## 269. *The Paper Chromatography of Cyclitols.*

By S. J. Angyal, D. J. McHugh, and P. T. Gilham.

Cyclitols are particularly suitable for paper chromatography: they are in most cases easily separated and readily detected, and the separations can be translated to a preparative scale by the use of cellulose-powder chromatography. $R_F$ values for several inositols in aqueous acetone were reported [1] and recently Posternak [2] gave values for many cyclitols and related compounds in several solvent systems. In the Table we now list $R_F$ values for all the inositols and for the known quercitols and inositol methyl ethers. Aqueous acetone is the solvent of choice in most cases because by its use chromatograms can be run, dried, and developed within 3—4 hr. In the authors' laboratory chromatograms are now run as a routine matter in aqueous acetone before the working-up of reaction mixtures.

The best method for detecting cyclitols on paper is the silver nitrate–sodium hydroxide reagent described by Trevelyan *et al.*,[3] as modified by Anet and Reynolds; [4] fixation by thiosulphate gives black spots which can be preserved as a permanent record. The older ammoniacal silver nitrate reagent [1] is less sensitive and usually causes darkening of the whole paper. The sensitivity of the reagent decreases with decreasing number of hydroxyl groups; while 10 μg. of an inositol is readily detected, about 50 μg. of a monomethyl inositol and 500 μg.

*$R_F$ values of cyclitols.*

Solvents: *A*, acetone–water (4 : 1, v/v); *B*, phenol–water (4 : 1, w/w); *C*, butanol–acetic acid–water (4 : 1 : 1); *D*, ethanol–water–conc. ammonia solution (20 : 4 : 1).

| Solvent | *A* | *B* | *C* | *D* |
|---|---|---|---|---|
| D-Glucose | 0·43 | 0·35 | 0·175 | 0·64 |
| *Inositols* | | | | |
| *scyllo*- (1 : 3 : 5/2 : 4 : 6) | 0·17 | 0·155 | 0·07 | 0·40 |
| (+)- (1 : 2 : 4/3 : 5 : 6) | 0·27 | 0·195 | 0·10 | 0·50 |
| *neo*- (1 : 2 : 3/4 : 5 : 6) | 0·19 | 0·24 | 0·085 | 0·42 |
| *myo*- (1 : 2 : 3 : 5/4 : 6) | 0·185 | 0·205 | 0·08 | 0·41 |
| *muco*- (1 : 2 : 4 : 5/3 : 6) | 0·35 | 0·265 | 0·145 | — |
| *allo*- (1 : 2 : 3 : 4/5 : 6) | 0·30 | 0·29 | 0·135 | — |
| *epi*- (1 : 2 : 3 : 4 : 5/6) | 0·22 | 0·33 | 0·105 | 0·46 |
| *cis*- (all-*cis*) | 0·22 | 0·35 | 0·125 | — |
| *Quercitols* | | | | |
| *scyllo*- (1 : 3 : 5/4 : 6) | 0·31 | 0·37 | 0·145 | 0·63 |
| *proto*- (1 : 4/2 : 3 : 5) | 0·405 | 0·38 | 0·20 | 0·67 |
| *vibo*- (1 : 2 : 4/3 : 5) | 0·33 | 0·42 | 0·155 | 0·63 |
| *epi*- (1 : 2 : 3 : 5/4) | 0·34 | 0·41 | 0·16 | — |
| *cis*- (all-*cis*) | 0·39 | 0·54 | 0·205 | — |
| *Inositol methyl ethers* | | | | |
| 1-Me-*myo*- (bornesitol) | 0·30 | 0·50 | 0·15 | 0·58 |
| 2-Me-*myo*- | 0·35 | 0·50 | 0·16 | 0·61 |
| 4-Me-*myo*- (ononitol) | 0·33 | 0·50 | 0·16 | — |
| 5-Me-*myo*- (sequoyitol) | 0·33 | 0·47 | 0·165 | 0·58 |
| 1-Me-(−) | 0·43 | 0·49 | 0·19 | 0·64 |
| 2-Me-(−) (quebrachitol) | 0·39 | 0·46 | 0·185 | 0·64 |
| 3-Me-(+) (pinitol) | 0·44 | 0·45 | 0·20 | 0·64 |
| 1 : 3-diMe-*myo*- (dambonitol) | 0·50 | 0·69 | 0·27 | 0·69 |

of dambonitol are required to cause a similar spot: heating the paper for a short time increases the sensitivity to methyl ethers. For dambonitol, Lemieux and Bauer's permanganate–periodate reagent [5] is more suitable; it is a good reagent for all cyclitols and its sensitivity does

[1] Ballou and Anderson, *J. Amer. Chem. Soc.*, 1953, **75**, 648.
[2] Posternak, Reymond, and Haerdi, *Helv. Chim. Acta*, 1955, **38**, 1911.
[3] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.
[4] Anet and Reynolds, *ibid.*, 1954, **174**, 930.
[5] Lemieux and Bauer, *Analyt. Chem.*, 1954, **26**, 920.

not vary much with the number of hydroxyl groups, but the spots are not permanent. The Scherer reagent [6] is specific for inositols only but lacks sensitivity. In some cases Hockenhull's [7] borate–phenol-red reagent is useful because it is more sensitive to those cyclitols which form complexes readily with borate,[8] *e.g.*, small amounts of *cis*inositol can be detected in the presence of *myo*inositol. It is also useful when the cyclitols are to be preserved, for example, for elution; all the other reagents referred to destroy the compounds.

