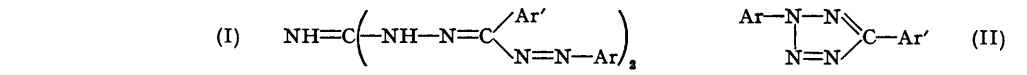
772. *A New Route to 2 : 5-Disubstituted Tetrazoles.*

By F. L. Scott, D. A. O'Sullivan, and J. Reilly.

As an introduction to a general investigation into the production of condensed heterocyclic compounds from the polyaminoguanidines, the oxidation of the " bisformazans " (I), from



(I) (II)

diaminoguanidines, has been studied. Fission results, with the production of 2 : 5-disubstituted tetrazoles (II).

Experimental.—Microanalyses are by Drs. Weiler and Strauss, Oxford. All m. p.s are uncorrected.

Hydrazone formation. Typical examples are as follows :

Redistilled furfuraldehyde (11 ml.; an excess) was added to a concentrated aqueous solution of diaminoguanidine nitrate (7·1 g., 1 mol.); the resulting deep-brown solution on cooling deposited whitish-yellow needles of NN'-*bisfurfurylideneaminoguanidine nitrate*, which after recrystallisation from aqueous ethanol, melted at 121—122° (Found : C, 40·8; H, 4·5; N, 25·2. $C_{11}H_{12}N_6O_5,H_2O$ requires C, 40·5; H, 4·3; N, 25·8%). This hydrazone, which readily discoloured on exposure to light, forms a picrate, m. p. 253°.

When equimolecular quantities of *m*-nitrobenzaldehyde and diaminoguanidine nitrate are similarly mixed, a quantitative precipitation of NN'-*bis*-m-*nitrobenzylideneaminoguanidine nitrate* results. This compound, after recrystallisation from aqueous ethanol in which it was very sparingly soluble, melted at 250—252° (Found : C, 41·2; H, 3·9; N, 24·4. $C_{15}H_{14}O_7N_8,H_2O$ requires C, 41·3; H, 3·7; N, 24·5%). Recrystallisation from pyridine affords the anhydrous material (Found : C, 43·9; H, 3·6; N, 27·8. $C_{15}H_{14}O_7N_8$ requires C, 43·1; H, 3·4; N, 26·8%).

" *Bisformazan* " *formation.* *NN'*-Bisbenzylideneaminoguanidine hydrochloride (1·06 g., 1 mol.) was suspended in ethanol (95%) and an excess of concentrated potassium hydroxide solution added. The suspension was cooled to below 10°, the mixture well-stirred mechanically, and the calculated quantity of benzenediazonium chloride (2 mols.) was added. A deep purple colour immediately developed and the solution was set aside in an ice–salt mixture overnight. *Formimidobis-3 : 5-diphenylformazan* (6-*imino*-1 : 3 : 9 : 11-*tetraphenyl*-3 : 6 : 9-*tricarbaundeca-az*-1 : 3 : 8 : 10-*tetraenes* *) separated as a deep-red solid which was extremely soluble in the usual organic solvents and was purified by repeated boiling with water in which it was insoluble. It was thus obtained as a fine red amorphous powder, m. p. 137—138° (Found : C, 68·5; H, 5·15; N, 26·4. $C_{27}H_{23}N_9$ requires C, 68·5; H, 4·9; N, 26·6%).

When, similarly, diazotized potassium sulphanilate (2 mols.) was run into a well-agitated suspension of bisbenzylideneaminoguanidine nitrate (1 mol.) in excess of ethanolic potassium hydroxide solution (40%), the temperature being maintained below 10° during the addition, an analogous coupling results and during 24 hours, deep reddish-purple crystals of the *potassium* 6-*imino*-3 : 9-*diphenyl*-3 : 6 : 9-*tricarbaundeca-az*-1 : 3 : 8 : 10-*tetraene*-1 : 11-*disulphonate* separated (Found : C, 46·3; H, 2·6; N, 16·9. $C_{27}H_{21}O_6N_9S_2K_2$ requires C, 45·7; H, 3·0; N, 17·8%). The diacid was characterised as its p-*toluidine* salt, m. p. 227—229° (Found : C, 57·5; H, 4·9. $C_{41}H_{41}N_{11}O_6S_2$ requires C, 58·1; H, 4·8%).

