458. 1 : 1 : 1-*Trifluoro-2* : 3-*dione Dioximes and Related Compounds.*

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The direct bromination of ethyl trifluoromethyl ketone in sulphuric acid gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one. With bromine in sodium acetate–acetic acid each of these ketones gave 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one. This was converted by hydroxylamine into 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime, which showed unusual properties when treated with ammoniacal nickel solutions. Hydrolysis of the dioxime, or treatment of ethyl trifluoromethyl ketone with selenium dioxide, gave the diketone, isolated as the quinoxaline derivative. 3 : 3-Dibromo-1 : 1 : 1-trifluoroacetone and hydroxylamine gave the dioxime of 3 : 3 : 3-trifluoropyruvaldehyde; with semicarbazide, either the analogous disemicarbazone, or the semicarbazone of the parent ketone, was formed according to the conditions.

CERTAIN 1 : 2-dioximes are well known as analytical reagents for the determination of nickel and some other metal ions.[1] In connection with our studies of fluorine-containing compounds as possible analytical reagents, an investigation of dioximes possessing trifluoromethyl substituents was undertaken. No success was achieved in attempts to make a hydroxyimino-derivative from ethyl trifluoromethyl ketone, and so the desired dioximes were made by extensions of the work of McBee and Burton [2] who brominated 1 : 1 : 1-trifluoroacetone with bromine in concentrated sulphuric acid to give 3 : 3-dibromo-1 : 1 : 1-trifluoroacetone which, with semicarbazide, gave the disemicarbazone of 3 : 3 : 3-trifluoropyruvaldehyde, with loss of bromine. We found that, in the cold, the dibromo-ketone gave a monosemicarbazone in the usual way. The disemicarbazone of the keto-aldehyde was formed only at elevated temperatures. The dioxime was prepared similarly.

Ethyl trifluoromethyl ketone with bromine (0·5 mol.) in concentrated sulphuric acid gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one. In this reaction only half-molar quantities of bromine are necessary,[2] but 1 mol. of bromine under these conditions also gave only the monobromo-compound and no dibromide. However, the latter ketone, 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one, was prepared by direct bromination of ethyl trifluoromethyl ketone or of 3-bromo-1 : 1 : 1-trifluorobutan-2-one in sodium acetate–acetic acid.

α-Nitrato-ketones have been made [3] by the action of silver nitrate on solutions of α-bromo-ketones in dry acetonitrile, and aryl α-diketones have been prepared from them [4] by the action of a base. 3-Bromo-1 : 1 : 1-trifluorobutan-2-one reacted with silver nitrate in dry acetonitrile to give silver bromide in 92% yield, but the attempted isolation of the α-nitrato-ketone, and subsequent conversion into an α-diketone, failed. When treated with semicarbazide in the cold, 3-bromo-1 : 1 : 1-trifluorobutan-2-one gave a monosemicarbazone.

Treatment of 3 : 3-dibromo-1 : 1 : 1-trifluorobutan-2-one with hydroxylamine hydrochloride in sodium acetate solution gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime as a crude mixture, from which one form was isolated as a crystalline solid, m. p. 89°. This compound reacted with nickel ions in ammoniacal solution to give a drab green precipitate, which was virtually insoluble in carbon tetrachloride, chloroform, etc. Analysis of this precipitate gave poor results but indicated that it was a 1 : 1 compound of the dioxime with nickel. However, the oily residues remaining after the separation of this crystalline

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[1] (*a*) Tschugaeff, *Z. anorg. Chem.*, 1905, **46**, 144; (*b*) Diehl, "The Applications of the Dioximes to Analytical Chemistry," G. F. Smith Chemical Co., Colombus (Ohio), 1940.

[2] McBee and Burton, *J. Amer. Chem. Soc.*, 1952, **74**, 3902.

[3] Ferris, McLean, Marks, and Emmons, *ibid.*, 1953, **75**, 4078.

