EEREACTION OF ISATOIC ANHYDRIDE WITH AMINOAZOBENZENE DERIVATIVES: SYNTHESIS OF SOME NEW ANTHRANILAMIDE AND QUINAZOLIN-2,4-DIONE DYES

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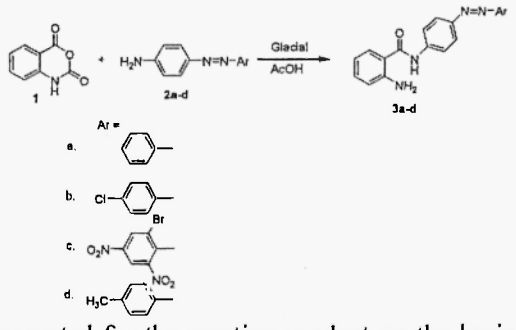
Abstract: A new synthesis of quinazolin-2,4-dione derivatives and substituted anthranilamide based on the reaction of isatoic anhydride (1) with different aminoazobenzene derivatives in presence of glacial acetic acid is described. Structures of the newly prepared compounds were established by chemical and spectral data.

Introduction

The last few decades have seen significant developments in the use of heterocyclic compounds in dyestuff and pigment chemistry. The design of newer heterocyclic systems has been a major target area and has focused on economically viable synthesis, absence of effluent problems and freedom from carcinogenic and mutagenic effects. The present article reviews the chromophoric potential of the anthranilamide derivatives and 2, 4-(*1H,3H*)-quinazolin-dione ring system, including dyes. The relationship between structure and color, dyeing and fastness properties has been studied[1-3]. It can be concluded that dyes derived from benzanilide have superior substantively and wash fastness on cotton compared to the other dyes Studied[4,5].

Results and Discussions

As a part of our program directed for development of new simple and efficient procedures for the synthesis of anthranilamides, utilizing a readily obtainable arylaminoazobenzene containing intermediates, we have previously reported several new approaches for the synthesis of different heterocycles[6] utilizing arylaminoazobenzene derivatives as starting materials. From the above facts in conjunction of our current interest in the synthesis of heterocyclic derivatives incorporating arylazo moiety, we disclose here a facile synthesis of the highly versatile, hitherto unreported anthranilamide derivatives. In view of the considerable biological importance of anthranilamide, the synthesized compounds containing this structure moiety could possess interesting, useful biological and pharmaceutical properties. It has been found that, treatment of isatoic anhydride (1) with p-aminoazobenzene derivatives (**2a-d**) in boiling glacial acetic acid afforded N-[4-arylazophenyl] anthranilamide (**3a-d**) as a single isolable product (TLC control) in high yield (72-90%).



Structure **3a** was suggested for the reaction product on the basis of elemental analysis and spectral evidence. The infrared spectrum of **3a** showed absorption bands at 3350-3540, 3286, 1640 and 1586 cm^{-1} attributable to NH_2, NH, amidic carbonyl and azo group respectively, while its ^1H NMR spectrum δ (ppm) revealed .multiplet bands at 7.1-8.2 ppm assigned for aromatic protons, and

two broad signals at 6.8, and 11.3 ppm corresponding to NH_2 and NH protons, respectively. The signals of NH_2 and NH protons were disappeared on the addition of few drops of deuterium oxide. Moreover, structure **3a** was also proved by mass spectroscopic measurement which gave molecular ion peak 316 (M^+, 75%) in accord with its molecular weight.

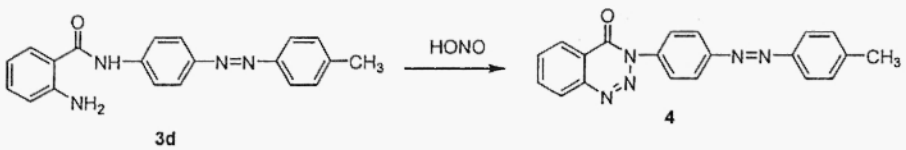
Similarly, when **1** was refluxed with p-chlorophenylazoaniline (**2b**) in glacial acetic acid afforded a product of molecular formula $C_{19}H_{15}N_4OCl$ which assigned as N-[4-chlorophenylazophenyl] anthranilamide (**3b**) in good yield (90%).

