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" BISCYCLISATION" SYNTHESIS OF 1,8-DIHYDROXY-9, 10-ANTHRAQUINONE (1,8-DHA)

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Abstract

The synthetic route in this work is based on the classical Friedel-Crafts strategy, and began with 1,4-dimethoxybenzene (1), followed by alkylation and selective demethylation of 2-methoxy function in oxo-acid (3). The orthoformylation to synthesize aldehyde (6) was based on the Reimer-Tieman reaction. Chain extension of this aldehyde required methylation of the hydroxyl group and condensation with pyruvic acid which afforded acid (8) in 85% yield. Two steps reduction process of this acid led to diacid (11) in good yield. A direct "biscylisation" of (11) afforded diketone (12) as the main product. This compound was converted to (1, 8-DHA), 15, via an aromatization process.

Introduction

"Biscyclisation" processes are rarely reported in the literature as a synthetic method in organic chemistry and are often described as impractical for ring closure purposes in aromatic moieties [14a-d]. We have been able to develop a new method using the "biscyclisation" in which four main steps in the synthesis of 1,8-DHA are avoided.

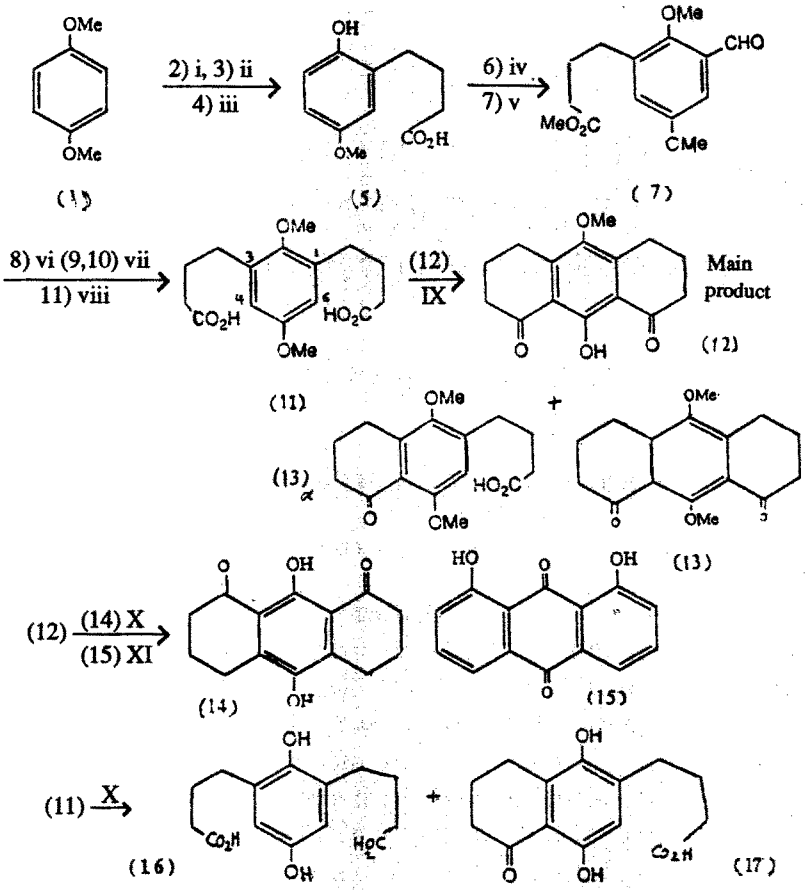
Results and Discussion

This article describes our synthetic approach to the preparation of 1,8-DHA (15). The oxo-acid (3) was prepared from condensation of succinic anhydride (2) in the presence of aluminium chloride in nitrobenzene in very good yield [1]. The reagent for selective demethylation of the oxo-acid (3) was boron tribromide in dichloromethane at -5 to 0°C which yielded oxo-acid (4) in 90% yield. The selectivity of boron tribromide can be attributed to complexation with the carbonyl which makes the methyl group more vulnerable to attack by bromide. Reduction of the carbonyl group in this acid using triethylsilane (TES) in trifluoroacetic acid (TFA) at room temperature led to acid (5) in high yield [2,3].

