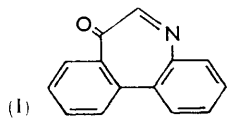
977. *The Anils of Phenylglyoxal.*

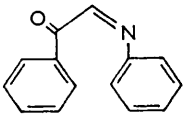
By E. Fraser, W. Paterson, and G. R. Proctor.

The *cis*- and the *trans*-anil of phenylglyoxal have been prepared by two routes; they differ from the material previously described as the anil, but the latter, which has been obtained from phenacylaniline, has been characterised. A compound previously obtained from the anils is shown not to be a 1,4-oxazine. Synthesis of 1,4-oxazines and 3,4-diaminofurans has been examined.

There is only one reference in the literature to the anil of phenylglyoxal.[1] The formal similarity between the azatropone (I) and phenylglyoxal *cis*-anil (II) aroused our interest in the anil. We found that condensation of phenylglyoxal with aniline in acetic acid solution [1] gave very erratic results and, by thin-layer chromatography,[2] we could detect at least five yellow products, two of which were isolated. One (m. p. 70°) appears to be a dimer of the anil; we consider the other (m. p. 145°) to be the *trans*-anil. Yates [1] gives the m. p. of the anil as 164°.



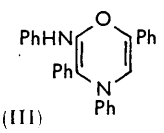
(I)



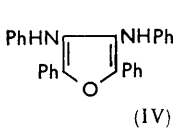
(II)

N-toluene-*p*-sulphonylphenacylaniline underwent a mild base-catalysed elimination [3] to give the *cis*-anil (m. p. 210°) of phenylglyoxal, which was converted on a palladium catalyst into the *trans*-anil. The stereochemistry of these compounds was assigned from their ultraviolet spectra.[4] Compared with the *cis*-anil, the *trans*-anil shows a bathochromic shift (10 mμ) of the longer-wave absorption band. The presence of two replaceable hydrogen atoms adjacent to the nitrogen atom and uncertainty about the conformation of *N*-toluene-*p*-sulphonylphenacylaniline made it impossible to forecast which anil would be produced from a heterolytic elimination reaction.[5]

Direct confirmation of the structures of the anils could not be obtained by reduction to phenacylaniline; both zinc in dilute acetic acid and hydrogen on a palladium catalyst gave a substance (m. p. 187°) which we formerly believed to be a 1,4-oxazine (III).[6] Analyses and molecular-weight measurement by mass spectroscopy indicated a molecular formula $C_{28}H_{22}N_2O$. The infrared spectrum revealed an amino-group and an ether linkage but neither carbonyl nor hydroxy-groups. The compound was unaffected by boiling with acids and alkalis and by heating with alcoholic ammonia under pressure, and it did not react with toluene-*p*-sulphonyl chloride, methyl iodide, or acetic anhydride. The n.m.r.



(III)



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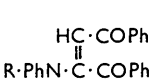

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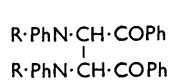


(VI)

spectrum showed twenty aromatic protons (τ from 2 to 3·2) as expected for (III) but the other two protons were both attached to nitrogen atoms (singlet τ 5·65). This excludes

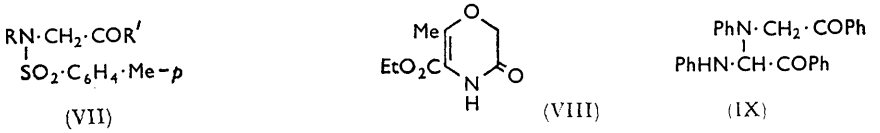
[1] Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 5380.
[2] Stahl, *Arch. Pharm.*, 1959, **65**, 531.
[3] Paterson and Proctor, *Proc. Chem. Soc.*, 1961, 248.
[4] Gillam and Stern, "Electronic Absorption Spectroscopy," E. Arnold, London, 1957, p. 232.
[5] Cram, "Steric Effects in Organic Chemistry," ed. Newman, J. Wiley and Sons, New York, 1956, p. 315.
[6] Paterson and Proctor, *Chem. and Ind.*, 1961, 254.

formula (III) but suggests a tetrasubstituted furan [*e.g.*, (IV)] of which there are several positional isomers.