When a solution of benzenediazonium chloride was treated in an analogous fashion with an aqueous ethanolic suspension of bis-*m*-nitrobenzylideneaminoguanidine hydrochloride in a strongly alkaline medium no coupling resulted. 6-*Imino*-3 : 9-*di*-m-*nitrophenyl*-1 : 11-*diphenyl*-3 : 6 : 9-*tricarbaundeca-az*-1 : 3 : 8 : 10-*tetraene* was obtained however in the following fashion. A solution of benzenediazonium chloride was neutralized with solid sodium carbonate and then added to a solution of the hydrazone (1 mol.) in pyridine, the temperature being kept below 10° during the addition and with constant agitation; a deep red colour immediately developed and the addition of water precipitated the desired formazan as a dark-red amorphous material which after repeated extraction with boiling water had m. p. 148—149° (Found : C, 57·4; H, 4·1; N, 28·0. $C_{27}H_{21}O_4N_{11}$ requires C, 57·5; H, 3·7; N, 27·4%).

Oxidation of the formazans. Oxidation of the tetraphenyl compound with either lead tetra-acetate or nitrous oxide in anhydrous chloroform solution resulted in the production of 2 : 5-diphenyltetrazole, m. p. 101° (Dimroth and Merzbacher, *Ber.*, 1907, **40**, 2402, reported m. p. 102°) (Found : C, 70·2; H, 4·55; N, 24·4. Calc. for $C_{13}H_{10}N_4$: C, 70·3; H, 4·5; N, 25·2%).

Oxidation of both the tetraphenyl compound and the di-*m*-nitrophenyldiphenyl analogue with nitric acid resulted again in the production of tetrazole, with two nitro-groups substituted in the aryl residues. The orientation of the isomeric materials from these experiments is at present under consideration.

University College, Cork. [*Received, June 5th*, 1951.]

* The nomenclature is based on the use of " carba " to indicate replacement, by CH or CH_2 as appropriate, of one of a chain of hetero-atoms; in this case replacement by CH of one of a chain of nitrogen atoms, named in accordance with I.U.P.A.C. rule 43 f.

773. *Diglycine Hydrochloride.*

By Ronald Bentley.

In the preparation of isotopically labelled glycine ($H_2{}^{15}N{\cdot}CH_2{\cdot}CO_2H$) ethyl phthalimidoacetate is hydrolysed by concentrated hydrochloric acid (Schoenheimer and Ratner, *J. Biol. Chem.*, 1939, **127**, 301). After the removal of phthalic acid and evaporation of the solution to dryness, a residue of glycine hydrochloride is obtained. Free glycine is conveniently obtained by solution of the hydrochloride in ethanol and addition of pyridine. During one preparation of labelled glycine, a white crystalline solid, m. p. 182°, was obtained at this stage. It was shown qualitatively to contain chlorine and it seemed most likely that this compound was diglycine hydrochloride, $(H_2N{\cdot}CH_2{\cdot}CO_2H)_2,HCl$ (literature m. p. 186—187°). Since this was an isotopic preparation, the material was not further investigated; it was dissolved in aqueous ethanol and treated with more pyridine; glycine, m. p. 230°, was then obtained.

In further experiments with non-isotopic material, glycine was dissolved in concentrated hydrochloric acid and such solutions evaporated to dryness *in vacuo*. These preparations of glycine hydrochloride which must have contained a little free hydrochloric acid, were dissolved in ethanol and treated with an equimolar quantity of pyridine; diglycine hydrochloride, m. p. 185°, was regularly obtained. Use of a good excess of pyridine was necessary to precipitate free glycine.

Previously, diglycine hydrochloride had been prepared by the action of gaseous ammonia on an alcoholic solution of glycine hydrochloride (Kraut and Hartmann, *Annalen*, 1865, **133**, 101) and by reaction of glycine hydrochloride with glycine in boiling glacial acetic acid (Frost, *J. Amer. Chem. Soc.*, 1942, **64**, 1286).

Experimental.—Glycine (5 g.) was dissolved in concentrated hydrochloric acid (10 c.c.) with warming. The solution was evaporated to dryness *in vacuo*, and the residue further evaporated with ether (20 c.c.). The residue, which still contained free acid, was dissolved in warm ethanol (75 c.c.) and pyridine (5·5 c.c.) added with swirling. After 1 hour at 0° the white crystalline solid was filtered off; it had m. p. 186° (yield, 5·62 g.). When the compound was recrystallised from water by addition of ethanol its m. p. decreased to 181° [Found: N, 14·5. Calc. for $(C_2H_5O_2N)_2,HCl$: N, 15·0%].

