Communications to the Editor

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THE REACTION OF 1,4-DIHYDROCYCLOPENT[b]INDOLES WITH DIMETHYL ACETYLENEDICARBOXYLATE

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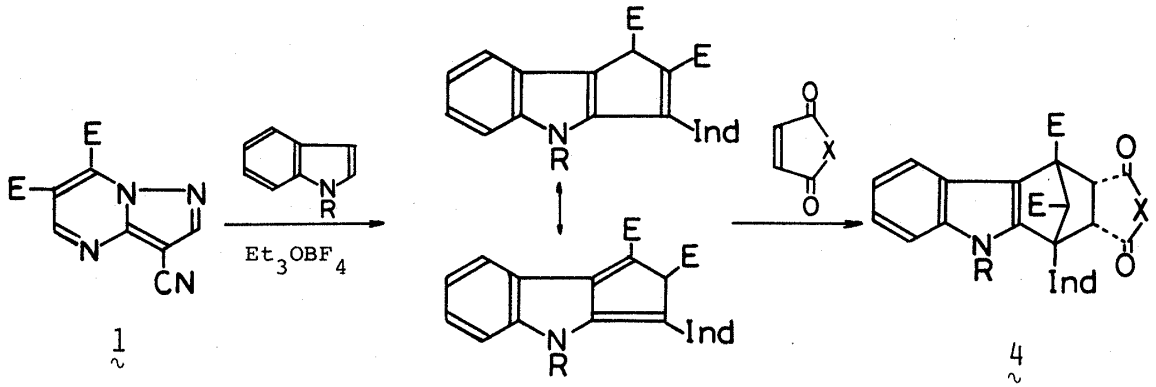
Diethyl 1,4-dihydro-4-methyl-3-(N-methyl-3-indolyl)cyclopento[b]indole-1,2-dicarboxylate (3) reacted with dimethyl acetylenedicarboxylate (DMAD) in acetonitrile under reflux to give the 5,10-dihydrocyclopent[b]indole (5). The same reaction in benzene gave the maleate (or fumarate) (6) and the 1,1a,3a,4-tetrahydrocyclobut[2,3]cyclopent[b]indole (8). Thermolysis of 8 resulted in the formation of 5. In contrast to a [2 + 2] cycloaddition reaction of 3 and DMAD, 2 reacted with two molecules of DMAD to give the 1,1a,5a,6-tetrahydrocyclohex[2,3]cyclopent[b]indole (10).

KEYWORDS ——— 1,4-dihydrocyclopent[b]indole; dimethyl acetylenedicarboxylate; [2 + 2]cycloaddition; 5,10-dihydrocyclohept[b]indole; tetrahydrocyclobut[2,3]cyclopent[b]indole; tetrahydrocyclohex[2,3]cyclopent[b]indole; thermolysis

In a preceding paper,[1] we reported that heating the 1,4-dihydrocyclopent[b]indoles (2 and 3), prepared by the reaction of the pyrazolo[1,5-a]pyrimidine derivative (1) with indoles in the presence of triethyloxonium fluoroborate,[2] resulted in the formation of intermediate 2,4-dihydrocyclopent[b]indoles, which reacted with olefins to yield [4 + 2] cycloadducts, bicyclo[2,2,1]hept[2,3-b]indoles (4).

The reaction of indoles with DMAD has been extensively investigated.[3] Neckers reported[4] photocycloaddition of DMAD to 1,3-dimethylindole to yield derivatives of cyclobutenes which are transformed to benzazepines by ring-opening. Taylor reported[5] the reaction of 1,3-dimethylindole with DMAD in the presence of boron trifluoride (BF_3)-etherate to give the benzazepine which might be obtained by thermal decomposition of an intermediate cyclobutene adduct. The cyclobutene was afterward isolated as a red oil in only 0.6% yield by Neckers[4] under the same conditions. Rodorigues also reported[6] that the thermal reaction of 1,2,3-

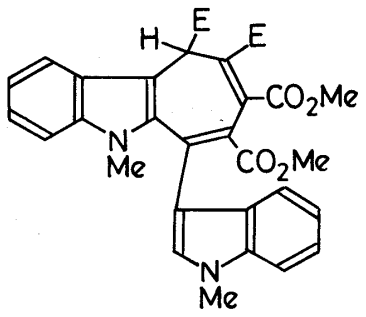


trimethylindole and 1,3-dimethylindole with DMAD in the presence of BF_3 -etherate gave the cyclobutene adducts in good yields. In these connections, we now describe the results of cycloaddition of 2 and 3 with DMAD without a catalyst in which we isolated the cyclobutene (8).

