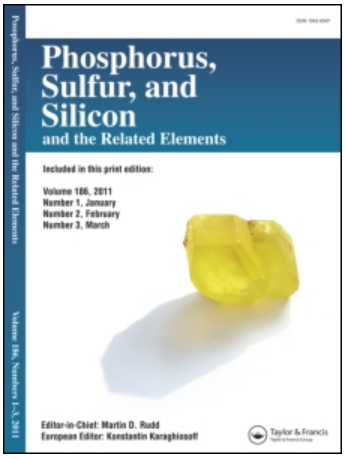

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CONDENSATION OF o-PHENYLENEDIAMINE WITH α-DIKETONES. PREPARATION AND PHOSPHORYLATION OF NEW α-DIKETONE MONOANILS

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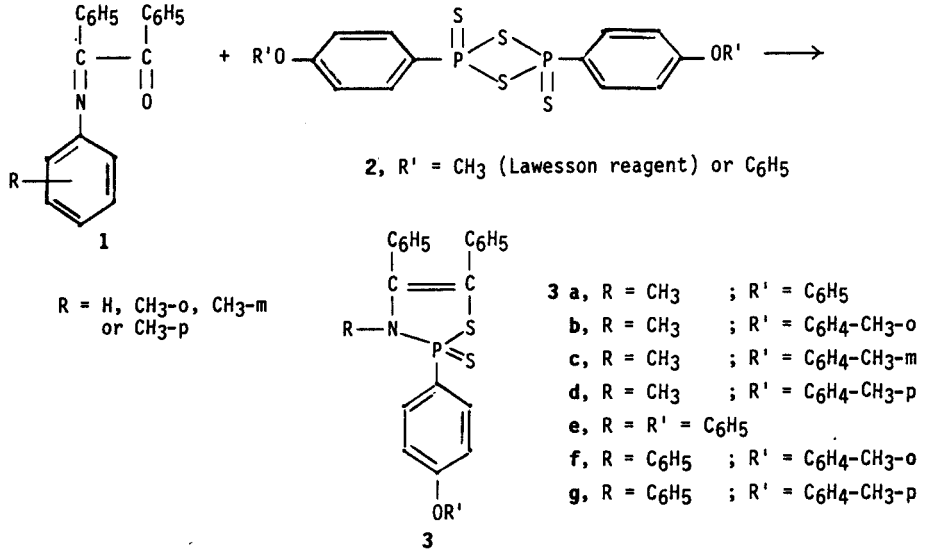
Condensation of o-phenylenediamine 5 with N-methylisatine **4b** and with benzocoumaranedione **12** under different conditions was studied. Monoanils N-methyl-3-(2-aminophenylimino)-indoline-2-one **6b** and benzocoumaran-3-(2-aminophenylimino)-2-one **13** were isolated. Dimethyl phosphite add to anils **6b** and/or **13** to give the corresponding quinoxalines **7** and **14** respectively. On the other hand, diethyl phosphite add to carbonyl-oxygen double bond in compounds **6b** & **13** to give the respective phosphate adducts **16** & **17a**. Structural reasonings are based on chemical and spectroscopic results.

Key words: α-Diketones; α-diketone monoanils; schiff base; quinoxalines; dialkyl phosphites; phosphates.

INTRODUCTION

Recently,[1] we have shown that α-diketone monoanils, namely benzil monoanils **1** act as suitable synthones for producing new heterocyclic structures incorporating N, P and S atoms (thiazaphospholines, **3**), (Scheme I). This together with our



SCHEME I

growing interest[2-4] in the chemistry of α-diketone monoanils has prompted us to prepare new candidates belonging to this class of compounds, to study their behavior toward some phosphorus reagents.

RESULTS AND DISCUSSION

The reaction of N-methylisatine **4b** with o-phenylenediamine **5** was studied under different solvent conditions (cf. Table I). Thus, when THF, benzene and/or absolute methanol were used as reaction media, a mixture of N-methylisatine monoanil **6b** and N-methylindolo (**2,3-b**) quinoxaline **7** was obtained in each case. The percentage yields of **6b** and **7** depended upon the reaction conditions (cf. Table I).

When the reaction of **4b** and **5** was carried out in acidic medium, quinoxaline **7** was obtained almost exclusively. The reaction conditions and the yields of products are summarized in Table I (Scheme II).

