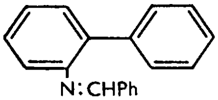
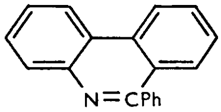
# 227. *Anils. Part I. Syntheses of* 9-*Phenylphenanthridine.*

By C. A. Bartram, D. Harrison, and (the late) W. F. Short.

2-Benzylideneaminodiphenyl is converted into 9-phenylphenanthridine by stannic chloride in boiling *o*-dichlorobenzene or less rapidly in chlorobenzene. Phosphorus pentachloride in 1 : 2 : 4-trichlorobenzene is also a good cyclising agent, but aluminium chloride in tetrachloroethane, and phosphoryl chloride in nitrobenzene, are less effective. Rough rate measurements on the phosphorus pentachloride and stannic chloride reactions have been made, and possible reaction mechanisms are discussed. 2-Benzylaminodiphenyl with stannic chloride in boiling chlorobenzene also gave 9-phenylphenanthridine.

The successful application [1] of the Bischler–Napieralski reaction to the synthesis of phenanthridines from 2-acylaminodiphenyls prompted us to investigate the possible extension of the Pictet–Spengler reaction to the synthesis of phenanthridines from 2-arylideneaminodiphenyls. Whilst our work was in progress, Whaley and White [2] failed to cyclise 2-aminodiphenyl by means of formaldehyde, and from 2-benzylideneamino-3′ : 4′-di- and -3′ : 4 : 4′ : 5-tetra-methoxydiphenyl with hydrogen chloride in various solvents recovered only 2-aminodiphenyl hydrochloride; these anils yielded tars on treatment with phosphoric oxide. However, Wildman and Norton,[3] by keeping 4-*m*-methoxyphenyl-5-methyleneamino*cyclo*hexene overnight with 6N-hydrochloric acid, obtained 1 : 4 : 4*a* : 9 : 10 : 10*a*-hexahydro-6-methoxyphenanthridine in 64% yield.

(I)




(II)

The present paper describes the conversion of 2-benzylideneaminodiphenyl (I) into 9-phenylphenanthridine (II) by various reagents.[4] Experiments using other anils will

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[1] Morgan and Walls, *J.*, 1931, 2447.
[2] Whaley and White, *J. Org. Chem.*, 1953, **18**, 184.
[3] Wildman and Norton, *J. Amer. Chem. Soc.*, 1954, **76**, 152.
[4] Cf. B.P. Appl. 36,203/1953.

be described later. Phosphorus pentachloride in boiling 1 : 2 : 4-trichlorobenzene gave good yields of the phenanthridine (II) (cf. Table 1). A plot of these results indicates a first-order reaction ($k_1 \simeq 0{\cdot}17$ hr.$^{-1}$), which is consistent with rapid reaction to form an intermediate which undergoes slow cyclisation, but absence of accurate temperature control prevents further kinetic considerations. No phenanthridine was isolated from a reaction in chlorobenzene, suggesting that cyclisation of the intermediate is very slow at the boiling point of this solvent. However, hydrogen chloride was evolved rapidly and from the residue after steam-distillation 2-benzamidodiphenyl was obtained in 18% yield: since imidoyl chlorides are easily hydrolysed to amides, the intermediate may be *N*-2-diphenylylbenzimidoyl chloride. Further work on the action of phosphorus pentachloride on simple anils (*e.g.*, benzylideneaniline) is planned in order to clarify this point.

TABLE 1.

| Time (hr.) | 1 | 2 | 4 | 6 | 7·3 |
|---|---|---|---|---|---|
| Yield (as picrate; %) | 24·4 | 33·4 | 45·4 | 64·0 | 73·6 |

The anil (I) with stannic chloride in boiling *o*-dichlorobenzene gave the phenanthridine (II) in 72·4% yield after only 30 min. Longer heating had little effect on the yield (*e.g.*, 75·5% after 3 hr.), equilibrium apparently being attained. The method is very convenient for preparative purposes, but may have limitations with other anils. Addition of stannic chloride to the solution of the anil produced a change in colour, possibly due to complex formation; benzylideneaniline and stannic chloride give a yellow compound [5] $2CHPh{:}NPh,SnCl_4$.

