

1309. *The Removal of Toluene-*p*-sulphonyl Groups from Sulphonamides. Part II.* Phenylglyoxal Anil Dimers*

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N-Toluene-*p*-sulphonyl phenacyl anilines (I) undergo the base-catalysed elimination to give dimers (III) where R = H: when R = Ph, a monomer was obtained.

In a previous Paper¹ we described how a dimer (m. p. 76°) of phenylglyoxal anil had been isolated along with other products from the reaction of aniline with phenylglyoxal using the method of Yates:² the only other crystalline product (m. p. 145°) we supposed to be the *trans*-anil monomer (10% yield), the molecular weight being measured by isothermal distillation. What we formulated as the *cis*-anil monomer (m. p. 210°) was obtained in good yield by a base-catalysed elimination³ from *N*-phenacyl-*N*-toluene-*p*-sulphonyl-aniline (I; R = R' = H). We have discovered that both these supposed monomers are in fact dimeric; the error was detected in the following way.

* Part I, W. Paterson and G. R. Proctor, *J.*, 1965, 485.

¹ E. Fraser, W. Paterson, and G. R. Proctor, *J.*, 1963, 5107.

² P. Yates, *J. Amer. Chem. Soc.*, 1952, **74**, 5380.

³ W. Paterson and G. R. Proctor, *Proc. Chem. Soc.*, 1961, 284; *J.*, 1965, 485.

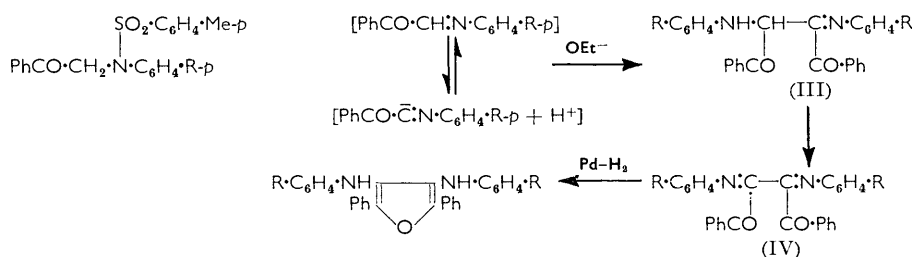
When the sulphonamides (I; $R' = H$, $R = Me$ and Br) were treated with sodium methoxide in toluene, the red-orange products resembled the parent compound (m. p. 210°) in appearance and in solubility but exhibited strong N-H absorption in the infrared



spectra. Re-examination of the parent "anil" (m. p. 210°) revealed that while in Nujol it had negligible absorption in the region $3300\text{--}3500\text{ cm.}^{-1}$; in a potassium chloride disc a sharp peak (N-H) was present. These findings made it impossible to formulate the elimination reaction products as anil monomers.

The compound from (I; $R = Me$, $R' = H$) was chosen for further study. The n.m.r. spectrum, obtained with difficulty owing to poor solubility, contained an amino or hydroxyl proton. The latter signal disappeared after treatment with palladised charcoal in ethanol;¹ the product (m. p. 162°) resembled the material described previously¹ as the *trans*-anil monomer (m. p. 145°), and its infrared spectrum contained no peaks that could be ascribed to amino or hydroxyl groups. The results prompted a mass-spectroscopic examination, which showed that the product of elimination is a dimer (M , 446) of the expected anil and that the substance obtained by palladised charcoal treatment has a molecular weight of 444. The possibility of dissociation in solution was excluded when the anil was shown to be a dimer in benzene solution (vapour pressure osmometer). The reason for failure of the isothermal distillation method is not understood, but we now realise that this method was known to be unreliable.⁴ Details of the mass spectra are in accord with structures (III) and (IV) for the dimer and its dehydrogenation product, respectively. For instance, in (III) the parent ion (m/e 446) appears to shed two successive PhCO groups; the presence of metastable ions at m/e 260.9 and 163.1 confirm this. Other peaks at m/e 224 ($\text{Me}\cdot\text{C}_6\text{H}_4\cdot\ddagger\text{NH}\cdot\text{CH}\cdot\text{CO}\cdot\text{Ph}$) and 188 ($\text{Me}\cdot\text{C}_6\text{H}_4\cdot\ddagger\text{N}\cdot\text{CH}$) fit into a logical degradation pattern, and, although the latter peak had no corresponding metastable ion, a subsequent elision of fragment m/e 27 (HCN) led to m/e 91 (tropylium) with a corresponding metastable ion at m/e 70.1. The slight difference in structure (IV) is reflected in the cracking pattern of this molecule, from which the initial loss of one PhCO group is followed by two successive expulsions of a fragment m/e 117 (presumably $\text{Me}\cdot\text{C}_6\text{H}_4\cdot\text{NC}$).