Compound **6b** was easily converted into **7** by heating in glacial acetic acid. This facile conversion is accounted for by a *syn-anti*-isomerization of the Schiff base.[5] Apparently, the base **6b** takes the *anti*-form preferably but it should be required to isomerize to the *syn*-form which provides the geometry necessary for the cyclodehydration to afford **7**. Under acidic conditions, the C—N double bond can be protonated[5] and the *anti-syn* interconversion is thus facilitated *via* the conjugate acid **8** of the Schiff base **6b**. Formation of **6b** and **7** may be explained in terms of initial formation of an adduct of type **9** which simulates the intermediate **10** formed *via* the reaction of isatine **4a** with ammonia.[6] The reaction of the amino group with the α-carbonyl of **9** followed by removal of two molecules of water would give **7**, while removal of one molecule of water from **9** appears to give **6b** (Scheme III).

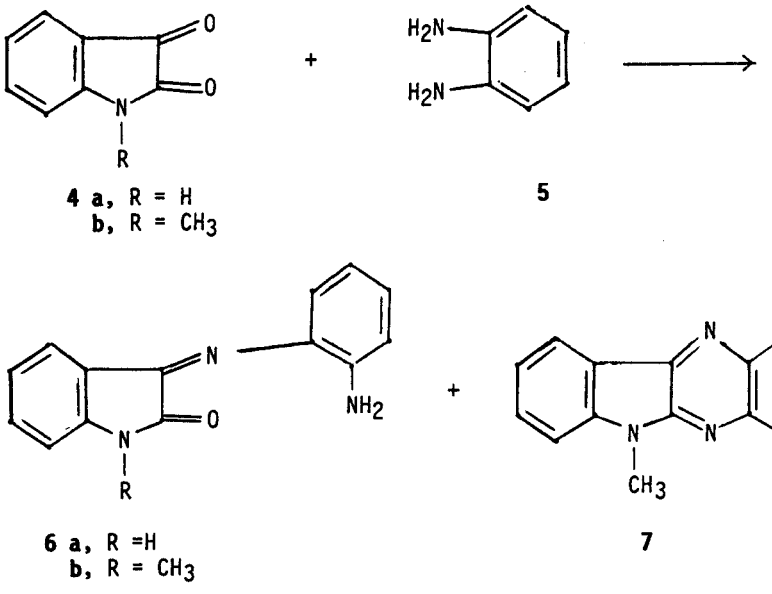
A spiro-compound like **11**—expected from nucleophilic attack of the NH_2 group on the β-carbon in intermediate **9**—was not obtained under the reaction conditions depicted in Table I, despite isolation of analogous structure (**11**, R=H) among the reaction products of isatine **4a** with aromatic o-diamines.[7,8]

Structural support for the Schiff base **6b** are. Its elemental analysis and molecular weight determination (MS) corresponded to $C_{15}H_{13}N_3O$ (m/z 251 M^+, base peak). The IR spectrum of **6b** (in kBr, expressed in cm^{-1}) showed strong absorption bands