National Institute for Medical Research, London, N.W.7. [*Received, August 1st*, 1951.]

---

774. *The Mechanism of Amide Formation from Acids and Urea.*

By H. R. V. Arnstein and Ronald Bentley.

Cherbuliez and Landolt (*Helv. Chim. Acta*, 1946, **29**, 1438) have described a new general method for preparation of amides. When an acid was heated with urea, carbon dioxide and ammonia were evolved and the corresponding amide was obtained in good yield:

$$R{\cdot}CO_2H + H_2N{\cdot}CO{\cdot}NH_2 \longrightarrow R{\cdot}CO{\cdot}NH_2 + CO_2 + NH_3$$

Although it seemed likely that the reaction was the straightforward acidolysis postulated by Cherbuliez and Landolt, it was also possible that direct decarboxylation of the acid occurred, perhaps leading to a free radical, or that an intermediate $R{\cdot}CO{\cdot}O{\cdot}CO{\cdot}NH_2$ decomposed with loss of the original carboxyl-carbon atom as carbon dioxide. In order to decide whether decarboxylation of the acid was involved, the reaction has been carried out with acids labelled in the carboxyl group with ^{13}C.

When $H{\cdot}{}^{13}CO_2H$ was used, the evolved carbon dioxide contained only the normal atom % of ^{13}C. The formamide produced was characterised as formylphenylhydrazide; after correction for the carbon of the phenyl group, this contained the same atom % excess ^{13}C as the formic acid. Similarly, with $CH_3{\cdot}{}^{13}CO_2H$, the evolved carbon dioxide had only the normal atom % of ^{13}C, and the acetamide isolated had the same atom % excess of ^{13}C as the acetic acid. It is clear therefore that all of the carbon dioxide produced in this reaction is derived from the urea.

The decomposition of urea oxalate (which yields carbon monoxide, carbon dioxide, ammonia, and cyanuric acid; Berzelius, "Lehrbuch der Chemie," 3rd edn., Dresden–Leipzig, 1840, vol. IX, p. 443) was also investigated, by use of urea oxalate prepared from ^{14}C-urea. Barium carbonate obtained from the carbon monoxide was not radioactive, indicating that the oxalic

acid moiety was the sole source of this product. The carbon dioxide produced in the reaction contained a substantial amount of ^{14}C, indicating that it was derived both from the oxalic acid and the urea.

Experimental.—[^{13}C]*Formic acid* (cf. Grant and Turner, *Nature*, 1950, **165**, 153). Potassium cyanide (1·252 g., 79·5% potassium cyanide, 56 atom % ^{13}C) in water (10 c.c.) was heated for 2 hours at 250° in a specially designed small autoclave (Kantorowicz, *J. Soc. Chem. Ind.*, 1950, **69**, Suppl. No. 2, S 76). After removal of a water-insoluble polymer (56 mg.) the solution was evaporated *in vacuo* (yield of crude potassium formate, 1·462 g.). Formic acid was steam-distilled after addition of excess of 2N-sulphuric acid, and the distillate treated with 1·01N-sodium hydroxide (16·9 c.c.). The solution was neutralised by addition of 6 c.c. of a solution of non-isotopic formic acid (=52·92 mg. of formic acid). On evaporation *in vacuo*, 1·137 g. sodium formate were obtained.

Reaction of [^{13}C]*formic acid and urea.* Sodium [^{13}C]formate (10 mg., prepared as above) was refluxed briefly with anhydrous formic acid (0·2 c.c.) to effect the exchange reaction, $H\cdot{}^{13}CO_2Na + H\cdot CO_2H \rightleftharpoons H\cdot CO_2Na + H\cdot{}^{13}CO_2H$. The labelled formic acid was distilled in a closed vacuum system into a tube cooled in alcohol–carbon dioxide. The residual sodium formate was oxidised with van Slyke and Folch's chromic acid mixture (*J. Biol. Chem.*, 1940, **136**, 509); the carbon dioxide evolved was collected as barium carbonate which was treated with mineral acid in a special vacuum sample tube before analysis in a mass spectrometer (Arnstein and Bentley, *Quart. Reviews*, 1950, **4**, 174) (Found: atom % excess of ^{13}C, 1·17, 1·15).