Introduction of a second butanoic acid substituent to phenol (5) was required in this step. We took advantage of a modified Reimer-Tiemann formylation [4], using methanol as co-solvent. The condensation of puruvic acid in basic media is carried out for extension of the side chain. This condensation process is covered extensively in the literature [5-11]. We found crucial factors were pH, which must be high (about 14), and the ratio of methanol to aqueous potassium hydroxide (20%), which should be about 10:1. The diacid (8) was obtained in 85% yield. Since the hydroxyl group interferes with such a condensation reaction, it was protected by methylation using known conditions (Me_2SO_4/K_2CO_3/acetone/reflux). (Scheme 1).

The reduction of α, β-unsaturated keto-acid side chain in product (8) was carried out by two steps hydrogenation process. Treatment of this compound with TES/TFA for a short time led mainly to keto-diacid (10). Then the carbonyl

Keywords: Biscyclisation synthesis; Condensation; 1,8-Dihydroxy-9, 10-anthraquinone; Pyruvic acid



Scheme I

i; Succinic Anhydride, $AlCl_3$, $PhNO_2$, ii; BBr_3, CH_2Cl_2, O°C, iii; TES/TFA, iv; $HCCl_3$, OH^-, H^+, v; Me_2SO_4, K_2CO_3, Acetone, ReFluX, vi; $MeCOCO_2H$, aq. KOH/MeOH, vii; TES/TFA, ice-bath, viii; NH_2NH_2, Diethyleneglycol, ix; PPA, x; aq. 48% HBr, xi; KOH/H_2O, O_2

group was reduced by the Wolf-Kishner procedure [12].

Using the "diacylation" process with a more activated benzenoid moiety, the one pot "bicyclisation" of diacid took place with polyphosphoric acid (PPA) alone and TFA/TFAA in dichloramethane. Under both conditions, bicyclisation took place, but the reaction, in the presence of PPA, was much clearer. Using either condition, it was possible to isolate the monocyclised product (13a) after a short time. Over a longer period the major product from both conditions was (12). The refluxing of diketone (12) with aqueous 48% HBr afforded diketone (14).

The diacid (16) was obtained by demethylation of its dimethyl ether (11) using aqueous 48% HBr.[1] H NMR spectroscopic analysis of the product indicated that not only had demethylation taken place, but intramolecular acylation had also occurred leading to the tetralone (17) as the major product under these conditions. This tetralone could be converted to the diketone (14) by treatment wi PPA. The activating effects of the two hydroxyl grou facilitate such a cyclisation.

Aromatization of the diketone (14) was carried o under aerial oxidation in alkaline solution leading to targ 1,8-DHA (15).

Conclusion

"BisCyclisation" of the diacid (16), a precursor of 1, DHA (15) can be achieved without protection of t carbonyl group of the intermediate tetralone (13a) becau the deactivating effect of this carbonyl group is minimal the position meta to it, at which cyclisation occu Interestingly, PPA effects this cyclisation with concomita mono-demethylation affording (12).

Also notable is the fact that demethylation of (11) wi concentrated HBr is accompanied by monocylisation

tetralone (17), subsequent cyclisation of which with PPA affords the diketone (14) from which 1,8-DHA (15) can be obtained by aerial oxidation under alkaline conditions.

This work demonstrates the potential usefulness in organic synthesis of combining traditional and modern methods in novel approaches to anthraquinones.

Experimental Section

4- [3-Formyl - 2- hydroxy-5- methoxyphenyl] butanoic acid (6)