Derivatives of diaminofurans are not well known and our preliminary investigations of an alternative route to the isomer (IV) were not encouraging; when dibromodibenzoylethane was allowed to react with substituted anilines we obtained the substituted ethylenes (V; R = $SO_2 \cdot C_6H_4 \cdot Me$-*p* or Me) rather than the desired intermediates for furan synthesis (VI; R = $SO_2 \cdot C_6H_4 \cdot Me$-*p*). We also failed to synthesise (VI; R = H) from dianilinosuccinic acid.

In order to find out more about the reductive self-condensation of phenylglyoxal anil we attempted to prepare further intermediates of the type (VII; R = $Ph \cdot CH_2$, R′ = Ph and Me) from which " keto-anils " could be obtained for comparison. It is interesting that, although monophenacylaniline is readily available from ω-bromoacetophenone and aniline,[7] benzylamine invariably gives diphenacylbenzylamine (cf. ref. 8). We found that bromoacetone and benzylamine gave only benzylamine hydrobromide. In this case the use of *N*-toluene-*p*-sulphonylbenzylamine (potassium salt) was no improvement. We are now investigating other methods of preparing compounds (VII); for example, ω-bromoacetophenone reacts with potassium toluene-*p*-sulphonamide, giving (VII; R = H, R′ = Ph) and (VII; R = $PhCO \cdot CH_2$, R′ = Ph) which can be separated by chromatography.

It is of interest that in 1893, Mason and Winder [8] claimed (without analyses) to have converted the hydrobromide of diphenacylbenzylamine by treatment with alkali into a 1,4-oxazine; we have repeated their work and found that only diphenacylbenzylamine itself or ketonic polymers therefrom were obtained under a variety of dehydrating conditions. Since our own claim [6] to have made a 1,4-oxazine was also incorrect, the only examples of this class are those named by Newbold, Spring, and Sweeny [9] as 5-hydroxy-1,4-oxazines although formulated by them as lactams, *e.g.*, (VIII). We have examined the infrared spectrum of one of their compounds (VIII) (kindly supplied by Dr. Newbold) and find that it is to be regarded as a lactam, since amide-carbonyl absorption is present (ν 1660 $cm.^{-1}$). In the strict sense, then, no 1,4-oxazine has ever been obtained.



(VII) (VIII) (IX)

When *N*-toluene-*p*-sulphonylphenacylaniline was treated with sodamide in toluene, no anil was obtained, an amino-ketone (m. p. 187°) being the only product. The amino-ketone also arose when solutions of phenacylaniline were aerated or shaken with a palladium–carbon catalyst, or when solid phenacylaniline was left in a stoppered bottle for one year. Yates [1] described this material as the anil, but, after considering its spectra, analyses, and molecular weight, we conclude that the amino-ketone probably has structure (IX). This is readily explained by assuming that phenancylaniline and phenylglyoxal anil undergo a Michael-type reaction. Mass spectroscopy indicated both the expected molecular weight and a number of fragments consistent with structure (IX). It was not possible to convert (IX) into (IV), so we conclude that the former is not a precursor of the latter.[10]

Experimental

Phenacylaniline.[7]—This formed needles (from ethanol), m. p. 98° (Found: C, 80·0; H, 6·15; N, 6·6. Calc. for $C_{14}H_{13}NO$: C, 79·6; H, 6·15; N, 6·6%), $\nu_{max.}$ (Nujol) 3342, 1695, 1605 $cm.^{-1}$, $\lambda_{max.}$ (ethanol) 208, 246, 286 mμ (ε 17,200, 29,150, 3870). The 2,4-*dinitrophenylhydrazone*

[7] Verkade and Janetzky, *Rec. Trav. chim.*, 1943, **62**, 772.
[8] Mason and Winder, *J.*, 1893, **63**, 1355.
[9] Newbold, Spring, and Sweeny, *J.*, 1950, 909.
[10] We thank the Referees for suggesting this point.

formed needles (from nitrobenzene), m. p. 220° (Found: C, 60·8; H, 4·15. $C_{20}H_{17}N_5O_4$ requires C, 61·4; H, 4·3%). The N-*toluene*-p-*sulphonyl derivative* formed needles (from methanol), m. p. 130° (Found: C, 68·85; H, 5·3; N, 3·95. $C_{21}H_{19}NO_3S$ requires C, 69·0; H, 5·2: N, 3·85%), $\nu_{max.}$ (Nujol) 1740, 1600, 1156, 1105 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 212, 225 (infl.) mμ (ε 25,630, 18,720).

