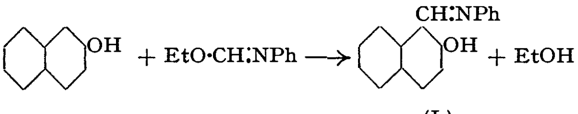
185. *Reactions of Alkyl*iso*formanilides. Part III. With Phenols.*

By Edward B. Knott.

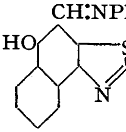
Ethyl*iso*formanilide will react with polycyclic phenols containing a free, active *o*- or *p*-position to form hydroxyanils. Phenol does not react, but various substituted monocyclic phenols showed slight activity. The reagent may be formed *in situ* by using mixtures of ethyl orthoformate and aniline or diphenylformamidine. Replacement of the aniline by other aromatic amines leads to analogues. The reaction may be used as a qualitative test for reactive phenols since all the anils are highly coloured.

In Parts I and II (*J.*, 1945, 686; *J.*, 1946, 120) of this series the activity of alkyl*iso*formanilides towards substances containing reactive or ionisable hydrogen has been described. It was of interest to determine the reactivity of these reagents towards polycyclic phenols, since the latter contain both ionisable and reactive hydrogen atoms.

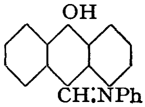
Although phenol did not react with ethyl*iso*formanilide at temperatures up to 220°, the naphthols showed considerable reactivity even in boiling ethanol, and particularly at temperatures above 100°. The product from β-naphthol, an intensely yellow compound, was homogeneous, and was 2-hydroxy-1-naphthaldehyde anil (I). The orange solid from α-naphthol appeared to be a mixture of anils. The naphthols function therefore like substances containing a reactive methyl or methylene group, and the reaction is not dissimilar to the coupling with diazonium salts. A variety of phenols were then heated with the reagent, the formation of colour being taken as an indication of reaction. Amongst the monocyclic phenols, the cresols and polyhydroxybenzenes all gave yellow colours but no products were isolated. Polycyclic phenols with active *o*- or *p*-positions gave colours varying from yellow to red. Substances of this type not containing an active hydrogen in the *o*- or *p*-position, such as 1-bromo-2-naphthol,



(I.)



(II.)



(III.)

8-hydroxyquinoline, 4′-hydroxy-2 : 3′-dimethylnaphtha-1′ : 2′ : 4 : 5-thiazole, or 2-acetyl-1-naphthol, did not give any colour. Two other anils were isolated, *viz.*, 4′-*hydroxy*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole*-3′-*aldehyde anil* (II) and 9-*hydroxy*-10-*anthraldehyde anil* (III). The latter gave an intense red solution in aqueous sodium hydroxide. Its solution in acetic acid developed a similar intense red colour on the addition of concentrated hydrochloric acid, the colour fading rapidly as hydrolysis to the aldehyde occurred. The aldehyde differed in m. p. from that given in F.P. 648,069 for the product obtained from 9-hydroxyanthracene formomethylanilide and phosphorus oxychloride; but since in no case was reaction observed where both *o*- and *p*-positions were blocked, it is most likely that the aldehyde group in the present substance was introduced into the 10-position. Somewhat lower yields of anil may be obtained by the formation of the reagent *in situ*. This can be achieved (cf. Claisen, *Annalen*, 1895, **287**, 365) by fusing the phenol with mixtures of aniline or diphenylformamidine and ethyl orthoformate. Other aromatic amines may replace the aniline to give analogues.

Substance.	Colour.
Phenol	None
m-Cresol	Yellow
o- and *p*-Cresol	Faint yellow
Resorcinol	Yellow
Adrenalin	Red
o-Hydroxybenzylideneacetone	Yellow
2 : 5-Dihydroxydiphenyl	Orange-yellow
β-Naphthol	Yellow
a-Naphthol	Orange
1 : 5-Dihydroxynaphthalene	,,
1-Bromo-2-hydroxy-naphthalene	None
1-Hydroxy-2-acetylnaphthalene	,,
1-Hydroxy-4-phenylnaphthalene	Yellow
1-Hydroxy-4-furylnaphthalene-3-carboxylic acid	,,
9-Hydroxyanthracene	Orange-red
4-Hydroxy-7-phenylcoumarone-6-carboxylic acid	Yellow
8-Hydroxyquinoline	None
2-Amino-6-hydroxypyridine sulphate	Orange
Aesculin	,,
2-Hydroxy-3 : 4-benzfluorene	Red
4′-Hydroxy-2-methylnaphtha-1′ : 2′ : 4 : 5-thiazole	Orange-red
2-Acetamido-4′-hydroxynaphtha-1′ : 2′ : 4 : 5-selenazole	Red
4′-Hydroxy-2 : 3′-dimethylnaphtha-1′ : 2′ : 4 : 5-thiazole	None
4′-Hydroxy-2-methylphenanthra-1′ : 2′ : 4 : 5-thiazole	Red
1′-Hydroxy-2-methylphenanthra-4′ : 3′ : 4 : 5-thiazole	,,
4′-Hydroxy-2-methylthionaphtheno-7′ : 6′ : 4 : 5-thiazole	Orange

The reaction may be used as a sensitive test for many phenols since the reaction products are highly coloured. The table indicates the colours obtained on boiling a small quantity of the phenol with an excess of reagent in a test-tube over a free flame.