For the separation of *cis*- and *epi*-inositol ethyl acetate–acetic acid–water (3 : 1 : 1; v/v) is useful, the $R_F$ values being: *myo*- 0·15, (±)- 0·20, *epi*- 0·20, and *cis*-inositol 0·25.

The $R_F$ values were determined on descending chromatograms (although the ascending technique is used for routine testing). With butanol–acetic acid–water, the chromatograms were run for 24 hr., the solvent dripping off the serrated end of the paper to give relative $R_F$ values; absolute values were calculated by comparison with a chromatogram of a few substances (of higher $R_F$ values) for which the solvent was run only to the end of the paper. Whatman No. 1 paper was used throughout. Papers wetted with phenol or butanol were dried overnight but those with acetone require only a few minutes' drying. The $R_F$ values vary considerably, unless stringent precautions are taken to assure constant conditions, but their ratio to the $R_F$ value of glucose (the $R_G$ value) is easily reproducible; glucose was therefore incorporated in all chromatograms and its $R_T$ values are given in the Table.

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[6] Fleury, Courtois, and Malangeau, *Bull. Soc. Chim. biol.*, 1953, **35**, 537.
[7] Hockenhull, *Nature*, 1953, **171**, 982.
[8] Angyal and McHugh, preceding paper.

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## 270. *Conversion of Methyltrichlorosilane into Chloromethyl Derivatives of Silane.*

By H. D. Kaesz and F. G. A. Stone.

Silicon compounds containing chloromethyl groups have been widely studied; [1] however, few chloromethyl derivatives of silane with silicon–hydrogen bonds are known. Only $CH_2Cl{\cdot}SiHMe_2$ and $CH_2Cl{\cdot}SiHEt_2$ are well characterised,[2] although chloromethylsilane, $CH_2Cl{\cdot}SiH_3$, has been reported,[3] having been obtained in poor yield by refluxing chloromethyltrichlorosilane with lithium hydride in di*iso*pentyl ether for two days. A convenient general method for preparing chloromethyl derivatives of silane, *e.g.*, $CHCl_2{\cdot}SiH_3$, by reducing chloromethylchlorosilanes with lithium aluminium hydride, is now described. Reaction occurs rapidly at 0°. Diethyl or dibutyl ether may be used as solvent, the choice depending on the boiling point of the product. The chloromethylsilane produced was recovered by distillation *in vacuo* at or below room temperature and purified by fractional distillation at atmospheric pressure. In this way chloromethylsilanes were quickly isolated from metal halides, in the presence of which they exchanged hydrogen on silicon for chlorine. Chloromethylsilane, $CH_2Cl{\cdot}SiH_3$, was obtained in nearly 80% yield, and dichloromethylsilane, $CHCl_2{\cdot}SiH_3$, and chloromethyldimethylsilane, $CH_2Cl{\cdot}SiHMe_2$, in nearly 90% yield. During reduction of $CHCl_2{\cdot}SiCl_3$ and of $CCl_3{\cdot}SiCl_3$ some difficulty was caused by production of silane as a by-product, perhaps through cleavage of carbon–silicon bonds by lithium aluminium hydride. Indeed, attempts to make $CCl_3{\cdot}SiH_3$ were abandoned owing to the large amounts of silane formed from $CCl_3{\cdot}SiCl_3$ and more particularly owing to explosions that occurred during distillation of $CCl_3{\cdot}SiH_3$ in dibutyl ether. Thus the thermal stability of the chloromethylsilyl compounds apparently decreases in the order $CH_2Cl{\cdot}SiH_3$, $CHCl_2{\cdot}SiH_3$, $CCl_3{\cdot}SiH_3$.

Chloromethylchlorosilanes, from which chloromethylsilanes are prepared, are made principally by photochemical chlorination of methylchlorosilanes. Nevertheless, the

[1] Burkhard, Rochow, Booth, and Hartt, *Chem. Rev.*, 1947, **41**, 97.
[2] Seyferth and Rochow, *J. Amer. Chem. Soc.*, 1955, **77**, 907.
[3] Ponomarenko and Mironov, *Bull. Acad. Sci. U.S.S.R.*, 1954, 423 (*Chem. Abs.*, 1955, **49**, 9495).

tendency of entering chlorine atoms completely to chlorinate one methyl group in a methylchlorosilane presents a problem as yields of the monochloro-derivatives are lowered, and these are the products usually desired. However, satisfactory yields of ***monochlorinated*** methylchlorosilanes have been obtained by maintaining the starting material in large excess. With methyltrichlorosilane one such process gave $CH_2Cl{\cdot}SiCl_3$ in 22% yield.[4] In the work described below, the photochemical chlorination technique was improved, and applied to a variety of compounds, giving any required chloromethyl compound in high yield.

