"ONE POT" SYNTHESIS OF 1,5-DIAZA-2,3,6,7-TETRAHYDRO- 4-METHYL-PHENANTHRENE-4,8-DIONE FROM CORRESPONDING BIS-β-AMINO ACID

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ABSTRACT: *The cyclization of β−anilino propionic acids in the presence of polyphosphoric acid (PPA) afforded the 2,3-Dihydroquinoline-4-(1H)-ones in good yields. N,N'-bis(2-carboxyethyl)-4-methyl-1,2-diaminobenzene (7) is cyclized under this condition to produce the 1,5-diaza-2,3,6,7-tetrahydro-4-methyl-pheranthrene-4,8-dione(bis-quinolone) (8).*

KEY WORDS: *Quinolone, Quinoline, Bis-β-amino propionic acid.*

"Biscyclization" strategy is a useful method for synthesis of compounds with three or more rings. *Scholl* et al. have used PPA for preparation of a tetraketone [1]. *Miller* synthesised an anthracenedione via biscyclization in the presence of PPA [2]. We have succeeded in synthesis of precursor of 1,8-dihydroxy-9,10-anthraquinone in the presence of PPA [3]. This method is used for synthesis of different quinolones by *Forbis* [4] and *Kelly* [5]. PPA is also used for simultaneous cyclization of a diacid to obtain a diketone containing nitrogen [6]. The "biscyclization" process was carried out on the bis-β-amino acid (**7**) in the presence of PPA, using the similar procedure [3]. It is notable that "biscyclization" did not take place on para-isomer (**9**). This might be due to the protonation and deactivation of the two nitrogen atoms with PPA.

EXPERIMENTAL

N-(2-cyanoethyl)-2,4-dimethoxyaniline (2)

In a 50 mL round-bottom flask equipped with a reflux condenser, 15.3 g (0.1 mol) 2,4-dimethoxyaniline, 20 mL acrylonitrile and 0.8 g (5% weight of amine) cupric acetate was heated at 60°C for 8 h and then poured in 100 mL water. The cyanoethylated product was separated as oil-like red layer. It had ν_{max} (film) 3360(s), 3020(s), 2960(s), 2240(s), 1600(s), 1520(s), 1460(s).

^{1}H NMR, δ(60 MHz, $CDCl_3$) 2.6(t, J= 6 Hz, 2H), 3.3 (t, J=6 Hz, 2H), 3.6(s, 1H), 3.8(6H), 6.5(3H).

N,N'-Bis-(2-cyanoethyl)-4-methyl-1,2-diaminobenzene (8)

In a 100 mL round-bottom flask equipped with a reflux condenser were place 12.2 g (0.1 mol) 4-methyl-

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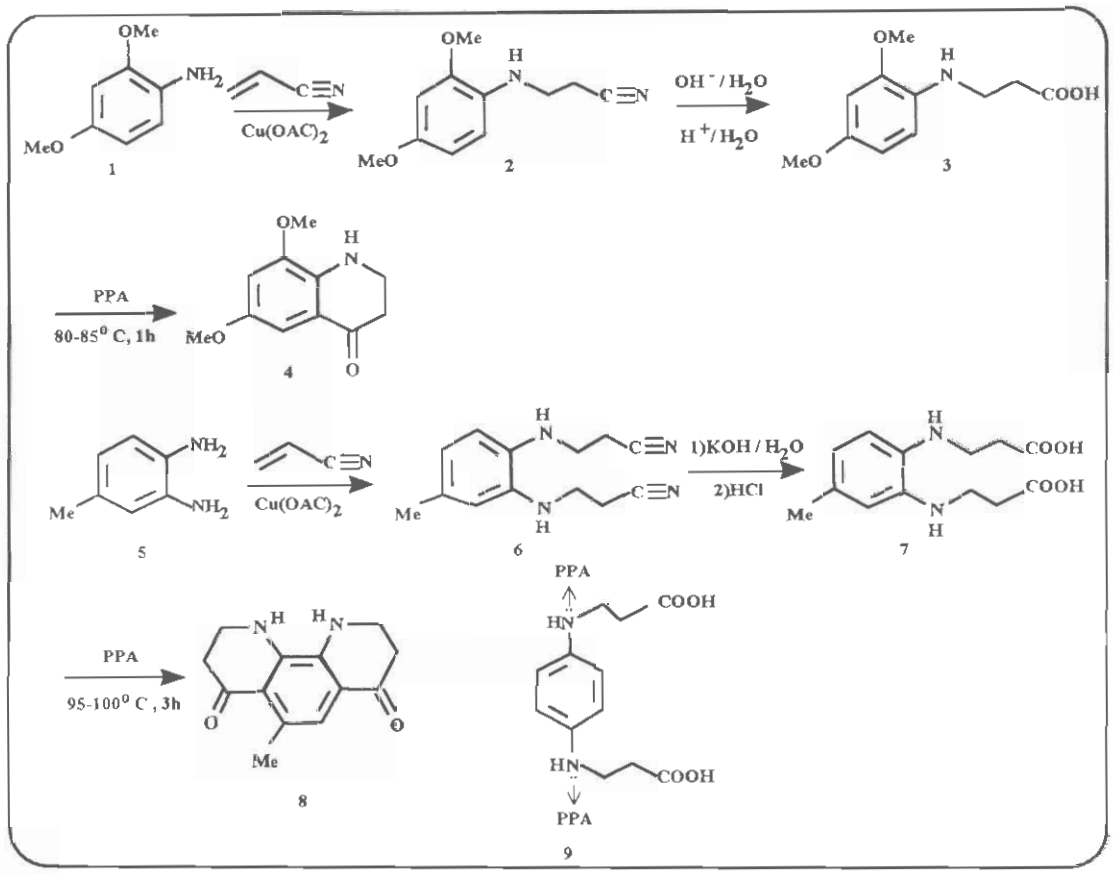
1021-9986/99/1/24 3/$/2.30