A solution of 4-(2-hydroxy-5-methoxyphenyl) butanoic acid (5) (9.4 g 0.045 mol) in a mixture of methanol (80 ml) and water (50 ml) was prepared in a 500 ml three-necked, round - bottomed flask equipped with condenser, pressure equalizing separatory funnel and mechanical stirrer. Sodium hydroxide pellets (54 g, 1.35 mol) were added to the flask slowly, with vigorous stirring. The temperature was then adjusted to about 30°C using a water bath. Chloroform (75 ml) was then added dropwise over two hours. The reaction was exothermic. The mixture was then refluxed with vigorous stirring for 90 min. It was then cooled and poured into a mixture of 20% hydrochloric acid (500 ml) and ice (200 g) with cooling using an ice-bath. The product was extracted with ether, (5×20 ml), and the combined ether extracts were washed with water (5×50 ml), dried with sodium sulphate and the solvent evaporated. A deep red oily material (11. 4 g) was obtained. It was purified by column chromatography on C60 - 40/60 silica gel eluting with 10:7 CH_2Cl_2-MeOH. The product was collected in the third fraction as a pale yellow oil. Recrystallization in CH_2Cl_2 gave yellow small needles (3. 14 g, 30%), m. p. 70-72°C. (Found: C, 59.7%; H, 6.1 $C_{12}H_{14}O_5$ requires; C, 60.5%, H, 5.88%). νmax (film) 3600-2600 (m and broad), 2938 (m), 1707 (s), 1655 (s), 1602 (m), 1463 (s), 1439 (s), 1272 (s), 1209 (s), 1158 (m), 1062 (s) cm^{-1}; ^1H NMR, δ (300 MHz, $CDCl_3$) 2.0 (quintet, **J** = 7.5, 2H), 2.4 (t, **J** = 7.5, 2H), 2.72 (t, **J**=7.5, 2H), 3.81 (s, OMe), 6.85 (d, **J** = 3, H-6), 7.05 (d, J_3, H-4), 9.88 (s, CHO), 10.98 (s, OH); **m/z** (EI) 239 [7.5, $(M + 1)^{\cdot+}$] 238 [56.5, $M^{\cdot+}$], 221 [0.8, $(M\text{-}OH)^+$], 220 [7.2, $(M\text{-}H_2O)^{\cdot+}$], 179, 178 {3.1, 10.3, [MeO(OH)CHO) $C_6H_2CH_2]^+$}, 165 {100.0, [MeO(OH)(CHO) $C_6H_2CH_2]^+$}; **m/z** (Cl/NH_3) 257 {3.2, $[(M+1+NH_4)]^+$}, 256 [25.5, $(M+NH_4)^+$], 240 [14.3, $(M+1+H)^+$], 239 [100.0, $(M+H)^+$], 238 (20.8, M^+).

Methyl 4- (3- formyl - 2,5-dimethoxyphenyl)-butanoate (7)

A solution of 4-(3-formyl-2-hydroxy-5-methoxyphenyl)-butanoic acid (6) (2.3 g, 0.0097 mol) in acetone (150 ml; dried with 4A molecular sieves) was prepared in a 250 ml three-necked, round-bottomed flask equipped with condenser and pressure equalizing separatory funnel. Solid anhydrous potassium carbonate (13.4 g, 0.097 mol) was added with vigorous stirring by a magnetic stirrer. Dimethyl sulphate (18.3 g, 13.7 ml, 0.144 mol) was added dropwise over 7 min, and the suspension was then stirred and heated (water bath) at reflux temperature for 75 min. A cloudy colourless suspension was obtained. After cooling, 20% hydrochloric acid (100 ml) was added slowly. The mixture was then extracted with ether (1 ×150 ml, 3 × 15 ml), and the combined ether extracts were washed with water (4×15 ml) and then evaporated at a temperature below 55°C. A red oily material was obtained. This was extracted with hexane (4×15 ml), and the solvent was then evaporated to give a colourless oil (2.5 g, 97%). It had ν max (film) 2951 (m), 1737 (s), 1687 (s), 1603 (m), 1476 (s), 1390 (m), 1216 (m), 1136 (s), 1066 (m) cm^{-1}; δ (200 MHz, $CDCl_3$) 1.99 (quintet, **J**=7.5, 2H), 2.40 (t, **J**= 7.5, 2H), 2.71 (t, **J**=7.5, 2H), 3.68 (s, OMe), 3.8 (s, OMe), 3.88 (s, OMe), 7.01 (d, **J**=2.4, 6-H), 7.19 (d, **J**=2.4, 4-H), 10.32 (s, CHO); **m/z** (EI) 268 [1.7, $(M+2)^{\cdot+}$], 267 [15.4, $(M+1)^{\cdot+}$], 266 [100.0, $M^{\cdot+}$], 252 [0.7, $(M\text{-}Me)^+$], 221 [3.7, $(M\text{-}CO_2H)^+$], 193 [23.0, $(MeO)_2C_6H_2(CHO)(CH_2)_2^+$], 179 [28.1, $(MeO)_2C_6H_2(CHO)CH_2^+$]; **m/z** (Cl/NH_3) 285 (14.9), 284 [100.0, $(M + NH_4)^+$], 268 {15.0, $[(M+1)+H]^+$}, 267 [88.9, $(M+H)^+$], 266 [19.7, M^+], 253 {9.1, $[(M\text{-}Me)+H]^+$}, 252 [13.8, $(M\text{-}Me)^+$]. (Found **m/z**: $M^{\cdot+}$, 266.144. $C_{14}H_{18}O_5$ requires 266.1154).

