The abnormal behaviour of glyoxaline-carboxlic esters and anilides towards diazonium salts / by Robert George Fargher and Frank Lee Pyman.

Contributors

Fargher, Robert George.
Pyman, Frank Lee.
Wellcome Chemical Research Laboratories.

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LXXXVII.—*The Abnormal Behaviour of Glyoxalinecarboxylic Esters and Anilides towards Diazonium Salts.*

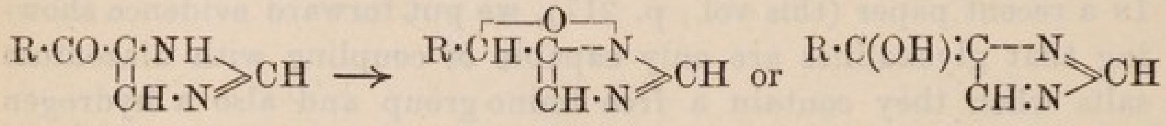
By Robert George Fargher and Frank Lee Pyman.

In a recent paper (this vol., p. 217), we put forward evidence showing that glyoxalines are only capable of coupling with diazonium salts when they contain a free imino-group and also a hydrogen atom or some other displaceable group, such as the carboxyl group, in one of the 2-, 4-, or 5-positions. Numerous derivatives of glyoxaline, in which these conditions are fulfilled, have been shown to couple with sodium diazobenzene-*p*-sulphonate in aqueous sodium carbonate, but an exceptional behaviour is shown by the esters of 5-methylglyoxaline-4-carboxylic acid (Gerngross, *Ber.*, 1912, **45**, 513) and the esters of glyoxaline-4-carboxylic acid (Pyman, T., 1916, **109**, 186). These give a negative result, whereas the corresponding acids behave normally, giving deep red solutions with the reagent.

With the object of finding some clue to this abnormality, we have examined the behaviour of a number of carboxylic acids containing the glyoxaline nucleus and their esters towards sodium diazobenzene-*p*-sulphonate in aqueous sodium carbonate. All the acids examined gave a positive result, and so also did the esters of those acids, such as glyoxalineacetic acid, in which the carbonyl group is separated from the glyoxaline nucleus by a chain of one or more carbon atoms. The esters of the 2-alkylglyoxaline-4-carboxylic acids, however, like those of glyoxaline-4-carboxylic acid and 5-methylglyoxaline-4-carboxylic acid, gave a negative result, and so also did the anilides of glyoxaline-4-carboxylic acid and its 2-alkyl derivatives. In order to ensure that the difference in behaviour was not due to the particular conditions selected for the test, the action of benzenediazonium chloride and *p*-nitrobenzenediazonium chloride on glyoxaline-4-carboxylic acid and ethyl glyoxaline-4-carboxylate was examined. In the presence of hydrochloric acid or acetic acid, neither of the derivatives coupled, whilst in the presence of sodium carbonate or sodium hydroxide the acid coupled but the ester did not.

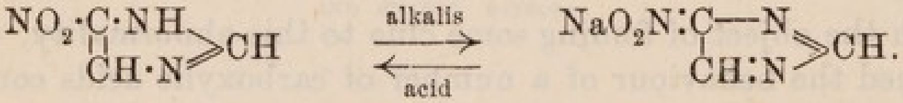
The abnormality is thus seen to be connected with the direct attachment of the carboxyalkyl or carboxyanilide group to the glyoxaline nucleus, and would seem to be due to the mutual influence of the imino- and carbonyl groups.

Further than this we do not as yet feel able to offer any explanation of the abnormality. The fact that all the glyoxalinecarboxylic esters and anilides behave normally towards silver nitrate in ammoniacal solution, yielding insoluble silver salts, rules out any formula such as (I) not containing a free iminic or acidic hydrogen atom, whilst their stability towards potassium permanganate in acid solution would appear to indicate that they exist as true glyoxalines in the presence of mineral acids.



(I.) (II.)

There is, however, the possibility of a molecular rearrangement, such as that represented by formula (II), taking place under the influence of alkalis. The nitroglyoxalines also fail to couple with diazonium salts, and here the explanation seems clear, since these compounds dissolve in alkalis with a yellow colour, yielding salts which are no doubt derived from the corresponding nitronic acids, as Windaus (*Ber.*, 1909, **44**, 758) has suggested, and no longer contain an imino-group.



The glyoxalinecarboxylic esters and anilides, however, yield colourless solutions with alkalis, and although, bearing in mind that the nitroglyoxalines themselves are colourless and their alkaline solutions only comparatively pale yellow, the lack of colour would alone seem insufficient to preclude a formula such as (II), we do not feel justified in advancing it as more than a possibility until further experimental evidence has been accumulated.