The structure of **3b** was inferred from its spectral and analytical data. Thus, the infrared spectrum of **3b** showed strong absorption bands at 3352-3461, 3283, 1636 and 1596 cm^{-1} assigned for NH_2, NH, amidic carbonyl and azo groups, respectively. The ^1H NMR δ (ppm) for compound **3b** exhibited multiplet signals at 7.4-8.2 ppm attributable to aromatic protons, the NH_2 and NH protons appeared at 6.8 and 11.2 ppm as a broad bands. The mass spectroscopic measurement of compound **3b** showed molecular ion peak at m/e 350 (M^+).

Moreover, N- [6-bromo-2,4-dinitro-phenylazophenyl] anthranilamide (**3c**) could be synthesized as the only isolable product by reaction of **1a** with 2,4- dinitro-6- bromophenylazoaniline (**2c**), as evidenced by TLC analysis.

The structure of **3c** was established by its IR spectrum which showed absorption bands at 3356-3448, 3328, 1648 and 1611 cm^{-1}corresponding to NH_2, NH, C=0 and N=N groups, respectively, while its ^1H NMR spectrum revealed the presence of two D_20 exchangeable protons at δ 6.6 and 11.7 ppm attributable to NH_2, NH, respectively, besides, multiplet band, at δ 7.3-8.2 ppm corresponding to aromatic protons, two singlet signals at δ 8.4, 8.6 ppm due to two protons in benzene ring that containing two nitro groups which make them appeared highly deshielded. The mass spectroscopic measurement of **3c** showed m/e 485 (M^+, 18%).

In a similar way, N-[4.-methylphenylazophenyl] anthranilamide (**3d**) was prepared by reaction of isatoic anhydride (**1**) with 4-(p.-tolyl)azoaniline (**2d**) in boiling glacial acetic acid. The reaction sequence is assumed to be proceeding by attacking of arylazoaniline the nucleus of isatoic anhydride via losing a molecule of carbon dioxide affording the final isolable product **3d**.. The structure of **3d** was confirmed by its spectral data and analytical analysis. Thus, the infrared spectrum showed stretching frequencies at 3356-3464, 294, 1636 and 1598 cm1 assigned for NH_2, NH, lactam C=O and N=N groups, respectively. Moreover, the mass spectroscopic measurements showed the molecular peak at 330 (M^+, 40%). In addition, structure **3d** was also proved chemically by its reaction with nitrous acid to give the corresponding 1,2,3-benzotriazin-4-one derivatives **4**, this reaction confirm the presence of o-aminobenzamide moiety.