(E) - 4 [3 - (Carboxypropyl) - 2,5 - dimethoxyphenyl] - 2- oxobutenoic acid (8)

A solution of methyl 4-(3-formyl-2,5-dimethoxyphenyl) butanoate (7) (0.618 g, 0.00232 mol), pyruvic acid (1.023 g, 0.81 ml, 0.0116 mol) and 20% potassium hydroxide (0.023 mol, about 7 ml) was prepared in a 100 ml round-bottomed flask. The pH of the solution was about 13-14. Methanol (50 ml) was added and the mixture was stirred magnetically at rt, for 4h. 20% HCl (50 ml) was added and the resulting light green solution was extracted with ether (1 × 50 ml, 4 × 15 ml), the combined ether extracts being washed with water (3 × 15 ml), and then dried with sodium sulphate. The ether was evaporated giving a colourless oil (0.55 g, 73%). It had ν max (film) 3600-2400 (m and broad), 3050 (m), 2940 (m), 1709 (s and broad), 1599 (s), 1474 (s), 1215 (s), 1093 (m), 1064 (m) cm^{-1}; ^1H NMR δ (200 MHz, $CDCl_3$) 2.0 (quintet, **J**=7.9, 2H), 2.45 (t, **J** = 7.9, CH_2), 271 (t, **J**=7.9, CH_2), 3.73 (s, OMe), 3.82 (s, OMe), 6.9 (d, **J**=2.4, 4-H), 7.05 (d, **J**= 2.4, 6-H), 7.55 (d, **J**=15.1, 3'-H), 8.35 (d, **J**=15.1, 4'-H); **m/z**, -veFAB (M-nitrobenzylalcohol) 322 (**M** -, 50), 321 (M-1)-, 100]. (Found **m/z**: $M^{\cdot+}$, 321.0980. $C_{16}H_{18}O_7$ requires 321.0974).

4 - [3 - (3- Carboxypropyl) -2, 5- dimethoxyphenyl] - 2 - oxobutenoic acid (10)

