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ISOINDOLO [2,1-b] ISOQUINOLINIUM BROMIDE PREVIOUSLY DESCRIBED AS ISOQUINOLYL-BENZOIC ACID BROMIDE¶

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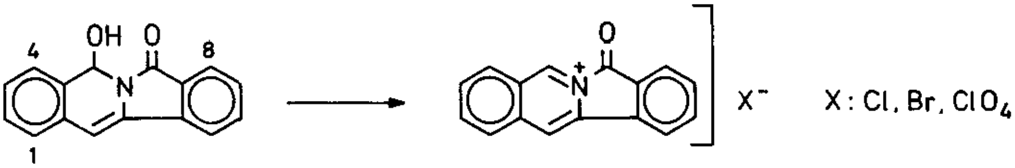
Abstract - Treatment of 3 with bromine in chloroform affords the isoindolo [2,1-b] isoquinolinium salt 5a and not the 2-(3-isoquinolyl)-benzoyl bromide 4a. Compound 5a was also obtained from 4c and thionyl bromide. Reactions of 5a with alcohols and acetone led to 6a-c.

Up to now the chemistry of N-acylpseudobases (so-called carbinolamides) of isoquinoline-type has only been rarely investigated[1a,b]. Recently we reported the synthesis of the tetracyclic carbinolamide 1 and its transformation to stable N-acyliminium salts 2[2].



1 2

Marsili and Scartoni assumed the formation of an acid bromide 4a when treating 3 with bromine[3]. Taking our findings into account we doubted the structure of the reaction product 4a.

The compound isolated by Marsili and Scartoni is a yellow crystalline substance, exhibits a high melting point, and is insoluble in solvents of low polarity. Its ir (Nujol) shows a strong band at 1810 cm^{-1}. It reacts with methanol to yield an ester 4b, which can be hydrolyzed to give 4c.

In contrast to the substance in question the compounds 4b and 4c are colourless and can be easily dissolved in solvents of low polarity.

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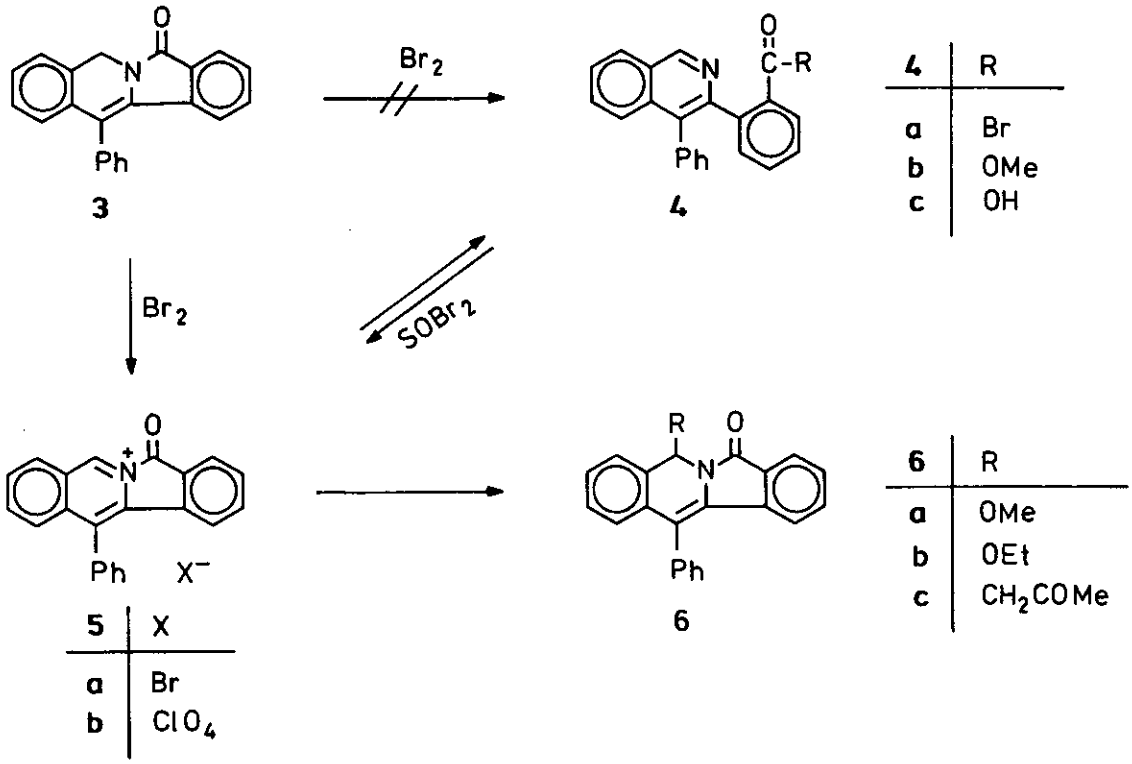