Phenylglyoxal cis-*Anil*.—A nitrogen-saturated suspension of *N*-toluene-*p*-sulphonylphenacylaniline (8·4 g.) in dry toluene (300 ml.) was added to a nitrogen-saturated suspension of sodium methoxide (9 g.) in dry toluene (200 ml.). After 24 hr. at 20°, the mixture was poured into water (500 ml.) and filtered; the residue (4·6 g.) gave yellow plates (from methanol), m. p. 210° [Found: C, 80·4; H, 5·3; N, 6·6%; *M* (isothermal distn.), 218. $C_{14}H_{11}NO$ requires C, 80·4; H, 5·25; N, 6·7%; *M*, 209], $\nu_{max.}$ (Nujol) 1666, 1600 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 207, 250 mμ (ε 13,920, 13,800). The 2,4-*dinitrophenylhydrazone* formed pale red needles (from nitrobenzene), m. p. 235° (Found: N, 17·95. $C_{20}H_{15}N_5O_4$ requires N, 17·95%).

Phenylglyoxal trans-*Anil*.—(*a*) The previous anil (88 mg.) was shaken in ethanol (100 ml.) with 5% palladised charcoal (100 mg.) at 20° for 16 hr. The product (75 mg.), obtained by evaporation of the filtrate, formed yellow prisms (from ethanol), m. p. 145° [Found: C, 80·6; H, 4·8; N, 7·05%; *M* (isothermal distn.), 214], $\nu_{max.}$ (Nujol) 1666, 1590 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 207, 260 mμ (ε 22,360, 13,800).

(*b*) A mixture of phenylglyoxal hydrate [11] (7·94 g.), freshly distilled aniline (4·6 ml.), glacial acetic acid (10 ml.), and ethanol (50 ml.) was heated on the steam-bath for 30 min. After addition of water (12 ml.), and cooling, a yellow oil separated. Thin-layer and paper chromatography showed that this contained at least five products. It was chromatographed on alumina; elution with benzene–light petroleum (b. p. 60—80°) (9 : 1) gave a *dimer* of phenylglyoxal anil, yellow needles [from light petroleum (b. p. 100—120°)], m. p. 76° (32%) [Found: C, 80·3; H, 5·25; N, 7·2%; *M* (Rast), 408. $C_{28}H_{22}N_2O_2$ requires C, 80·4; H, 5·25; N, 6·75%; *M*, 418], $\nu_{max.}$ (Nujol) 1666, 1500 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 205, 247, 337 mμ (ε 44,640, 33,640, 10,050). Elution with chloroform gave the *trans*-anil (10·5%), m. p. and mixed m. p. 145°. The remaining fractions gave oils which did not crystallise.

Reactions of Phenylglyoxal Anils.—(*a*) A solution of phenylglyoxal *cis*-anil (76 mg.) in ethanol (100 ml.) was shaken at 20° for 24 hr. with hydrogen and 5% palladised charcoal (100 mg.). Evaporation of the filtrate gave the *product*, colourless cubes (from methanol), m. p. 188° (63 mg.) [Found: C, 83·6; H, 5·5; N, 7·3%; *M* (mass spectroscopy), 402. $C_{28}H_{22}N_2O$ requires C, 83·6; H, 5·5; N, 7·0%; *M*, 402], $\nu_{max.}$ (Nujol) 3310, 1575, 1235 cm.$^{-1}$, $\lambda_{max.}$ (ethanol) 210, 242, 286, 337 mμ (ε 26,500, 28,600, 24,400, 18,600).