Cyclisation by means of stannic chloride in chlorobenzene is rather slow for preparative use, but was studied in more detail in the hope of obtaining information about the mechanism of the reaction (cf. Table 2). The reaction follows a first-order law ($k_1$ ~0·34 hr.$^{-1}$) for only the first 4 hr. and extrapolation of the appropriate plot indicates an induction period of *ca.* 30 min. during which presumably there is no cyclisation; the end of the induction period coincides roughly with the beginning of evolution of hydrogen chloride and separation of stannous chloride. This suggests that cyclisation requires the presence of a certain concentration of hydrogen chloride, normally produced by very slow reaction between the anil and stannic chloride. Table 2 shows how saturation of the chlorobenzene with hydrogen chloride reduces the induction period; and the value of $k_1$ for the first-order process occurring during the first 2 hr. is almost the same as in the absence of added hydrogen chloride. We conclude that the same species is being cyclised in each case, and a possible scheme is that illustrated.

TABLE 2. *Yields of* 9-*phenylphenanthridine picrate obtained* (*a*) *in* PhCl *and* (*b*) *in* PhCl *saturated with* HCl.

| Time (hr.) | | 0·25 | 0·5 | 1·0 | 2·0 | 3·0 | 4·0 | 6·0 | 12·0 |
|---|---|---|---|---|---|---|---|---|---|
| Yield (%) | (*a*) | — | 0·4 | 12·7 | 39·9 | 56·0 | 65·1 | 68·0 | 72·0 |
| | (*b*) | 9·6 | 24·1 | 33·4 | 52·0 | 61·0 | 66·4 | — | 74·9 |

$$\text{(I)} + \text{SnCl}_4 \xrightarrow{\text{Fast}} \text{Complex} + \text{HCl} \xrightarrow{\text{Slow}} \text{9 : 10-Dihydro-compound (III)} \xrightarrow{\text{Oxidn.}} \text{(II)}$$

9 : 10-Dihydro-9-phenylphenanthridine (III) was obtained by reduction of 9-phenylphenanthridine with lithium aluminium hydride in tetrahydrofuran. It formed a picrate as deep red needles which became plae yellow on exposure to air or heat. The picrate of 9 : 10-dihydrophenanthridine behaved similarly.[6] 9 : 10-Dihydro-9-phenylphenanthridine with the anil (I) in boiling tetrachloroethane gave the phenanthridine (II) and 2-benzylaminodiphenyl. Hence, although other observations (see below) suggest that the compound (III) is a probable intermediate in the cyclisation, it is not isolated because it is unstable under the conditions used.

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[5] Hieber and Sonnekalb, *Annalen*, 1927, **456**, 104.

[6] Bates and Cymerman-Craig, *J.*, 1954, 1153.

In the cyclisation experiments both with 4 and with 12 hours' heating, appreciable amounts of 2-aminodiphenyl and 2-benzylaminodiphenyl were isolated. The origin of the primary amine is not clear since appreciable hydrolysis of the anil, under the alkaline conditions employed in working up the reaction mixture, is not to be expected.[7] The 2-benzylaminodiphenyl would be accounted for if the oxidation step is effected partly by stannic chloride and partly by unchanged anil, which would thereby be reduced to the secondary amine. The approximate agreement with a first-order law during the early stages of the reaction suggests that conversion of the complex into the phenanthridine [probably *via* the dihydro-compound (III)] is initially the only important process, but that other reactions later supervene as 2-benzylaminodiphenyl, etc., accumulate. The present reaction is clearly more complex than that with phosphorus pentachloride.

2-Benzylaminodiphenyl with stannic chloride in boiling chlorobenzene also gave the phenanthridine (II) (cf. Table 3). First-order plots are not linear even in the early stages, and the reaction is much slower than for the anil under the same conditions. Further, hydrogen chloride decreases the rate of formation of phenanthridine. A possible explanation is that, at least in the early stages, the reaction rate measured is the oxidation of secondary amine to anil by stannic chloride: $\mathrm{R{\cdot}NH{\cdot}CH_2Ph + SnCl_4 \rightleftharpoons R{\cdot}N{:}CH{\cdot}Ph + SnCl_2 + 2HCl}$; hydrogen chloride should promote the reverse reaction, and hence hinder the formation of phenanthridine. Such equilibria may add a further complication to the mechanism of cyclisation of the anil discussed above.