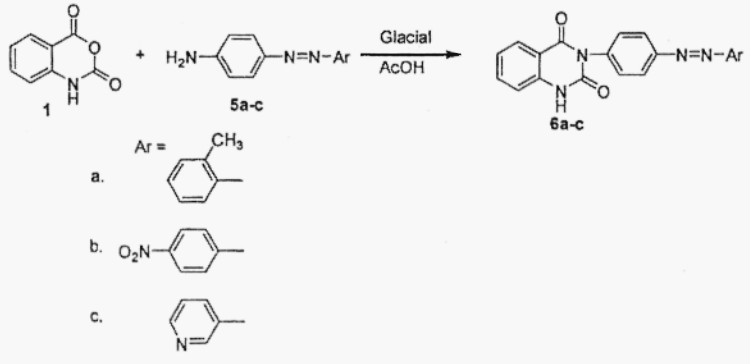


3d 4

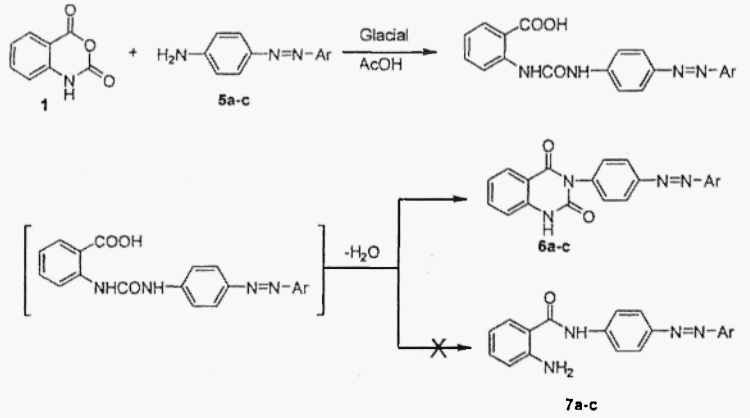
If diazotization of anthranilamide **3d** should proceed like that of anthranilic acid or its amide, then benzenediazonium carboxamide intermediate would be expected. Instead, diazotization of **3d** provides a stable, yellow solid which has properties not expected in a diazonium salts. In contrast to any diazonium salt, this solid is soluble in organic solvent and virtually insoluble in water. Elemental analysis and molecular weight determination showed that $C_{20}H_{15}N_5O$ is the empirical and molecular formula. Rather than the IR spectrum showed absorption at 1596 and 1530 cm^{-1}, which are characteristics of two N=N stretching frequencies of triazine and azo groups, respectively. In addition,

the infrared spectrum has a sharp, strong band at 1670 cm^{-1}, assigned to lactam carbonyl group. (Absorptions normally assigned to N_2 in the 2280 cm^{-1} region and the NH_2 in the 3400 cm^{-1} area are absent). As expected, only aromatic proton is observed in the ^1H NMR spectrum (except the methyl protons at δ 2.4 ppm). Thus, the structure of the stable yellow solid is assigned as 1,2,3-benzotriazine-4-one derivative **4**.

On the other hand, it has been found that, 4-(o-tolyl)azoanilne, 4-(p- nitrophenyl) azoaniline and 4-(m- pyridylazo) aniline (**5a-c**) behaved differently towards isatoic anhydride (**1**) when heated in glacial acetic acid affording 3-(4- arylazophenyl)quinazoline-2,4(1H,3H)-dione (**6a-c**)

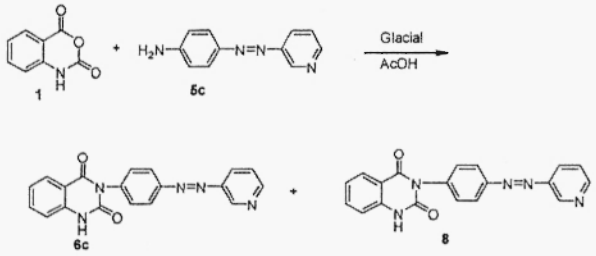


The formation of **6b**, **6a-c** is assumed to proceed via the formation of o-uridobenzoic acid intermediate which followed by loss of water molecule to give the final isolable product **6.**



The formation of 2-(1H)-quinazolin-2,4-dione derivative **6a** instead of the expected anthranilamide **7a** was established by its elemental and spectral data. The IR spectrum showed no absorption bands in the region 3340-3 550 cm^{-1} confirming the absence of amino group indicating that it was involved in the intramolecular cyclization process. In addition, stretching frequencies at 3226, 1648, 1608 and 1583 cm^{-1} corresponding to NH, lactam carbonyl and azo groups, respectively.

