

CXXV.—6-*Aminocoumarin*.

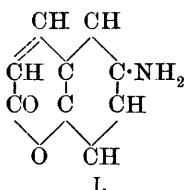
By GILBERT THOMAS MORGAN and FRANCES MARY GORE MICKLETHWAIT.

THE greater reactivity towards diazonium compounds exhibited by the amines of the naphthalene series when compared with the benzenoid bases is intimately connected with the existence in their molecules of two unsaturated cyclic systems, for when the unsubstituted ring is completely hydrogenated, the tetrahydronaphthalene bases thus produced are found to be endowed with the properties of the amines of the benzene series.

Tetrahydro- $\beta$ -naphthylamine, in its interaction with nitrous acid or diazonium salts, behaves as an analogue of *p*-toluidine (C. Smith, *Trans.*, 1902, 81, 900), and although tetrahydro- $\alpha$ -naphthylamine still retains the naphthalenoid character of yielding azo-derivatives without the intermediate formation of diazo-amines (Bamberger and Bordt,

*Ber.*, 1889, **22**, 625), yet its para-substituted derivatives behave in this respect exactly like the corresponding compounds of aniline (Morgan, Micklethwait, and Winfield, this vol., p. 739).

Comparative experiments have now been made on 6-aminocoumarin \*



(Frapolli and Chiozza, *Annalen*, 1855, **95**, 252) with the view of ascertaining whether the presence of the unsaturated lactonic ring would, as in the case of the unsaturated hydrocarbon ring in the naphthalene compounds, bring about any increase in the reactivity of the amine towards diazonium salts.

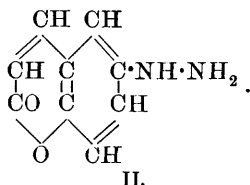
6-Aminocoumarin, when treated with nitrous acid, yields a very sparingly soluble compound which undergoes fission on treatment with concentrated mineral acids into a mixture of the salts of the original base and its diazonium compound. Diazonium salts, such as *p*-nitrobenzenediazonium chloride, furnish similar diazo-amines, and hence the base behaves in this respect like any other para-substituted benzenoid amine, the presence of the lactonic ring having no apparent influence on the course of the foregoing changes.

In carrying out these experiments, the singular colour of 6-aminocoumarin and its derivatives attracted attention, and the investigation was extended in order to ascertain whether any connection could be traced between the colour of these coumarin derivatives and their chemical nature.

Although derived from coumarin, a colourless lactone, 6-aminocoumarin, is a bright yellow compound and retains its colour after repeated crystallisations. Its salts with the mineral acids are, however, colourless, and so are its acyl derivatives containing formyl, acetyl, lactyl, benzoyl, and benzenesulphonyl groups. The quaternary methobromide and methiodide, obtained by completely methylating the base, are likewise devoid of colour, as are also its diazonium salts, the acyl derivatives, and salts of its hydrazine and monoalkylated derivatives, the nitrosoamines of the latter bases, and the salts of the tertiary base, dimethyl-6-aminocoumarin.

\* The constitution of this base follows from the synthesis of 6-nitrocoumarin from 5-nitrosalicylaldehyde and the oxidation of the nitro-compound to 5-nitrosalicylic acid (Taegge, *Ber.*, 1887, **20**, 2109), additional evidence being furnished by the synthesis of 6-aminocoumarin itself by the electrolytic reduction of *m*-nitrocinnamic acid (Gattermann, *Ber.*, 1894, **27**, 1937).

On the other hand, the mono- and di-alkylated 6-aminocoumarins are distinctly coloured like the parent substance, and 6-coumarylhydrazine,



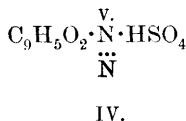
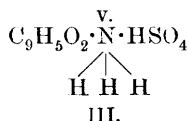
obtained by the partial reduction of the colourless diazonium salts, is also distinctly yellow.

*Benzylidene-6-aminocoumarin* occupies an intermediate position between the free base and its acyl derivatives, for, although it is distinctly coloured, the shade of yellow is much paler than that of the original base.

