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Peculiar Reaction Behaviour of Barbituric Acid Derivatives Towards Aromatic Amines.

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Abstract: 5-Benzoylethyl barbituric acid derivatives 2a-c were prepared as useful precursors for the synthesis of pyrimidine fused heterocycles. Their behaviour as 1,5-diketocompounds towards aniline derivatives afforded the pyrimidoquinoline derivatives 6a-e. On the other hand, fusion of $\underline{0}$ -substituted anilines with 1,3-dimethyl barbituric acid derivatives 8a,b gave the corresponding benzazoles 10a-e. Furthermore, the reaction of 1,3-dimethyl barbituric acid (1) with catechol/K₃[Fe(CN)₆] or β -ketoester (19)/SiCl₄ gave the benzofuro adduct 13a and the diphenylphenyl barbituric acid derivative 18, respectively. Copyright © 1996 Elsevier Science Ltd

Pyrimidine annelated heterocycles belong to an important class of biologically active compounds. These compounds such as xanthines and other purines contain a characteristic pyrimidine-2,4-dione ring system. The importance of purine bases and analogous compounds in pharmaceutical and biological fields is well known.^{1,2}

With the development of clinically useful pyrimidine-based anticancer (5-Fluorouracil ³) and antiviral drugs (AZT, BVDU⁴), there has been noticeable interest in the synthetic manipulations of uracils.^{5,6,7}

This persuaded us to investigate the C_5 and C_6 reactivities the oxo-analogues of uracil, e.g., barbituric acid and its derivatives, as centers of heteroannulation. The synthetic exploitation of these C_5 and C_6 reactivities is considered to be an important undeveloped field in view of the great variety of potential products.

Therefore, 5-benzoylethyl barbituric acid derivatives 2a-c were prepared as useful precursors for the synthesis of pyrimidine fused heterocycles. Thus the base catalysed addition of 1,3-dimethyl barbituric acid (1) to appropriate α,β -unsaturated ketones afforded the Michael adducts **2a-c**. Their structures were confirmed by elemental analysis, IR and ¹H-NMR spectra. The ¹H-NMR spectrum of **2a** not only confirms the structure, but also indicates its stereochemistry. The small coupling of 4Hz between H-5 and H-7 of compound **2a** suggested the eclipsed conformation of H-5 and H-7 in this compound.

In view of the significant therapeutic value of pyridines it was considered worthwhile to incorporate pyridine moieties into the C_5/C_6 position of the pyrimidine nucleus. To this end, it seemed desirable to investigate the reactivity of benzoylethylbarbituric acids **2a-c**, 1,5-diketo compounds, towards primary amines.

Unexpectedly, the reaction of diketones 2a-c by refluxing them in xylene with aniline derivatives in the presence of a catalytic amount of <u>p</u>-toluene sulphonic acid does not give either the hoped for





pyridopyrimidines **3a-c** or pyrimidoazocines **4a-c** through cyclization of the expected intermediate schiff bases **5a-c**. Instead, the pyrimidoquinoline derivatives **6a-c** were produced. Their structures were confirmed from the elemental analyses as well as the spectral data. The ¹H-NMR spectrum of **6a** does not show the expected AA' BB' system for a p-substituted benzene ring; however, it showed a 1,2,4-trisubstituted benzene moiety indicated by presence of three proton signals at δ 7.13 br<u>s</u> (attributed to H-10), 7.92 <u>d</u> (J=8.5 Hz) (attributed to H-7) and 7.62 <u>dd</u> (J=8.5, 2 Hz) (attributed to H-8). The molecular ion peak in the mass spectrum of **6a** was 331 (m/z). Also, the mass spectrum of **6b** showed a molecular ion peak at (m/z) (rel. int.) 368, 366 (33:100, i.e., 1:3).