TABLE 3. *Conversion of* 2-*benzylaminodiphenyl into* 9-*phenylphenanthridine by* $\mathrm{SnCl_4}$ *in* (*a*) PhCl *and* (*b*) PhCl *saturated with* HCl.

| Time (hr.) | 0·25 | 0·5 | 1·0 | 2·0 | 4·0 | 6·0 | 8·0 | 12·0 |
|---|---|---|---|---|---|---|---|---|
| Yield (as picrate; %) ......(*a*) | 5·1 | 8·5 | 17·5 | 23·2 | 31·0 | 34·4 | — | 46·7 |
| (*b*) | — | 5·9 | 9·8 | 17·6 | 21·2 | — | 33·1 | — |

The anil (I) with aluminium chloride in boiling tetrachloroethane gave only moderate yields (<50%) of the phenanthridine (II), probably owing to the absence of an oxidising agent. The 9 : 10-dihydro-compound formed as the initial product of cyclisation is converted into phenanthridine by unchanged anil; only half the anil would then be available for cyclisation. Similarly, phosphoryl chloride in 1 : 2 : 4-trichlorobenzene gave only very small yields of phenanthridine; use of nitrobenzene as solvent caused some improvement, perhaps owing to its oxidising properties or to formation of a complex with phosphoryl chloride; however, even under very vigorous conditions the yields were not as good as those obtained by using phosphorus pentachloride or stannic chloride.

## EXPERIMENTAL

2-*Benzylideneaminodiphenyl*.—2-Aminodiphenyl (60 g., 1 mol.) and benzaldehyde (37·6 g., 1 mol.) were heated under reflux in glacial acetic acid (90 c.c.) for 30 min. and the solvent was then removed at *ca.* 100 mm. Distillation of the residue afforded 2-*benzylideneaminodiphenyl* as a pale yellow viscous oil (63·9 g., 70%), b. p. 154—157°/0·1—0·2 mm. (Found: N, 5·4. $\mathrm{C_{19}H_{15}N}$ requires N, 5·45%). The yellow *styphnate* had m. p. 148—150° (Found: N, 11·3. $\mathrm{C_{25}H_{18}O_8N_4}$ requires N, 11·5%).

2-*Benzylaminodiphenyl*.—2-Aminodiphenyl (67·6 g., 4 mol.) and sodium hydrogen carbonate (20·1 g., 1·25 mol.) in water (20 c.c.) were stirred and heated under reflux whilst benzyl chloride (24·3 g., 1 mol.) was added during 2 hr. The mixture was stirred overnight, cooled, and extracted with ether. The ether extract was washed with 10% sodium chloride solution, then dried ($\mathrm{MgSO_4}$), and the ether removed. Distillation of the residue under reduced pressure and crystallisation of the product from methanol furnished prisms of 2-*benzylaminodiphenyl* (15·1 g., 47%), m. p. 89—91° (Found: C, 87·7; H, 6·6; N, 5·7. $\mathrm{C_{19}H_{17}N}$ requires C, 88·0; H, 6·55; N, 5·45%).

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[7] Willi and Robertson, *Canad. J. Chem.*, 1953, **31**, 365

*Cyclisation of* 2-*Benzylideneaminodiphenyl*.—(a) *By phosphoryl chloride and nitrobenzene.* The anil (5·14 g., 1 mol.) in nitrobenzene (52 c.c.) was heated under reflux with phosphoryl chloride (3·07 g., 1 mol.) for 6 hr., hydrogen chloride being evolved. The dark brown mixture was evaporated under reduced pressure and the residue steam-distilled in the presence of dilute sulphuric acid (25 c.c.). The residue was made alkaline with 5N-sodium hydroxide, and the oily solid collected. A solution of it in acetone (25 c.c.) was treated with picric acid (5·18 g., 1 mol.) in acetone (25 c.c.). The 9-phenylphenanthridine picrate (4·58 g., 54%), m. p. 247—249°, which separated was collected, washed with acetone (2 × 5 c.c.), and dried *in vacuo*. Cymerman and Short [8] give m. p. 246—247°. The crude picrate was decomposed by warming it with a slight excess of an aqueous solution of lithium hydroxide. The cooled mixture was extracted with chloroform. The chloroform solution was washed with water, dried ($MgSO_4$), and evaporated, leaving 9-phenylphenanthridine (2·65 g., 51%), m. p. 102—104°. Crystallisation from light petroleum (b. p. 80—100°) raised the m. p. to 104—106°. Morgan and Walls [1] and Cymerman and Short [8] give m. p. 105—106°.