The distillate ($H\cdot{}^{13}CO_2H$) was mixed with urea (0·23 g.) and heated in a stream of carbon dioxide-free nitrogen at 140—150° for 1½ hours. The carbon dioxide produced was absorbed in saturated barium hydroxide solution and analysed for ^{13}C in the usual way (Found: atom % excess of ^{13}C, 0·00, 0·00). The residue, consisting mainly of formamide, was distilled *in vacuo* (free flame) at water-pump pressure, to yield a viscous oil. For further purification, this product was warmed with an equal volume of phenylhydrazine at 135° until there was no further evolution of ammonia (15 minutes). A reddish crystalline solid was formed on storage overnight; it was washed first with water, then with 2N-hydrochloric acid, and recrystallised from a small volume of ethanol. The white plates, m. p. 144°, showed no m. p. depression on admixture with authentic formylphenylhydrazide (Found: atom % excess of ^{13}C, 0·16, 0·17. Hence, calc. atom % excess of original formamide = 1·16).

Reaction of [*carboxy*-^{13}C]*acetic acid with urea.* (*a*) Sodium [*carboxy*-^{13}C]acetate, $CH_3\cdot{}^{13}CO_2Na_2$ (50 mg., atom % excess of ^{13}C, 7·6; prepared at the Chemical Research Laboratory, Teddington) was dissolved, with warming, in glacial acetic acid (1 c.c.). The labelled acetic acid was then distilled off in a closed vacuum system (Found: atom % excess of ^{13}C, 0·20). The bulk of the acid was warmed with urea (1 g.) in a stream of carbon dioxide-free nitrogen at 110—120°. Evolution of carbon dioxide (which was collected as barium carbonate) took place slowly. After 20 minutes, carbon dioxide was collected for 30 minutes (Found: atom % excess of ^{13}C, 0·00). After a further 4 hours, a second sample of carbon dioxide was collected during 30 minutes (Found: atom % excess of ^{13}C, 0·00). (*b*) Sodium [*carboxy*-^{13}C]-acetate (10 mg., atom % excess of ^{13}C, 7·6) was equilibrated with glacial acetic acid (0·2 c.c.) as previously described. After distillation of the acetic acid, the residual sodium acetate was oxidised to carbon dioxide (Found: atom % excess of ^{13}C, 0·20, 0·20). The distilled [*carboxy*-^{13}C]acetic acid was warmed with urea (200 mg.) in a stream of carbon dioxide-free nitrogen at 185° for 3 hours. The residue was treated with saturated sodium hydrogen carbonate solution, a little insoluble material filtered off, and the solution extracted with chloroform (6 × 15 c.c.). The aqueous solution was evaporated to dryness *in vacuo* and the acetamide extracted from the residue with warm chloroform. The acetamide obtained on removal of solvent was oxidised to carbon dioxide (Found: atom % excess of ^{13}C, 0·22, 0·23).

Decomposition of [^{14}C]*urea oxalate.* The [^{14}C]urea oxalate was prepared by adding oxalic acid (624 mg.) to a solution of [^{14}C]urea (596·9 mg.) in water (6 c.c.). The product was crystallised from aqueous ethanol. This material gave 438·5 counts/min. when counted as a infinite thickness sample of 1 cm.^{2} area on a thin-window bell-shaped Geiger–Müller counter (Popják, *Biochem. J.*, 1950, **46**, 560).

The above [^{14}C]urea oxalate was decomposed by heating it in a tube immersed in an oil-bath. A slow stream of dry carbon dioxide-free air was passed through the reaction tube; the exit gases were passed successively through three barium hydroxide traps to absorb carbon dioxide, a tube containing copper oxide heated to red heat, and a further three traps to absorp the carbon dioxide arising from the oxidation of carbon monoxide in the copper oxide tube.

The urea oxalate began to decompose at about 165° and the bath-temp. was kept at 170° till gas evolution ceased. The barium carbonate (224·7 mg.) arising from the carbon dioxide gave 197 counts/min. when counted in the same way as the starting material; the barium carbonate (95·7 mg.) derived from the carbon monoxide was completely non-radioactive.

We are indebted to the Chemical Research Laboratory, Teddington, for synthesis of the [*carboxy*-^{13}C]-acetate and to Mr. H. L. Kornberg for a gift of [^{14}C]urea.

NATIONAL INSTITUTE FOR MEDICAL RESEARCH,
LONDON, N.W.7.

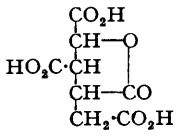
[*Received, August 17th*, 1951.]