Refluxing a solution of 3 and DMAD in acetonitrile for 12 h afforded 9,10-bis(ethoxycarbonyl)-7,8-bis(methoxycarbonyl)-5,10-dihydro-5-methyl-6-(N-methyl-3-indolyl)cyclohept[b]indole (5)[7] as orange-red needles, mp 202-203°C, in 64.5% yield ; $C_{33}H_{32}N_2O_8$: m/z 584 (M^+) ; IR ν_{max}^{KBr} cm^{-1} 1730, 1720, 1620 ; UV λ_{max}^{EtOH} nm (log ε) 250 (sh), 270 (3.97), 290 (3.84), 450 (3.88) ; ^{1}H-NMR (DMSO-d_6) δ 0.65 and 1.15 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2\underline{C}H_3$), 2.95, 3.40, 3.87, 3.93 (each 3H, each s, 2 × CO_2CH_3 and 2 × NCH_3), 4.05 (1H, s, C_{10}-H), 3.50-4.20 (4H, m, 2 × $CO_2\underline{C}H_2CH_3$), 6.50-7.70 (8H, m, Ar-H), 7.30 (1H, s, C_2-H of indole ring). Cyclohept[b]indole, which is an aza-analog of benz[b]azulene, has been prepared by vapor-phase dehydrogenation with 5% palladium-charcoal on manganese oxide[8] or iodine oxidation[9] of 5,6,7,8,9,10-hexahydrocyclopent[b]indole. However, dihydrocyclopent[b]idole was hitherto unknown.

On the other hand, heating 3 and DMAD in benzene for 12 h gave, after silica gel column chromatography, pale yellow needles (6), mp 142-145°C, in 67% yield ; $C_{33}H_{34}N_2O_9$: m/z 602 (M^+), 583 as base peak (M^+-H_2O) ; IR ν_{max}^{KBr} cm^{-1} 3500, 1745, 1720, 1600 ; ^{1}H-NMR (DMSO-d_6) δ 0.65 and 0.90 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2\underline{C}H_3$), 2.53 and 3.60 (each 3H, each s, 2 × NCH_3), 3.73 and 3.83 (each 3H, each s, 2 CO_2CH_3), 3.15 (1H, s, C_1-H), 5.05 (1H, s, vinyl-H), 5.50 (1H, s, OH, exchangeable with D_2O), 6.45-7.80 (8H, m, Ar-H), 6.79 (1H, s, C_2-H of indole ring).

Reaction of 3 with DMAD in benzene followed by treatment with ethanol gave the 3-ethoxy derivative (7), mp 157-160°C, in low yield. On the basis of these results, the structure of 6 was presumed to be dimethyl 1,2-bis(ethoxycarbonyl)-3-hydroxy-4-methyl-3-(N-methyl-3-indolyl)-1,2,3,4-tetrahydro-2-(cyclopent[b]indole)maleate (or fumarate). Abnormal high-field olefinic proton (δ 5.05) of 6 in ^{1}H-NMR spectrum, which is not comparable to those of diethyl fumarate (δ 6.83) and diethyl maleate (δ 6.28), is supposed to result from the anisotropic effect of the C_3-indole ring. However, the stereochemistry of 6 and 7 was not determined at this stage.



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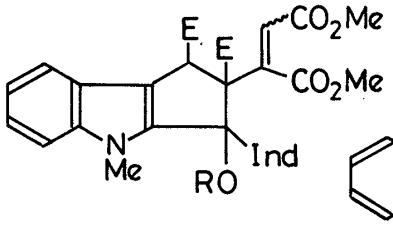
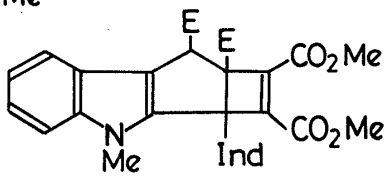