The probable mechanism for production of the pyrimidoquinolines 6a-c is believed to be through the formation of the ylidene derivatives^{8,9} 8a-c via elimination of an acetophenone molecule from the diketones 2a-c with subsequent addition of the aniline derivatives to the formed ylidene followed by cyclization to dihydropyrimido[5,4-c]quinoline intermediate (A) which subsequently underwent oxidation in presence of the ylidene derivatives¹⁰ 8a-c as portrayed in scheme (2).

The structure proof of the pyrimidoquinoline derivatives 6a-c was further supported by an independent synthesis. This involved, fusion of benzal barbituric acid derivatives 8a-c with the corresponding aniline derivatives to yield 6a,d,e. This was confirmed in the case of 6a by undepressed mixed melting point of the

products obtained by the two methods and identify of their R_f value on TLC (silica gel, pet. ether 40-60/EtOAc, 1:1).



Scheme (2)

However, the pyridopyrimidine derivatives 7**a-c** were obtained by treatment of the diketones 2**a-c** with ammonium carbonate in acetic acid.

The structure of 7a-c were established on the basis of their analytical and spectral data. Also, the structure of 7a was further confirmed through its identical melting point with that reported in literature¹¹.

On the other hand, fusion of \underline{o} -phenylenediamine, \underline{o} -aminothiophenol, or \underline{o} -aminophenol with 1,3-dimethyl-5-arylidene barbituric acid derivatives 8a,b in attempts to obtain the corresponding azepines 11a-e were unsuccessful. Benzimidazole, benzthiazole and benoxazole derivatives 10a-e, in addition to the corresponding benzyl barbituric acid derivatives 9a,b were obtained instead of the anticipated azepines 11a-e.

This reaction was followed by TLC then the products column chromtographed on silica gel using a mixture of petroleum ether 40-60/ EtOAc as elution solvent. TLC showed three spots, the upper one corresponds to the benzalbarbituric acid derivatives 9a,b, the middle spot corresponds to the benzazoles 10a-e, whilst, the lower spot is for 1,3-dimethyl barbituric acid.

The structure of benzyl barbituric acid derivatives 9a,b were confirmed through their identical melting points with those reported in the literature^{10,12}. The IR and ¹H-NMR spectra of 1,3-dimethyl-5-(p-methoxybenzyl) barbituric acid 9b showed further evidence of its structure.

Also, the benzazole structures 10a-e were proved by the identical melting points with those reported in literature¹³⁻¹⁵, besides the IR, ¹H-NMR, MS spectra. Considering compound 10b, its IR showed C=C of the aromatic system, whilst its ¹H-NMR showed the signals of two aromatic rings, one a 1,4-disubstituted benzene indicated by the AA'BB' system [at $\delta 8.00 (J = 9Hz)$ and 7.01 (J=9 Hz)] and the second a 1,2-disubstituted benzene ring represented by the multiplet at $\delta 7.25$ of four aromatic protons. In addition the mass spectrum gave a molecular ion peak as a base peak 224 (m/z). The probable reaction mechanism for formation of benzazoles 10a-e and benzyl barbituric acid derivatives 9a,b is displayed in the following scheme (3).

It is thought that the arylidene 8 serves as oxidizing agent. This behavior was investigated previously by Tanaka and co-workers¹⁰ who have reported the oxidation of thiols to disulphides at the expense of 5-arylidene-1,3-dimethyl barbituric acid derivatives 8 with concomitant formation of their dihydro derivatives 9.

Again, the reaction of 1,3-dimethyl barbituric acid (1) with catechol in the presence of potassium ferricyanide does not give the anticipated benzofuro[2,3-d] pyrimidine 12^{16} , but gave the benzofuro adduct 13a ¹⁷. Its structure was ascertained by elemental analysis, IR, ¹H-NMR and Ms.

The ¹H-NMR spectrum of 13a showed, in addition to four N-CH₃ singlets (at δ 3.25, 3.42. 3.75 and at 3.35), a doublet and triplet (at δ 4.15, 4.00) due to H-5 and H-6, respectively. Also there is a doublet (at δ 6.9) due to H-7 and one singlet (at δ 7.1) due to H-10. Furthermore, the small coupling of 2 Hz between H-5 and H-6 suggests the *cis*- configuration of these two protons. In addition, its mass spectrum gave a molecular ion peak 418 (m/z).