775. *Chebulinic Acid.*

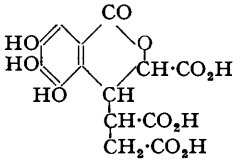
By Robert D. Haworth and Leslie B. de Silva.

The work of Freudenberg and his collaborators (*Ber.*, 1919, **52**, 1238; 1920, **53**, 1728; *Annalen*, 1927, **452**, 303) indicated that chebulinic acid, the crystalline constituent of the fruits of *Terminalia chebula*, commonly called Myrobalans, had the molecular formula, $C_{41}H_{34}O_{27}$. Partial hydrolysis gave equimolecular proportions of gallic acid, 3 : 6-digalloyl glucose (see Schmidt and his co-workers, *Annalen*, 1951, **571**, 19, 29), and the so-called " split acid," which was isolated as the crystalline thallium and the brucine salt, gave a blue ferric test, and on pyrolysis yielded a small amount of pyrogallol. Later Schmidt and his colleagues (*Ber.*, 1947, **80**, 510; *Annalen*, 1951, **571**, 1) showed that " split acid," $C_{14}H_{12}O_{11}$, contains one lactonic, three hydroxyl, and three carboxyl groups, and methylation of the hydroxyl groups with diazomethane yielded the trimethyl derivative of " split acid," which gave a crystalline triamide. Oxidation of this trimethyl derivative with permanganate in acid solution gave a crystalline acid, $C_8H_8O_8$, containing one lactonic and three carboxyl groups, and structures (I) and (II) were suggested for this acid, $C_8H_8O_8$, and for " split acid," respectively, on the

(I)



(II)



following grounds. (i) The acid, $C_8H_8O_8$, resists decarboxylation; consequently it is not a malonic acid derivative, and the three carboxyl groups and the lactonic group are associated with different carbon atoms. (ii) The lactonic group is derived from a α-hydroxy-acid, because sodium cyanate was obtained by the action of sodium hypochlorite on the triamide of trimethyl-" split acid." (iii) The acid, $C_8H_8O_8$, yielded a mixture of acetic, oxalic, and succinic acids on fusion with potassium hydroxide, and oxalic acid on oxidation with alkaline permanganate. (iv) The formula proposed for " split acid " is attractive because (II) may be derived from ellagic acid by oxidative degradation of one of the phenolic rings.

It was assumed that the aromatic ring of (II) was destroyed during the formation of (I), but on the basis of formula (II) it would be expected that oxidation of the trimethyl derivative of " split acid " under appropriate conditions would give 3 : 4 : 5-trimethoxyphthalic acid. In our hands oxalic acid was the only product of the oxidation of the trimethyl derivative with alkaline permanganate, but welcome support of the suggestion of the aromatic nucleus has been obtained by the isolation of 3 : 4 : 5-trimethoxyphthalic acid, in yields exceeding 40% by the action of alkaline potassium ferricyanide on the trimethyl derivative of " split acid."

Experimental.—Potassium hydroxide (35 g.) was added to a solution of the trimethyl derivative of " split acid " (1 g.) in water (1·5 l.), and after the temperature had been raised to 80—90°, potassium ferricyanide (200 g.) was added with stirring. Further quantities of potassium ferricyanide (200 g.) and potassium hydroxide (35 g.) were added at the end of 12, 24, and 36 hours, and the stirred solution was maintained at 80—90° for 72 hours.

The solution was cooled, and the yellow crystals were collected and washed thoroughly with cold water. The combined filtrate and washings (1·5 l.) were acidified with dilute sulphuric acid and heated for several hours on a steam-bath to remove hydrogen cyanide, and the blue acidified solution was saturated with ether and allowed to cool in the refrigerator for 24 hours. The precipitated Prussian-blue was removed and the filtrate and the precipitate were continously extracted with ether during 48 hours. The ether was removed, the moist residue was evaporated under reduced pressure, and the yellow solid was sublimed twice at 140—150°/0·5 mm. Recrystallisation from ether gave 3 : 4 : 5-trimethoxyphthalic anhydride (256 mg.) as needles, m. p. 144° not depressed by admixture with an authentic specimen. Identity was confirmed by the preparation of *N*-methyl-3 : 4 : 5-trimethoxyphthalimide, m. p. 127° undepressed by admixture with an authentic specimen.

Our thanks are due to The Calder and Mersey Extract Company Ltd. for a supply of myrobalans, to the Government of Ceylon for a scholarship, and to Imperial Chemical Industries Limited for a grant.

The University, Sheffield, 10. [*Received, August 18th*, 1951.]