A solution of (**E**)-4-[3- (3-carboxypropyl) -2,5 -

dimethoxy-phenyl] -2- oxobutanoic acid (8) (47 mg, 0.146 mmol) in trifluoroacetic acid (5 ml) was prepared in a dry 10 ml round-bottomed flask at 0-3°C (ice-bath). A red orange solution was obtained. Triethylsilane (0.128 ml, 0.0933 g, 0.8 mmol) was added dropwise with vigorous magnetic stirring. The reaction mixture became colourless after 1 min. Stirring was continued for two more minutes and then water (5 ml) was added to stop the reaction. The mixture was diluted with 50 ml water and extracted with ether (4 × 10 ml). The combined ether extracts were washed with water several times until the washings were neutral and then dried with sodium sulphate. The ether was evaporated to give an almost colourless oil (0.042 g, 89%). HPLC analysis indicated the presence of less than 10% of impurities but purification by other procedures was unsuccessful. It had ν max (film) 3600-2400 (s and broad), 2944 (s), 1726 (s and broad), 1604 (m), 1478 (s), 1217 (s), 1064 (s), 1008 (m) cm^{-1}; ^1H NMR δ (300 MHz, $CDCl_3$) 1.9 (quintet, **J**=7.5, 3'-CH_2 collapsed to triplet by irradiation at 2.6 and 2.35, 2.35 (t, **J**= 7.5, 4'-CH_2 collapsed to singlet by irradiation at 1.9), 2.65 (t, **J** = 7.5, 2'-CH_2, collapsed to singlet by irradiation at 1.9), 2.96 (t, **J** = 7.5, 4-CH_2 changed to singlet by irradiation at 3.18), 3.18 (t, **J**= 7.5, 3-CH_2, collapsed to singlet by irradiation at 2.96), 3.58 (s, OMe), 3.72 (s, OMe), 6.55 (d, **J** =3, ArH_2); **m/z** (EI) 326 (22.6), 325 (24.9), 324 (95.4, $M^{+\cdot}$), 279 [15.4, $(MeO)_2C_6H_2(CH_2)_3CO_2H(CH_2)_2CO^+$], 251 [3.1, $(MeO)_2C_6H_2(CH_2)_3CO_2H(CH_2)_2^+$], 237 [6.6; $(MeO)_2C_6H_2(CH_2)CO_2H(CH_2)^+$], 179 [8.0, $(MEO)_2C_6H_2(CH_2)_3^+$]. (Found **m/z**: $M^{+\cdot}$, 324.1216. $C_{16}H_{20}O_7$ requires 324.1209).

2,5 - Dimethoxy-1,3 - benzenebisbutanoic acid (11)

A mixture of 4-[3-(3-carboxypropyl)-2,5-dimethoxyphenyl]- 2-oxobutanoic acid (10) (2 g, 0.0062 mol, diethylene glycol (35 ml), 99% hydrazine hydrate (4.5 ml, 0.093 mol), water (2 ml) and potassium hydroxide (5 g, 0.102 mol) was prepared in a 100 ml two-necked round-bottomed flask equipped with condenser and magnetic stirrer. The mixture was heated (water-bath) until all the potassium hydroxide had dissolved, and then heated with a free flame at reflux temperature for 1 h. A pale yellow solution was obtained, which was cooled and poured into 20% hydrochloric acid (100 ml) and then extracted with ether (1 × 30 ml, 3 × 7 ml). The combined ether extracts were extracted with saturated sodium hydrogen carbonate (5 × 10 ml). The sodium hydrogen carbonate solution was washed with ether (2 × 7 ml), acidified with concentrated hydrochloric acid and then extracted with ether (4 × 10 ml). The combined ether extracts were washed with water (3 × 7 ml), dried with sodium sulphate and evaporated (rotavap, water-pump and oil-pump). A colourless oily material (1.69 g, 89%) was obtained. Attempts to purify it were unsuccessful. It had ν max (film) 3650-2400 (s and broad), 2941 (s), 170 (s) 1603 (m), 1477 (m), 1216 (s), 1066 (m) cm^{-1}; ^1HNMF δ (200 MHz, $CDCl_3$), 1.95 (quintet, **J**= 7.5, 2 × CH_2), 2.4 (t, **J** = 7.5, 2 × CH_2), 2.68 (t, **J**= 7.5, 2 × CH_2), (3.68 (s OMe), 3.78 (s, OMe), 6.6 (s, ArH_2); **m/z** (EI) 311 (15.6) 310 (100.0, $M^{+\cdot}$). (Found **m/z**: $M^{+\cdot}$, 310.1421. $C_{16}H_{22}O$ requires 310.1416).

1,2,3,4,5,6,7,8 - Octahydro-9 - hydroxy-10 - methox anthracene - 1,8 - dione (12)

A solution of 2,5 - dimethoxy- 1,3 - benzenebisbutanoi acid (11) (0.5 g, 1.6 mmol) in an excess of polyphosphori acid (about 25 ml) was prepared in a dry 50 ml round bottomed flask and stirred with a glass rod at 125-130°((oil - bath). Stirring was continued for 20 min, giving a re solution. The mixture was poured into a mixture of wate (80 ml) and ice (about 80 g), and then extracted with eth (4 × 10 ml). The combined ether extracts were washed wi saturated sodium hydrogen carbonate (5 × 7 ml) and the with water until the washings were no longer basic. Th ether layer was then dried with sodium sulphate ar evaporated.