The formation of the adduct 13a was probably through the addition 17 of 1,3-dimethyl barbituric acid (1) to the diene of the furan ring in compound 12.

Acetylation of 13a with acetic anhydride/pyridine mixture afforded the diacetate derivative 13b. Its IR spectrum showed the carbonyl absorption at 1770 cm⁻¹ (-OCOCH₃) besides, the absorption at 1685 cm⁻¹ (H₃C-N-CO).

Furthermore, refluxing equimolar ratios from 1,3-dimethyl barbituric acid (1) and salicylaldehyde or its bromo derivative in methanol in the presence of hydrochloric acid resulted in cyclo-condensation to give benzopyrano[2,3-d]pyrimidines 14a,b¹⁸. Follow up of this reaction by TLC (silica gel, EtOAc/Acetone, 9:1) displayed a complete disappearance of 1,3-dimethyl barbituric acid (1) and the presence of a considerable amount of the unreacted salicylaldehyde derivative used. This favours the formation of 14a,b from 1,3-dimethyl barbituric acid (1) and salicylaldehyde derivative in a 2:1 ratio. The structures of 14a,b was supported by analytical and spectral studies. Their IR spectra showed the presence of C=C, CO, CH₃ and CH functions. The ¹H-NMR spectrum of 14a showed, in addition to four N-CH₃ singlets (at δ 3.02, 3.23, 3.33 and 3.55), a two broad singlets at δ 5.10 and 4.10 due to H-5 and H-5⁺, respectively. Also, there is a multiplet at δ 7.00-7.40 of four aromatic protons (H-6, H-7, H-8, H-9).

Treatment of 14a,b with POCl₃ produced the corresponding chloroderivatives 15a,b. The main characteristic features of their IR spectra was the absence of the OH group. Further confirmation of structures 15a,b was illustrated by the mass fragmentation pattern of 15a which is consistent with the proposed structure.



Scheme (3)



An attempt to obtain the anilino derivative 16a through fusion of chloroderivative 15a with p-toluidine failed. Instead, the 5-anilinobenzopyrano [2,3-d] pyrimidine derivative 17 was produced.

The 5-anilinobenzopyrano[2,3-d]pyrimidine structure for derivative 17 was adopted in view of elemental analysis as well as its IR, ¹H-NMR and Ms spectra. Its ¹H-NMR spectrum showed only two N-CH3 singlets (at $\delta_{3.50}$ and 3.80). In addition, the mass spectrum of 17 revealed the presence of molecular ion peak at 349, m/z. The loss of 6-(p-toludino)-1,3- dimethyl uracil was in line with that reported by Wawzonek ¹⁹.

The plausible pathway for the formation of 17 is depicted in scheme (4).

Attempts to obtain the α,β -unsaturated ketone 20 through condensation of 1,3-dimethyl barbituric acid (1) with the cyclic β -ketoester 19²⁰ in presence of either methanol/hydrochloric acid or polyphosphoric acid were unsuccessful. However, when this reaction was conducted in absolute ethanol and in presence of silicon tetrachloride²¹ compound 18 was obtained (Scheme 5).

Structure of 18 was supported by elemental analysis, IR, ¹H-NMR and mass spectra. Its IR spectrum showed absorptions at 2950 (CH₃, CH_{str}.) 1680, 1741 (CO), 1600 (C=C). The ¹H-NMR of 18 showed the presence of 6H (two N-CH₃) and a singlet (3H of 1,3,5-trisubstituted benzene moiety) at δ 7.60, the latter in a ratio of 3 : 10 (with other aromatic protons). Additionally, the Ms fragmentation pattern of compound 18 was in good agreement with the proposed structure. It showed fragments at 229 (m/z) (1,3-diphenylbenzene) and at 155 (m/z) (1,3-dimethyl barbituric acid).