(*b*) As in (*a*), with palladised barium carbonate as catalyst. The yield of material, m. p. and mixed m. p. 188°, was 19%. The remainder was starting material.

(*c*) Phenylglyoxal *cis*-anil (314 mg.), glacial acetic acid (150 ml.), and water (10 ml.) were heated together on the steam-bath for 1 hr. with zinc dust (6 g.). After filtration, the mixture was diluted with water (200 ml.), and extracted with chloroform, the extract was washed with dilute ammonium hydroxide and water, dried, and evaporated, to leave the product (217 mg.), m. p. 187°, identical with that obtained as in (*b*). It was recovered unchanged after (*a*) being heated with aniline for 5 hr., (*b*) being heated with liquid ammonia in a sealed tube at 140° for 40 hr., (*c*) being heated with concentrated hydrochloric acid at 120° for 3 hr., (*d*) being heated with toluene-*p*-sulphonyl chloride in pyridine at 100° for 3 hr.

1,2-*Dibromodibenzoylethane*.—*trans*-Dibenzoylethylene [12] (4·2 g.) and water were stirred together to form a paste. Bromine (1 ml.) was added at once to the refluxing mixture. The solid (4 g.) which separated was filtered off, washed with water, and dried; it formed cubes (from ethanol), m. p. 190° (Found: C, 48·3; H, 2·9. Calc. for $C_{16}H_{12}Br_2O_2$: C, 48·5; H, 3·05%), $\nu_{max.}$ (Nujol) 1684 cm.$^{-1}$. A mixture of the product (0·93 g.), sodium iodide (1·5 g.), and acetone (150 ml.) was refluxed for 2 hr. and cooled. Sodium thiosulphate solution was added dropwise until the colour of iodine was discharged and the solution was diluted with water (250 ml.). The residue obtained on filtration was washed and dried; it formed needles (95%; from methanol), m. p. 111° undepressed by dibenzoylethylene.

1,2-*Dibenzoyl*-1-N-*methylanilinoethylene* (V; R = Me).—A mixture of 1,2-dibromodibenzoylethane (6·6 g.), methylaniline (7·0 g.), and ethanol (150 ml.) was refluxed for 8 hr., the solution evaporated to small volume, and the resultant semi-solid mass dissolved in chloroform; this

[11] Riley and Gray, *Org. Synth.*, 1935, **15**, 67.
[12] (*a*) Conant and Lutz, *J. Amer. Chem. Soc.*, 1923, **45**, 1305; (*b*) Lutz, *Org. Synth.*, 1940, **20**, 29.

solution was washed with dilute hydrochloric acid, dilute ammonium hydroxide, and water, dried, and evaporated. The *product* (5·6 g.) formed needles (from methanol), m. p. 142° (Found: C, 81·15; H, 5·95; N, 4·0. $C_{23}H_{14}NO_2$ requires C, 80·95; H, 5·6; N, 4·1%), $\nu_{max.}$ (Nujol) 1666, 1626 cm.$^{-1}$. The n.m.r. spectrum showed 15 aromatic protons, 1 vinyl proton (τ = 3·9), and 3 methyl protons (singlet, 7·5 τ).

1,2-*Dibenzoyl*-1-(N-*toluene*-p-*sulphonylanilino*)*ethylene* (V; R = SO_2·C_6H_4·Me-*p*).—A solution of 1,2-dibromodibenzoylethane (6·5 g.) in dry benzene (200 ml.) was refluxed with the sodium salt of *N*-toluene-*p*-sulphonylaniline (9 g.) for 18 hr. and cooled. After filtration, the filtrate was washed with dilute sulphuric acid and water, dried, and evaporated. The *product* (6·45 g.) formed needles (from ethanol) m. p. 172° (60%) (Found: C, 72·35; H, 4·8; N, 2·85. $C_{29}H_{23}NO_4S$ requires C, 72·35; H, 4·8; H, 2·9%), $\nu_{max.}$ (Nujol) 1686, 1658 cm.$^{-1}$. The n.m.r. spectrum showed 1 vinyl proton (τ = 3·85).