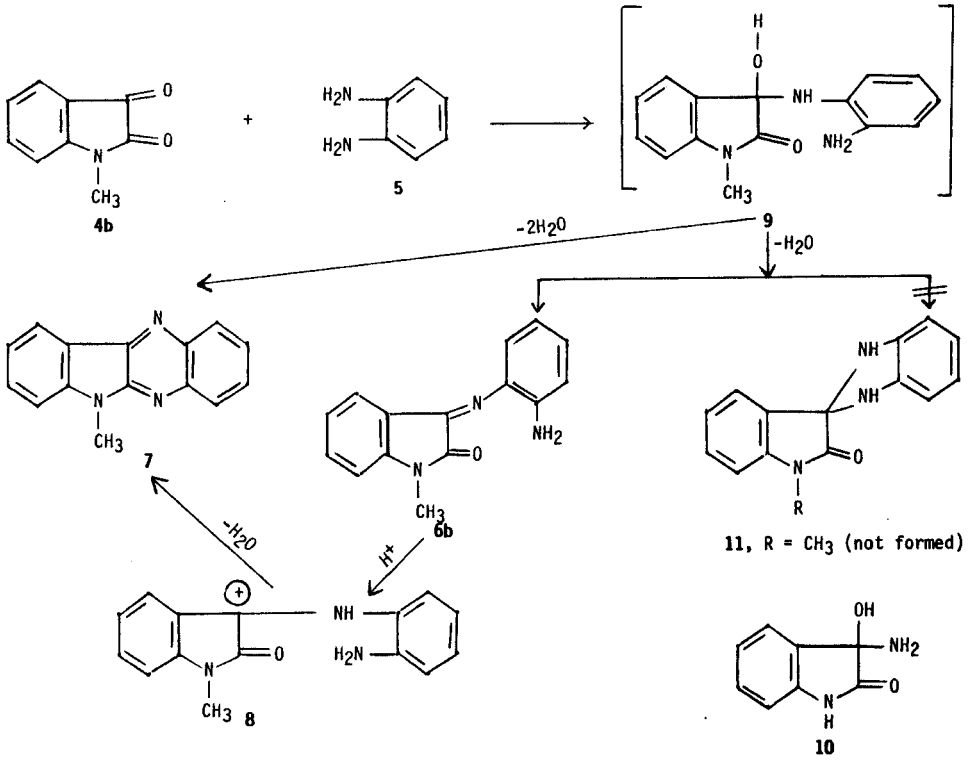
TABLE I

The reaction conditions and products of N-methylisatine with o-phenylenediamine

Solvent	Reaction conditions		Yields %	
	Temp. °C	Time/hr	6b	7
THF	60	24	90	<5
Benzene	80	8	90	<5
Methanol	65	4	50	50
Water / HCl (9.5 : 0.5 v/v)	90	2	<5	90
Acetic acid	118	3	<5	90



SCHEME II



SCHEME III

at 3480, 3200 (NH_2), 1630–1530 (C=N, C=C) and 1715 (C=O).[9] Its PMR spectrum (in DMSO/$CDCl_3$, expressed in δ-scale ppm) showed signals at 2.95 (N—CH_3, s), 6.60–8.60 (8H, aromatics, m) and 11.50 (2H, exchangeable with D_2O, NH_2).

Elemental analysis and molecular weight determination (MS) for compound **7** corresponded to $C_{15}H_{11}N_3$. Its mass spectrum showed the molecular ion peak at m/z 233 (100%). Its IR spectrum (in kBr, expressed in cm^{-1}) showed no NH_2 bands in the 3400–3300 region. It showed strong bands at 1605 (C=N) and 1580–1460 (C=C). The PMR spectrum of **7** (in $CDCl_3$, expressed in δ-scale ppm), showed signals at 2.95 (N—CH_3, s) and 6.50–8.60 (8H, aromatics, m).

The reaction of o-phenylenediamine **5** with 5,6-benzocoumaran-2,3-dione **12** was also studied under different conditions. Percentage yields of the produced monoanil **13** and quinoxaline **14** depended upon the reaction conditions (Table II).

Structural assignment for **13** was based upon presence of a strong lactone-carbonyl band at 1740 cm^{-1} in its IR spectrum. This rules out an alternative structure like **13a** (Scheme IV).

Elemental and spectral measurements for **13** and **14** agree with the proposed structures (cf. experimental).

This work is now extended to study the action of dialkyl phosphites on the new α-diketone monoanils **6b** and **13**. It has been found that dimethylphosphite DMP **15a** reacted with monoanil **6b** to give a yellow crystalline substance proved to be **7** (mixed melting point and comparative IR spectra).

Diethylphosphite DEP **15b** added to monoanil **6b** yields the phosphate product **16** (cf. experimental).