*Experimental.*—Lithium aluminium hydride solutions were analysed immediately before use.[5]

*Chloromethylsilane.* Chloromethyltrichlorosilane (41·0 g.) was added to dibutyl ether (20 ml.), stirred at 0°, in a flask connected to a high-vacuum apparatus through a trap cooled to −78° and another at −196°. Then 574 ml. of a 1·164N-dibutyl ether solution of lithium aluminium hydride were added dropwise. The reaction vessel and traps which had previously contained purified nitrogen were then evacuated. In this manner liquid product, together with some solvent, was distilled into the trap at −78° while the reaction flask was at 0°. The trap cooled to −196° was intended to collect any silane formed during the reduction, but none was detected. The liquid collected at −78° was fractionally distilled at atmospheric pressure under nitrogen, through a 12″ vacuum-jacketed Vigreux column equipped with a partial-take-off total reflux still-head. At 32° *chloromethylsilane* (13·9 g., 78·5%), $n_D^{20}$ 1·4149 (Found: C, 15·0; H, 6·4; Si, 35·0%; *M*, 81·9. $CH_5ClSi$ requires C, 14·9; H, 6·2; Si, 34·8%; *M*, 81·4) was obtained. Vapour pressures were as tabulated. They correspond to $\log_{10} p(\text{mm.}) = 7{\cdot}593 - 1436T^{-1}$, an extrapolated b. p. of 31·5° (obs. 32°), a Trouton constant of 21·6 cal. deg.$^{-1}$ mole$^{-1}$, and a heat of vaporisation 6·572 kcal. mole.$^{-1}$.

*Vapour pressure of* $CH_2Cl{\cdot}SiH_3$.

| Temp. | −27·2° | −21·3° | −18·0° | −5·2° | 5·2° | 9·8° | 19·9° | 24·4° |
|---|---|---|---|---|---|---|---|---|
| $p_{mm.}$ (obs.) | 57·2 | 78·2 | 92·6 | 171·0 | 271·0 | 330·1 | 495·5 | 589·0 |
| $p_{mm.}$ (calc.) | 57·0 | 78·1 | 92·5 | 171·8 | 272·4 | 330·4 | 494·2 | 586·0 |

*Dichloromethylsilane.* 675 ml. of 0·942N-lithium aluminium hydride solution in dibutyl ether, with dichloromethyltrichlorosilane (44·3 g.) in dibutyl ether (25 ml.) at 0°, gave a considerable amount of silane and *dichloromethylsilane* (20·0 g., 86%), b. p. 68°, $n_D^{20}$ 1·4478 (Found: Si, 24·1; Cl, 62·0%; *M*, 116. $CH_4Cl_2Si$ requires Si, 24·4; Cl, 61·6%; *M*, 115). Vapour pressures (tabulated) correspond to $\log_{10} p(\text{mm.}) = 7{\cdot}869 - 1698T^{-1}$, extrapolated b. p. 67·3° (obs. 68°), Trouton constant 22·8 cal. deg.$^{-1}$ mole$^{-1}$, and heat of vaporisation 7·771 kcal. mole$^{-1}$.

*Vapour pressure of* $CHCl_2{\cdot}SiH_3$.

| Temp. | 10·4° | 15·1° | 20·5° | 24·8° | 29·8° | 35·2° | 40·2° | 45·6° |
|---|---|---|---|---|---|---|---|---|
| $p_{mm.}$ (obs.) | 76·1 | 95·2 | 123·0 | 149·3 | 185·1 | 231·7 | 282·4 | 346·4 |
| $p_{mm.}$ (calc.) | 76·1 | 95·1 | 122·2 | 148·0 | 184·2 | 230·2 | 282·1 | 348·4 |

In attempted preparations of trichloromethylsilane from trichloromethyltrichlorosilane and lithium aluminium hydride at low temperatures much silane was formed. Attempted removal of $CCl_3{\cdot}SiH_3$ from its dibutyl ether solution, by distillation under nitrogen, led to explosions. The b. p. of the presumed derivative $CCl_3{\cdot}SiH_3$ was recorded as 81°/760 mm.

*Chloromethyldimethylsilane.* 1·430N-Lithium aluminium hydride solution (125 ml.) in diethyl ether was added to $CH_2Cl{\cdot}SiMe_2Cl$ (24·6 g.) in diethyl ether (30 ml.) at 0°. Further treatment was as for the isolation of chloromethylsilane, except that dibutyl ether was added as chaser. Distillation under nitrogen gave chloromethyldimethylsilane (16·1 g., 86%), b. p. 81°, $n_D^{20}$ 1·4178 (lit.,[2] b. p. 80—81°).

*Rearrangement of Chloromethylsilanes.*—(i) During reduction of freshly distilled chloromethyldimethylchlorosilane, recovery of chloromethyldimethylsilane was attempted by distillation through a column having a Chromel spiral. While $CH_2Cl{\cdot}SiHMe_2$ was being collected at 81°, the temperature at the still-head fell to 57°, and $Me_3SiCl$ ($n_D^{20}$ 1·3890; lit.,[1]

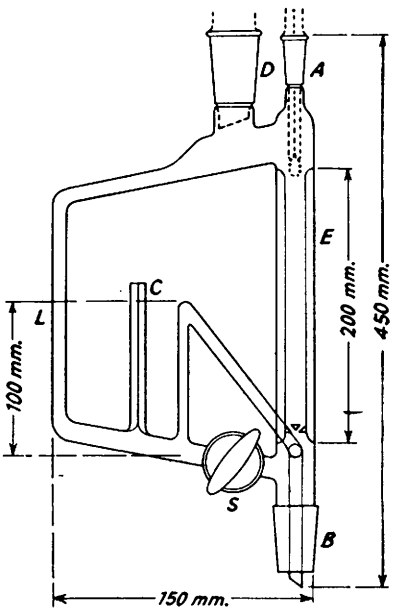
[4] Speier, B.P. 629,719/1949 (*Chem. Abs.*, 1950, **44**, 3518).
[5] Felkin, *Bull. Soc. chim. France*, 1951, 347.

b. p. 57·3°, $n_D^{20}$ 1·3878) in 53% yield was obtained. The final yield of $CH_2Cl{\cdot}SiHMe_2$ was only 36%.