Treatment of Bromoacetone with Benzylamine.—Benzylamine (5·3 g.) in ethanol (25 ml.) and bromoacetone [13] (7·3 g.) in ethanol (15 ml.) were chilled to 0° and mixed by slowly adding the latter solution to the former. After several hours, the precipitate was removed; it yielded benzylamine hydrobromide (4·9 g.) (from carbon tetrachloride), m. p. and mixed m. p. 216°.

Potassium Salt of N-*Toluene*-p-*sulphonylbenzylamine.*—To *N*-toluene-*p*-sulphonylbenzylamine (5 g.) in ethanol (100 ml.) was added potassium (760 mg.), and the solution evaporated *in vacuo* to leave a solid, m. p. 236° (5·2 g.).

Treatment of N-*Toluene*-p-*sulphonylbenzylamine with Bromoacetone.*—(*a*) Amberlite resin [14] IRA 400 (OH^- form) (100 g.) was suspended in benzene (100 ml.), *N*-toluene-*p*-sulphonylbenzylamine (4·5 g.) in benzene (100 ml.) was added and, after shaking, bromoacetone (9 g.) and water (25 ml.). After 48 hr. the resin was removed and the benzene was shaken with dilute ammonium hydroxide, dilute hydrochloric acid, and water, dried, and evaporated, giving a solid (620 mg.) (from carbon tetrachloride), m. p. 117° undepressed by *N*-toluene-*p*-sulphonylbenzylamine.

(*b*) *N*-Toluene-*p*-sulphonylbenzylamine (5·3 g.), bromoacetone (3 g.), and freshly roasted potassium carbonate (10 g.) were refluxed for 48 hr. in dry toluene. The filtrate was washed with ammonium hydroxide solution, dilute hydrochloric acid, and water. The product (4·1 g.), which crystallised from carbon tetrachloride, was *N*-toluene-*p*-sulphonylbenzylamine, as before. The use of ethanol as solvent was no improvement.

(*c*) The potassium salt of *N*-toluene-*p*-sulphonylbenzylamine (3 g.) and bromoacetone (800 mg.) were refluxed in benzene (50 ml.) for 2½ hr. *N*-Toluene-*p*-sulphonylbenzylamine (2·55 g.), m. p. 117°, was recovered.

Reaction of ω-*Bromoacetophenone with the Potassium Salt of Toluene*-p-*sulphonamide.*—The potassium salt [15] (7·95 g.) and ω-bromoacetophenone (7·6 g.) were refluxed in dry benzene (40 ml.) for 3 hr. The solution was extracted with chloroform, washed with dilute hydrochloric acid and water, dried, and the solvent removed *in vacuo*, leaving a red oil (7·8 g.) which was chromatographed on neutral alumina. Elution with light petroleum (b. p. 60—80°) gave *NN*-diphenacyltoluene-*p*-sulphonamide (VII; R = PhCO·CH_2, R′ = Ph), m. p. 135° (2·56 g.) (Found: C, 67·7; H, 5·15; N, 3·55. $C_{23}H_{21}NO_4S$ requires C, 67·7; H, 5·2; N, 3·45%), $\nu_{max.}$ (Nujol) 1695 cm.$^{-1}$. Elution with benzene gave ω-(N-*toluene*-p-*sulphonylamino*)*acetophenone* (VII; R = H, R′ = Ph), m. p. 108° (from ethanol) (3·32 g.) (Found: C, 62·15; H, 5·05; N, 4·5. $C_{15}H_{15}NO_3S$ requires C, 62·3; H, 5·25; N, 4·85%), $\nu_{max.}$ (Nujol) 3333, 1695 cm.$^{-1}$. When this product was treated with methyl iodide on an ion-exchange resin, as before, there was obtained (~20% yield) an oil having no absorption in the infrared spectrum that could be attributed to N–H or C=O chromophores.

Diphenacylbenzylamine Hydrobromide (cf. ref. 8).—Benzylamine (5·3 g.) and ω-bromoacetophenone (20 g.) were separately dissolved in ethanol (50 ml.). When the solutions were mixed, an exothermic reaction ensued; after several hours, the solid was filtered off and yielded the *product*, m. p. 203° (16 g.) (from ethanol) (Found: C, 65·6; H, 5·6; Br, 18·75; N, 4·05. Calc. for $C_{23}H_{22}BrNO_2$: C, 65·1; H, 5·2; Br, 18·8; N, 3·3%), $\nu_{max.}$ (Nujol) 1698 cm.$^{-1}$.