776. 2- *and* 5-*Fluoronicotinic Acids.*

By R. D. Beaty and W. K. R. Musgrave.

It has been reported (Hawkins and Roe, *J. Org. Chem.*, 1949, **14**, 328) that attempts to prepare 5-fluoronicotinic acid by a modified Schiemann reaction, the 5-amino-acid and ester being used as starting materials, failed because of the solubility of the diazonium fluoroborate. Eventually the required ester was prepared, *via* the diazonium silicofluoride, in approximately 15% crude yield. The preparation is now reported of methyl 5-fluoronicotinate, in a slightly lower yield than that from the diazonium silicofluoride, by the preparation and decomposition of the diazonium fluoroborate in fluoroboric acid; and also the preparation of 2-fluoronicotinic acid, in much better yield, by a similar procedure. The method of isolation of the 2-fluoronicotinic acid has been simplified, and this may be one reason for the increased yield, which in this case, is as good as that obtained in the preparation from 2-amino-3-methylpyridine (Minor, Hawkins, VanderWerf, and Roe, *J. Amer. Chem. Soc.*, 1949, **71**, 1125). Usually in the Schiemann reaction, the presence of a carboxyl group in the molecule greatly reduces the yield of fluorine-containing compound, when compared with that in the hydrocarbon reaction, but in this case the yields are about the same. Application of the process to the preparation of 3-fluoropicolinic acid from 3-aminopicolinic acid failed.

Experimental.

5-Fluoronicotinic Acid.—5-Aminonicotinic acid (3·0 g.) was dissolved in 40% fluoroboric acid (20 c.c.) and cooled to −5°. Sodium nitrite (2·5 g.) was added slowly with constant stirring, and after one hour in the ice-bath the product was heated to 50° for 30 minutes. When cooled, the solution was neutralised with sodium carbonate and the solvent removed by distillation under reduced pressure. After being dried *in vacuo* (P_2O_5) at 60°, the resulting salt was refluxed with 3% methyl-alcoholic sulphuric acid (50 c.c.) for 2—3 hours. The methanolic solution was filtered, neutralised with sodium methoxide, filtered again, and concentrated by distillation to about 2 c.c. On cooling, crystals of methyl 5-fluoronicotinate (0·3 g.), m. p. 48°, separated.

The methyl ester was dissolved in dry methyl alcohol (10 c.c.), and the solution saturated with ammonia at 0°. Next day the methyl alcohol was evaporated and the solid residue recrystallised from water, giving 5-fluoronicotinamide (0·2 g.), m. p. 174° (Found: F, 13·3. Calc. for $C_6H_5ON_2F$: F, 13·5%).

2-Fluoronicotinic Acid.—2-Aminonicotinic acid (2·0 g.) was dissolved in 40% fluoroboric acid (10 c.c.) and diazotised at 0° to −5° by the addition of aqueous sodium nitrite (1·0 g. in 10 c.c.). After 1 hour at 0° the solution was heated to 50—60° for a further hour. It was then cooled and basified to pH 5 by the addition of sodium hydroxide solution. The solid was filtered off and recrystallised from water, giving 2-fluoronicotinic acid (0·7 g., 33%), m. p. 164—165° (Found: F, 13·4. Calc. for $C_6H_4O_2NF$: F, 13·5%).

Esterification by refluxing the acid for 2 hours with 3% methanolic sulphuric acid followed by neutralisation of the solution with sodium methoxide, filtration, and evaporation to a small volume, gave, on cooling, crystals of the methyl ester, m. p. 74—75°.

The methyl ester (0·2 g.) was dissolved in absolute alcohol, saturated with ammonia at 0°, and set aside at 0° for one day. Evaporation of the solvent gave crystals of 2-fluoronicotinamide (0·16 g.) which, after recrystallisation from water, had m. p. 124° (Found: F, 13·4. Calc. for $C_6H_5ON_2F$: F, 13·5%).

One of us (R. D. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

The University, South Road, Durham. [*Received, August 22nd,* 1951.]

---

777. *Fluorene-2-aldehyde.*

By S. J. Angyal, G. B. Barlin, and P. C. Wailes.