The ^1H NMR δ(ppm) spectrum of this product revealed singlet signal at δ 2.3 ppm attributable to methyl group, multiplet signal for aromatic protons at δ 7.2-8.3 ppm and at 10.8 ppm due to NH proton. Moreover, mass spectroscopic measurement gave molecular ion peak at 356 (M^{+1}, 25%) in accord with molecular weight of this compound. These data could be interpreted for structure **6a.** An analogues results were obtained when **1** was refluxed **5b** produced structure **6b** which was also established from its analytical and spectral data; Thus, the IR spectrum of compound **6b** showed stretching frequencies at 1587 cm^{-1} (N=N) and 1647 cm^{-1} due to lactam carbonyl group only, the other caxbonyl one not observed, indicating the existence of this compound in the enol form in the solid state. The ^1H NMR spectrum of this compound showed multiplet band at δ 7.3-8.6 ppm assigned for aromatic protons, in addition to one exchangeable proton at δ 11.9 ppm corresponding to NH. The mass spectroscopic of **6b** showed molecular ion peak at 387 (M^+, 18%). Unexpectedly, when **1** was allowed to react with 5c in glacia acetic acid, it afforded a mixtutre of two products which analyzed correctly for $C_{18}H_{15}N_5O$ (**8**) and $C_{19}H_{13}N_5O_2$ **6c.** The components of this mixture were separated by fractional crystallization and formulated as N-[4-(m-pyridylazo)phenyl]anthranilamide (**8**) and 3-[4-(m-pyridylazo)phenyl]-2(1H)-dihydroquinazloline-2,4-dione (**6c**).



Structure **6c** was suggested for this product based on its spectral data. The IR spectrum of **6c** showed no absorption bands of amino group which involved in the ring closure and showed bands at 1636, 1659 cm^{-1} assigned for two lactam CO groups, 1584 cm^{-1} due to azo group and bands at 3282, 3346 cm^{-1} corresponding to NH and enolic OH groups, respectively. This indicate that compound **6c** exist in a mixture of keto-enol form in solid state. The ^1H NMR of **6c** showed multiplet signals at δ 7.4-8.3 ppm attributable to eight aromatic protons, multiplet at δ 8.6-8.9 ppm due to four pyridine protons and broad signal D_20 exchangeable proton observed at δ 11.4 ppm corresponding to NH proton. The structure of **6c** was confirmed also by mass spectroscopic measurement, which showed the molecular ion peak at 343. (M^+, 8%).

Experimental

All melting points are uncorrected. FTIR spectra (KBr) were recorded on a Nicolet Magna Model 550 IR spectrophotometer. ^1H-NMR spectra were determined on a Brucker WP Spectrometer at 200 MHz with TMS as internal standard. Mass spectrometer recorded at 70 eV with a Varian MAT 311 instrument. Elemental analyses (C,H) agree satisfactorily with the calculated values.

General procedure for synthesis compound 3a-d and 6a-c: A mixture of isatoic anhydride (1.63g. 0.01 mol) and substituted arylazobenzene derivatives (2a-d) and (5a-c) (0.01 mol) in glacial acetic acid was refluxed for 2-4 h.(TLC controlled), the reaction mixture filtered while hot then cooled to room temperature, the separated crystals were collected by filtration and recrystallized from diluted acetic acid

N-14-phenylazophenyljanthranilatnide 3a: m.p. 165°C; yield (80%); IR (KBr) cm^{-1} 3350 3540, 3286,1640 and 1586 (attributable to NH_2, NH, ainidic carbonyl and azo groups, respectively); ^1H NMR (DMSO), δ (ppm); 7.1-8.2 (m, 13H, Ar-H), 6.8 (br, 2H, NH_2), 11.3 (s, 1H, NH); mass (m/z); (316, M^+); Anal. calcd. for $C_{19}H_{16}N_4O$. C, 75.15; H, 5.06. Found: C, 75.14; H, 5.05.
N-[4-chIorophenylazophenyl]anthranilamide (3b): m.p. 165°C; yield 90(90%); IR(KBr) cm-1 3352-3461, 3283, 1636 and 1596 (due to NH2NH, amidic carbonyl and azo groups, respectively); ^1H NMR (DMSO), (ppm); 7.4-8.2 (m, 12H, Ar-H), 6.8 (br, 2H, NH2) and 11.2 (s, 1H, NH); mass (m/z); (350,M+). Anal. calcd. for $C_{19}H_{15}N_4OCl$: C, 65; H, 4.3. Found: C, 64.8; H, 4.2.