The m. p.s of the phenanthridine and its picrate, where not quoted below, were identical with those above. The volume of solvent used in all cyclisation experiments was 10 c.c. per g. of anil or amine.

(b) *By phosphoryl chloride and* 1 : 2 : 4-*trichlorobenzene.* The anil (1 mol.) was boiled in 1 : 2 : 4-trichlorobenzene with phosphoryl chloride (1 mol.) for 6 hr., then worked up as above. The yield of picrate was 1·8%.

(c) *By aluminium chloride and tetrachloroethane.* The anil (1 mol.) in tetrachloroethane was boiled with aluminium chloride (1 mol.) for 6 hr. The green solution was evaporated under reduced pressure and the residue steam-distilled, first in the presence of 5N-sulphuric acid (25 c.c.), and then in alkaline solution. The residue was cooled, and the solid collected and dissolved in acetone. The acetone solution gave a picrate (48·5%) from which the phenanthridine (45·0%) was regenerated as in (a). The filtrate from the picrate was evaporated, and the residue treated with warm aqueous lithium hydroxide. The mixture was extracted with chloroform, and the chloroform solution washed with water, dried ($MgSO_4$), and evaporated. Distillation of the residue gave an oil (32·6%), b. p. 172°/0·3 mm., which, crystallised from methanol, gave 2-benzylaminodiphenyl, m. p. and mixed m. p. 89—91°.

(d) *By phosphorus pentachloride and chlorobenzene.* The anil (10·0 g., 1 mol.) in chlorobenzene was boiled with phosphorus pentachloride (9·7 g., 1·2 mol.) for 2 hr. Evolution of hydrogen chloride was vigorous at first, but ceased after 30 min. The mixture was evaporated under reduced pressure and the residue steam-distilled first in an acid, and then in an alkaline medium. The residual liquor was extracted with chloroform, the extract washed with water, and dried ($MgSO_4$), and the chloroform removed. The residual oil was distilled giving fractions (1), b. p. 125—150°/2—2·5 mm., and (2), b. p. 225—230°/2—2·5 mm. Fraction (1) was redistilled twice, giving a colourless oil (2·4 g.), b. p. 120—125°/1—1·5 mm. (Found: Cl, 4·1; N, 7·8%), which was not investigated further. Fraction (2), when redistilled (1·9 g.; b. p. 225—228°/1 mm.), solidified. Crystallisation from light petroleum (b. p. 60—80°) gave needles of 2-benzamidodiphenyl, m. p. and mixed m. p. 87—88°.

(e) *By phosphorus pentachloride and* 1 : 2 : 4-*trichlorobenzene.* The anil (1 mol.) in 1 : 2 : 4-trichlorobenzene was boiled with phosphorus pentachloride (1·2 mol.) for 6 hr. The mixture was evaporated under reduced pressure and the residue warmed on the steam-bath with 5N-sodium hydroxide for 10 min., then cooled and extracted with chloroform. The extract was washed with water, dried ($MgSO_4$), and evaporated. The residue in acetone was converted into the picrate (64%), decomposition of which gave the phenanthridine (62·4%).

(f) *By stannic chloride and* o-*dichlorobenzene.* The anil (1 mol.) in *o*-dichlorobenzene was boiled with anhydrous stannic chloride (2 mol.) for 15 min. As soon as boiling began, the colour changed from yellow to dark green, and stannous chloride separated. The mixture was warmed with an excess of 40% sodium hydroxide solution for 10 min., then kept at room temperature for a further hour. Extraction with chloroform, evaporation, and treatment of the residue in acetone with picric acid (1 mol.) in acetone gave the picrate (68·0%).