It is now much clearer why a substituted furan was previously obtained by catalytic hydrogenation of the "anils"; in the present case analogous furans were obtained starting from (I; $R = Br$ or Me , $R' = H$). The sequence of reactions can be rationalised as shown in the Scheme. The dimerisation is thus seen as a Michael-type addition of a carbanion and a proton to the monomer; anils are known to undergo such reactions.⁵ Precedents for the dehydrogenation step (III) \rightarrow (IV) exist.⁶



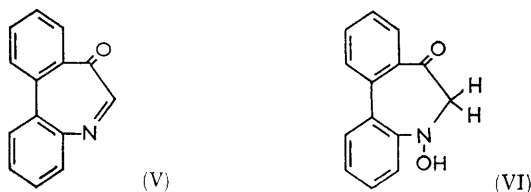
⁴ N. D. Cheronis, "Technique of Organic Chemistry," ed. A. Weissberger, Interscience, New York, vol. VI, 1954, p. 227.

⁵ E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, 1959, **10**, 209; A. H. Blatt and N. Gross, *J. Org. Chem.*, 1964, **29**, 3306.

⁶ P. L. Julian, E. W. Meyer, A. Magnani, and W. Cole, *J. Amer. Chem. Soc.*, 1945, **67**, 1203.

One would expect that if the crucial cause of this dimerisation were the readiness of the monomer to ionise as indicated, the reaction should be wholly or partly suppressed by (a) steric effects hindering attack at the double bond, (b) electron-donating groups *ortho* and *para* to the nitrogen atom, (c) use of weaker bases, and (d) replacement of the α -hydrogen atom by alkyl or aryl groups. We have not yet examined factor (b) and have failed to discover a weaker base that was effective. The *p*-nitrobenzaldehyde anil obtained³ by the elimination reaction was shown to be a monomer; whether this is a manifestation of a steric or electronic effect cannot be decided without examination of other examples. Finally, factor (d) was tested thus: the sulphonamide (I; R = H, R' = Ph) reacted with sodium methoxide giving a product (II; R = H, R' = Ph) as a crystalline monomer in reasonable yield. The monomer could also be obtained directly from desylaniline by treatment with manganese dioxide.

While this work was in progress, Negishi and Day⁷ reported that, when using the same elimination reaction, they had encountered the same dimerisation. The model synthesis of the anil (II; R = H, R' = Ph) illustrates how the dimerisation can be avoided in synthetic problems employing the elimination reaction. The original successful prepar-



ation of the azatropone (V) monomer⁸ was presumably made possible by its enhanced stability due to electron delocalisation; indeed, the addition of water⁸ to (V) [yielding the hydroxy-ketone (VI)] has to be explained by assuming that the normal polarisation of the C=N bond is reversed, and consequently the Michael reaction is less likely to occur.

EXPERIMENTAL

*Phenacyl-p-toluidine.*⁹—This substance had m. p. 127° (Found: C, 79.65; H, 6.5; N, 6.1. Calc. for C₁₅H₁₅NO: C, 80.0; H, 6.7; N, 6.25%). The 2,4-dinitrophenylhydrazone crystallised from methanol in red needles, m. p. 207—208° (Found: N, 16.95. C₂₁H₁₉N₅O₄ requires N, 16.7%). The *N*-toluene-*p*-sulphonyl derivative formed needles, m. p. 133° (from methanol) (Found: C, 69.3; H, 5.6; N, 3.5. C₂₂H₂₁NO₃ requires C, 69.65; H, 5.6; N, 3.7%). ν_{\max} (Nujol) 1689 (C=O), 1333 and 1247 cm.⁻¹ (N·SO₂).

Treatment of N-Phenacyl-N-toluene-p-sulphonyl-p-toluidine with Sodium Methoxide.—A nitrogen-saturated solution of *N*-phenacyl-*N*-toluene-*p*-sulphonyl-*p*-toluidine (740 mg.) in dry toluene (50 ml.) was added to a nitrogen-saturated suspension of sodium methoxide (110 mg.) in dry toluene (50 ml.). After 24 hr. at 20°, the mixture was poured into ice-water (100 ml.). The organic layer was extracted with ether (100 ml.) and dried. The product (390 mg.), obtained on evaporation of the solvent, crystallised from methanol in bright yellow needles, m. p. 217—218° [Found: C, 80.35; H, 5.75; N, 6.05%; *M* (mass spectrum), 446. C₃₀H₂₆N₂O₂ requires C, 80.7; H, 5.85; N, 6.25%; *M*, 446], ν_{\max} (KCl disc) 3333 (N-H), 1658 cm.⁻¹ (C=O). The n.m.r. spectrum in deuteropyridine showed a singlet at 7.72 τ (area 6), a broad peak around 5.2 τ (area 1), and a multiplet at 2—3.2 τ (area 19). The substance smelled strongly of carbylamine.