Two apparently different compounds have been described in the literature as fluorene-2-aldehyde. One was prepared by von Braun and Engel (*Ber.*, 1924, **57**, 191) by heating 2-bromomethylfluorene with hexamine in aqueous solution; they reported m. p. 174—175° for this compound and m. p. 245—247° for its semicarbazone. Hinkel, Ayling, and Beynon (*J.*, 1936, 339) prepared an aldehyde from fluorene by treating it with $AlCl_3$,HCN and hydrogen chloride; the position of the aldehyde group was established by reduction to 2-methylfluorene, and by oxidation to fluorene-2-carboxylic acid. This aldehyde melted at 90° and was characterised by its phenylhydrazone, oxime, anil, and semicarbazone (m. p. 278°).

In connection with our work on the Sommelet reaction, we have investigated von Braun's results by using the more readily prepared 2-aminomethylfluorene instead of the bromomethyl derivative. It has been established (Angyal, Morris, Tetaz, and Wilson, *J.*, 1950, 2141) that the use of an amine salt and hexamine in the Sommelet reaction is equivalent to the use of the addition compound made from a halogenomethyl compound and hexamine. When 2-aminomethylfluorene hydrochloride and hexamine were boiled in aqueous solution, a solid was formed, with a m. p. similar to that of von Braun's compound; but it was not an aldehyde. It contained nitrogen, and on acid hydrolysis it yielded 2-aminomethylfluorene and formaldehyde. Thus, von Braun's " aldehyde " is 2-methyleneaminomethylfluorene, a conclusion confirmed by its direct synthesis from the amine and formaldehyde.

A methyleneamine is always formed in the Sommelet reaction. In this case its low solubility in water prevented its further reaction. When the Sommelet reaction has been carried out in 50% acetic acid, which is a better solvent for the methyleneamine, the fluorenealdehyde described by Hinkel *et al.* has been obtained in 77% yield.

Experimental.—2-Aminomethylfluorene hydrochloride (von Braun and Engel, *loc. cit.*) was prepared in 81% yield by the hydrogenation of 2-cyanofluorene in the presence of Raney nickel at room temperature and atmospheric pressure.

2-Methyleneaminomethylfluorene. 2-Aminomethylfluorene hydrochloride (0·5 g.), hexamine (0·3 g.), formaldehyde (0·2 c.c., 40%), and water (7 c.c.) were boiled for 1 hour. During the whole time a solid was present which was filtered off (0·45 g.) and crystallised from ethanol; it then melted at 178°. When this compound was boiled with ethanol and concentrated hydrochloric acid (10 : 1) for 1½ hours, 2-aminomethylfluorene hydrochloride, m. p. 274°, crystallised on cooling, and from the mother-liquor formaldehyde was precipitated as its 2 : 4-dinitrophenylhydrazone, m. p. 160°. Both compounds were identified by their mixed m. p. with authentic samples.

A purer sample of *2-methyleneaminomethylfluorene* was obtained by dissolving 2-aminomethylfluorene hydrochloride (0·3 g.) in ethanol (15 c.c.; 65%), and adding sodium hydroxide solution (1 c.c.; 10%) and formaldehyde (1 c.c.; 40%). The precipitate was crystallised from much ethanol, or from pyridine–water, giving the fluorene, m. p. 181° (Found : N, 6·95. $C_{15}H_{13}N$ requires N, 6·75%).

When this Schiff's base was warmed with semicarbazide hydrochloride and sodium acetate in ethanol, a small amount of crystals, m. p. about 250°, was obtained. This was not a semicarbazone, however, but impure 2-aminomethylfluorene hydrochloride.

Fluorene-2-aldehyde. 2-Aminomethylfluorene hydrochloride (0·6 g.), hexamine (0·5 g.), and 50% acetic acid solution (6 c.c.) were boiled under reflux for ½ hour. After the addition of concentrated hydrochloric acid (0·5 c.c.) the mixture was cooled, diluted with water, and the precipitated aldehyde (0·39 g.) was collected and crystallised from dilute ethanol. The m. p., 85·5—86°, could not be raised by repeated crystallisation of the aldehyde from ethanol or from light petroleum, or by sublimation *in vacuo*. Hinkel *et al.* report m. p. 90°. In an attempt to purify the aldehyde further, it was converted into the anil, m. p. 159° (Hinkel *et al.* report m. p. 158°), and the anil was hydrolysed. When the anil (0·6 g.) was boiled with ethanol (10 c.c.) and concentrated hydrochloric acid (0·5 c.c.) for 1 minute, yellow crystals of the *anil hydrochloride*, m. p. 226—227° (0·4 g.), separated on cooling (Found : N, 4·8. $C_{20}H_{15}N$,HCl requires N, 4·6%); but when the anil (0·5 g.) was boiled with ethanol (10 c.c.), water (5 c.c.), and concentrated hydrochloric acid (0·7 c.c.) for ½ hour, the aldehyde was obtained in nearly theoretical yield, but the m. p. was still 85·5—86°. The oxime, the phenylhydrazone, and the semicarbazone all had the m. p.s reported by Hinkel *et al.*

THE UNIVERSITY OF SYDNEY. [*Received, August 27th*, 1951.]