[4] Emmons and Freeman, *ibid.*, 1955, **77**, 4415.

dioxime reacted differently with nickel ions in ammonia solution, giving, as well as the green form, a bright red precipitate which could be extracted by chloroform and by carbon tetrachloride. Accordingly, the preparation of the dioxime was repeated, the crude product was treated with ammoniacal nickel sulphate solution and the red precipitate, which was formed simultaneously with the drab green one, was extracted into chloroform. Analysis of the red solid obtained from the chloroform extracts confirmed that this compound contained 2 molecules of dioxime and 1 atom of nickel and was thus analogous to the complexes formed by dimethylglyoxime and similar reagents.[1]

In an attempt to liberate the parent dioxime from the red nickel derivative, the complex was decomposed with hydrochloric acid. However, the dioxime which was isolated had m. p. and mixed m. p. 89° and reacted with an ammoniacal nickel solution to give only the drab green precipitate. The dioxime preparation was again repeated and a sample of the crude product treated with an ammoniacal nickel solution to demonstrate the formation of the two compounds. When the remainder of the crude dioxime was treated with hydrochloric acid, recovered by ether-extraction, and then treated with an ammoniacal nickel solution, only the green precipitate was formed. Thus, the form of the dioxime giving the red complex was unstable to acid, being converted into the crystalline form, m. p. 89°. Accordingly, the dioxime preparation was carried out in sodium carbonate solution, but it was possible to isolate only the same solid, m. p. 89°, although treatment of a sample of the crude product with nickel ions, in the usual way, gave both nickel compounds, thus showing that both forms of the dioxime were again present. As an alternative, an attempt was made to convert the dioxime, m. p. 89°, into the form which gave the red complex by digestion with 2N-ammonia (pH 12), but the organic compound was degraded and fluoride ion was found in the aqueous solution. Both the crystalline dioxime and the oily residues reacted with palladium ions in aqueous solution. The former gave a cream-coloured precipitate, insoluble in chloroform and in carbon tetrachloride, while the latter gave a golden-yellow one, soluble in these solvents. Though analyses of them were rather unsatisfactory, these compounds resembled those formed by nickel.

From aromatic 1 : 2-dioximes, such as benzil dioxime, three different stereochemical forms have been isolated and shown [5, 6] to react differently with nickel ions. The α(*anti*)-form gave a red (2 : 1) complex, the β(*syn*)-form gave no precipitate, and the γ(*amphi*)-form gave a yellow (1 : 1) compound. The green nickel derivative of the crystalline dioxime isolated in the present work resembles those from γ-dioximes.[5, 1b] In the formation of the compound between one molecule of dioxime and one atom of nickel the hydrogen atoms of both oxime groups are replaced by the metal, so that the resulting product is salt-like rather than a chelate compound, and this will account for its insolubility in organic solvents. So far as we can ascertain, known examples of aliphatic 1 : 2-dioximes react with nickel ions to give only the red (2 : 1) precipitates, although a transient yellow compound is first formed when a solution of dimethylglyoxime in acetone is added to a dilute and very weakly acidic solution of a nickel salt.[1b] The evidence therefore indicates that the dioxime, m. p. 89°, described here is unique, at least in the aliphatic series, in being a stable γ(*amphi*)-form. Since $R = Me$ and $R' = CF_3$, two such forms are possible, so that the compound might be a mixture. Since the crude dioxime also yields the red (2 : 1) nickel complex, the *anti*-form of the dioxime is presumably also present, though it appears to be less stable.

Hydrolysis of the crystalline dioxime with hydrochloric acid gave the parent diketone, which could not be isolated in a pure condition. The crude product was characterised, however, since with *o*-phenylenediamine, 2-methyl-3-trifluoromethylquinoxaline was formed. The oxidation of ethyl trifluoromethyl ketone with selenium dioxide was also studied. In aqueous solution, the reaction was slow, only half complete after 15 hr., as

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[5] Atack, *J.*, 1913, **103**, 1317.