Diphenacylbenzylamine.—The above hydrobromide (2·7 g.), in chloroform, was shaken successively with dilute ammonium hydroxide, dilute hydrochloric acid, and water. After

[13] Weygand, Schmid, and Kowanzik, *Chem. Ber.*, 1949, **82**, 333.
[14] Barner, Borgulya, Proctor, and Schmid, *Chimia* (*Switz.*), 1961, **15**, 492.
[15] Harington and Moggridge, *J.*, 1940. 706.

drying and removal of the solvent, the *product* (1·8 g.) was an oil, b. p. 142°/0·2 mm., $\nu_{max.}$ (liquid film) 1697 cm.$^{-1}$ (Found: C, 79·35; H, 6·4. $C_{23}H_{21}NO_2$ requires C, 80·4; H, 6·2%). The *bis-2,4-dinitrophenylhydrazone* was a dark orange solid, m. p. 184° (Found: N, 17·7. $C_{35}H_{29}N_9O_8$ requires N, 18·05%).

The above amine was treated with the following dehydrating agents. (a) Concentrated hydrochloric acid at 100° for 2 hr. (b) Polyphosphoric acid at 100° for 1 hr. (c) Potassium hydroxide in glycol or ethanol at the reflux temperature for 3 hr. (d) Acetic anhydride containing concentrated sulphuric acid at room temperature for 1 month. In all cases the product had an infrared spectrum containing strong C=O absorption (ν 1700 cm.$^{-1}$) and in each case, except (c), 50—60% of the starting material was recovered by distillation *in vacuo*. The remaining materials appeared to be polymeric.

Attempted Preparation of ω-(benzylamino)acetophenone (cf. ref. 8).—ω-Bromoacetophenone (10 g.) and ethanol (50 ml.) were slowly added (20 min.) to benzylamine (5·3 g.) in ethanol (25 ml.). After 15 hr., the crystalline *diphenacylbenzylamine hydrobromide* had m. p. and mixed m. p. 203° (from ethanol) (13 g.). From the liquors was obtained only benzylamine (infrared spectrum, and hydrobromide, m. p. 216°).

Amino-ketone (IX) *from Phenacylaniline.*—(*a*) Phenacylaniline (1·2 g.) and ethanol (150 ml.) were shaken at 20° for 16 hr. with 5% palladised charcoal (100 mg.). The *product* formed yellow needles (from ethyl acetate), m. p. 187° (90%) [Found: C, 79·6; H, 5·9; N, 6·5%; *M* (mass spectroscopy), 420. $C_{28}H_{24}N_2O_2$ requires C, 79·95; H, 5·75; N, 6·65%; *M*, 420], $\nu_{max.}$ (Nujol) 3330 (NH), 1668 cm.$^{-1}$ (C=O), $\lambda_{max.}$ ($CHCl_3$) 249, 283 mμ (ε 38,360, 6610). The mass spectrum showed peaks at 420, 327, 315, 222, 210, 116, and 79. The material was too poorly soluble in most solvents to obtain an n.m.r. spectrum.

(*b*) A nitrogen-saturated solution of *N*-toluene-*p*-sulphonylphenacylaniline (1·2 g.) in dry toluene (200 ml.) was added to a nitrogen-saturated suspension of sodamide (1 g.) in dry toluene (100 ml.). After 14 days at 20°, the reaction mixture was poured into water (200 ml.) and extracted with chloroform. The product (600 mg.), crystallised as before, had m. p. and mixed m. p. 187°.

(*c*) When phenacylaniline in ethanol was agitated by a stream of oxygen for six days, the product (2%; cf. ref. 1) was identical with that in (*a*) and (*b*).

The amino-ketone (III, 600 mg.) was recovered after being shaken in ethanol (100 ml.) and hydrogen for 16 hr. at atmospheric pressure.

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