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SYNTHESIS OF 1,9a-DIHYDRO-9a-SUBSTITUTED FLUORENONES AND THEIR 4-AZA ANALOGUES

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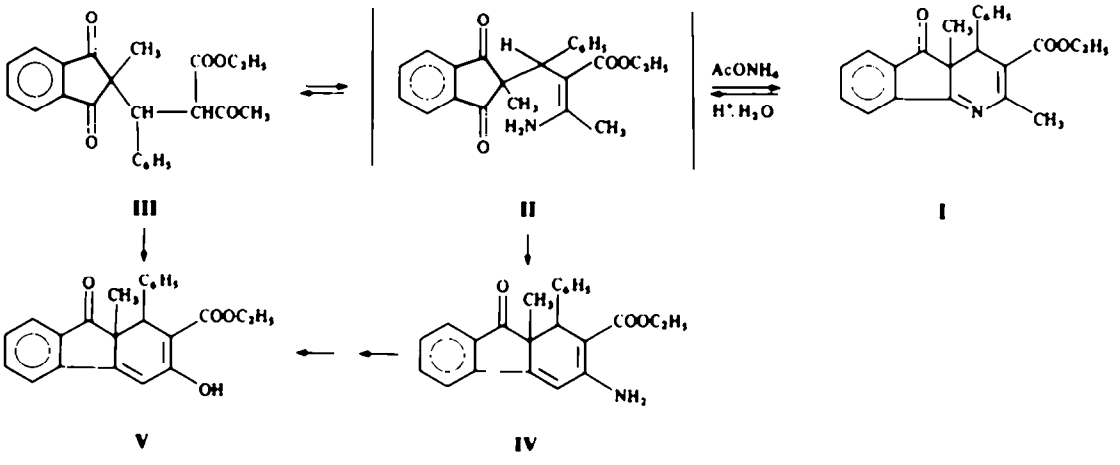
Abstract—Cyclization of 2,2-disubstituted indan-1,3-dione with CH_3COONH_4 yields 9a-substituted 1,9a-dihydrofluorenone and 9H-4a,5-dihydroindeno(1,2-b)pyridine derivatives.

The synthesis of hydrogenated fluorenone derivatives with angular substituents meets with certain obstacles, the 9a-substituted 1,9a-dihydrofluorene-9-one derivatives being unknown. Recently, 4-aza analogues of 9a-alkyl-1,9a-dihydrofluorene-9-one have been obtained by alkylation of 2-methyl-3-ethoxycarbonyl-4-aryl-5-oxo-1H-4,5-dihydroindeno(1,2-b)pyridines.[1] By examining the chemical properties of the compounds mentioned above we found a transition from 2,2-disubstituted indan-1,3-dione to 9a-substituted 1,9a-dihydrofluorene-9-one and a new synthetic route to its earlier known 4-aza analogue was proposed.

On boiling 2,4a-dimethyl-3-ethoxycarbonyl-4-phenyl-5-oxo-4H-4a,5-dihydroindeno(1,2-b)-pyridine (I) in acid medium the $N{=}C_{9b}$ bond undergoes hydrolysis resulting in dihydropyridine cycle breakage to give ethyl α-acetyl-β-(2-methylindan-1,3-dione-2-yl)-β-phenylpropionate (III) and also, unexpectedly, 1,9a-dihydrofluorene-9-one derivatives IV and V.

The hydrolysis of I yields III as the main product resulting from enamic group cleavage in the intermediate II. Recyclization of the primary hydrolysis product, i.e. intramolecular interaction of the terminal CH_3 group with the CO group of the indan-1,3-dione moiety producing IV proceeds in parallel to substitution. 3-Hydroxyfluorene V does not result directly from hydrolysis, but is formed upon intramolecular condensation of III, as supported by experimental evidence. Compound V (yield: 37%) is obtained by boiling of III with 0.6 M HCl in ethanol for 20 hr. 3-Aminofluorene IV readily affords the N-acetyl derivative, but undergoes diazotization under rigid conditions, which is characteristic of amines in the fluorenone series. The hydrolysis of the corresponding diazonium salt provides V.