(ii) When $CH_2Cl{\cdot}SiHMe_2$ was distilled through the same column using a glass spiral no rearrangement to $Me_2SiCl$ occurred.

(iii) Chloromethyldimethylsilane decomposed very slowly at room temperature when sealed *in vacuo* in glass containers. In 3 months pure $CH_2Cl{\cdot}SiHMe_2$ suffered about 2% of rearrangement, as found by determination of hydrolysable chlorine.

*Chlorination of the Methylchlorosilanes.*—The apparatus shown in the Figure was used; essentially only unchlorinated material was in contact with chlorine, and exposed to radiation. Water and solid carbon dioxide condensers were placed at *D*, and a thermometer at *A*. The compound to be chlorinated was heated in a distillation flask at *B*. As soon as liquid collected at *L*, chlorine was admitted through the capillary-tube *C*. Only the tube *L* was irradiated with ultraviolet light. The stopcock *S* was closed, and opened only at the end of reaction. The vacuum-jacketed column *E* packed with glass helices serves to return most higher-boiling chlorinated material to the flask. The temperature of the latter gradually rises to the b. p. of the desired product, whereas the temperature at *A* remains near the b. p. of the starting material, until towards the end of reaction when it rises rapidly. The course of reaction may also be followed by passing the hydrogen chloride gas issuing from the condensers into standard base.




Methyltrichlorosilane was thus chlorinated to give a 46% yield of chloromethyltrichlorosilane, b. p. 117° (Found : C, 6·8; H, 1·3; Si, 15·3; hydrolysable Cl, 58·0. Calc. for $CH_2SiCl_4$ : C, 6·5; H, 1·1; Si, 15·3; hydrolysable Cl, 57·8%) (the b. p. is reported [6] as 116·5°), and a 17% yield of *dichloromethyltrichlorosilane*, b. p. 142°, $n_D^{20}$ 1·4727 (Found : C, 5·7; H, 0·5; Si, 13·2; hydrolysable Cl, 48·9. $CHSiCl_5$ requires C, 5·5; H, 0·5; Si, 12·9; hydrolysable Cl, 48·7%). The constitution of the latter was confirmed by hydrolysis with base : methylene chloride (infrared spectrum identical with that of a pure sample) was obtained rather than a mixture of methyl chloride and chloroform.

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[6] Yakubovitch and Ginsburg, *J. Gen. Chem.* (*U.S.S.R.*), 1952, **22**, 1783.

## 271. *The Preparation of Cyclic Ketones by Use of Trifluoroacetic Anhydride.*

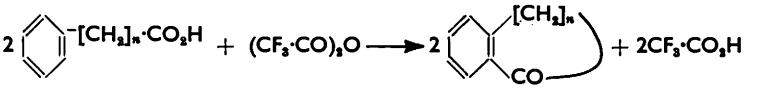
By R. J. FERRIER and J. M. TEDDER.

IT has been shown that trifluoroacetic anhydride will promote condensation of carboxylic acids with activated aromatic compounds to form ketones.[1] This reaction has now been applied to intramolecular condensation of two aromatic acids. γ-Phenylbutyric acid ($n = 3$) has been converted into α-tetralone in good yield in mild conditions, but β-phenylpropionic acid ($n = 2$) gave very poor yields of indan-1-one. Although a better yield of indan-1-one was obtained by using heptafluorobutyric anhydride at a higher temperature the product was contaminated with tar and was hard to purify. As a reagent for promoting this type of ring closure, trifluoroacetic anhydride would appear valuable for the

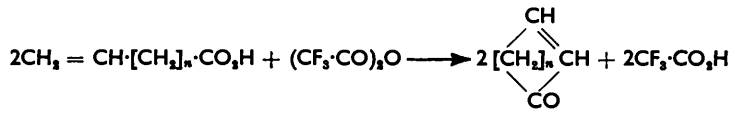
[1] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1951, 718.

synthesis of six-membered rings ($n = 3$) from compounds too sensitive to be treated with anhydrous hydrogen fluoride or polyphosphoric acid; however it would not appear to be very useful for the synthesis of five-membered rings ($n = 2$).