The formation of 5-(3',5'-diphenylphenyl)barbituric acid derivative 18 may be assumed to proceed via formation of the intermediate disilyl derivative of β -keto ester 19 followed by decarboxylation to give the siloxy derivative, which is attacked by 1,3-dimethyl barbituryl anion with subsequent dehydrogenation of the product formed to obtain compound 18 (Scheme 5).



Scheme (4)



Scheme (5)

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EXPERIMENTAL

Melting points °C (uncorrected) were taken on a Fisher electric melting point apparatus. Proton NMR spectra were recorded in CDCl3 unless otherwise specified. ¹H-NMR spectra were obtained on Varian-Gemini 200 MHz, 270 MHz and Bucker 250 MHz machines. Chemical shifts are reported in ppm (δ) downfield from internal tetramethyl silane. IR spectra were recorded using KBr wafer technique. Mass spectra were recorded on GC-Ms GP-1000 EX. Schiwadzu (Japan) machine.

1,3-Dimethyl-5-(1'-aryl-2'benzoyl ethane) barbituric acids 2a-c:

A solution of 1 (5g, 0.03mol), α , β -unsaturated ketones (0.03mol) and triethyl amine (0.3ml) in methanol (50ml) was refluxed at 80-5°C for 4 hrs. On cooling the reaction mixture, the product was precipitated, filtered off and crystallised from ethanol to give **2a**,**b**. However, compound **2c** was separated as an oily substance which was purified with column chromatography on silica gel using pet. ether 40-60/EtOAc as eluent. The product solidified after evaporation of most of the eluent, then was left for three days at room temperature.

2a : (76%); mp 150°C (lit.²² mp 148°C); ¹H-NMR δ 3.05 (s,3H), 3.12 (s,3H), 3.53 (dd, J=5.5, 18.5Hz, 1H), 3.99 (d, J=4Hz, 1H), 4.09 (dd, J=9, 18.5 Hz, 1H), 4.36 (ddd, J=4, 5.5, 9Hz, 1H) and 7.06-8.10 (m,10H). **2b** : (67%); mp. 139-140°C; IR 1600(C=C), 1650(CO), 1700(CO) cm⁻¹; ¹H-NMR δ 3.10 (s,3H), 3.20 (s,3H), 3.50 (dd, 1H), 4.00 (d, 1H), 4.10 (dd, 1H), 4.40 (ddd, 1H) and 7.10-8.00 (m,9H). Anal. Calcd. for C₂₁H₁₉ClN₂O₄ : C, 63.24; H, 4.80. Found C, 62.94; H, 5.00. **2C** : (70%); mp 140-1°C, IR 1590(C=C), 1650(CO), 170(CO), 170(CO) cm⁻¹; ¹H-NMR δ 3.10 (s,3H), 3.15 (s,3H), 3.50 (dd, 1H), 3.75 (s,3H), 4.0 (d, 1H), 4.05 (dd, 1H), 4.35(ddd, 1H), 6.8-8.05 (m,9H). Anal. Calcd. for C₂₂H₂₂N₂O₅ C, 66.99; H, 5.62. Found C, 66.59; H, 5.47.

Pyrimido[5,4-c]quinolines 6a-e: Method (A):

A solution of the diketone 2a-c (0.01 mol), aryl amine (0.012 mol) and p-toluene sulphonic acid (20 mg) in xylene (30 ml) was refluxed with a Dean-Stark trap for 8hrs. after which the xylene was evaporated at reduced pressure, the residue was treated with ethanol, the products were separated by filtration, and purified by recrystallization from glacial acetic acid.

Method (B):

A mixture of 1,3-dimethyl barbituric acid arylidene derivative **8a-c** (0.01 mol) and arylamine (0.01 mol) was fused in an oil bath at 150°C for one hour. The reaction mixture was cooled and treated with ethanol. The precipitated products were filtered off and purified by recrystallization from glacial acetic acid as yellow crystals.