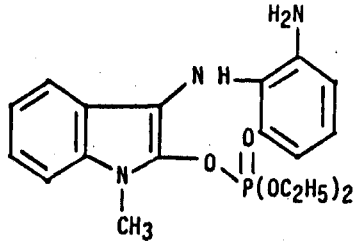


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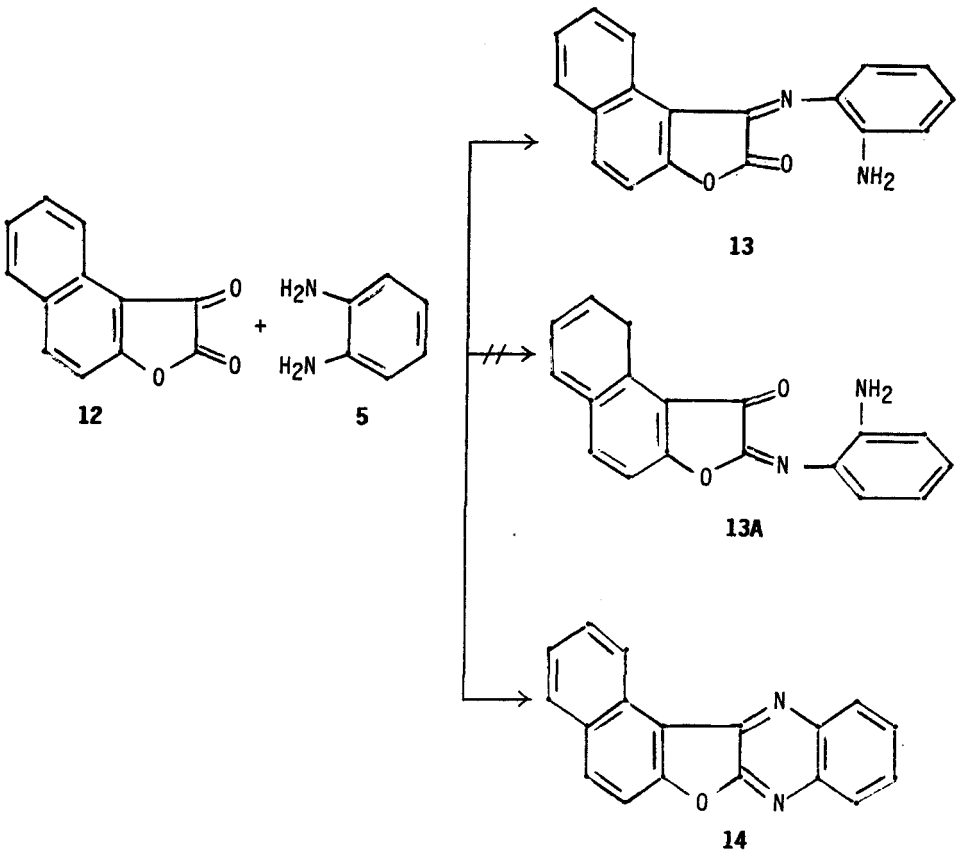
TABLE II

The reaction conditions and products of 5,6-benzocoumaran-2,3-dione with o-phenylenediamine