[6] Tschugaeff, *Ber.*, 1908, **41**, 1678.

indicated by the recovery of selenium; about 40 hr. was required for the completion of the oxidation. The product was heterogeneous and contained selenium, probably as organic complexes, which have been obtained from other oxidations with selenium dioxide. Attempts to prepare a more tractable product by carrying out the reaction in ethyl alcohol or dioxan were not successful. The crude α-diketone gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime (m. p. 89°) when treated with hydroxylamine hydrochloride in sodium acetate solution, whilst treatment with *o*-phenylenediamine gave 2-methyl-3-trifluoromethylquinoxaline. It is probable that isolation of this diketone from these experiments was complicated by hydrate formation.

EXPERIMENTAL

Ethyl Trifluoromethyl Ketone.—Trifluoroacetic acid was treated with ethylmagnesium iodide by the method of Sykes, Tatlow, and Thomas [7] to give the desired ketone (52%), b. p. 45—45·5°.

Preparation of 3-*Bromo*-1 : 1 : 1-*trifluorobutan*-2-*one.*—Ethyl trifluoromethyl ketone (39·2 g.) and concentrated sulphuric acid (130 c.c.) were stirred at 15—20° whilst bromine (25·0 g.) was added slowly. The stirring was continued at 15—20° for 6 hr. and then at 60—70° for ½ hr., sulphur dioxide being collected in a trap cooled by solid carbon dioxide–ethyl alcohol. The mixture was cooled and the two layers were separated. Volatile components were distilled from the lower (acid) layer through a 1′ column packed with 4 mm. single-turn Fenske glass helices. The distillate was added to the upper layer, which was distilled (1′ column) to give a fraction (48·5 g.), b. p. 92·5—93·5°. This was shaken with silver powder and redistilled, to give 3-bromo-1 : 1 : 1-trifluorobutan-2-one (47·3 g.), b. p. 92·5—93·5°, n_D^{20} 1·3792 (Found : C, 23·2; H, 2·0. Calc. for $C_4H_4OBrF_3$: C, 23·4; H, 2·0%). This compound had a strong infrared absorption band at 1757 cm.$^{-1}$. It has been prepared also by Rausch, Lovelace, and Coleman.[10]

In a similar experiment, ethyl trifluoromethyl ketone (20·0 g.) was stirred with concentrated sulphuric acid (100 c.c.) at 15—20° while bromine (29·1 g.) was added slowly. The stirring was continued for 24 hr. at 15—20° and then for 15 min. at 60°. Separation and distillation of the two layers as described above gave 3-bromo-1 : 1 : 1-trifluorobutan-2-one (13·6 g.), b. p. 92—93°, n_D^{20} 1·3790. This sample was shown by analytical gas-liquid partition chromatography [8] to be identical with that described above.

The monobromo-ketone (1·45 g.) was added to a filtered solution of semicarbazide hydrochloride (0·90 g.) and sodium acetate trihydrate (1·35 g.) in water (8 c.c.). After 2 hr. at 0° the *semicarbazone* (1·02 g.) was filtered off and washed with a little cold water. It had m. p. 113—114° (Found : C, 22·55; H, 2·9. $C_5H_7ON_3BrF_3$ requires C, 22·9; H, 2·7%).

3 : 3-*Dibromo*-1 : 1 : 1-*trifluorobutan*-2-*one.*—3-Bromo-1 : 1 : 1-trifluorobutan-2-one (17·8 g.), fused sodium acetate (7·8 g.), and glacial acetic acid (65 c.c.) were stirred together at 15—20° while bromine (15·3 g.) was added slowly. The solution was stirred for 7 hr. and kept for 10 hr. at 15—20°, then filtered, and the filtrate was cooled in a cold-water bath and stirred while concentrated sulphuric acid (300 c.c.) was added. The lower layer was separated, washed with concentrated sulphuric acid (50 c.c.), and fractionated (1′ glass-packed column), to give 3 : 3-*dibromo*-1 : 1 : 1-*trifluorobutan*-2-*one* (15·2 g.), b. p. 124°, n_D^{22} 1·4302 (Found : C, 17·2; H, 1·4. $C_4H_3OBr_2F_3$ requires C, 16·9; H, 1·1%).