A yellow orange solid (0.198 g, 46%) was obtaine Crystallization from carbon tetrachloride gave yellowi needles, m.p. 129-130°C. It had ν max (film) 2926 (s 2854 (s), 1687 (s), 1630, 1592 (s), 1460 (s), 1374 (s), 13 (m), 1191 (s), 1018 (s) cm^{-1}; ^1HNMR δ (200 MHz, CDC 2.03 [quintet, **J** = 6.5, 3-CH_2 + 6-CH_2], 2.65 [t, **J** = 6.5, CH_2 + 5-CH_2], 2.98 [t, **J** = 6.5, 2-CH_2 + 7- CH_2], 3.68 OMe]; **m/z** (EI) 261 (15.9), 260 (100.0, $M^{+\cdot}$), 245 [71. (M-Me)$^+$], 232 [24.5, (MeO)(OH) C_6 (CH_2)(CO) $(CH_2)_3$ 218 [8.0, (MeO) (OH)C_6 $(CH_2)_3$(CO) $(CH_2)_2^+$], 20.4 [10. (MeO) (OH) C_6 (CO) CH_2^+]; **m/z** (Cl/NH_3) 262 (16.9), 2 [100.0, (**M**+ H)$^+$], 260 [14.4, M^+].

6 - (3 - Carboxypropyl) - 5, 8 - dimethoxy - 1 - tetralo (13a)

This compound was obtained as a by-product duri the cyclisation of diacid (11) with PPA. It was obtained a light pink oily material (0.1 g, 22%) by acidification the sodium hydrogen carbonate solution with concentrat hydrochloric acid and extraction with ether (3 × 7 m decolourization with activated charcoal, washing w water (3 × 10 ml), drying over sodium sulphate a evaporation. It had νmax (film) 3600 - 2400 (m and broa 2930 (s), 2850 (s), 1701 (s), 1686 (s), 1610 (m), 1590 (1462 (s), 1373 (m), 1353 (s), 1210 (s), 1020 (s) cm^{-1}; NMR δ (200 MHz, $CDCl_3$), 2.05 (m, 3-CH_2 + 3'-CH_2), 2. (t, J = 7.5, 4'- CH_2), 2.61 (t, **J** = 6.5, 4-CH_2), 2.70 (t, **J** = 7 2'-CH_2), 2.98 (t, **J** = 6.5, 2-CH_2), 3. 70 (s, OMe), 3.90 OMe), 6.68 (s, 7-H); **m/z** (EI) 293 (14.9), 292 (100.0, M 277 [18.0, (M-Me)+], 260 [35.9; (compound 343).$^+$], **n** (Cl/NH_3), 294 (16.2), 293 [100.0, (M+ H)$^+$], 292 [13

$M^{+\cdot}$], 261 [37.5, (compound 343 + H)$^+$]. (Found **m/z**: $M^{+\cdot}$, 292.1300. $C_{16}H_{20}O_5$ requires 292.1311).

1, 2, 3, 4, 5, 6, 7, 8 -Octahydro - 9, 10 - dihydroxy-anthracene - 1, 8 - dione (14)

A solution of 1, 2, 3, 4, 5, 6, 7, 8 -octahydro - 9 - hydroxy-10 - methoxyanthracene - 1, 8-dione (12) (0.03 g, 0.115 mmol) in an excess of 48% hydrobromic acid (7 ml) was refluxed (oil bath) for 2 h. The solution was cooled and then poured into water (40 ml) and then extracted with ether (4 × 7 ml). The combined ether extracts were washed with water (3 × 10 ml), decolourized with activated charcoal and dried over sodium sulphate. The ether was evaporated giving a yellow oily material (0.016 g, 56%). Spectroscopic data indicated that demethylation had taken place accompanied by formation of a by-product which might be the tetralone (17). More work is required to find the best condition for this demethylation. Demethylation in the presence of boron tribromide was not as clean as that under the above conditions. The crude product had ν max (film) 3500 (m and broad), 2920 (s), 2851 (s), 1639 (s), 1464 (m), 1358 (m), 1182 (m) cm^{-1}; ^{1}H NMR δ (200 MHz, $CDCl_3$), 2.1 (quintet, **J**= 6.6, 3-CH_2 + 6 - CH_2), 2.68 (t, **J** = 6.6, 4 - CH_2 + 5-CH_2), 2.90 (t, **J** = 6.6, 2- CH_2 + 7-CH_2), 6.6 (s, 10-OH), 12 (s, 9-OH); **m/z** (EI) 246 [17.7, M^+], 218 (40.3, (**M** - 28).$^+$]; **m/z** (Cl/NH_3) 265 [100.0, (compound 350 + H)$^+$], 264 (compound 353)$^+$]. (Found **m/z**: $M^{+\cdot}$, 246.0899. $C_{14}H_{14}O_4$ requires 246.0892).