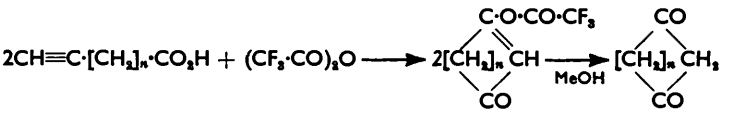
The second reaction of trifluoroacetic anhydride adapted for the preparation of cyclic ketones was the acyl addition of carboxylic acids to olefins.[2] Two ω-olefinic acids have



been treated with trifluoroacetic anhydride and one of these, hex-5-enoic acid ($n = 3$), yielded *cyclo*hex-2-enone in good yield. Pent-4-enoic acid ($n = 2$) on the other hand gave



only a trace of *cyclo*pent-2-enone together with a small yield of a linear dimer. The closely related acyl addition of carboxylic acids to acetylenes [2] was also developed for the preparation of cyclic 1 : 3-diketones. Hex-5-ynoic acid ($n = 3$) when treated with



trifluoroacetic anhydride gave a 25% yield of *cyclo*hexane-1 : 3-dione, but pent-4-ynoic acid ($n = 2$) failed to yield *cyclo*pentane-1 : 3-dione, and hept-6-ynoic acid ($n = 4$) failed to yield either *cyclo*heptane-1 : 3-dione or 1-hydroxymethylene*cyclo*hexanone.

*Experimental.—Successful cyclisations.* (*a*) γ-Phenylbutyric acid [3] (0·18 g.) was dissolved in trifluoroacetic anhydride (0·3 c.c.). The reactants were warmed at 60—70° for 3 hr. and the product was isolated by pouring the mixture into aqueous sodium hydrogen carbonate and extracting it with chloroform. The extract was dried ($MgSO_4$) and the solvent evaporated to leave crude α-tetralone (0·17 g.). The crude product was treated with a methanolic solution of semicarbazide hydrochloride from which α-tetralone semicarbazone (0·17 g.; m. p. 213—214°) was isolated.

In another experiment γ-phenylbutyric acid (0·39 g.) was warmed with trifluoroacetic anhydride (0·6 c.c.) for 1 hr. at 40° and the crude α-tetralone (0·21 g.) isolated as before.

(*b*) Hex-5-enoic acid (8·5 g.) was added to ice-cold trifluoroacetic anhydride (15·6 c.c.). The temperature rose spontaneously to 45°, and the reactants were set aside at room temperature for 2 hr., warmed at 30—40° for 0·5 hr., poured into aqueous sodium hydrogen carbonate, and left overnight. The *cyclo*hexenone was isolated by extraction with chloroform, and the product was distilled under reduced pressure. Three fractions were taken: (i) 0·42 g., $n_D^{20}$ 1·4710, b. p. 50°/20 mm., (ii) 3·06 g., $n_D^{20}$ 1·4860, b. p. 67—68°/18 mm., and (iii) 0·20 g., $n_D^{20}$ 1·4730, b. p. 68—80°/20 mm. (undistilled residue 1·33 g.). Fraction (ii) was essentially pure *cyclo*hex-2-enone. Both fractions (i) and (iii) contained some ketone which was estimated by quantitatively preparing the 2 : 4-dinitrophenylhydrazone, the yields of which corresponded to 0·15 g. and 0·10 g. respectively of ketone, making the overall yield 3·31 g. (46%) [2 : 4-dinitrophenylhydrazone, m. p. 163—164° (Found: C, 52·3; H, 4·35; N, 19·7. Calc. for $C_{12}H_{12}O_4N_4$: C, 52·2; H, 4·38; N, 20·3%). Bartlett and Woods [4] report *cyclo*hex-2-enone, b. p. 61—63°/14 mm., $n_D^{18}$ 1·4842 (2 : 4-dinitrophenylhydrazone, m. p. 163°)].

(*c*) Trifluoroacetic anhydride (8·0 c.c.) was added to hex-5-ynoic acid (5·09 g.) at 0°. After 6 hr., during which the solution darkened considerably, the reactants were allowed to warm to room temperature (18°) and were left overnight. Methanol (30 c.c.) was then added and the mixture was refluxed for 1 hr. before methyl trifluoroacetate and the excess of methanol were

[2] Henne and Tedder, *J.*, 1953, 3628.
[3] Overbaugh, Allen, Martin, and Fieser, *Org. Synth.*, 1935, **15**, 64; 1937, **17**, 97.
[4] Bartlett and Woods, *J. Amer. Chem. Soc.*, 1940, **62**, 2933.

distilled off at atmospheric pressure. The residue was distilled *in vacuo*; the distillate (1·72 g.), a yellow oil, which partly solidified, had b. p. 120—140° (bath-temp.)/0·1 mm. The distillate was rubbed with ether to yield a pale yellow solid, m. p. 99—103°, which was recrystallised from ether–light petroleum to yield *cyclo*hexane-1 : 3-dione, m. p. and mixed m. p. 105° (1·01 g.).

*Syntheses of ω-unsaturated acids used in the cyclisation experiments.* (*a*) Hex-5-enoic acid. Pent-4-en-1-ol [5] was converted into hex-5-enoic acid by way of 4-bromo- and 4-cyano-pentene according to the method of LaForge, Green, and Gersdorff.[6] The acid used for cyclisation had b. p. 102—104°, $n_D^{16}$ 1·4368 (*p*-toluidide, m. p. 54—55°).

(*b*) Pent-4-ynoic acid was prepared by the oxidation of pent-4-yn-1-ol [7] according to Eglington and Whiting's method.[8] Acid used for the attempted cyclisation had m. p. 55—56°.