In an alternative preparation, ethyl trifluoromethyl ketone (33·0 g.), fused sodium acetate (45·1 g.), and glacial acetic acid (355 c.c.) were stirred at 15—20° while bromine (88·0 g.) was added during 45 min. The solution was stirred for 5 hr. and then kept for 65 hr. at 15—20°. It was decanted from the solid and treated with concentrated sulphuric acid (1200 c.c.) as described above. Separation and distillation of the lower layer gave the dibromo-ketone (40·1 g.), b. p. 124—125°.

1 : 1 : 1-*Trifluorobutane*-2 : 3-*dione Dioxime.*—3 : 3-Dibromo-1 : 1 : 1-trifluorobutan-2-one (8·30 g.) was heated for 3 hr. at 100° with hydroxylamine hydrochloride (9·5 g.) and sodium acetate trihydrate (19·0 g.) in water (60 c.c.). The solution was cooled and extracted thrice with ether. The extracts were dried ($MgSO_4$) and concentrated under diminished pressure. The residue (4·14 g.) was recrystallised from benzene, to give 1 : 1 : 1-*trifluorobutane*-2 : 3-*dione*

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[7] Sykes, Tatlow, and Thomas, *J.*, 1956, 835.

[8] Evans and Tatlow, *J.*, 1955, 1184.

dioxime (1·17 g.), m. p. 89·5—90·5° (Found: C, 28·2; H, 3·0; F, 33·5. $C_4H_5O_2N_2F_3$ requires C, 28·2; H, 3·0; F, 33·5%). The mother-liquors from the recrystallisation were concentrated and the residue distilled under diminished pressure, to give an oil (b. p. 74—76°/0·2 mm.). This solidified partly, giving after filtration and recrystallisation a further quantity of the dioxime (0·4 g.), m. p. and mixed m. p. 88·5—89·5°. A semi-solid (1·0 g.) and a viscous liquid (0·7 g.) were left.

The dibromo-ketone (5·67 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (5·5 g.) in 2M-sodium carbonate solution (30 c.c.). Extraction of the solution and treatment as described above gave the same dioxime (0·75 g.), m. p. and mixed m. p. 88·5—89·5°, and a viscous liquid (1·85 g.).

The dibromo-ketone was refluxed with hydroxylamine hydrochloride in methyl alcohol for 8 hr. The solution was diluted with water and extracted with ether. Concentration and distillation of the extracts gave only the dibromo-ketone (80%).

Reaction of 1 : 1 : 1-*Trifluorobutane*-2 : 3-*dione Dioxime with Nickel Ions in Ammoniacal Solutions.*—The crystalline dioxime (m. p. 89°) was dissolved in water and added to a solution of nickel sulphate (6·7 mg. per c.c.) in 0·67N-ammonia. The drab green *nickel derivative* was filtered off, washed with water, and dried at 100°. It was insoluble in carbon tetrachloride, chloroform, and other organic solvents. It was poorly defined and difficult to purify.

A known weight of the precipitate (about 0·065 g.) was digested with potassium sulphate (1·25 g.) and concentrated sulphuric acid (4·5 c.c.) in a Kjeldahl flask.[9] Hydrogen peroxide was added and the solution was boiled until colourless. The solution was diluted with water, and the nickel was precipitated with dimethylglyoxime in the usual way (Found: Ni, 24·4; 24·6. $C_4H_3O_2N_2F_3Ni$ requires Ni, 25·9%).

The semi-solid and viscous liquid products from the oximation described above, when similarly treated with ammoniacal nickel sulphate solution, gave a precipitate, part of which was extracted by chloroform to give a red solution, leaving a drab green precipitate suspended in the aqueous layer.