Depending on reaction conditions, ethyl α-acetyl-β-(2-indan-1,3-dione-2-yl)-β-phenylpropionate (III) with ammonium acetate readily undergo cyclization to 1,9a-dihydrofluorene and 4a,5-dihydroindenopyridine



After boiling the mixture of 5 mmol I with 0.1 M HCl (75 ml) in 80% ethanol for 5 hr it was diluted with water and extracted with chloroform (3 × 50 ml). The resulting extract was evaporated and chromatographed on a silica gel column using chloroform:hexane:acetone (9:7:1) as eluent to afford the colourless ethyl α-acetyl-β-(2-methylindan-1,3-dione-2-yl)-β-phenylpropionate (III)[2] (yield: 74%) and two yellow coloured substances—1-phenyl-2-ethoxycarbonyl-3-hydroxy-9a-methyl-1,9a-dihydrofluorene-9-one (V)[3] (yield: 10%) and 1-phenyl-2-ethoxycarbonyl-3-amino-9a-methyl-1,9a-dihydrofluorene-9-one (IV)[4] (yield: 12%).

derivatives. The cyclization of 2-(2-acetyl-1'-arylethyl)indan-1,3-diones with CH_3COONH_4 in acetic acid is known to give 1H-4,5-dihydroindeno(1,2-b)pyridines,[5] however, the cyclization of 2,2-disubstituted indan-1,3-dione to 4H-4a,5-dihydroindeno(1,2-b)pyridine as well as to the dihydrofluorenone derivative with an angular methyl group at C_{9a} was carried out for the first time. Thus, a convenient new method for the preparation of 9a-methyl derivatives of 1,9a-dihydrofluorenone and its 4-aza analogue from readily available 2,2-disubstituted indan-1,3-diones[6] is presented.

The quantitative ratio of the indenopyridine I and

aminofluorenone IV obtained during the cyclization of III depends on the reactivity of the reaction medium. If after boiling of 5 mmol of III with CH_3COONH_4 (1.4 g) in acetic acid (15 ml) the reaction mixture is diluted with 100 ml H_2O and the yellow sediment is subjected to column chromatography the reaction yield will be 84% (I) and 14% (IV). This ratio remains practically unchanged in alcohol–acetic acid, but in the presence of water (50% aqueous acetic acid) compound I is not formed at all, the yield of aminofluorenone IV being 30%. Addition of aprotic solvents (benzene, dioxan) to the reaction medium favours the formation of indenopyridine I.

REFERENCES AND NOTES

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[2] M. Bundule, A. Mishnow, J. Bleidelis, V. Lusis, D. Muceniece and G. Dubur, *Ibid.* 1388 (1984).

[3] M.p. 165°, PMR spectrum (DMSO-D_6): 1.14 (t, 3H, OCH_2CH_3), 1.32 (s, 3H, 9a-CH_3), 4.12 (s, 1H, 1-H), 4.12 (k, 2H, OCH_2CH_3), 6.91 (s, 1H, 4-H), 7.07 (s, 5H, 1-C_6H_5), 7.51–7.64 (m, 2H), 7.69–7.92 (m, 1H) and 8.18 (d, 1H, protons at C_5—C_8), 12.31 ppm (s, 1H, 3-OH, involved in deutero-exchange with D_2O). Mass spectrum: 360 (3) $[M]^+$, 314 (100) $[M-C_2H_5OH]^+$, 299 (33) $[M-C_2H_5OH-CH_3]^+$, 286 (9) $[M-C_2H_5OH-CO]^+$, 271 (8) $[M-C_2H_5OH-CH_3-CO]^+$. IR spectrum: 1712 cm^{-1} (CO).

[4] M.p. 184–186°, PMR spectrum ($CDCl_3$): 1.18 (t, 3H, OCH_2CH_3), 1.44 (s, 3H, 9a-CH_3), 4.07 (k, 2H, OCH_2CH_3), 4.33 (s, 1H, 1-H), 6.47 (s, 1H, 4-H), 6.91–7.16 (m, 5H, 1-C_6H_5), 7.27–7.78 ppm (m, 6H, 3-NH_2 and protons at C_5—C_8). Mass spectrum: 359 (100) $[M]^+$, 358 (4) $[M-H]^+$, 344 (19) $[M-CH_3]^+$, 330 (5) $[M-C_2H_5]^+$, 313 (25) $[M-C_2H_5OH]^+$, 298 (19) $[M-CH_3-C_2H_5OH]^+$, 286 (90) $[M-COOC_2H_5]^+$, 282 (29) $[M-C_6H_5]^+$, 271 (15) $[M-CH_3-COOC_2H_5]^+$. IR spectrum: 3320 (NH_2), 1720 cm^{-1} (CO).

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[6] G. Vanags and E. Ozola, *Zhurn. Org. Khimii* 1(3), 529 (1965).