(*c*) Hex-5-ynoic acid. 1-Bromo-3-chloropropane (158 g.) was treated with sodium acetylide in liquid ammonia, to yield 5-chloropent-1-yne [9] (56 g.), b. p. 112°/748 mm., $n_D^{17}$ 1·4451. The chloropentyne (55 g.) was refluxed with a solution of sodium cyanide to yield 5-cyanopent-1-yne (35 g.), $n_D^{18\cdot5}$ 1·4362. The cyanopentyne (30 g.) was hydrolysed by 10% sodium hydroxide solution on a water-bath for 6 hr., to yield hex-5-ynoic acid (27·6 g.), b. p. 122—124°/20 mm., $n_D^{18\cdot5}$ 1·4495. Eglington and Whiting,[8] who prepared the cyanide by a different route, report $n_D^{17}$ 1·4409 for the cyanopentyne and m. p. −8°, b. p. 106°/9 mm., $n_D^{17}$ 1·4500, for the acid.

(*d*) Hept-6-ynoic acid. Tetramethylene dibromide (93 g.) was treated with sodium cyanide in aqueous ethanol, to yield δ-bromovaleronitrile [10] (17 g.), b. p. 105—110°/14 mm., $n_D^{18}$ 1·4669 (19·2 g. of tetramethylene bromide were recovered). The bromovaleronitrile (16 g.) with sodium acetylide in liquid ammonia yielded hex-5-ynyl cyanide (8·0 g.), which was hydrolysed with 10% sodium hydroxide solution to hept-6-ynoic acid (6·0 g.), b. p. 78—80° (bath-temp.)/0·04 mm., $n_D^{26}$ 1·4371 (*p*-toluidide, m. p. 80°). Taylor and Strong [11] who prepared hept-6-ynoic acid by a different route report b. p. 93—94°/1 mm., $n_D^{25}$ 1·4495 (*p*-toluidide, m. p. 84—85°).

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[5] Brooks and Synder, *Org. Synth.*, 1945, **25**, 84.
[6] LaForge, Green, and Gersdorff, *J. Amer. Chem. Soc.*, 1948, **70**, 3709.
[7] Jones, Eglington, and Whiting, *Org. Synth.*, 1953, **33**, 68.
[8] Eglington and Whiting, *J.*, 1953, 3052.
[9] Henne and Greenlee, *J. Amer. Chem. Soc.*, 1945, **67**, 484.
[10] Cloke and Ayers, *ibid.*, 1934, **56**, 2144.
[11] Taylor and Strong, *J. Amer. Chem. Soc.*, 1950, **72**, 4264.

## 272. *The Reversibility of Aromatic Nitration.*

By P. H. GORE.

EXAMPLES of acid-catalysed migrations of aromatic nitro-groups have recently been recorded.[1] These involve two systems (I; R = H or Ac) and (II) in which the central nitro-group slowly moves to give isomeric dinitro-compounds on treatment with concentrated sulphuric acid at 112°.

The scheme suggested [1] for the rearrangement of the dinitroaniline (I; R = H) involves, as an initial step, a reversal of Bamberger's phenylnitramine rearrangement [2] to give the nitramine (III; R = H). The latter either undergoes the normal intramolecular rearrangement to give two of the products isolated, 2 : 5-dinitroaniline and a part, at least, of the 3 : 4-dinitroaniline, or undergoes acidolysis to *m*-nitroaniline. The nitronium cation thus formed is considered to react further with *m*-nitroaniline to give most of the 3 : 4-dinitroaniline, and possibly a little 2 : 5-isomer as well. This is supported by the isolation of a much reduced yield of 3 : 4-dinitroaniline as well as some 15% of *m*-nitroaniline when the rearrangement is carried out in the presence of anisole as acceptor. This observation clearly establishes the presence of a free nitrating agent (presumably $NO_2^+$) but provides no evidence for a reversal of the phenylnitramine change. In any case, this suggested first step becomes highly unlikely in the reaction with the dinitrophenol (II) (it would involve formation of an analogous phenyl nitrate). Moreover the acidolysis

[1] Pausacker and Scroggie, *Chem. and Ind.*, 1954, 1290; *J.*, 1955, 1897.
[2] Cf. Hughes and Ingold, *Quart. Rev.*, 1952, **6**, 48.

of phenylnitramine is considerably slower [3] than its rearrangement, whilst Pausacker and Scroggie's mechanism [1] requires the two processes to be comparable in rate.

An attractive alternative mechanism, by which the formation of each of the products may be simply accounted for, involves an acid-controlled removal of the " migrating " nitro-group directly from the dinitro-aniline (I) or -phenol (II), followed by renitration. Such a mechanism seems to require that aromatic nitration is reversible, although it is generally understood to be irreversible. However, evidence now presented shows that such a reversal of nitration is indeed possible, in the special systems here considered.