The dibromo-ketone (2·00 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (2·0 g.) and sodium acetate trihydrate (4·0 g.) in water (10 c.c.). Extraction and distillation in the usual way gave the crude mixed dioxime (1·1 g.). This was dissolved in water and added to an ammoniacal solution of nickel sulphate as described above, and the resulting mixture was extracted with chloroform.

The aqueous layer was acidified with dilute acetic acid and extracted with ether. Concentration of the extracts gave the dioxime (15%), m. p. and mixed m. p. 88—89°, which reacted with nickel ions in ammonia solution to give only the drab green precipitate.

The red chloroform solution was dried ($MgSO_4$) and concentrated, to leave a red *nickel derivative* (0·33 g., 24%) (Found: C, 24·5; H, 2·3; Ni, 14·8. $C_8H_8O_4N_4F_6Ni$ requires C, 24·2; H, 2·0; Ni, 14·8%).

Treatment of the red nickel complex (0·2 g.) with hydrochloric acid and extraction with ether in the usual way gave the dioxime (0·1 g.), m. p. and mixed m. p. 88·5—90·5°, which reacted with an ammoniacal nickel solution to give the drab green precipitate, no red complex being re-formed.

Treatment of the Crude Dioxime Mixture with Hydrochloric Acid.—The dibromo-ketone (1·4 g.) was converted into the crude mixed dioxime in the usual way, and a test sample was treated with ammoniacal nickel sulphate solution as described above. A mixture of the red complex, soluble in chloroform, and the green compound, insoluble in chloroform, was formed.

The crude dioxime was dissolved in hydrochloric acid, and the solution extracted with ether. The extracts afforded in the usual way the crystalline dioxime (0·19 g., 21%), m. p. and mixed m. p. 85—87°, which reacted with nickel ions to give the green compound. No red complex was formed.

Action of Ammonia Solution on the Dioxime.—The dioxime (0·62 g.; m. p. 89°) was heated at 100° for 3 hr. with 2N-ammonia (10 c.c.). Ether-extraction of the solution afforded an unidentified product (0·035 g.) which did not react with nickel ions. Acidification of the aqueous solution with acetic acid and treatment with cerous nitrate solution gave a copious precipitate of cerous fluoride.

Hydrolysis of 1 : 1 : 1-*Trifluorobutane*-2 : 3-*dione Dioxime.*—The dioxime was heated at 100°

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[9] Nyholm, *J.*, 1950, 2061.

[10] Rausch, Lovelace, and Coleman, *J. Org. Chem.*, 1956, **21**, 1328.

for 3 hr. with 5N-hydrochloric acid, and the resulting solution was extracted with ether. The extracts were dried ($MgSO_4$) and concentrated, to leave a residue which could not be purified but was refluxed for 1 hr. with *o*-phenylenediamine in ethyl alcohol. Water was added and the precipitate was filtered off and recrystallised from aqueous ethyl alcohol, to give *2-methyl-3-trifluoromethylquinoxaline*, m. p. 83—84° (Found : F, 26·6. $C_{10}H_7N_2F_3$ requires F, 26·9%).

Reaction of Ethyl Trifluoromethyl Ketone with Selenium Dioxide.—The ketone (10·9 g.) was heated at slightly below the b. p. for 15 hr. with selenium dioxide (12·0 g.) in water (30 c.c.). The aqueous solution was then distilled, to give ethyl trifluoromethyl ketone (4·3 g.) which gave a peak coincident with that from the authentic ketone in gas chromatography.[8] The selenium (3·47 g., 51%) was filtered off and the filtrate was extracted with ether. The extracts were dried ($MgSO_4$) and concentrated and distilled, to give a heterogeneous liquid, b. p. 60—120°.

Part of the distillate (1·0 g.) was heated at 100° for 3 hr. with hydroxylamine hydrochloride (1·1 g.) and sodium acetate trihydrate (2·2 g.) in water (6 c.c.). Ether-extraction and treatment in the usual way gave 1 : 1 : 1-trifluorobutane-2 : 3-dione dioxime (0·13 g.), m. p. and mixed m. p. 87—89°.