(g) *By stannic chloride and chlorobenzene.* The anil (1 mol.) in chlorobenzene was boiled with anhydrous stannic chloride (2 mol.) for 4½ hr. After 30 min. the mixture became dark green, and stannous chloride began to separate. The mixture, treated as in (f), gave the

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[8] Cymerman and Short, *J.*, 1949, 703.

picrate (66·3%) which was decomposed to the phenanthridine (64·9%). In experiments with heating for 4·5 and 12 hr. the filtrates from the picrate were treated as in (c). Distillation, under reduced pressure, of the residues from the chloroform extracts yielded 2-aminodiphenyl (identified as the acetyl derivative) and 2-benzylaminodiphenyl (identified by mixed m. p. with an authentic specimen). The yields of these products after respectively 4½ and 12 hr. were 2-aminodiphenyl 6·6, 8·5, 2-benzylaminodiphenyl 17·9, 10·6, and 9-phenylphenanthridine 66·3, 72·0% (total recovery: 90·8; 91·1%).

(h) *By stannic chloride, chlorobenzene, and hydrogen chloride.* The anil (1 mol.) in chlorobenzene saturated with anhydrous hydrogen chloride was boiled under reflux with anhydrous stannic chloride (2 mol.) for 0·25—12 hr. By-products isolated after 4 and 12 hr. respectively, as described above, were: 2-aminodiphenyl 9·2, 4·2, 2-benzylaminodiphenyl 16·5, 13·6, and 9-phenylphenanthridine 66·4, 74·9% (total recovery: 92·1, 92·8%).

*Cyclisation of 2-Benzylaminodiphenyl.*—(*a*) 2-Benzylaminodiphenyl (1 mol.) in chlorobenzene was boiled under reflux with stannic chloride (2 mol.) for 0·25—12 hr. Isolation of 9-phenylphenanthridine picrate and treatment of the filtrate were as for the corresponding cyclisation of the anil. Yields of by-products after respectively 4 and 12 hr. were: 2-aminodiphenyl 5·6, 8·0, 2-benzylaminodiphenyl 55·0, 38·0, and 9-phenylphenanthridine 30·0, 46·7% (total recovery: 90·6, 92·7%).

(*b*) 2-Benzylaminodiphenyl (1 mol.) in chlorobenzene saturated with hydrogen chloride was boiled under reflux with stannic chloride (2 mol.) for 0·5—8 hr. The mixtures were treated as before.

9 : 10-*Dihydro*-9-*phenylphenanthridine.*—A suspension of lithium aluminium hydride (0·64 g., 0·8 mol.) in tetrahydrofuran (100 c.c.) was stirred and boiled under reflux. 9-Phenylphenanthridine (5·1 g., 1 mol.) in tetrahydrofuran (100 c.c.) was added during 30 min. and the heating continued for a further 24 hr. The excess of lithium aluminium hydride was destroyed by water, and the mixture poured into excess of sodium hydroxide solution and extracted with ether. The ethereal solution, which had a blue fluorescence, was dried ($MgSO_4$) and evaporated. The residual straw-coloured oil was triturated with light petroleum (b. p. 60—80°) and the nearly colourless prisms (3·62 g.), m. p. 107—111°, were collected and dried *in vacuo*. Crystallisation from ethanol gave 9 : 10-*dihydro*-9-*phenylphenanthridine* (2·92 g., 57%), m. p. 114—115° (Found: C, 88·6; H, 5·9; N, 5·7. $C_{19}H_{15}N$ requires C, 88·7; H, 5·8; N, 5·45%). The *acetyl derivative* separated from aqueous ethanol as needles, m. p. 138—139° (Found: N, 4·9. $C_{21}H_{17}ON$ requires N, 4·7%).

*Reaction of the Dihydrophenanthridine with 2-Benzylideneaminodiphenyl.*—9 : 10-Dihydro-9-phenylphenanthridine (2·0 g.) and 2-benzylideneaminodiphenyl (2·0 g.) in tetrachloroethane were boiled under reflux for 2½ hr. The mixture was evaporated under reduced pressure and the residue taken up in acetone (30 c.c.). With picric acid (3·6 g.) in acetone (20 c.c.) it yielded 9-phenylphenanthridine picrate (3·33 g.). Regeneration of the base with lithium hydroxide gave the phenanthridine (1·0 g.). Treatment of the filtrate from the picrate preparation as in the cyclisation experiments gave 2-benzylaminodiphenyl, m. p. and mixed m. p. 88—90°.

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RESEARCH LABORATORIES, MESSRS. BOOTS PURE DRUG CO. LTD.,
NOTTINGHAM.
NOTTINGHAM & DISTRICT TECHNICAL COLLEGE.

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