6a : (60%), mp > 300°C; ¹H-NMR δ 2.40 (s,3H), 3.35 (s,3H), 3.87 (s,3H) 7.10-7.40 (m,5H), 7.55 (brs, 1H), 7.60 (brd, 1H) and 7.92 (d,1H); Ms, m/z (relative intensity) 331(100, M⁺). Anal. Calcd. for C₂₀H₁₇N₃O₂ C, 72.49; H, 5.17; N, 12.68. Found C, 72.09; H, 4.94; N, 12.72. **6b** : (55%); mp > 300°C; ¹H-NMR δ 2.40 (s,3H), 3.38 (s,3H), 3.85 (s,3H), 7.10-8.00 (m,7H); Ms, m/z (relative intensity) 366,368(100 and 33, M⁺, M⁺+2). Anal. Calcd. for C₂₀H₁₆ClN₃O₂ : C, 65.66; H, 4.40. Found C, 66.00; H, 4.10. **6c** : (50%); mp 250°C; Anal. Calcd. for C₂₀H₁₆N₄O₄ : C, 63.82; H, 4.29. Found C, 69.50; H, 5.20. **6d** : (60%); mp > 300°C; ¹H-NMR δ 3.40 (s,3H), 3.70 (s,3H), 3.87 (s,3H), 6.62-7.90 (m,8H). Anal. Calcd. for C₂₀H₁₇N₃O₃ : C, 69.15; H, 4.93. Found C, 69.30; H, 4.90.

Pyrido[2,3-d]pyrimidines 7a-c:

To a solution of 1,5-dicarbonyl compound 2a-c (0.005 mol) in acetic acid (25 ml) was added ammonium carbonate (2.5g). The mixture was refluxed for 8hrs. The solvent was evaporated and the residue was treated with dilute ammonium hydroxide (40 ml). The formed precipitate was removed by filtration, washed to neutrality with water and recrystallised from ethanol to give 7a-c.

7a : (68%); mp 248°C (lit.¹¹ mp 250-2°C). 7b : (60%); mp 198-200°C; ¹H-NMR δ 2.95 (§,3H), 3.40 (§,3H), 7.00-8.23 (m,10H); Ms, m/z (relative intensity) 377,379(15.3, 8.8, M⁺, M⁺+2), 105(100). Anal. Calcd. for C₂₁H₁₆ClN₃O₂: C, 66.76; H, 4.27. Found C, 67.05; H, 4.32. 7c:(58%); mp 220-1°C; ¹H-NMR δ 2.85 (§,3H), 3.45 (§,3H), 3.80 (§,3H), 6.86-8.10 (m,10H). Ms, m/z (relative intensity) 373(18, M⁺), 105(100). Anal. Calcd. for C₂₂H₁₉N₃O₃: C, 70.76; H, 5.13. Found C, 71.08; H, 4.80.

2-Aryl benzazoles 10a-e and 5-benzyl barbituric acids 9a,b:

A mixture of the 1,3-dimethyl-5-arylidene barbituric acid derivatives 8a,b (0.01 mol) and aniline derivatives (<u>o</u>-phenylenediamine, <u>o</u>-aminothiophenol or <u>o</u>-aminophenol) was fused in an oil bath at 140°C for one hour. The reaction was followed by TLC which showed three products. They were separated by column chromatography on silica gel using a mixture of pet. ether 40-60/EtOAc as eluent. The first fractions afforded compounds 9 and the second fractions correspond to compounds 10, while the last fraction was 1,3-dimethyl barbituric acid.