---

778. *The Reaction of Sodiomalonic Ester with a Halogenocarboxylic Acid.*

By M. D. POTTER and E. P. TAYLOR.

THERE is apparently no reference in the literature to the reaction of sodiomalonic ester with a halogeno-compound containing a free carboxyl group. In cases where the product of such a reaction has been required, the carboxyl group has always been protected by esterification before treatment of the halogeno-compound with sodiomalonic ester. However, in one such case, conditions have now been developed for the direct condensation of the free acid with sodiomalonic ester.

Brassylic acid (undecane-1 : 11-dicarboxylic acid) has hitherto been prepared from 11-bromoundecanoic ester and sodiomalonic ester (see Chuit, *Helv. Chim. Acta*, 1926, **9**, 270). It has now been found that a much improved yield is obtained if the free 11-bromoundecanoic acid is used, provided that the quantity of sodiomalonic ester be increased. The results are

summarised in the table (the yields recorded are in each case the mean of at least two experiments).

Quantities of reactants			% yield of brassylic acid based on	
11-Bromoundecanoic acid (*a*) or ester (*b*) (mol.)	Sodium (mols.)	Malonic ester (mols.)	11-bromoundecanoic ester	11-bromoundecanoic acid
(*b*) 1	1·05	1·1	76	68·5
(*b*) 1	2·1	2·2	83	74
(*a*) 1	1·03	1·1	—	nil
(*a*) 1	2·06	2·2	—	53
(*a*) 1	3·09	3·3	—	87

It appears probable that the first mol. of sodiomalonic ester is immediately decomposed by the 11-bromoundecanoic acid to form the sodium salt, which then reacts with further quantities of sodiomalonic ester in the normal manner. In support of this, brassylic acid was obtained when equimolar quantities of sodiomalonic ester and sodium 11-bromoundecanoate were allowed to react, although the yield was poor (39%). In those experiments in which equimolar quantities of sodiomalonic ester and the acid were used, the crude product was not completely identified. Its melting point (approximately 56—60°) was higher than that of 11-bromoundecanoic acid. On fractional distillation of the derived methyl ester, a fraction was obtained corresponding in boiling point to methyl 11-hydroxyundecanoate, and which yielded 11-hydroxyundecanoic acid on hydrolysis (the melting point was unaltered on admixture with an authentic specimen). The presence of 11-hydroxyundecanoic acid in the reaction product may arise from the hydrolysis stage of the working up, since 11-bromoundecanoic acid readily yields the 11-hydroxy-acid in 92% yield when boiled with alkali.

Experimental.—Sodium (2·7 g., 3·09 mol.) was dissolved in dry absolute alcohol (60 ml.), and, with the temperature maintained at approximately 50°, ethyl malonate (19·8 g., 3·3 mol.) was run in with continuous stirring during 15 minutes. The solution was then refluxed and stirred whilst a solution of 11-bromoundecanoic acid (10 g., 1 mol.) (Ashton and Smith, *J.*, 1934, 435) in dry absolute alcohol (30 ml.) was added during 45 minutes. Stirring and refluxing were continued for another 30 minutes, water was added, and the alcohol was distilled off. The cooled solution was then made alkaline with sodium hydroxide, washed with ether, acidified with dilute hydrochloric acid, and extracted with ether. After removal of the solvent, the crude oily residue was refluxed with aqueous potassium hydroxide (22 g.; in 100 ml.) for 16 hours. The cooled mixture was then acidified, extracted with ether, dried (Na_2SO_4), and filtered, and the solvent removed. The residue was then partially decarboxylated by heating it at 170° for 70 minutes with gentle stirring. After cooling, the product was recrystallised once from dry benzene, whereupon 8·0 g. (87%) of brassylic acid, of m. p. 111° (uncorr.), were obtained.

We thank the Directors of Messrs. Allen and Hanburys Ltd. for permission to publish this note.

RESEARCH DIVISION, ALLEN AND HANBURYS LTD.,
WARE, HERTS.

[*Received, September 19th*, 1951.]