While seeking for comparable instances of the mutual influence of imino- and carbonyl groups, we have observed that whereas anthranilic acid couples with sodium diazobenzene-*p*-sulphonate or *p*-nitrobenzenediazonium chloride in sodium carbonate solution, ethyl anthranilate gives a negative result. Both, of course, couple in acid solution. Further, it is perhaps worth noting that whereas the hydrochloride of anthranilic acid is stable in aqueous solution, the hydrochlorides of its methyl and ethyl esters are readily hydrolysed in cold aqueous solution with liberation of the free ester (compare Kolbe, *J. pr. Chem.*, 1884, [ii], **30**, 474; Fränkel and Spiro, *Ber.*, 1895, **28**, 1686; E. and H. Erdmann, *Ber.*, 1899, **32**, 1213), and whilst *s*-ethylenebisanthranilic acid dissolves readily in dilute mineral acids, the corresponding methyl ester is insoluble even in excess (Fränkel and Spiro, *loc. cit.*).

EXPERIMENTAL.

The esters described in this communication were prepared by boiling the acids with absolute alcohol saturated with hydrogen chloride. After removing the excess of alcohol and adding cold saturated aqueous potassium carbonate, the esters of the 2-alkylglyoxaline-4-carboxylic acids separated in a crystalline state. The other esters were extracted from the solutions by means of chloroform, and crystallised either as base or as hydrogen oxalate.

Ethyl 2-methylglyoxaline-4-carboxylate crystallises from ethyl acetate in clusters of fine, shimmering needles, which melt at 156° (corr.) and are anhydrous. It is sparingly soluble in water, but readily so in alcohol or ethyl acetate.

Found: C=54·3; H=6·7; N=17·9.

$C_7H_{10}O_2N_2$ (154·1) requires C=54·5; H=6·5; N=18·2 per cent.

The ester gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

2-*Ethylglyoxaline-4-carboxylic Acid and its Derivatives.*

2-*Ethylglyoxaline-4-carboxyanilide* is prepared from 2-ethylglyoxaline-4:5-dicarboxylic acid in a yield amounting to 45 per cent. of the theoretical by the general method described in a previous communication (this vol., p. 217). It is readily soluble in alcohol but very sparingly so even in boiling water, from which it crystallises in clusters of fine needles; these are anhydrous and melt at 193° (corr.), sintering from 190°. It gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found: C=66·6; H=5·8; N=19·2.

$C_{12}H_{13}ON_3$ (215·2) requires C=66·9; H=5·6; N=19·5 per cent.

2-*Ethylglyoxaline-4-carboxylic acid* is obtained in good yield by the hydrolysis of the corresponding anilide by dilute hydrochloric acid at 130°. It is readily soluble in hot water, but sparingly so in cold, and crystallises from the former in well-defined, prismatic needles which contain two molecules of water of crystallisation. After drying at 110°, it melts at 252° (corr.), sintering from 248°. It gives an immediate blood-red coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found, in air-dried acid: loss at 110°=20·7.

$C_6H_8O_2N_2,2H_2O$ requires 20·5 per cent.

In acid dried at 110°, C=51·3; H=5·7; N=19·9.

$C_6H_8O_2N_2$ (140·1) requires C=51·4; H=5·8; N=20·0 per cent.

The *picrate* crystallises from water in large, prismatic needles containing one and a-half molecules of water of crystallisation. After drying at 60° in a vacuum, it sinters above 170° and forms a turbid liquid, which becomes clear at about 195°.

Found, in air-dried salt, $H_2O=6·9$.

$C_6H_8O_2N_2,C_6H_3O_7N_3,1\frac{1}{2}H_2O$ requires 6·8 per cent.

In dried salt, N=18·7.

$C_6H_8O_2N_2,C_6H_3O_7N_3$ (369·2) requires N=19·0 per cent.

Ethyl 2-ethylglyoxaline-4-carboxylate crystallises from ethyl acetate, in which it is readily soluble, in prismatic needles which melt at 129° (corr.), and are anhydrous. It is readily soluble in alcohol, but sparingly so in water. It gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found: C=56·8; H=7·2; N=16·5.

$C_8H_{12}O_2N_2$ (168·2) requires C=57·1; H=7·2; N=16·6 per cent.

2-*Phenylglyoxaline-4-carboxylic Acid and its Derivatives.*

2-*Phenylglyoxaline-4-carboxyanilide* is prepared by the action of boiling aniline on 2-phenylglyoxaline-4:5-dicarboxylic acid in a yield amounting to 74 per cent. of the theoretical. As it is practically insoluble in boiling water, it is left behind after the steam distillation somewhat contaminated by resinous impurities, which are readily removed by grinding and washing with ice-cold alcohol. It is sparingly soluble in alcohol or the other usual organic solvents, and separates from alcohol in minute, glistening needles, which melt at 263° (corr.) and are anhydrous. It gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found: C=72·6; H=5·3; N=15·9.