9a : (40%); mp 115°C (lit.¹² mp 116-17°C); IR 1610(C=C), 1700 (CO), 1749(CO) cm⁻¹. 9b : (37%); mp 90°C (lit. mp 90-2°C); ¹H-NMR δ 3.14 (§,6H), 3.41 (d, J=4.5Hz, 2H), 3.74 (t, J=4.5 Hz, 1H), 3.76 (§,3H), 6.75 (AA'BB' system, J=8.5Hz, 2H) and 6.95 (AA'BB' system, J=8.5 Hz, 2H). 10a : (36%); mp 289°C (lit.¹³ mp 285°C); IR 1600 (C=C), 3200(NH) cm⁻¹ 10b : (35%); mp 230°C (lit.¹⁴ mp 227°C); IR 1600 (C=C), 3200(NH) cm⁻¹; ¹H-NMR δ 3.82 (§,3H), 7.01 (AA'BB' system, J=9Hz, 2H), 7.25 (m,4H), 7.62 (brs, 1H) and 8.00 (AA'BB' system, J=9Hz, 2H). 10c : (40%); mp 112°C (lit.¹⁵ mp 114°C); IR 1600 (C=C) cm⁻¹. 10d: (38%); mp 129-131°C (lit.¹⁵ mp 134°C); IR 1600 (C=C) cm⁻¹; ¹H-NMR δ 3.88 (§,3H), 7.00 (AA'BB' system, J=9Hz, 2H), 7.20-7.90 (m,4H) and 8.05 (AA'BB' system, J=9Hz, 2H). 10e : (37%); mp 102 °C (lit.¹⁵ mp 102-4°C); IR 1600 (C=C) cm⁻¹.

Benzofuro[2,3-d]pyrimidine adduct 13a:

Catechol (0.01 mol) was added to a suspension of 1 (1.56g, 0.03 mol) and sodium acetate (4.08g, 0.03 mol) in aqueous acetone (1:1, 50 ml). To this solution, an aqueous solution of potassium ferricyanide (9.87g, 0.03 mol) containing sodium acetate (4.08g, 0.03 mol) was added dropwise with constant stirring. The precipitate that formed was filtered off, washed several times with water and purified by dissolving it in a sodium hydroxide solution then precipitating by hydrochloric acid to give 13a, (86%); mp > 300°C; IR 1600 (C=C), 1650(CO), 3300(OH) cm⁻¹; ¹H-NMR (DMSO) δ 3.20 (g, 3H), 3.35 (3H under peak of solvent), 3.42 (g,3H), 3.75 (g,3H), 4.10 (t, J=2Hz, 1H, H-6), 4.15 (d, J=2Hz, 1H, H-5), 6.90 (d, J=2Hz, 1H, H-7)7.10 (g,1H), 8.50 (brg, 1H, OH) and 9.50 (brg, 1H, OH.); Ms, m/z (relative intensity) 418(1.9, M⁺), 416(27.5, M⁺-2), 326(100). Anal. Calcd. for C₁₈H₁₈N₄O₈: C, 51.68; H, 4.34; N, 13.39. Found C, 51.32; H, 4.50; N, 13.24.

Acetylation of benzofuro[2,3-d] pyrimidine: formation of the diacetate 13b:

Compound 13a (0.005 mol) was dissolved in acetic anhydride/pyridine mixture (1:1, 25 ml). The reaction mixture was left overnight at room temperature and the crushed ice was added to it. The separated solid was filtered off, washed with water and recrystallised from ethanol to give 13b as colorless crystals, (82%); mp 290°C; IR 1600(C=C), 1650(CO), 1685(CO), 1770(OCOCH₃) cm⁻¹. Anal. Calcd. for $C_{22}H_{22}N_4O_{10}$: C, 52.59; H, 4.41. Found C, 52.24; H, 4.30.

