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BENZO- AND INDOLOQUINOLIZINE DERIVATIVES †

PART IX. A NOVEL ROUTE TO THE TRIBENZO[a,c,h]QUINOLIZINE SYSTEM BY ELECTROPHILIC AND PHOTOLYTIC CYCLISATION OF IMMONIUM SALTS

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SUMMARY

Photocyclisation of immonium salts, followed by reduction, has been used successfully in the synthesis of tribenzo[a,c,h]quinolizine systems, in cases where the electrophilic cyclization failed.

In a previous communication[2] we reported the synthesis of 11,15b-dihydro-10H-isoquino[2,1-f]phenanthridine (7a ; Scheme 1) by photocyclisation and subsequent reduction of a 1,2-diphenylisoquinolinium salt and its 3,4-dihydro derivative. In view of our continuous interest in the synthesis and the spectroscopic properties of benzo- and indoloquinolizines, a novel approach to the tribenzo[a,c,h]quinolizine system was developed by cyclisation of the readily accessible 2-(2'-biphenyl)-3,4-dihydroisoquinolinium bromide (5a).

† Part VIII : see ref. 1

Intramolecular electrophilic cyclisation of immonium salts on the strongly activated 2-position of an indole nucleus is a well-known method for the synthesis of the β-carboline system[3]. This method is *however unsuccessful for the synthesis of the dibenzo[a,h]quinolizine* system [2], even when electrophilic cyclisation is strongly favoured by the high activation of the p.methoxy-substituent of [1]. Earlier claims to have prepared compound [2] by the synthetic sequence outlined from 2-(2'-phenetyl)-3,4-dihydroisoquinolinium bromide [1] were unjustified, as proven by Dyke[5].

When the 3,4-dihydroisoquinolinium salt [5a] was treated with polyphosphoric acid (PPA) at 175 - 185 °C for 2.5 hrs, cyclisation occured to give 11,15b-dihydro-10H-isoquino[2,1-f]phenanthridine† [7a]. Reaction of the nitro derivative [5b] under identical conditions failed however. The only product isolated from the reaction mixture was the hydrolysed starting material.

Photocyclisation, followed by reduction, is an alternative method for the preparation of the quinolizines (7a) and (7b) from the immonium salts (5a) and (5b). In the literature only one example of a photocyclisation between an aromatic carbon atom and the carbon atom of a $>C=\overset{+}{N}<$ moiety has been found. N-Styrylpyridinium salts undergo photocyclisation to give phenanthridizinium salts, as shown by Bradsher[6]. The quaternary salts (5a) (0.01 mol), dissolved in ethanol (750 ml) with a trace of iodine (5 mg) was irradiated during 30 hrs, using a high pressure 450 W mercury vapour Hanovia lamp. The reaction product was immediately reduced,

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† The isolated compound was completely identical with an authentic sample (ref. 2).

using petroleum ether/benzene (1/1) as eluant. A first fraction gave the reduced starting material : 2(2'-biphenyl)-1,2,3,4-tetrahydroisoquinoline [m.p. 85° (EtOH) ; NMR ($CDCl_3$) : δ 2.56 ppm, t, 2H - δ 3.02 ppm, t, 2H) δ 4.13 ppm, s, 2H and δ 7.02-7.64 ppm, m, 13H ; $M^{+\cdot}$ = 285] in a yield of 10 %. A second fraction gave the expected 11,15b-dihydro-10H-isoquino-[2,1-f]phenanthridine (7a) in a yield of 46 %.

When applying the same procedure to the nitro derivative,(5b), the ringclosed 11,15b-dihydro-6-nitro-10H-isoquino[2,1-f]phenanthridine (7b) could be isolated in a yield of 18 % [m.p. NMR ($CDCl_3$ - 270 MHz) : δ 2.93 ppm, m, 1H - δ 3.38 ppm, m, 1H - δ 3.77 ppm, m, 1H - δ 4.26 ppm, m, 1H - δ 5.66 ppm, s, 1H - δ 6.87-7.49 ppm, m, 8H - δ 7.84 ppm, dd, 1H - δ 8.07 ppm, dd, 1H and δ 8.57 ppm, d, 1H ; $M^{+\cdot}$ = 328].