The remainder of the distillate, refluxed with *o*-phenylenediamine in ethyl alcohol, gave 2-methyl-3-trifluoromethylquinoxaline, m. p. and mixed m. p. 83—84° (Found : C, 56·9; H, 3·2. Calc. for $C_{10}H_7N_2F_3$: C, 56·6; H, 3·3%).

3 : 3-*Dibromo*-1 : 1 : 1-*trifluoroacetone*.—Trifluoroacetic acid with methylmagnesium iodide (method of Sykes, Tatlow, and Thomas[7]) gave 1 : 1 : 1-trifluoroacetone (57%), which was brominated by McBee and Burton's method[2] giving 3 : 3-dibromo-1 : 1 : 1-trifluoroacetone (61%), b. p. 113°, n_D^{16} 1·4335 (Found : C, 12·8; H, 0·4. Calc. for $C_3HOBr_2F_3$: C, 13·3; H, 0·4%). McBee and Burton[2] gave b. p. 113·3—113·4°/735·5 mm., n_D^{20} 1·4311.

The dibromo-ketone (2·05 g.) was heated at 100° for 1 hr. with semicarbazide hydrochloride (1·75 g.) and sodium acetate trihydrate (2·7 g.) in water (15 c.c.) and then cooled. The solid was filtered off and recrystallised from aqueous ethyl alcohol, to give a disemicarbazone (1·0 g.), m. p. 208—210° (decomp.), which contained no bromine. McBee and Burton[2] gave m. p. 218° (decomp.).

The dibromo-ketone (0·7 g.) was added to a filtered solution of semicarbazide hydrochloride (0·5 g.) and sodium acetate trihydrate (0·75 g.) in water (4 c.c.) at 10—15°. Filtration after 30 min. gave a *semicarbazone* (0·51 g.), m. p. 134·5—135° (decomp.), which contained bromine (Found : C, 14·6; H, 1·6. $C_4H_4ON_3Br_2F_3$ requires C, 14·7; H, 1·2%).

3 : 3 : 3-*Trifluoropyruvaldehyde Dioxime.*—3 : 3-Dibromo-1 : 1 : 1-trifluoroacetone (8·0 g.) was heated at 100° for 90 min. with hydroxylamine hydrochloride (8·2 g.) and sodium acetate trihydrate (16·4 g.) in water (50 c.c.). After extraction with ether the extracts were dried ($MgSO_4$) and concentrated under diminished pressure. Recrystallisation of the residue from benzene gave 3 : 3 : 3-*trifluoropyruvaldehyde dioxime* (2·7 g.), m. p. 117·5—119·5° (Found : C, 22·9; H, 2·2; F, 36·9. $C_3H_3O_2N_2F_3$ requires C, 23·1; H, 1·9; F, 36·5%).

Sensitivities of the Dioximes towards Nickel Ions.—The crystalline trifluorobutanedione dioxime, m. p. 89°, gave precipitates with about 1·5 mg./c.c. or more of Ni^{++} in solutions which were 0·5—0·67N with respect to ammonia. No precipitate was formed even with 6·7 mg./c.c. of Ni^{++} in solutions which were neutral, acidic with acetic acid (0·67N), or more than 0·8N with respect to ammonia.

The sensitivity of the supposed α-form in the oxime residue was not easily determined, but a red precipitate was still formed in solutions containing about 0·5 mg./c.c. of nickel in 0·5N-ammonia.

3 : 3 : 3-Trifluoropyruvaldehyde dioxime gave only a blood-red colour even with 10 mg./c.c. of Ni^{++} in 0·5N-ammonia solution.

The authors thank Professor M. Stacey, F.R.S., for his close interest in this work, and Miss J. M. Lazenby for the analyses. One of them (A. S.) is grateful to the University of Birmingham for a Research Fellowship.

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[*Received, December 27th, 1956.*]