In short, all the bases of this series are coloured, whilst their salts and acyl derivatives are colourless. The appearance of colour in this group of substances seems to depend on the presence in the molecule of the free basic radicles,  $\text{NH}_2$ ,  $\text{NHR}$ , or  $\text{NR}_2$ , for when the basic character of these groups is destroyed by the substitution of one hydrogen by an acyl radicle or by the formation of a salt, then the colour disappears. As, however, the amino-derivatives of benzene are in general colourless substances, the development of colour in this particular case is probably due to some mutual interaction of the amino-group and the unsaturated coumarin residue. It is hardly likely that the group  $\text{CH}:\text{CH}$  in the latter complex participates in the production of this effect, otherwise it might be expected that the naphthylamines would be coloured owing to the presence in their molecules of an unsaturated ring containing, at least potentially, two of these ethylenic groups. It is probably the residue  $-\text{CO}\cdot\text{O}-$  acting in conjunction with the amino-group which brings about this appearance of colour.

The lactonic oxygen is in the para-position with respect to the amino-group, and, with this orientation, the unsaturated groups  $-\text{O}\cdot\text{CO}-$  and  $\text{NH}_2$  ( $\text{NHR}$  or  $\text{NR}_2$ ) are especially likely to exercise some action on each other in virtue of their residual affinities, but although these considerations suggest a probable rearrangement of the valencies in the molecule of the compound, the exact nature of this alteration can scarcely be rigidly formulated until further experimental data are available. The colour effect in the case of the 6-aminocoumarin can, however, scarcely be due to any migration of its aminic hydrogen atoms, inasmuch as these phenomena are not appreciably modified by the replacement of both hydrogens by alkyl groups, as in the case of *dimethyl-6-aminocoumarin*.

In this connection, the colour relationship of the diazo-derivatives is of interest. According to the prevailing view, a diazonium salt is regarded as containing pentadic nitrogen as in formula IV, and the fact that colourless 6-aminocoumarin sulphate gives rise to a colourless diazonium salt supports the hypothesis that the two compounds have a similar configuration :



On the contrary, the unstable diazocyanide derived from the latter substance is yellow, and probably contains only tervalent nitrogen.

#### EXPERIMENTAL.

Coumarin (100 grams) was dissolved in 120 c.c. of glacial acetic acid and treated with a mixture of 56 c.c. of nitric acid of sp. gr. 1.5 and 40 c.c. of glacial acetic acid ; no appreciable rise of temperature was observed, but, on adding 100 c.c. of concentrated sulphuric acid, a vigorous reaction took place ; the mixture was therefore cooled at first, and finally heated for a short time on the water-bath. A portion of the nitrocoumarin crystallised, and the remainder was precipitated by pouring the acid mother liquor into ice-water. The first product, when recrystallised from benzene, separates as a mass of white, prismatic crystals melting at 181—182° ; Taege, *loc. cit.*, gives 185°.

The nitro-compound (2 parts) was suspended in 50 parts of hot water acidified with 1 part of concentrated hydrochloric acid, and reduced by the gradual addition of 4 parts of iron filings ; the mixture was finally heated on the sand-bath, rendered alkaline with sodium hydrogen carbonate, and rapidly filtered at the pump. The filtrate, on cooling, yielded 1.2—1.4 parts of 6-aminocoumarin, which separated from the solution in long, yellow needles. A portion of the base was crystallised once from alcohol, and then thrice from benzene ; it then had the form of clear, straw-yellow needles melting at 163—164°. Frapolli and Chiozza give the melting point as 168—170°, whilst Taege and Gattermann found it to be 161° and 168° respectively.

The salts of 6-aminocoumarin are well-defined, crystalline, colourless substances soluble in water, the hydrochloride dissolves only sparingly in alcohol, whilst the sulphate may be precipitated in colourless crystals from glacial acetic acid.

*Formyl-6-aminocoumarin*,  $\text{C}_9\text{H}_5\text{O}_2 \cdot \text{NH} \cdot \text{COH}$ , prepared in the usual

way, crystallised from water in colourless crystals melting at  $175-176^\circ$ :  $N = 7.59$ ;  $C_{10}H_7O_3N$  requires  $N = 7.40$  per cent.

*Lactyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot NH \cdot CO \cdot CH(OH) \cdot CH_3$ , gradually separated on warming a saturated solution of the base in lactic acid; the precipitation was completed by diluting the mixture with aqueous ammonia; the substance, when recrystallised from hot water, separated as a felted mass of colourless, silky needles melting at  $159-160^\circ$ :  $N = 5.95$ ;  $C_{12}H_{11}O_4N$  requires  $N = 6.00$  per cent.

*Benzenesulphonyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot NH \cdot SO_2 \cdot C_6H_5$ , was prepared from the base and benzenesulphonic chloride by the Schotten-Baumann method, using sodium carbonate instead of sodium hydroxide; it crystallises from water or benzene in colourless crystals melting at  $159^\circ$ :  $N = 4.02$ ;  $C_{15}H_{11}O_4NS$  requires  $N = 4.38$  per cent.

