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SYNTHESIS AND X-RAY CRYSTAL STRUCTURE DETERMINATION OF 1,4-DIHYDROCYCLOPENT[b]INDOLES(1)

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Diethyl 1,4-dihydro-3-β-indolyl-4-methylcyclopent[b]indole-1,2-dicarboxylates (2 and 5) were synthesized and their structures were unambiguously established by the X-ray analysis of 5.

KEYWORDS ——— pyrazolo[1,5-a]pyrimidine; triethyloxonium fluoroborate; indole; N-methylindole; 1,4-dihydrocyclopent[b]indole; X-ray analysis

Recently, we reported the reaction of 6,7-diethoxycarbonylpyrazolo[1,5-a]pyrimidine-3-carbonitrile (1) with a variety of nucleophiles, such as phenol, naphthol, aniline, enamine of cyclohexanone and their analogs, in the presence of boron trifluoride (BF_3)-etherate(1) or triethyloxonium fluoroborate(2) (Et_3OBF_4) to give the respective addition products in a 1,4-fashion in the pyrimidine ring of 1. Here we would like to report a synthesis and X-ray crystal structure determination of novel 1,4-dihydrocyclopent[b]indoles (2 and 5), which were prepared by reaction of 1 with indoles in the presence of excess Et_3OBF_4.

Cyclopent[b]indole itself was first isolated by Paul and Weise(3) as a hydrobromide salt in 1963, and many kinds of its 1,2,3,4-tetrahydro derivatives have been reported.(4) However, to our knowledge 1,4-dihydrocyclopent[b]indole has so far been unknown, probably because of the presence of an unstable cyclopentadiene moiety in its molecule.

Two equivalents of N-methylindole added to a mixture of 1 and Et_3OBF_4 in CH_2Cl_2 at room temperature furnished a 69.6% yield of 2 as orange needles, $C_{27}H_{26}N_2O_4$ [MS m/z : 442 (M^+)], mp 171-173°C, IR ν_{max}^{KBr} cm^{-1} : 1720 and 1690 (CO), ^1H NMR (DMSO-d_6) δ : 0.97 and 1.24 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2CH_3$), 3.44 and 3.91 (each 3H, each s, 2 × NCH_3), 3.80-4.35 (4H, m, 2 × $CO_2CH_2CH_3$), 4.84 (1H, s, CH, disappeared upon D_2O addition), 7.00-7.70 (8H, m, Ar-H), 7.79 [1H, s, C(2)-proton of indole ring], UV λ_{max}^{EtOH} nm (log ε) : 369 (4.25), 260 (4.25), 218 (4.73). These analytical and spectral data clearly indicate lack of an aminopyrazole moiety in the molecule of 2. These data show that 2 consists of two N-methylindoles and three carbons and one hydrogen as well as two $CO_2C_2H_5$ groups derived from the starting material. Treatment of 1 with N-methylindole in the presence of BF_3-etherate as a catalyst yielded 3(1), which, by methylation with dimethylsulfate and KOH in acetone, was converted quantitatively to 4, mp 172-173°C. When this compound was then subjected to reaction with indole in the presence of Et_3OBF_4, it furnished an 8.0% yield of 5 as orange needles, $C_{26}H_{24}N_2O_4$ [MS m/z : 428 (M^+)], mp 190-191°C, together with a complex mixture. This product exhibited spectroscopic data similar to those of 2.

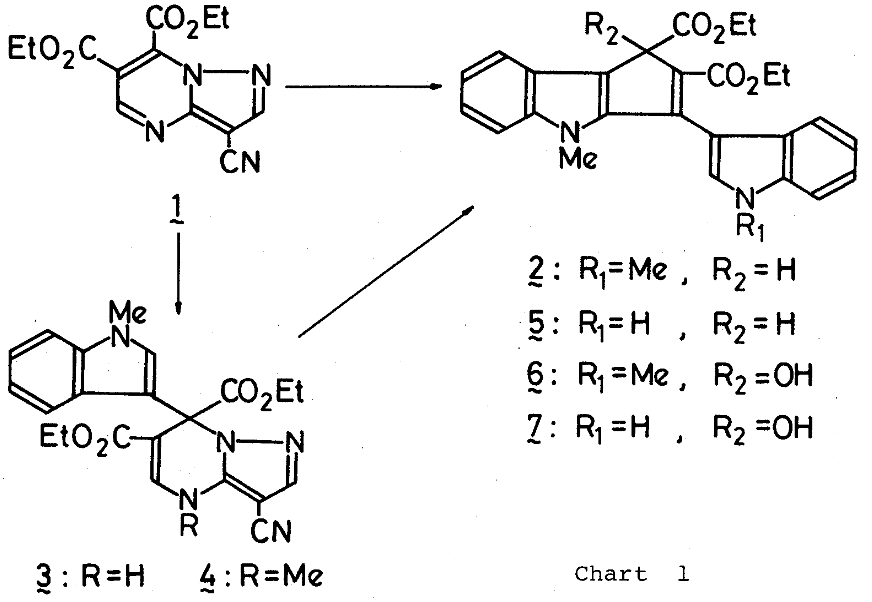

Chart 1

Thus, in order to obtain definitive evidence for the structure of **2** and **5**, an X-ray crystallographic analysis of **5** was carried out.