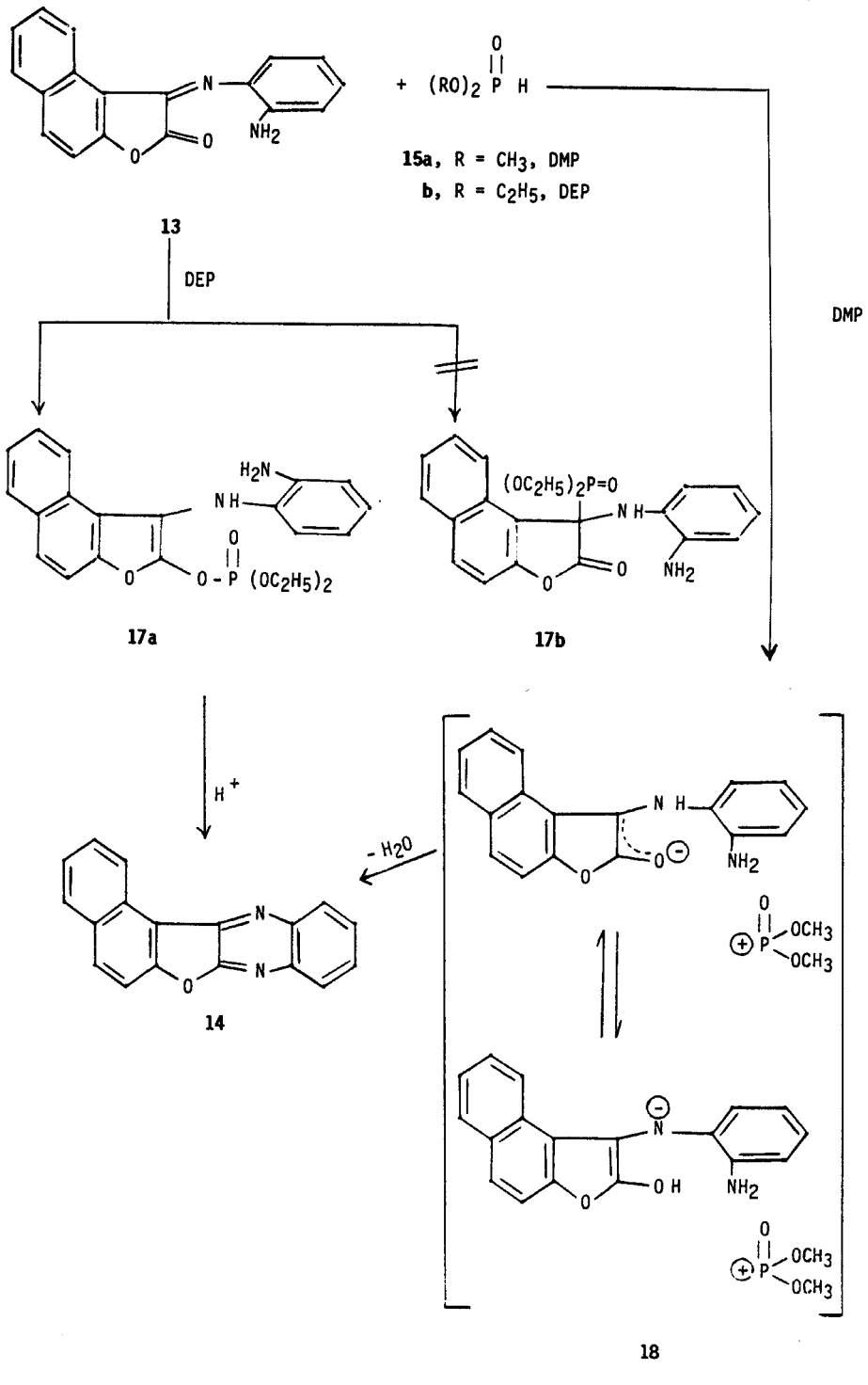
Solvent	Reaction conditions		Yields %	
	Temp. °C	Time/hr	13	14
THF	60	24	80	<10
Benzene	80	6	90	< 5
Methanol	65	3	60	40
Water/HCl (9.5:0.5 v/v)	90	2	<10	80
Acetic acid	118	3	< 5	90



SCHEME IV

Dimethylphosphite DMP **15a** reacted with benzocoumarandione monoanil **13** at 100°C in absence of solvent for 6 hr to give a pale yellow crystalline substance which proved to be quinoxaline **14**. Elemental analysis and molecular weight determination (MS) corresponded to $C_{18}H_{10}N_2O$ (m/z 270, M^+, base peak). Its PMR spectrum (in $CDCl_3$, δ-scale ppm) showed a multiplet due to the aromatic protons at 7.6–8.5 (10 H). Its IR spectra showed no absorption bands at 1650–1750 cm^{-1} due to the carbonyl group. A band at 1630 cm^{-1} appeared due to the C═N group absorption band.

Diethyl phosphite DEP **15b** added to monoanil **13** in absence of solvent at 100°C gives a substance assigned the structure **17a**. Elemental analysis and molecular weight determination (MS) corresponded to $C_{22}H_{23}N_2O_5P$ (m/z 426). Its ^{1}H-NMR spectrum (in DMSO-d_6, in δ-scale ppm) showed signals at 1.3 (6H, ethoxy-CH_3, t) and at 3.6 (4H, ethoxy-CH_2, quintet). The aromatic protons appeared at 7.90–7.10 (10 H, m). The NH protons appeared as a singlet at 9.30 (1 H, s, exchangeable with D_2O) and another singlet at 12.4 due to the NH_2 protons (2H, also exchangeable with D_2O). Its IR spectrum showed bands at 1030 cm^{-1} (P—O—C_2H_5) and at 1180 cm^{-1} (P═O, bonded). The spectrum revealed the absence of a band due to the carbonyl group around 1740 cm^{-1} and a band at 3200 cm^{-1} due to the NH group absorption (Scheme V).



SCHEME V

CONCLUSION

Monoanils **6b** and **13** behave toward addition of DMP in a manner completely different from DEP. Apparently, addition of DMP to Schiff base **6b** (or **13**) creates a quasiphosphonium intermediate of type 18 wherein phosphorus acts as a Lewis acid and the anil is existing preferably in the syn-form. Heating **18** facilitates formation of quinoxaline **7** (or **14**) by loss of one molecule of water (Scheme V).