6- (3 - Carboxypropyl) - 5, 8 - dihydroxy - 1 - tetralone (17)

A solution of 2,5-dimethoxy -1,3 - benzenebisbutanoic acid (11) (0.06 g, 0.193 mmol) in 48% aqueous hydrobromic acid (15 ml) was heated at reflux temperature for one and a half hours. A deep red solution was obtained which was cooled, poured into cold water (50 ml) and then extracted with ether (4 × 7 ml). The combined ether extracts were washed with water several times until the washings were no longer acidic, dried with sodium sulphate and evaporated giving a light yellow green solid (0.039 g, 77%). It had ν max (film) 3600 - 2400 (m and broad), 2921 (s), 2851 (s), 1708 (s), 1638 (s and broad), 1465 (m), 1359 (m), 1184 m cm^{-1}; ^{1}H NMR δ (200 MHz, $CDCl_3$), 1.95 (quintet, **J**= 6.2, 3-CH_2), 2.1 (quintet, **J** = 6.3, 3' - CH_2), 2.4 (t, **J** =6.3, 4'- CH_2), 2.65 (m, 2' - CH_2 and 4-CH_2), 2.85 (t, **J** 6.2, 2'-CH_2), 6.6 (s, 7- H), 6.8 (s, 5-OH), 12.04 (s, 8-OH); **m/z** (EI) 265 (11.8), 264 (55.0, $M^{+\cdot}$), 247 [8.8, (M^+-OH)$^+$; $(CH_2)_3COC_6H(OH)_2(CH_2)_3CO^+$], 246 [45.4, (M-$H_2O$)$^{+\cdot}$], 219 [18.4 $(CH_2)_3COC_6H(OH)_2(CH_2)_3^+$], 205 [6.6, $(CH_2)_3COC_6H(OH)_2(CH_2)_2^+$, 181 [1.5, $(CH_2)_2COC_6H(OH)_2(CH_2^+$]; **m/z** (Cl/$NH_3$), 282 [6.1, (**M** + NH_4)$^+$], 266 (16.4), 265 [100.0, (**M** + H)$^+$], 264 [10.9, M^+]. (Found **m/z**: $M^{+\cdot}$, 264.0996. $C_{14}H_{16}O_5$ requires 264.0998).

1, 8 - Dihydroxy - 9, 10 - anthraquinone (15)

A solution of 1, 2, 3, 4, 5, 6, 7, 8- octahydro- 9, 10 - dihydroxy-anthracene-1,8-dione (14) (0.024 g, 0.098 mmol) in 10% potassium hydroxide (25 ml) was prepared in a 50 ml two-necked, round-bottomed flask equipped with a condenser. A deep red solution was obtained. The solution was heated at reflux while air was bubbled into the reaction mixture for two hours. The mixture was cooled and then poured into 20% hydrochloric acid (80 ml). The resulting light yellow solution was extracted with ether (4 × 7 mol). The combined ether extracts were washed with water (3 × 10 ml), dried with sodium sulphate and evaporated (rotavap, water-pump and oil-pump). A yellowish solid, mostly flat needles (0.015, 65%), m.p. 187-191°C (lit. 15, m.p. 193°C) was obtained. Spectroscopic data and TLC analysis were in accord with those of authentic 1, 8-dihydroxy-9, 10- anthraquinone.

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