Crystal data: monoclinic, space group $P2_1/n$, a = 13.326(3) Å, b = 9.210(2) Å, c = 18.872(4) Å, β = 105.41(2)°, V = 2232.9(9) $Å^3$, Z = 4, Dm = 1.267(1) $g \cdot cm^{-3}$, and Dx = 1.274 $g \cdot cm^{-3}$. The structure was determined by the direct method (program MULTAN[5]) and refined by the block-diagonal least-squares method with anisotropic temperature factors for non-hydrogen atoms and aisotropic ones for hydrogen atoms. The R-value for 3800 independent reflactions is 0.071. The structure was unambigously established as diethyl 1,4-dihydro-3-β-indolyl-4-methylcyclopent[b]indole-1,2-dicarboxylate (**5**), whose stereoscopic view is presented in Fig. 1. Hence, the structure of **2** was determined to be diethyl 1,4-dihydro-4-methyl-3-β-N-methylindolylcyclopent[b]indole-1,2-dicarboxylate.

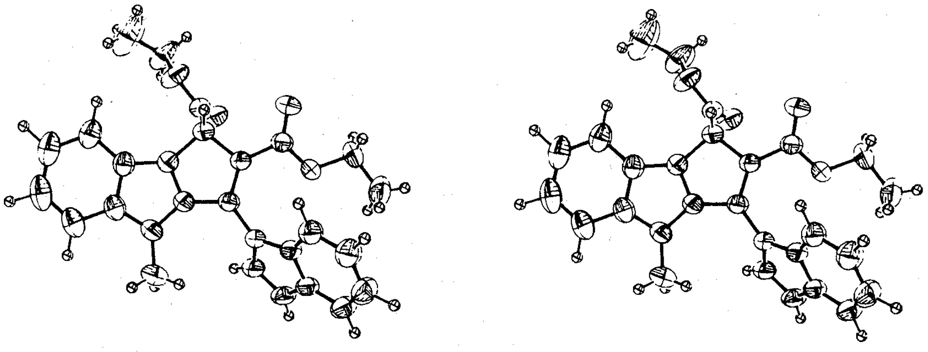

Fig. 1

The transformation of **1** into **2** probably involves the initial formation of the adduct (**8**). So the nucleophilic attack of the second N-methylindole at C(5)-position of **8** may form **9**. Subsequent intramolecular cyclization leaving the amino-

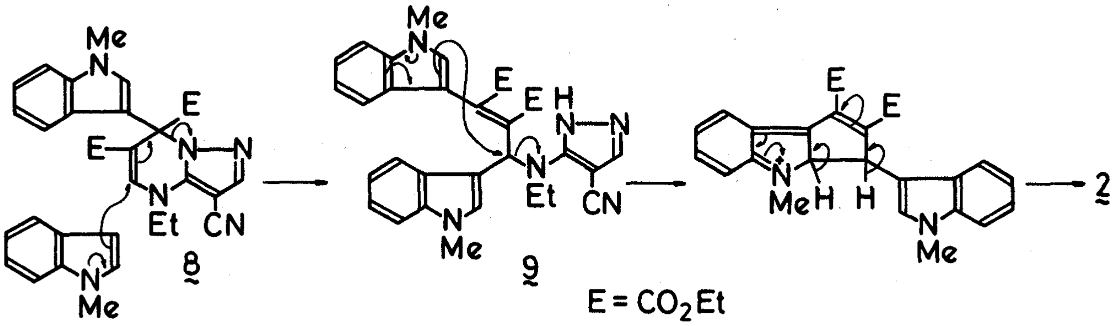

Chart 2

pyrazole moiety followed by prototropy would ultimately yield **2** as shown in Chart 2.

It should be noted that although the C(1)-proton signal of **2** or **5** disappeared upon D_2O addition in DMSO-d_6, no exchange was observed in $CDCl_3$ in its ^1H NMR spectrum, respectively. In addition, treatment of **2** with KOH in EtOH afforded the unexpected 1-hydroxycyclopent[*b*]indole (**6**),$^{6)}$ $C_{27}H_{26}N_2O_5$ [MS m/z : 458 (M^+), mp 197-198°C]. Compound **5** gave **7**, $C_{26}H_{24}N_2O_5$ [MS m/z : 444 (M^+), mp 173-174°C], under similar conditions.

The chemical reactivity of these 1,4-dihydrocyclopent[*b*]indoles is now under investigation.

REFERENCES AND NOTES

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6) Compound **6** : IR ν_{max}^{KBr} cm^{-1} : 3340 (OH), 1720 and 1690 (CO); ^1H NMR (DMSO-d_6) δ : 0.88 and 1.06 (each 3H, each t, *J*=7 Hz, 2 × $CO_2CH_2C\underline{H}_3$), 3.44 and 3.90 (each 3H, each s, 2 × NCH_3), 3.70-4.25 (4H, m, 2 × $CO_2C\underline{H}_2CH_3$), 5.91 (1H, broad s, OH), 6.95-7.60 (8H, m, Ar-H), 7.78 [1H, s, C(2)-proton of indole ring].

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