EXPERIMENTAL.

(Microanalyses are by Drs. Weiler and Strauss, Oxford; m. p.'s uncorrected.)

2-*Hydroxy*-1-*naphthaldehyde Anil* (I).—(a) *β*-Naphthol (14·4 g.; 0·1 mol.) and ethyl*iso*formanilide (14·9 g.; 0·1 mol.) were fused at 160° for 30 minutes, by which time the evolution of ethyl alcohol had ceased. Methyl alcohol (5 c.c.) was added to the melt. The yellow solid (17·0 g., 81%) crystallised as glossy needles, m. p. 92°, with an intense green fluorescence to ultra-violet light, when the methyl alcoholic solution was chilled, or shiny plates, m. p. 92°, with no fluorescence in ultra-violet light, if the same solution were allowed to cool (Found: C, 82·3; H, 5·4; N, 5·75. Calc. for $C_{17}H_{13}ON$: C, 82·55; H, 5·3; N, 5·65%).

(b) β-Naphthol (2·88 g.; 0·02 mol.), diphenylformamidine (2·92 g.; 0·02 mol.), and ethyl orthoformate (2·96 g.; 0·02 mol.) were fused at 150° for 60 minutes. After cooling, light petroleum was added and the whole shaken until the melt had solidified. From methyl alcohol (10 c.c.), 2·25 g. (46%) of the anil were obtained. If the ethyl orthoformate is omitted a yellow colour develops but the yield of anil is very low.

2-*Hydroxy*-1-*naphthaldehyde* p-*Methoxyanil*.—β-Naphthol (5·96 g.; 0·04 mol.), ethyl orthoformate (5·92 g.; 0·04 mol.), and *p*-anisidine (4·92 g.; 0·04 mol.) were fused at 145° for 60 minutes. The melt gave a crystalline *solid* on addition of methyl alcohol. From the same solvent it formed bright yellow needles, m. p. 111°, in 65% yield (Found: N, 5·1. $C_{18}H_{15}O_2N$ requires N, 5·05%).

9-*Hydroxy*-10-*anthraldehyde Anil* (III).—9-Hydroxyanthracene (3·84 g.; 0·02 mol.) and ethyl*iso*formanilide (3 g.; 0·02 mol.) were fused at 180° for 60 minutes. Ethyl alcohol (10 c.c.) was added to the red melt, and the orange-red crystalline *solid* (4·9 g., 82·5%) was collected and washed with alcohol. It formed garnet red crystals, m. p. 204°, from acetic acid (Found: N, 4·95. $C_{21}H_{15}ON$ requires N, 4·7%). 9-*Hydroxyanthracene*-10-*aldehyde*. The anil (2 g.) was dissolved in boiling acetic acid (20 c.c.), and concentrated hydrochloric acid (4 c.c.) added. The intense red colour so formed slowly faded as the *aldehyde* crystallised. It formed flat, creamy needles, m. p. 230° onwards, from benzene (Found: C, 81·3; H, 4·4. $C_{15}H_{10}O_2$ requires C, 81·05; H, 4·55%).

4′-*Hydroxy*-2-*methylnaphtha*-1′ : 2′ : 4 : 5-*thiazole*-3′-*aldehyde Anil* (II).—4′-Hydroxy-2-methylnaphtha-1′ : 2′ : 4 : 5-thiazole (10·75 g.; 0·05 mol.) and ethyl*iso*formanilide (14·9 g.; 0·1 mol.) were fused at 170° for 60 minutes. On cooling, the orange melt solidified. It was ground with alcohol and well washed with the same solvent. It formed orange needles (13·2 g. = 86% yield), m. p. 228°, from benzene (Found: N, 8·5; S, 9·8. $C_{19}H_{14}ON_2S$ requires N, 8·8; S, 9·75%). The *aldehyde* was obtained by dissolving the anil (2 g.) in dioxan (30 c.c.), adding concentrated hydrochloric acid (10 c.c.) and water (10 c.c.), and heating for 30 minutes on the steam-bath. The solid was dissolved in an excess of 2N-sodium carbonate, filtered from a little unhydrolysed anil, and the yellow solution acidified. From ethyl alcohol it formed yellow-green needles, m. p. 160° (Found: S, 13·1. $C_{13}H_9O_2NS$ requires S, 13·2%).

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