$C_{16}H_{13}ON_3$ (263·2) requires C=73·0; H=5·0; N=16·0 per cent.

2-*Phenylglyoxaline-4-carboxylic acid* is obtained in good yield by the hydrolysis of the corresponding anilide, which, however, is much more stable towards acid hydrolysis than the 2-alkyl derivatives. At 130° the reaction proceeds very slowly, but at 145—150° the reaction is complete after eight to nine hours' heating. The acid separates from boiling water, in which it is fairly readily soluble, in fan-shaped clusters of minute needles containing one and a-half molecules of water of crystallisation. After drying at 110°, it melts and effervesces at 239° (corr.). The acid gives an immediate red coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found, in air-dried material: loss at 110° = 12·7.

$1\frac{1}{2}H_2O$ requires 12·6 per cent.

In substance dried at 110°, C = 63·5; H = 4·5; N = 14·8.

$C_{10}H_8O_2N_2$ (188·1) requires C = 63·8; H = 4·3; N = 14·9 per cent.

Ethyl 2-phenylglyoxaline-4-carboxylate crystallises from ethyl acetate in minute needles, which melt at 189° (corr.), sintering above 183°. It is readily soluble in alcohol or hot ethyl acetate, less readily so in cold ethyl acetate, and very sparingly so in water. It gives no coloration with sodium diazobenzene-*p*-sulphonate in sodium carbonate solution.

Found, in air-dried substance: loss at 100° = 9·5.

Found, in dried substance: C = 66·5; H = 5·7; N = 12·9.

$C_{12}H_{12}O_2N_2$ (216·1) requires C = 66·6; H = 5·6; N = 13·0 per cent.

Ethyl Glyoxaline-4-acetate.—This was prepared previously by the action of alcoholic hydrogen chloride on 4-cyanomethylglyoxaline (T., 1911, **99**, 681), and can also be obtained by the esterification of the corresponding acid or by the action of alcohol on the hydrochloride of glyoxaline-4-acetyl chloride. It gives a deep red colour when mixed with sodium diazobenzene-*p*-sulphonate in aqueous sodium carbonate.

Glyoxaline-4-acetyl chloride hydrochloride can be prepared in a crystalline state by the method given below. The crude product contains less than the theoretical amount of chlorine, and we have been unable to devise a satisfactory method of purifying it.

Five grams of phosphorous pentachloride and 6 c.c. of thionyl chloride were heated on the water-bath to incipient ebullition (about 50°), and 4 grams of glyoxaline-4-acetic acid hydrochloride were added, the mixture being well stirred. Evolution of hydrogen chloride took place, and the pasty mass quickly became crystalline, forming minute leaflets. When the reaction had ended, the mass was diluted with chloroform, filtered, washed with chloroform, and dried in a vacuum over sulphuric acid and sodium hydroxide. The dry, crystalline powder obtained in this way was pale pink and amounted to 4·4 grams, that is, 97·7 per cent. of the theoretical. The specimen with the highest chlorine content melted and decomposed at 127° (corr.), the others at 125°.

Found: C = 33·2; H = 3·5; Cl = 35·5, 35·1, 36·8 (in different specimens).

$C_5H_5ON_2Cl,HCl$ (181·0) requires C = 33·2; H = 3·3; Cl = 39·2 per cent.

Ethyl β-Glyoxaline-4-propionate.—This was purified by crystallisation of the hydrogen oxalate from alcohol. The ester formed an oil, which gave an immediate blood-red colour with sodium diazobenzene-*p*-sulphonate in aqueous sodium carbonate.

The *hydrogen oxalate* separates from alcohol in colourless, shimmering leaflets, which are anhydrous and melt at 160° (corr.) after sintering from 155°. It is readily soluble in water or hot alcohol, but sparingly so in cold alcohol.

Found: C=48·1; H=6·0; N=11·8.

$(C_8H_{12}O_2N_2)_4(C_2H_2O_4)_3$ (942·7) requires C=48·4; H=5·8; N=11·9 per cent.

Ethyl α-hydroxy-β-glyoxaline-4-propionate crystallises from dry chloroform in minute, colourless plates which melt at 118—119° (corr.), and are anhydrous. It is readily soluble in water or alcohol, sparingly so in chloroform, and insoluble in ether. It gives a cherry-red colour with sodium diazobenzene-*p*-sulphonate in aqueous sodium carbonate.

Found: C=52·3; H=6·5.

$C_8H_{12}O_3N_2$ (184·1) requires C=52·2; H=6·6 per cent.

WELLCOME CHEMICAL RESEARCH LABORATORIES,
LONDON, E.C. 1.

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