6 : R=H
7 : R=Et

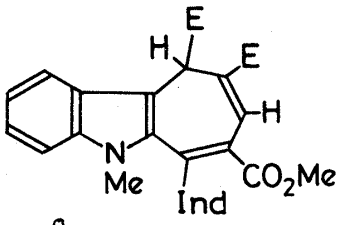


8

E=CO_2Et , Ind=3-N-methylindole

Next, attempts were made to isolate the cyclobutene adduct which might be a precursor of 5. The residual oil, which was obtained by treatment of 3 with DMAD in dry benzene followed by evaporation of the solvent, was heated at 80°C for 3 h in vacuo, and then subjected to silica gel column chromatography. The fraction of less polar component eluted with benzene gave a dark-brown solid 8 (6.3% yield), together with 6 (14%) and an unidentified crystalline compound. The product 8 showed the change of color to orange-red at around 125°C and melted at 202-203 °C when heated on a hot plate. The IR spectrum of the product obtained by heating at 120-125°C was completely identical with that of 5. Thus, 8 was assigned as the 1, 1a,3a,4-tetrahydrocyclobut[2,3]cyclopent[b]indole. When 8 was heated in ethanol under reflux, it was converted to 5 in good yield. Similarly, the reaction of 3 with methyl propiolate in toluene for 12 h under reflux afforded 9 as orange needles, mp 260-263°C, in 10.1% yield ; $C_{31}H_{30}N_2O_6$: m/z 526 (M^+) ; IR ν_{max}^{KBr} cm^{-1} 1740-1720 ; ^{1}H-NMR ($CDCl_3$) δ 0.74 and 1.21 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2CH_3$), 2.92 (3H, s, NCH_3), 3.45 and 3.80 (each 3H, each s, CO_2CH_3 and/or NCH_3), 3.88 (1H, d, J=2.5 Hz, C_1-H), 3.50-3.80 (2H, m, $CO_2CH_2CH_3$), 4.15 (2H, q, J=7 Hz, $CO_2CH_2CH_3$), 6.40-7.50 (8H, m, Ar-H), 6.82 (1H, s, C_2-H of indole ring), 7.85 (1H, d, J=2.5 Hz, C_3-H, collapsed to singlet by irradiation of C_1-H). The UV spectrum

was very similar to that of 5. In contrast to 3, compound 2 reacted with an excess of DMAD in benzene under reflux to give a complex mixture from which 1,1a-bis(ethoxycarbonyl)-6-methyl-5a-(N-methyl-3-indolyl)-2,3,4,5-tetrakis(methoxycarbonyl)-1,1a,5a,6-tetrahydrocyclohex[2,3]cyclopent[b]indole (10) was isolated as dark-red prisms, mp 205-207 ℃, in 17.3% yield ; $C_{37}H_{34}N_2O_{12}$: m/z 698 (M^+) ; IR ν_{max}^{KBr} cm^{-1} 3360, 1720 ; UV λ_{max}^{EtOH} nm (log ε) 240 (4.40), 293 (4.07), 405 (3.68) ; ^{1}H-NMR (DMSO-d) δ 0.65 and 1.17 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2CH_3$), 3.23, 3.80, 3.90, 4.07 (each 3H, each s, 4 × CO_2CH_3), 6.39 (1H, s, C_2-H of indole ring), 6.73 and 10.35 (each 1H, each s, 2 × NH), 6.85-7.70 (8H, m, Ar-H).



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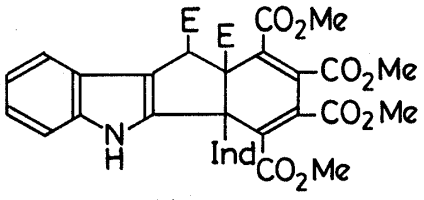
Ind=3-N-methylindole



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Ind=3-indole

These experiments revealed that the 1,4-dihydrocyclopent[b]indoles gave [4 + 2] cycloadducts with activated olefins, while [2 + 2] cycloadducts with DMAD.

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11) 8 : IR ν $_{max}^{KBr}$ cm^{-1} 1720-1700 ; ^{1}H-NMR (DMSO-d_6) δ 0.70 and 1.13 (each 3H, each t, J=7 Hz, 2 × $CO_2CH_2CH_3$), 3.20, 3.23, 3.80, 3.93 (each 3H, each s, 2 × NCH_3 and 2 × CO_2CH_3), 3.55 (1H, s, C_1-H), 5.97 (1H, s, C_2-H of indole ring), 6.55 - 7.60 (8H, m, Ar-H).

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