N- 16-bromo-2,4-dinitro-phenylazophenyll anthranilamide (3c):m.p. 350°C; yield (88%) IR (KBr) cm^{-1}; 3356-3448, 3328, 1648 and 1611 (attributable to NH_2, NH, CO and N=N groups, respectively), ^1H NMR (DMSO), (ppm); 7.3-8.2 (m, 10H, Ar-H), 6.6 (br, 2H, NH2), 11.7 (s, 1H, NH); mass (m/z); (485, M^+). Anal. calcd. for $C_{19}H_{13}N_6O_5Br$: C, 47; H, 2.7. Found: C, 46.9; H, 2.7

N-14-methylphenylazophenylj anthranilamide (3d):m.p. 140°C; yield (79%); IR (KBr) cm^{-1}; 33 56-3464, 3294, 1636 and 1598 (assigned for NH_2, NH, lactam, C=O and N=N groups, respectively); mass (m/z); (330, M^+). Anal. calcd. For $C_{20}H_{18}N_4O$: C, 72.72; H, 5.45. Found: C, 72.71; H, 5.43.

3-(4-o-Tolylazophenyl)quinazoline-2,4(1H,3H)-dione (6a):m.p. 290°C; yield (74%); IR (KBr) cm1; 3226, 1648, 1608 and 1583 cm^{-1}. (due to NH, lactam C=0 and azo groups respectively); ^1H NMR (DMSO), 8 (ppm); 2.3 (s, 3H, CH_3), 7.2-8.3 (m, 12H, Ar-H), 10.8 (s, 1H, NH); mass (m/z); (356, M^+ +1).Anal. calcd. for $C_{21}H_{16}N_4O_2$: C, 70.8; H, 4.5. Found: C, 70.7; H, 4.4.

3-(4-p-Nitrophenyazophenyl) quinazoline-2,4(1U,311)-dione (6b):m.p. 285°C; yield (74%); IR (KBr) cm^{-1}; 1647, 1587 (attributable to lactam carbonyl and N=N, respectively); ^1H NMR (DMSO), 8 (ppm); 7.3-8.6 (m, 1 8H, Ar-H), 11.9 (s, 1H, NH); mass (m/z); (387, M^+). Anal. calcd. for $C_{20}H_{13}N_5O_4$: C, 62; H, 3.36. Found: C, 61.8; H, 3.34.

3-(4-(3-Pyridyl)azophenyl)quinazoline-2,4(1H,3H)-dione (6c): m.p. 2 10°C; yield (70%); IR (KBr) cm^{-1} 3346, 3282, 1659. 1636 and 1584 (due to OH, NH, lactam CO and N=N groups, respectively); ^1H NMR (DM50), δ (ppm); 7A-8.3 (m,8H, Ar-H), 8.6-8.9 (m, 4H, Py-H), 11.4 (s, lH, NH); mass (m/z); (343, M^+). Anal. caled. for $C_{19}H_{13}N_5O_2$: C, 66.4; H, 3.8. Found: C, 66.2; H, 3.7.

Synthesis of 1,2,3-benzotriazine-4-one derivative (4): To a cold solution of (0.5g. 0.00 16 mol) of **3d** in 7ml concentrated hydrochloric acid and 7 ml water was added, sodium nitrate (0.24 g, 0.0035 mol) in 1.5 ml water dropwise at 0°C with continuous stirring for 5 min. The reaction mixture was made alkaline by adding ammonium hydroxide, then continued stirring for further 5 min. The separated precipitate was filtered off and washed with cooled ethanol and recrstallized from ethanol to yield (80%) of compound 4 : m.p 130°; IR (KBr) cm^{-1}; 1670, 1596 and 1530 (corresponding to lactam carbonyl group, two N=N of triazine and azo groups, respectively); ^1H NMR (DMSO), δ (ppm); 2.23 (s, 3H, CH_3), 7.2-7.7 (m, 12H, Ar-H); mass (m/z); (341, M^+). Anal. calcd. for $C_{20}H_{13}N_5O$: C, 70.38; H, 4.4. Found: C, 70.36; H, 4.38.

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