The foregoing acyl derivatives and the acetyl and benzoyl compounds described by Gattermann (*loc. cit.*) are all colourless substances.

*Benzylidene-6-aminocoumarin*,  $C_9H_5O_2 \cdot N : CH \cdot C_6H_5$ , produced by the condensation of its generators in glacial acetic acid solution, crystallised from benzene in pale yellow, flattened needles melting at  $150-152^\circ$ :  $C = 77.18$ ;  $H = 4.11$ ;  $C_{16}H_{11}O_2N$  requires  $C = 77.11$ ;  $H = 4.41$  per cent.

## I. The Diazo-reactions of 6-Aminocoumarin.

### 1. Action of Diazo-compounds on 6-Aminocoumarin.

*6:6'-Diazouminocoumarin*,  $C_9H_5O_2 \cdot N_2 \cdot NH \cdot C_9H_5O_2$ , produced by diazotising 1 molecular proportion of 6-aminocoumarin and adding the solution to an equal amount of the base dissolved in alcohol, separated at once as a brownish-yellow precipitate (m. p.  $230-234^\circ$ ), which was too sparingly soluble in the ordinary organic solvents to admit of recrystallisation:  $N = 12.47$ ;  $C_{18}H_{11}O_4N_3$  requires  $N = 12.61$  per cent. The diazo-amine dissolved in alcoholic potash to a green solution, and, when treated with cold concentrated solutions of the mineral acids, underwent the characteristic fission of a diazo-amine, yielding 6-aminocoumarin and the corresponding diazonium base; the solution, when diluted and filtered into an alkaline solution of  $\beta$ -naphthol, gave *coumarin-6-azo- $\beta$ -naphthol*,  $C_9H_5O_2 \cdot N_2 \cdot C_{10}H_6 \cdot OH$ , a substance which was also produced by the direct action of diazotised coumarin on the  $\beta$ -naphthol. This azo-compound, unlike the azo- $\beta$ -naphthols derived from aniline and its homologues, is somewhat soluble in aqueous alkali hydroxides; it crystallises from glacial acetic acid in well-defined, brownish-red needles melting at  $222^\circ$ :  $C = 72.83$ ;  $H = 3.91$ ;  $N = 8.59$ ;  $C_{19}H_{12}O_3N$  requires  $C = 72.15$ ;  $H = 3.80$ ;  $N = 8.86$  per cent.

*p-Nitrobenzenediazo-6-aminocoumarin*,  $NO_2 \cdot C_6H_4 \cdot N_2 \cdot NH \cdot C_9H_5O_2$ , prepared from *p*-nitrobenzenediazonium chloride and 6-aminocoumarin

in alcoholic solution, is very sparingly soluble in the ordinary organic media: a small portion dissolved in ethyl acetate or acetone separated in yellow crystals, which decomposed violently at  $218-225^{\circ}$  when slowly heated, but remained unchanged until  $230^{\circ}$  when immersed in the warm melting point bath:  $N=17.38$ ;  $C_{15}H_{10}O_4N_4$  requires 18.06 per cent. With alcoholic potash, this substance gives the magenta coloration characteristic of all diazo-amines derived from *p*-nitroaniline, but, on warming, the solution assumes a deep bluish-purple colour. This unsymmetrical diazo-amine, when decomposed by cold concentrated acid and poured on to ice, yielded a solution containing the diazonium salts of *p*-nitroaniline and 6-aminocoumarin; these substances, when coupled with  $\beta$ -naphthol in aqueous sodium hydroxide, gave rise to two azo-compounds, coumarin-6-azo- $\beta$ -naphthol, which remained dissolved in the alkali hydroxide, and *p*-nitrobenzeneazo- $\beta$ -naphthol, which was precipitated; the latter was crystallised from ethyl acetate and identified by its melting point ( $249^{\circ}$ ).

## 2. *Diazo-derivatives of 6-Aminocoumarin.*

The diazonium salts of 6-aminocoumarin are readily prepared by the ordinary process of diazotisation, and are fairly stable compounds yielding colourless solutions in water, alcohol, or glacial acetic acid. The authors have already employed solutions of the diazonium chloride in a comparative study of the action of diazo-compounds on the amines of the naphthalene and tetrahydronaphthalene series (this vol., pp. 750, 751).