Since it is unlikely that the derivatives of the same acid differ as much in their properties as in this case, we favoured the structure of an acyliminium salt 5a. This is in accordance with all physical and chemical data reported by the Italian authors. We were able to confirm the salt structure by additional investigations: The ^{1}H-nmr spectrum shows a singlet at 10.1 ppm due to the proton in position 5. The uv of 5a, exhibiting bands at 463 and 350 nm (shoulder), is similar to that of 2 and differs distinctly from that of 4b.

Upon treating the bromide with silver perchlorate anion exchange takes place and 5b is formed. The bromide and perchlorate have different stabilities[4]. In the cold 5a can be easily hydrolyzed whereas 5b remaines unchanged.

In the following reactions the tetracyclic structure was retained. 5a as well as 5b reacts with sodium methoxide and ethoxide in THF to give the acyl-O,N-acetals 6a and 6b respectively.

When suspending the salts in acetone the solvent attacks the carbonium ion and the acetonyl compound 6c results. In this case no base catalysis is necessary. Furthermore we found that the acyliminium bromide 5a can be obtained in pure form and good yield from the sodium salt of 4c by treating with thionyl bromide.

Future investigations will show whether this acyliminium salt may be useful as a synthon in alkaloid chemistry.

EXPERIMENTAL

Infrared spectra (KBr) were run on a Perkin-Elmer 297. Nmr spectra were recorded on a Bruker WP 60 and WM 250 with TMS as internal standard. Uv: Beckmann DK-1A and Varian Techtron 635; ms: Varian MAT CH-7A. The mps are uncorrected.

7-Oxo-12-phenyl-7H-isoindolo [2,1-b] isoquinolinium Bromide (5a)

A. According to the procedure[3] from 3 and bromine in chloroform.

B. To a stirred suspension of 90 mg of sodium salt of 4c (prepared by recrystallization from 5% NaOH) in 15 ml of dry chloroform, 15 drops of thionyl bromide were added. After filtration orange needles were formed. Yield: 60 mg (60%), mp 202-204^{0}C (decomp.), lit.[3] mp not indicated; ir: $\tilde{\nu}$/cm^{-1} 1810 und 1800 (C=O), 1620, 1570; nmr (CD_3NO_2) : δ/ppm 10.10 (s, 1H, 5-H), 8.77 (d, 1H, J = 7.90), 8.36-8.10 (m, 3H), 7.92-7.60 (m, 8H), 6.75 (m, 1H, 11-H); uv (conc. H_2SO_4) : λmax(log ε) : 235 (4.35), 270 (4.56), 305 (4.09, sh), 350 (3.73, sh), 463 nm (3.48).

7-Oxo-12-phenyl-7H-isoindolo [2,1-b] isoquinolinium perchlorate (5b)

To a solution of 100.mg of 5a in 10 ml of nitromethane 70 mg of silver perchlorate dissolved in 5 ml of nitromethane were added dropwise. After 5 min silver bromide was removed by filtration and ether was added to the filtrate. Orange crystals, mp 304-306^{0}C (decomp.), yield : 55 mg (53%); ir : $\tilde{\nu}$/cm^{-1} 1810 und 1795 (C=O), 1615, 1600, 1565, 1140-1120 and 1040 and 620 (ClO_4); nmr (CD_3NO_2) : δ/ppm 10.03 (s, 1H, 5-H), 8.72 (d, 1H, aromat.), 8.40-7.45 (m, 11H, aromat.) 6.70 (m, 1H, 11-H); ms (260^0) : m/z 323 (57%, M^++15), 309 (74%, M^++1), 308 (100%, M^+), 290 (5), 289 (7), 281 (12), 280 (44), 279 (28), 278 (26); $C_{22}H_{14}ClNO_5$(407.8), Calcd. : C 64.8; H 3.46; N 3.4; Found : C 64.6; H 3.12; N 3.6.