1,2-diamino benzene 30 mL acrylonitrile and 0.8 g (7% weight of diamine) cupric acetate. The temperature was adjusted at 80°C and kept for 14 h. The excess of acrylonitrile was evaporated at reduced pressure and the black oil residue was dissolved in 1:1 acetone-water mixture. After 24 h the crude cyanoethylated product was precipitated and filtered. Recrystalization in petroleum ether (60-80°C) gave N,N′-bis-(2-cyanoethyl)- 4- methyl- 1,2- diaminobenzene, brown powder (10.26 g, 45%) mp 70-74°C. It had ν_{max} (film), 3400(w), 3040(w), 3000(m), 2960(m), 2240(m), 1600 (s), 1520(s), 1480(m), 1400(s), 1360(m), 1240(s), 1200 (s).

^{1}H NMR(60 MHz, acetone-d_6), 2.2(s, 3H), 2.5(t, J= 6,4H), 3.1(t, J= 6, 4H), 6.5(s, 1H), 7.1(m, 2H).

Hydrolysis of cyanoethylated products

General procedure for alkaline hydrolysis

A solution of the nitrile (5 g) and potassium hydroxide (12 g) in 50 mL water was refluxed for 4-5 h. By addition of hydrochloric acid the *pH* reduced to the range of 6.5-7. Extraction followed by drying (with Na_2SO_4) and evaporation solvent at reduced pressure, gives the corresponding β−amino acids.

3-(2,4-Dimethoxyanilino) propionic acid (3)

ν_{max} (film), 3440(m, 3360-2200(s and broad), 1720 (s), 1640(s), 1520(s), 1480(m), 1440(m), 1440(s).

^{1}H NMR, δ (60 MHz, $CDCl_3$), 2.7(t, J= 7, 2H), 3.2 (t, J=6, 2H), 3.6(s, broad, 1H), 3.8(s, 6H), 6.5(s, 2H), 6.7(s, 1H).

m/z 225[57, $M^{\circ+}$], 166[80, $(M - CH_2CO_2H)^{\circ+}$], 150 [100], 136[30, $(M - NH\text{-}CH_2\text{-}CH_2\text{-}CO_2H)^{\circ+}$], 45(20).

N,N′-Bis-(2-carboxyethyl)-4-methyl-1,2-diamino-benzene (7)

ν_{max}(KBr), 3360(m), 3280-2080(b), 1720(s), 1640 (s), 1600(m), 1560(m), 1520(s), 1480(s), 1320(s), 1280 (m).

^{1}H NMR, δ(60 MHz, acetone-d_6), 2.2(s, 3H), 2.6(t, J= 6 Hz, 4H), 3.3(t, J= 6 Hz, 4 H), 7(s, 3H).

m/z 338 (3), 320(50), 277(100), 265(3), 261(30), 21

(75), 205 (70), 91(40).

Cyclization of β-amino acids with polyphosphoric acid (PPA)

General procedure: The β-amino acid was added to a mixture of di-phosphorous pentoxide (10.0 g for 0.3 g of β-amino acid) and phosphoric acid (4.0 mL) and heated to the optimum temperature 85-100. The solution was kept at this temperature for 1-3 h with occasional shaking. The solution was cooled, water (50 mL) and ice (50 g) was added with shaking and extracted with chloroform (5×10 mL).

The combined extracts was washed with saturated aqueous sodium hydrogen carbonate (7×10 mL) and then with water until the aqueous phase became neutral to the litmous indicator. Organic layer was dried with sodium sulphate. Evaporation of chloroform at reduced pressure leaves the quinolone.

6,8-Dimethoxy-2,3-dihydroquinoline-4-(1H)-one (4)

ν_{max}(KBr), 3400(s), 3360(s), 3120(w), 2960(s), 1640 (s), 1620(s), 1500(s), 1460(s), 1440(s), 1400(s).

^{1}H NMR, δ(60 MHz, $CDCl_3$), 2.7(t, J= 6Hz, 2H), 3.6 (t, J= 6 Hz, 2H), 3.8(s, 6H), 6.6(d, J= 3 Hz, 1H); 6.9(d, J= 3Hz, 1H).

m/z 279(10), 207(60), 192(100), 177(10), 164(10), 149 (40), 136(20).

1,5-Diaza-2,3,6,7-tetrahydro-4,methyl-phenanthrene-4,8- dione (8)

ν_{max}(film), 3360(m), 3040(s), 2960(s), 2880(s), 1680 (s), 1600(s), 1560(s), 1480(s), 1440(s), 1280(s).

^{1}H NMR, δ(60 MHz, acetone-d_6), 2.6(s, 3H), 2.8(t, J= 6Hz, 4H), 3.5(m, 4H), 7.1(s, 1H).

m/z, 284(60), 241(100), 230(30), 228(50), 221(20), 200 (35), 187(55), 175(20), 159(40), 147(30), 88(15), 43 (40).

Received, 11th November 1997; Accepted, 8th June 1998

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