*Coumarin-6-diazonium sulphate*,  $C_9H_5 \cdot O_2 \cdot N_2 \cdot HSO_4$ , was isolated in the solid form by dissolving 6-aminocoumarin in glacial acetic acid, precipitating the sulphate by the addition of 1 molecular proportion of concentrated sulphuric acid, and adding to the cooled mixture an excess of amyl nitrite, stirring vigorously until the insoluble sulphate had redissolved, and pouring the filtered solution into a mixture of ether and alcohol. The diazonium sulphate separated in colourless crystals, which became brown on exposure to the atmosphere; it was washed with ether and light petroleum and dried on a porous tile:  $S=12.04$ ;  $C_9H_5O_6N_2S$  requires  $S=11.85$  per cent. The diazonium salt underwent no further change on keeping, and after several days retained the property of coupling with  $\beta$ -naphthol-3:6-disulphonic acid ("R salt") in alkaline solution; it may therefore be regarded as an exceptionally stable example of its class.

*Coumarin diazocyanides*.—The preceding compound was extremely soluble in cold water, and its solution, when treated with aqueous potassium cyanide, yielded a voluminous, bright yellow precipitate

which rapidly assumed a green tinge before it could be separated from the mother liquor. Neither the yellow substance nor the green product formed an azo-compound with  $\beta$ -naphthol or "R salt."

### 3. 6-Coumarylhydrazine, $C_9H_5O_2 \cdot NH \cdot NH_2$ .

This primary hydrazine was obtained by diazotising 6-aminocoumarin (1 part) in cold concentrated hydrochloric acid with 20 per cent. aqueous sodium nitrite, and treating the product with excess of stannous chloride (4 parts) dissolved in 6 parts of concentrated hydrochloric acid diluted with an equal volume of water. A precipitate, which formed at first, redissolved, but after 12 hours the solution again became turbid; the precipitate was collected and cautiously treated with a saturated solution of sodium carbonate until it just gave an alkaline reaction with turmeric paper; the yellow product was then drained at the pump, the total yield being about 3.5 grams from 12 grams of the 6-aminocoumarin. The hydrazine crystallises from benzene, water, or the alcohols in canary-yellow needles melting at  $165-167^\circ$ , but the hydroxylic solvents seem to decompose it slightly; it is therefore preferably purified from benzene, the crystallisation being accelerated by the addition of light petroleum: C = 61.92; H = 4.98; N = 16.18;  $C_9H_5O_2N_2$  requires C = 61.36; H = 4.55; N = 15.90 per cent. The substance has the properties of a primary aromatic hydrazine; it readily reduces Fehling's solution, even in the cold, and when boiled with aqueous copper sulphate it loses the hydrazino-radicle and regenerates coumarin. The latter result is of interest, because it indicates that the unsaturated lactonic ring has not been affected by the changes involved in preparing this hydrazine from coumarin.

With pyruvic acid, the hydrazine gives a sparingly soluble, yellow hydrazone: the *benzylidene* compound,  $C_9H_5O_2 \cdot NH \cdot N : CH \cdot C_6H_5$ , separates from a glacial acetic acid solution of its generators, its formation being attended by an appreciable rise of temperature; it crystallises from benzene in aggregates of bright yellow needles melting indefinitely at  $190-194^\circ$ . When suspended in water and treated in the cold with acetic anhydride, the hydrazine yielded a colourless acetyl derivative melting at  $163^\circ$ : N = 12.44;  $C_{11}H_{10}O_3N$  requires N = 12.84 per cent. Repeated crystallisation of this acetylated compound seems to decompose it, a yellow solution being obtained having the odour of coumarin. The aqueous solution of the hydrazine salts of the mineral acids are also colourless.

## II. Alkylated 6-Aminocoumarins.

6-Coumaryltrimethylammonium bromide,  $C_9H_5O_2 \cdot N(CH_3)_3Br$ , was obtained in brown needles when 6-aminocoumarin hydrobromide was heated with excess of methyl alcohol in sealed tubes at  $160^\circ$ . After removal of the methyl alcohol on the water-bath, the crystalline residue was crystallised either from water, in which it was readily soluble, or from absolute alcohol, in which it dissolved only sparingly. The quaternary bromide separated from the latter solvent in colourless needles melting at  $229^\circ$ :  $Br = 27.97$ ;  $C_{12}H_{14}O_2NBr$  requires  $28.16$  per cent.