The immonium salts (5a) and (5b) were prepared using the method of Beke et al[7]. Condensation of 2-(β-bromoethyl)benzaldehyde[8] (3) and 2-aminobiphenyl (4a) or its 5-nitro derivative[9] (4b) gave (5a) and (5b) in a yield of 89 % and 84 % respectively. [(5a) : m.p. 204° (dioxane) ; IR (KBr) : 1640 cm^{-1} ($C=\overset{+}{N}$) ; NMR (CF_3COOH) : δ 3.07 ppm, t, 2H - δ 4.16 ppm, t, 2H - δ 7.40-7.89 ppm, m, 13H and δ 8.02 ppm, s, 1H] [(5b) : m.p. >250° (dioxane) ; IR (KBr) : 1630 cm^{-1} ($C = \overset{+}{N}$) ; NMR (DMSO d_6) : δ 3.0 ppm, t, 2H - δ 4.15 ppm, t, 2H - δ 7.4-8.5 ppm, m, 11H - δ 8.60 ppm, dd, 1H and δ 9.9 ppm, s, 1H].

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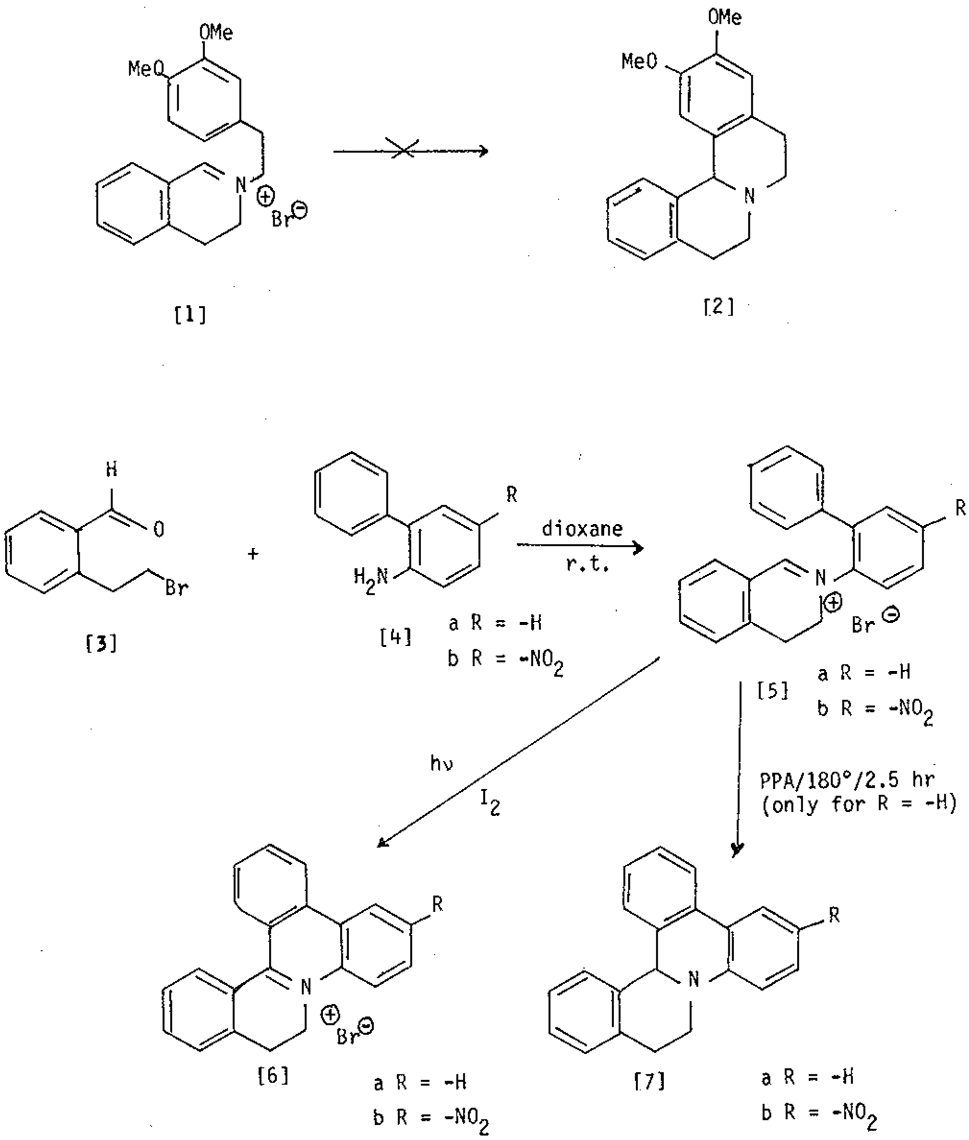
SCHEME 1



OMe
MeO
N
Br
[1]
OMe
MeO
N
[2]
H
O
Br
[3]
+
R
H_2N
[4]
a R = -H
b R = $-NO_2$
dioxane
r.t.
R
N
Br
[5]
a R = -H
b R = $-NO_2$
hν
I_2
PPA/180°/2.5 hr
(only for R = -H)
R
N
Br
[6]
a R = -H
b R = $-NO_2$
R
N
[7]
a R = -H
b R = $-NO_2$

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