Treatment of the "Anil Dimer" with Palladised Charcoal.—The previous product, m. p. 217—218°, (III; R = Me) was dissolved in ethanol (100 ml.) and shaken with palladised charcoal (10%; 50 mg.) at 20° for 12 hr. The filtrate gave a product (IV; R = Me) (85 mg.) which crystallised from methanol in yellow needles, m. p. 208—209° [Found: C, 80.75; H, 5.7; N, 6.2%; *M* (mass spectrum), 444, (osmometry in benzene) 453 \pm 6. C₃₀H₂₄N₂O₂ requires

⁷ E. Negishi and A. R. Day, *J. Org. Chem.*, 1965, **30**, 43.

⁸ W. Paterson and G. R. Proctor, *J.*, 1962, 3468.

⁹ A. Bischler, *Ber.*, 1892, **25**, 2860.

C, 81.0; H, 5.45; N, 6.3%; *M*, 444], ν_{\max} . (Nujol) 1669 (C=O), 1634 cm^{-1} (C=N). The n.m.r. showed a singlet at 7.7 τ (area 6) and a multiplet at 2—3.3 τ (area 18). This substance did not smell of carbylamine.

Treatment of the "Anil Dimer" with Hydrogen in the Presence of Palladised Charcoal.—The "anil dimer" (III; R = Me) (200 mg.) in ethanol (100 ml.) was hydrogenated at atmospheric pressure in presence of palladised charcoal (10%; 100 mg.). After removal of the solvent, the crude product (170 mg.) was chromatographed on silica (M.F.C.). Elution with benzene gave a *product* (130 mg.) which crystallised from light petroleum (b. p. 80—100°) in needles, m. p. 162° [Found: C, 83.3; H, 6.0; N, 6.6%; *M* (osmometry in benzene), 422 ± 6 . $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}$ requires C, 83.7; H, 6.1; N, 6.5%; *M*, 430], ν_{\max} . (Nujol) 3400 (N-H) and 1235 cm^{-1} (C-O-C). N.m.r., singlet at 7.75 τ (area 6), a broad peak at 5.22 τ (area 2), and a multiplet at 2—3.6 τ (area 18).

*Phenacyl-*p*-bromoaniline.*—*p*-Bromoaniline (34.4 g.) was dissolved in ethanol (50 ml.) and phenacyl bromide (19.3 g.) added at once. The mixture was mechanically stirred for 1 hr. at 20—25°, kept at 0° for 3 hr., and rapidly filtered. The residue (21 g.) was washed with cold ethanol; it crystallised from methanol in *prisms*, m. p. 168° (Found: C, 58.15; H, 4.15; N, 4.7. $\text{C}_{14}\text{H}_{12}\text{BrNO}$ requires C, 57.8; H, 4.15; N, 4.8%), ν_{\max} . (Nujol) 3378 (NH) and 1678 cm^{-1} (CO). The 2,4-dinitrophenylhydrazone crystallised from methanol, m. p. 222—223° (Found: N, 15.1. $\text{C}_{20}\text{H}_{16}\text{BrN}_5\text{O}_4$ requires N, 15.25%).

*N-Toluene-*p*-sulphonyl derivative* crystallised from light petroleum (b. p. 80—100°) as needles, m. p. 123° (Found: C, 56.6; H, 3.85; N, 3.1. $\text{C}_{21}\text{H}_{18}\text{BrNO}_3\text{S}$ requires C, 56.7; H, 4.05; N, 3.15%), ν_{\max} . (Nujol) 1689 (CO), 1342 and 1224 ($\text{N}\cdot\text{SO}_2$).

*Treatment of N-Phenacyl-N-toluene-*p*-sulphonyl-*p*-bromoaniline with Sodium Methoxide.*—To a nitrogen-saturated solution of *N*-phenacyl-*N*-toluene-*p*-sulphonyl-*p*-bromoaniline (850 mg.) in dry toluene (50 ml.) was added a nitrogen-saturated suspension of sodium methoxide (100 mg.) in dry toluene (50 ml.). After 20 hr. at 20° the mixture was poured into ice-water (50 ml.). The organic layer was separated, dried, and evaporated, leaving the *product* (570 mg.), which crystallised from acetone-methanol in orange-yellow needles, m. p. 228—229° (Found: C, 58.55; H, 3.35; N, 4.70. $\text{C}_{28}\text{H}_{20}\text{Br}_2\text{N}_2\text{O}_2$ requires C, 58.35; H, 3.45; N, 4.85%), ν_{\max} . (KCl disc) 3333 (NH) and 1653 cm^{-1} (CO). The substance smelled of carbylamine.