6-Coumaryltrimethylammonium iodide,  $C_9H_5O_2 \cdot N(CH_3)_3I$ , was prepared by heating for half an hour in a reflux apparatus 6-aminocoumarin (1 mol.), methyl iodide (3 mols.), and potassium hydroxide (2 mols.); all dissolved in alcohol, the iodide being added gradually. The deposit obtained when crystallised from absolute alcohol separated in colourless needles melting and decomposing somewhat indefinitely at  $202\text{--}207^\circ$ :  $N = 4.43$ ;  $I = 38.18$ ;  $C_{12}H_{14}O_2NI$  requires  $N = 4.23$ ;  $I = 38.27$  per cent.

Dimethyl-6-aminocoumarin,  $C_9H_5O_2 \cdot N(CH_3)_2$ , was obtained from the quaternary bromide by treating the latter with precipitated silver oxide, evaporating the filtered solution on the water-bath, and finally heating at  $130^\circ$  for 3 hours. When cooled, the product became semi-crystalline, and on extraction with light petroleum yielded a small amount of orange-yellow, flattened needles, sometimes of considerable length; the base melts at  $85\text{--}86^\circ$ :  $C = 69.42$ ;  $H = 5.77$ ;  $C_{11}H_{11}O_2N$  requires  $C = 69.84$ ;  $H = 5.82$  per cent.

A slightly better yield of dimethyl-6-aminocoumarin was obtained by heating the methobromide at  $120^\circ$  and then adding a small amount of water; a vigorous evolution of gas takes place; the liquid product which became solid on cooling furnished the tertiary base on extraction with light petroleum (b. p.  $60\text{--}80^\circ$ ). When heated with an alcoholic solution of methyl iodide, dimethyl-6-aminocoumarin gave rise to the foregoing quaternary iodide (m. p.  $202\text{--}207^\circ$ ).

### Monoalkylated 6-Aminocoumarins.

The secondary methyl and ethyl bases were prepared by heating benzenesulphonyl-6-aminocoumarin (p. 1234) in alcoholic solution with molecular proportions of potassium hydroxide and the appropriate alkyl iodide, and hydrolysing the alkylated sulphonamide thus produced with concentrated hydrochloric acid in sealed tubes at  $150\text{--}170^\circ$ , the heating in each step of this preparation being continued for about 3 hours.



*Benzenesulphonylethyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot N(C_2H_5) \cdot SO_2 \cdot C_6H_5$ , was prepared in the manner indicated and isolated by distilling off the alcohol and diluting the residual solution with water; when crystallised from a mixture of benzene and light petroleum, it separated in colourless prisms melting at  $124^\circ$ .

*Ethyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot NH \cdot C_2H_5$ , was obtained by hydrolysing the preceding compound with 4 parts of concentrated hydrochloric acid and neutralising the product with ammonia; it crystallised from light petroleum in yellow leaflets or flattened needles melting at  $83^\circ$ : C=70.11; H=5.89; N=7.77;  $C_{11}H_{11}O_2N$  requires C=69.84; H=5.82; N=7.40 per cent.

*6-Coumarylethylnitrosoamine*,  $C_9H_5O_2 \cdot N(C_2H_5) \cdot NO$ , separated as an oil, which rapidly changed to a pale brown solid, on treating the acid solution of the preceding base with sodium nitrite (1 mol.); it crystallised from light petroleum ( $80-100^\circ$ ) in well-defined, colourless needles (m. p.  $90^\circ$ ) which became brown on exposure to air: N=12.71;  $C_{11}H_{10}O_3N_2$  requires N=12.84 per cent. When dissolved in cold concentrated sulphuric acid containing a trace of phenol, the nitrosoamine developed a blue coloration.

*Benzenesulphonylmethyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot N(CH_3) \cdot SO_2 \cdot C_6H_5$ , prepared exactly like its ethyl homologue, crystallised in short, colourless, refractive prisms and melted at  $165-167^\circ$ .

*Methyl-6-aminocoumarin*,  $C_9H_5O_2 \cdot NH \cdot CH_3$ , obtained in the manner previously described, crystallised from light petroleum (b. p.  $80-100^\circ$ ) in yellow needles melting at  $105-106^\circ$ : N=8.61;  $C_{10}H_9O_2N$  requires N=8.00 per cent.

*6-Coumarylmethylnitrosoamine*,  $C_9H_5O_2 \cdot N(CH_3) \cdot NO$ , crystallised from a mixture of benzene and light petroleum in well-defined, colourless needles melting at  $168-169^\circ$ , and was only very sparingly soluble in light petroleum; it gave intense colorations in all the phases of Liebermann's reaction.

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