Apparently, the bulkiness of DEP in comparison to DMP directs attack on monoanils **6b** and **13** (preferably in the anti-form) to give the stable phosphates **16** and **17a** respectively. Diethyl phosphite adducts **16** and/or **17a** form the respective quinoxalines upon heating only in presence of a protonating agent (Scheme V).

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded in kBr, with Perkin-Elmer Infracord Spectrometer 197G, and expressed in cm^{-1}. The ^{1}H-NMR spectra were run on Varian spectrometers at 60 and/or 90 MHz, using TMS as an internal standard and expressed in the δ-scale ppm. The mass spectra were run at 70 eV on kratos MS-50 equipment provided with a data system. Dialkyl phosphites **15a, b** were prepared by known procedures[10] and twice distilled before use. Benzene (thiophene free) and petroleum ether 40–60°C and 60–80°C were dried over sodium.

Silica gel (kieselgel 60, particle size 0.2–0.5 mm, E. Merck, Darmstadt) was used for column chromatography. A pyrex glass column was used, 60 cm long and 2 cm diameter.

1-N-methyl-3-(2-aminophenylimino) indoline-2-one **6b**. A mixture of 0.01 mol of N-methyl isatine and 0.01 mol of o-phenylenediamine was dissolved in 70 ml of benzene. The solution was refluxed for 6 hr then allowed to stand overnight at room temperature to give deep orange needles which were collected by filtration and recrystallized from benzene-pet ether (60–80°C) to give 90% yield of **6b** m.p. 230°C.
Analysis, Calcd. for $C_{15}H_{13}N_3O$: C, 71.69; H, 5.21; N, 16.72. Found: C, 71.40; H, 5.09; N, 16.49. The spectrum of the crude product indicated the presence of a small quantity of compound identified to be **7** (TLC).

Benzocoumarane-3-(2-aminophenylimino)-2-one **13**. In a similar manner compound **13** was prepared, recrystallization from methanol gave 80% yield as a pale orange needles m.p. 298°C.
Analysis, Calcd. for $C_{18}H_{12}N_2O_2$: C, 75.00; H, 4.16; N, 9.72. Found: C, 74.72; H, 4.02; N, 9.50. A trace of compound identified to be **14** was detected (TLC).
IR: Bands at 1620, 1500 (C=N, C=C, aromatic); 3560, 3300 (NH_2) and at 1740 (lactone) ^{1}H-NMR: signals at 7.2–8 (10 H, aromatics) and at 12.4 (2H, NH_2, s).
MS: m/z. 288, M^+, 80%.

1-N-methyl-indolo (**2,3-b**) quinoxaline **7**. A solution of 0.01 mol of N-methylisatine and 0.01 mol of o-phenylenediamine in 50 ml of acetic acid was heated at 118°C for 3 hr. After cooling the solution was poured into 500 ml of water to give yellowish brown precipitate, which was collected by filtration, washed with water and dried. Recrystallization from cyclohexane gave 90% yield as yellow crystals of **7** m.p. 148°C.
Analysis, Calcd. for $C_{15}H_{11}N_3$: C, 77.25; H, 4.72; N, 18.03. Found: C, 76.98; H, 4.62; N, 17.86. The spectrum of the crude product indicated the presence of a trace of **6b**.

Similarly, **quinoxaline 14** was prepared, recrystallization from ethanol gave 80% yield of **14** as pale yellow crystals m.p. 215°C. The spectrum of the crude product indicated the presence of small quantity of **13**.
Analysis, Calcd. for $C_{18}H_{10}N_2O$: C, 75.52; H, 3.49; N, 9.79. Found: C, 75.30; H, 3.34; N, 9.53.
IR: No C=O absorption band at 1750–1680, instead strong C=N band at 1620.
^{1}H-NMR: signals at 7.4–8.2 (10 H, aromatic, m).
MS: m/z, 270, M^+, base peak.