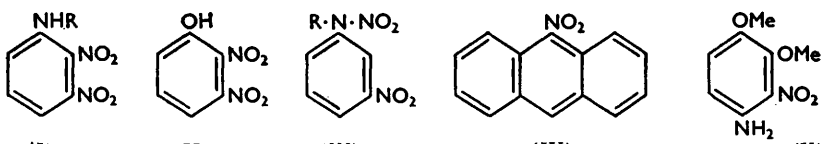
In 9-nitroanthracene (IV) any initial denitration on acid treatment is not followed by nitration in a different aromatic position, as postulated in the above cases, so that the fragments of the acidolysis can be sought. With 12N-sulphuric acid in trichloroacetic acid for 15 min. at 95° it gives a dark solution in which, after dilution with water, an 81% yield of free nitric acid was estimated. Free anthracene could not be isolated, but a 20% yield of anthraquinone * and appreciable amounts of polymer and soluble sulphonic acids were obtained. An experiment conducted in the presence of nitrobenzene failed to show the formation of a possible cross-nitration product. The system may be represented thus :

$$Ar{\cdot}NO_2 \overset{H^+}{\rightleftharpoons} [ArH{\cdot}NO_2]^+ \rightleftharpoons Ar{\cdot}H + \overset{+}{N}O_2$$

$$\downarrow \qquad \downarrow H_2O$$

$$\text{Products} \quad HNO_3 + H^+$$

It is seen, therefore, that a nitro-group in an " aromatic " position may be considered hydrolysable (or liable to rearrangement) when its position is activated and is sterically hindered, and the solvent conditions are sufficiently acidic. Activation of the position at which the nitro-group is replaced by hydrogen may occur by electron-releasing substituents (hydroxyl, methoxyl, amino, acetamido), or by the nature of the polycyclic residue. In the present case, the reactive aromatic position is flanked by two bulky *ortho*-substituents, or by two *peri*-hydrogen atoms, so that this central nitro-group may be displaced from the coplanar position with a lowering of its mesomeric deactivation of the ring. Also, if it may be assumed that the transition state of the denitration is a σ-complex,[4] there will be a reduction of steric repulsion by the nitro-group, *i.e.*, there will be little steric hindrance to the formation of the σ-complex. The acid concentration necessary to effect removal of a nitro-group is high in those examples where one of the *ortho*-substituents is a deactivating nitro-group. Thus, rearrangement of the nitrophenol (II) is far from complete after 7 hours with concentrated sulphuric acid at 112°. Where no such deactivation occurs, milder conditions suffice (see Experimental). In one case [5] the nitroaniline (V), where all three substituents are activating, a much less acidic medium (phosphoric acid in glacial acetic acid) can mobilise the nitro-group.




(I) (II) (III) (IV) (V)

We conclude that nitration can be reversed in certain cases, but emphasise that normal aromatic nitrations should continue to be regarded as essentially irreversible, because a nitro-group rarely enters a sterically hindered position of the type discussed here, and

* We do not attempt to explain its formation here.

[3] Cf. Hughes and Jones, *J.*, 1950, 2678.
[4] Wheland, *J. Amer. Chem. Soc.*, 1942, **64**, 900.
[5] Frisch, Silverman, and Bogert, *J. Amer. Chem. Soc.*, 1943, **65**, 2432.

conditions for the removal of a nitro-group appear to be far more strenuous than those for its introduction.

*Experimental.—Action of sulphuric acid on 9-nitroanthracene.* 9-Nitroanthracene (5 g.) was dissolved in a mixture of 36N-sulphuric acid (10 ml.) and trichloroacetic acid (30 g.) at 65°, and kept thereat for 10 min., and at 95° for a further 15 min. During this time the odour of " nitrous fumes " was noticeable. The precipitate formed on pouring the mixture on ice was extracted with hot benzene, leaving a black residue (4·5 g.). The dried extract was chromatographed on alumina; the main band (yellow) was eluted, the solvent evaporated, and the residue crystallised from acetic acid, giving anthraquinone (1·0 g., 21%), m. p. and mixed m. p. 283—284°. The aqueous mother liquor gave strongly positive tests for nitric acid (brown-ring, Lunge, " nitron "). Gravimetric precipitation [6] as nitron nitrate (0·287 g. on a 1/25th aliquot part) showed the presence of 1·20 g. (81%) of nitric acid.

I thank Dr. K. H. Pausacker for his comments.

ACTON TECHNICAL COLLEGE, LONDON, W.3. [*Received, May 31st*, 1956.]

[6] Treadwell and Hall, " Analytical Chemistry," John Wiley and Sons, Inc., New York, 1935, Vol. II, 401.

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## 273. *Anion-exchange Studies of Solutions of Stannic Chloride in Hydrochloric Acid.*

By D. A. EVEREST and J. H. HARRISON.

IT has been recently observed [1] that quadrivalent tin is sorbed by the strong base ion-exchange resin Amberlite I.R.A. 400 from 2M-hydrochloric acid. In view of the utility of ion-exchange methods in the study of complex systems,[2,3] we are studying ion-exchange of solutions of stannic chloride in hydrochloric acid.