5-Methoxy-12-phenyl-5,7-dihydroisoindolo [2,1-b] isoquinolin-7(5H)-one (6a)

A mixture of 200 mg of 5a and 50 mg of sodium methoxide in 10 ml of tetrahydrofuran was stirred at room temperature for 10 min. After evaporation of the solvent the residue was treated first with water and then with methanol to give a pale yellow powder, mp 156-158^{0}C (decomp.), Yield : 94 mg (54%); ir : $\tilde{\nu}$/cm^{-1} 1705 (C=O), 1635 (C=C), 1610; nmr ([D_6]DMSO) : δ/ppm 7.86-7.10 (m, 11H), 6.93-6.83 (m, 1H, aromat.), 6.65 (s, 1H, NCHO), 6.35-6.21 (m, 1H, aromat.), 3.19 (s, 3H, OCH_3); uv (methanol) : λmax(logε) 222 (4.38), 232 (4.35), 243 (4.06, sh), 298 (3.70), 311 (3.65), 362 (4.12), 381 nm (3.94, sh); ms (140^0) : m/z 339 (6%, M^+), 308 (100), 280, 279, 278, 277 (all 6-8%); $C_{23}H_{17}NO_2$ (339.4), Calcd. : C 81.4; H 5.05; N 4.1; Found : C 81.2; H 4.73; N 3.9.

5-Ethoxy-12-phenyl-5,7-dihydroisoindolo [2,1-b] isoquinolin-7(5H)-one (6b)

Following the same procedure indicated for 6a, 6b was prepared from 5a and sodium ethoxide. Pale yellow powder, which melts between 180 and 182°C (decomp.), yield : 80 mg (46%); ir : $\tilde{\nu}$/cm^{-1} 1710 (C=O), 1640 (C=C), 1610, 1600; nmr ($CDCl_3$) : δ /ppm 7.88-7.72 (m, 1H, aromat.), 7.55-6.85 (m, 11H, aromat.), 6.66 (s, 1H, OC<u>H</u>N), 6.36-6.21 (m, 1H, aromat.), 3.60 (m, 2H, O-$\underline{CH_2}$-CH_3), 1.08 (t, 3H, O-CH_2-$\underline{CH_3}$); uv (methanol) : λ max(log ε) 223 (4.35), 232 (4.33), 244 (4.02), 300 (3.69), 312 (3.65), 364 (4.16), 381 nm (3.92, sh); ms (130°) : m/z 353 (4%, M^+), 309 (29), 308 (100), 280, 279, 278, 277 (all 6-9%); $C_{24}H_{19}NO_2$(353.4); Calcd. : C 81.6; H 5.42; N 4.0; Found : C 81.3; H 5.12; N 3.7.

5-Acetonyl-12-phenyl-5,7-dihydroisoindolo [2,1-b] isoquinolin-7(5H)-one (6c)

200 mg of 5a and 20 ml of acetone were stirred for 20 h. After filtration the residue was recrystallized from acetone/petrol ether. Pale yellow crystals, mp 227-229°C (decomp.), yield : 80 mg (43%); ir : $\tilde{\nu}$/cm^{-1} 1680-1710 (C=O), 1630 (C=C), 1610, 1595; nmr ($CDCl_3$) : δ /ppm 7.85 (d, 1H, J = 7.5), 7.60-7.15 (m, 10H), 6.91 (d, 1H, J = 7.4), 6.35 (d, 1H, J = 7.8), 6.13 (ABX-system, 1H, $J_{AX} + J_{BX} = 11.2$, N-C<u>H</u>-CH_2-), 3.18 und 3.00 (2H; $J_{AB} = 15.7$, $J_{AX} = 7.1$, $J_{BX} = 4.1$, -CH_2-), 2.10 (s, 3H, -CH_3); uv (methanol) : λ max(log ε) 221 (4.33), 233 (4.33), 248 (4.03), 371 nm (4.15); ms (140°) : m/z 365 (6%, M^+), 309 (36), 308 (100), 280, 279, 278, 277 (4-11%); $C_{25}H_{19}NO_2$(365.4); Calcd. : C 82.2; H 5.24; N 3.8; Found : C 81.9; H 4.92; N 3.7.

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