Condensation of α-diketone **4b** *(and/or* **12***) with o-phenylenediamine in methanol.* A mixture of 0.01 mol of **4b** (and/or **12**) and 0.01 mol of o-phenylenediamine was dissolved in 60 ml methanol. The solution was refluxed for 4 hr (or 3 hr for **12**). After cooling to room temperature, the reaction mixture was evaporated till dryness, *in vacuo*, in the presence of 5 gm of silica gel. This mixture was introduced

into a column charged with silica gel and packed with the appropriate eluent. The following products were isolated and identified:

1. In case of α-diketone **4b**:
   a) Compound was separated in 50% yield and identified to be **6b**. Eluent used (ether-pet. ether, 2:8; v/v).
   b) Compound was separated in 50% yield and identified to be **7**. Eluent used (ether-pet. ether, 4:6, v/v).
2. In case of α-diketone **12**:
   a) Compound was separated in 60% yield and identified to be **13**. Eluent used (benzene-ethyl acetate, 8:2; v/v).
   b) Compound was separated in 40% yield and identified to be **14**. Eluent used (benzene-ethylacetate, 5:5; v/v).

Reaction of anils **6b** *and* **13** *with dimethyl phosphite.* A mixture of 0.01 mol of **6b** and 0.02 mol dimethyl phosphite was heated on a steam bath for 8 hr. The excess of dimethyl phosphite was removed *in vacuo* and the residue was washed several times with petroleum ether then recrystallized from cyclohexane to give yellow crystals m.p. 148°C proved to be **7** (m.p., mixed m.p. and comparative IR spectra).

Under the same conditions, quinoxaline **14** was obtained by reacting dimethyl phosphite with anil **13** as pale yellow crystals, m.p. 215°C (m.p., mixed m.p. and comparative IR spectra).

Reaction of anils **6b** *and* **13** *with diethyl phosphite.* A mixture of 0.01 mol **6b** and 0.02 mol diethyl phosphite was heated on a steam bath for 8 hr. The excess of diethyl phosphite was removed under vacuum, then the residue was triturated with petroleum ether (b.r. 40–60°C), the solid product so formed was collected in 70% yield and recrystallized from benzene-pet ether to give phosphate product **16** m.p. 162°C.

Analysis, Calcd. for $C_{19}H_{24}N_3O_4P$: C, 58.61; H, 6.16; N, 10.79; P, 7.96. Found: C, 58.40; H, 6.10; N, 10.85; P, 7.75.

IR: Bands at 1540 (C=C, aromatic); 1250 (P=O); 1040 (P—O—C_5H_5) and 3450 (NH).

^{1}H-NMR: signals at 2.9 (N—CH_3, s), 1.2 (6H, ethoxy—CH_3, t), 4.01 (4H, ethoxy—CH_2, q), 8.3–6.6 (8H, m) and at 9.1 & 11.8 due to NH and NH_2 protons.

Similarly, phosphate **17a** was prepared in 80% yield by reacting anil **13** with diethyl phosphite as a yellow crystals from ethanol m.p. 243°C.

Analysis, Calcd. for $C_{22}H_{23}N_2O_5P$: C, 61.97; H, 5.39; N, 6.57; P, 7.27. Found: C, 61.80; H, 5.15; N, 6.33; P, 7.39.

Action of heat on diethyl phosphite adduct 17a in absence and in presence of protonating agent

a) In absence of protonating agent

Diethyl phosphite adduct **17a** was dissolved in 70 ml benzene. The solution was refluxed for 6 hr then allowed to stand overnight at room temperature. After removal the volatile materials under reduced pressure, the residual substance was recrystallized from ethanol to give yellow crystals m.p. 243°C (proved to be **17a**; m.p. and mixed m.p.).

b) In presence of protonating agent

Diethyl phosphite adduct **17a** was heated in 50 ml acetic acid at 118°C for 3 hr. After cooling the solution was poured into 500 ml of water to give yellow precipitate, which was collected by filtration, washed with water and dried. Crystallization from ethanol gave pale yellow crystals m.p. 215°C (proved to be **14**; m.p. and mixed m.p.).

Degradation experiments with monoanils 6b and 13

Thermolysis. Compound **6b** (and/or **13**) was heated in a cold finger sublimator above its m.p. (bath temperature) under reduced pressure (2 mm/Hg) for 15 minutes. The solid product that sublimed was collected (ca. 60% yield) and recrystallized from the appropriate solvent to give crystals proved to be the parent α-diketone **4b** (and/or **12**), (m.p., mixed m.p.).

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