1,3-Dimethyl-5-(1`,3`-dimethyl-2`,4`,6`-trioxo-5`pyrimidinyl)-benzopyrano[2,3-d]pyrimidine-2,4-diones 14a,b:

A solution of 1 (1.56g, 0.01 mol) and the appropriate salicylaldehyde derivative (0.005 mol) in methanol (30 ml) in the presence of hydrochloric acid (2-3 drops) was refluxed for 30-45 min. The reaction mixture was cooled. The solid that separated was filtered off, dried and recrystallised from chloroform/methanol mixture as colorless crystals. 14a : (83%); mp 238-9°C (lit.²³ mp 237°C); ¹H-NMR δ 3.02 (s,3H), 3.23 (s,3H), 3.55 (s,3H), 4.10 (brs, 1H), 5.10 (brs, 1H) and 7.00-7.40 (m,4H).14b :

(85%); mp 261-3°C; IR 1595(C=C), 1640(CO), 1700(CO) cm⁻¹. Anal. Calcd. for $C_{19}H_{17}BrN_4O_6$: C, 47.81; H, 3.59. Found C, 48.20; H, 3.79.

1,3-Dimethyl-5-(6'-chloro-1',3'-dimethyl-2',4'-dioxo-5'pyrimidinyl)-benzopyrano[2,3-d]pyrimidine-2,4diones 15a,b:

A mixture of benzopyrano[2,3-d]pyrimidine 14a,b (0.01 mol) and phosphorous oxychloride (40 ml) was heated for one hour. The excess of phosphorous oxychloride was distilled under reduced pressure and the residue was treated with crushed ice then extracted with chloroform (3x100 ml), dried over Na₂SO₄ and then evaporated under reduced pressure. The residue was recrystallised from ethanol to give 15a,b as buff crystals. 15a : (72%); mp 279-280°C; Ms, m/z (relative intensity) 416, 418 (69.6 and 27.0, M^+ , M^+ +2), 381(100). Anal. Calcd. for C₁₉H₁₇ClN₄O₅: C, 54.75; H, 4.11. Found C, 54.90; H, 4.20. 15b : (69%); mp 291°C. Anal. Calcd. for C₁₉H₁₆BrClN₄O₅: C, 46.03; H, 3.25. Found C, 45.70;H, 3.40.

1,3-Dimethyl-5-(p-toluidino) benzopyrano-[2,3-d]pyrimidine-2,4-dione 17:

A mixture of compound 15a (2.08g, 0.005 mol) and p-toluidine (0.502g, 0.005 mol) was fused at 200°C in a sand bath for 2hrs. The residue was triturated with ethanol (5ml). The solid that formed was filtered off and recrystallised from ethanol to afford 17 as a grey needles, (65%); mp 297-8°C; IR 1595(C=C), 1660(CO), 1705(CO), 3200-3400(NH);¹H-NMR δ 2.40 (§,1H), 2.54 (§,3H), 3.38 (§,1H), 3.53 (§,3H), 3.84 (§,3H) and 7.00-8.00 (m, 8H); Ms, m/z (relative intensity) 349 (11.3, M⁺), 331(100). Anal. Calcd. for C₂₀H₁₉N₃O₃: C, 68.75; H, 5.48. Found C, 68.70; H, 5.37.

1,3-Dimethyl-5-(3',5'-diphenylphenyl)barbituric acid 18:

A solution of 1,3-dimethyl barbituric acid (1) (0.78g, 0.005 mol), β -keto ester 19, absolute ethanol (25 ml) and silicon tetrachloride (2.4 ml) was stirred at room temperature for 72hrs. The reaction mixture was poured into ice cold water and the separated product was filtered off and dried. It was dissolved in chloroform (15 ml) and filtered. The chloroform filtrate was evaporated under reduced pressure whereby an oily residue was obtained. It was purified by column chromatography on silica gel using pet. ether 40-60/EtOAc, (3 : 1) to give compound 18, (68%); mp 138-9°C; IR 1606(C=C), 1610(CO), 1741(CO), ¹H-NMR δ 3.05 (§, 6H), 3.80 (§, 1H), 7.00-7.58 (m, 10H) and 7.60 (§, 3H); Ms, m/z (relative intensity) 385,386 (0.7 and 0.7, M⁺, M⁺+1), 248(100), 229(26.7). Anal. Calcd. for C₂₄H₂₀N₂O₃: C, 74.98; H, 5.24. Found C, 75.27; H, 5.45.

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