*Treatment of Desylaniline with Toluene-*p*-sulphonyl Chloride.*—Desylaniline¹⁰ (2.72 g.) was dissolved in dry pyridine (10 ml.), toluene-*p*-sulphonyl chloride (2.1 g.) was added, and the mixture warmed on a steam-bath for 30 min. Excess pyridine was distilled off under reduced pressure and the residue poured into ice-cold dilute hydrochloric acid. It was then extracted with chloroform. The chloroform extract was repeatedly washed with sodium carbonate solution followed by water. After drying and removal of solvent, a yellow gum (3.5 g.) was obtained. Thin-layer chromatography revealed the presence of at least three substances. Chromatography on silica (M.F.C.), with light petroleum (b. p. 60—80°) as eluent, afforded toluene-*p*-sulphonyl chloride (15 mg.), m. p. and mixed m. p. 68—70°.

Elution with light petroleum (b. p. 60—80°)-benzene (1:1) gave a yellow substance (II; R = H, R' = Ph) (1.6 g.) which crystallised from methanol in yellow cubes, m. p. 103—106° [Found: C, 84.35; H, 5.5; N, 4.9%; *M* (mass spectrum), 285. Calc. for $\text{C}_{20}\text{H}_{15}\text{NO}$: C, 84.5; H, 5.6; N, 4.9%; *M*, 285], ν_{\max} . (Nujol) 1667 (CO), 1592 cm^{-1} (C=N). The n.m.r. spectrum showed only a multiplet at 2—3.2 τ . On further elution with benzene, a colourless *substance* (I; R = H, R' = Ph) (1.1 g.) was obtained. It crystallised from methanol in needles, m. p. 132—133° (Found: C, 73.2; H, 5.5; N, 3.1. $\text{C}_{27}\text{H}_{22}\text{NO}_2\text{S}$ requires C, 73.45; H, 5.25; N, 3.2%), ν_{\max} . (Nujol) 1684 (CO), 1340 and 1156 cm^{-1} ($\text{N}\cdot\text{SO}_2$). The n.m.r. spectrum showed a singlet at 7.62 τ (area 3) and a multiplet at 2—3.2 τ (area 20).

*Treatment of N-Toluene-*p*-sulphonyl Derivatives of Desylaniline with Sodium Methoxide.*—A nitrogen-saturated solution of desyl-*N*-toluene-*p*-sulphonylaniline (450 mg.) in dry toluene (50 ml.) was added to a nitrogen-saturated suspension of sodium methoxide (120 mg.) in dry toluene (50 ml.). After 15 hr. at 20°, the mixture was poured into ice-water (50 ml.) and worked up in the usual manner. The product (II; R = H, R' = Ph) crystallised from methanol in yellow cubes, m. p. and mixed m. p. 103—105° with the material described above (superimposable spectra). Julian *et al.*⁸ report m. p. 103—106° for desylaniline monoanil. The 2,4-dinitrophenylhydrazone crystallised from methanol in needles, m. p. 186—187° (Found: N, 14.3; $\text{C}_{26}\text{H}_{16}\text{N}_5\text{O}_4$ requires N, 14.55%).

¹⁰ D. S. James and P. E. Fanta, *J. Org. Chem.*, 1962, **27**, 3346.

Alternative Preparation of Desyl N-toluene-p-sulphonylaniline.—Desyl bromide¹¹ (m. p. 55°) (2.75 g.), *N*-toluene-*p*-sulphonylaniline (2.5 g.), and anhydrous potassium carbonate (1 g.) were refluxed for 22 hr. in dry acetone (100 ml.). The mixture was diluted with water and the organic matter extracted with chloroform, washed with sodium hydroxide solution (5%; 25-ml. portions), and finally with water, and dried. The residue (3.25 g.), obtained on evaporation of solvent, crystallised from methanol in needles, m. p. and mixed m. p. 132—133° with the material described previously (I; R = H, R' = Ph).

Treatment of Desylaniline with Manganese Dioxide.—Desylaniline (300 mg.), dry benzene (100 ml.), and freshly prepared manganese dioxide^{12,13} (105 mg.) were refluxed with a Dean and Stark apparatus for 6 hr. After filtration and removal of solvent, a yellow solid (230 mg.) was obtained which crystallised from methanol in yellow cubes, m. p. and mixed m. p. with desylaniline monoanil 103—106°.

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¹¹ G. Schroeter, *Ber.*, 1909, **42**, 2336.

¹² J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, and T. Walker, *J.*, 1952, 1094.

¹³ E. F. Pratt and T. P. McGovern, *J. Org. Chem.*, 1964, **29**, 1540.
