satisfactory elementary analyses.



VII



IX

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