The results are given in the Table. The ratios Cl : Sn in the complex tin anions sorbed

*Sorption of tin and chloride from solutions of stannic chloride in hydrochloric acid by Amberlite* I.R.A. 400-(Cl) (0·25 *g.*).

| Acid concn.* (M) | G.-atoms sorbed/ equiv. resin: Cl | Sn | Cl : Sn in sorbed complex ions: singly charged | doubly charged |
|---|---|---|---|---|
| *1·5 ml. of stannic chloride in 50 ml. of solution.* | | | | |
| 12 | 4·00 | 0·735 | 5·1 : 1 | 6·1 : 1 |
| 10 | 4·24 | 0·760 | 5·2 : 1 | 6·2 : 1 |
| 10 | 4·06 | 0·755 | 5·0 : 1 | 6·0 : 1 |
| 9 | 4·15 | 0·765 | 5·1 : 1 | 6·1 : 1 |
| 6 | 4·16 | 0·755 | 5·1 : 1 | 6·1 : 1 |
| 5 | 4·25 | 0·775 | 5·1 : 1 | 6·1 : 1 |
| 5 | 4·15 | 0·767 | 5·1 : 1 | 6·1 : 1 |
| 5 | 4·03 | 0·765 | 4·9 : 1 | 5·9 : 1 |
| 4 | 4·00 | 0·765 | 4·9 : 1 | 5·9 : 1 |
| 3 | 3·60 | 0·700 | 4·7 : 1 | 5·7 : 1 |
| 2 | 3·90 | 0·720 | 4·9 : 1 | 5·9 : 1 |
| 1 | 3·37 | 0·627 | 4·8 : 1 | 5·8 : 1 |
| 0·5 | 3·22 | 0·627 | 4·5 : 1 | 5·5 : 1 |
| 0·1 | 2·84 | 0·475 | 4·7 : 1 | 5·7 : 1 |
| 0·02 | 2·58 | 0·426 | 4·5 : 1 | 5·5 : 1 |
| 0·0 | 1·74 | 0·292 | 4·5 : 1 | 5·5 : 1 |
| *0·3 ml. of stannic chloride in 50 ml. of solution.* | | | | |
| 1·0 | 2·65 | 0·450 | 4·7 : 1 | 5·7 : 1 |
| 0·5 | 2·54 | 0·416 | 4·7 : 1 | 5·7 : 1 |
| 0·4 | 2·49 | 0·423 | 4·5 : 1 | 5·5 : 1 |
| 0·3 | 1·62 | 0·150 | 5·1 : 1 | 6·1 : 1 |
| 0·25 | 1·30 | 0·067 | 5·4 : 1 | 6·4 : 1 |
| <0·2 | 1·00 | 0·00 | — | — |

* Acid concentration before addition of stannic chloride.

by the resin, on the assumption that only a simple mixture of chloride ions and *n*-valent chloro-tin anions were taken up by the resin, were calculated as follows: the fraction of

[1] Hunter and Miller, *Analyst*, 1954, **79**, 483; 1956, **81**, 79.
[2] Everest, *J.*, 1955, 4415.
[3] Holroyd and Salmon, *J.*, 1956, 269.

the capacity of the resin sample taken up by simple chloride ions was [1 — ($n$ × g.-atoms of tin sorbed)]; the ratio Cl : Sn in the sorbed complex was then given by the expression (g.-atoms of total chloride sorbed — g.-atoms of simple chloride sorbed)/(g.-atoms of tin sorbed). The ratios so calculated indicated that in >1M-hydrochloric acid either $SnCl_5^-$ or $SnCl_6^{2-}$ ions were sorbed by the exchanger. As the amount of tin sorbed was greater than 0·5 g.-atom per equiv. of resin the sorption of $SnCl_5^-$ ions was favoured. As has been shown by Kraus and Moore,[4] in strong hydrochloric acid solutions the anions most strongly held by an anion-exchanger carry the smaller negative charge. This effect is the probable cause of the sorption of $SnCl_5^-$ rather than $SnCl_6^{2-}$ ions by the exchanger.

Hydrolysis was observed with the lower stannic chloride concentrations in <0·25M-hydrochloric acid: hydrous stannic oxide was precipitated and the sorption of tin by the resin fell to zero. No hydrolysis was observed with the higher stannic chloride concentrations, even when hydrochloric acid was not used. Pentachlorostannate or hexachlorostannate ions appeared to be the only tin species sorbed by the resin at all acid concentrations, although the slight decrease in the Cl : Sn ratios in <1M-hydrochloric acid at the higher stannic chloride concentrations may indicate sorption of some partly hydrolysed chlorostannate ions (*i.e.*, some $Cl^-$ ions replaced by $OH^-$). The fraction of the tin sorbed as these partly hydrolysed species was always small, however, even when hydrochloric acid was not used. In the latter solutions, the chloride ions liberated by the hydrolysis of a fraction of the stannic chloride combine with the rest of the stannic chloride to form penta- or hexa-chlorostannate ions, which were then sorbed by the resin. This would be in agreement with the views of Gueron,[5] who observed that the Raman spectrum of freshly prepared solutions of stannic chloride contained lines observed also in acid solutions of hexachlorostannates.

*Experimental.*—Stannic chloride (1·5 or 0·3 ml.) was dissolved in 0—12M-hydrochloric acid (50 ml.) and allowed to come to equilibrium with Amberlite I.R.A. 400-Cl resin (0·25 g.) over a period of two weeks. The solution was then separated from the resin phase by filtration through a column (10 cm. long above a sintered glass disc of No. 2 grade porosity), washed with *ca.* 25 ml. of water under suction, the resin-solution contact time during washing being of the order of 10 sec. The resin was then eluted with N-sodium hydroxide (*ca.* 300 ml.), tin in the eluate was estimated iodometrically,[6] and the chloride gravimetrically as silver chloride. As it is not possible entirely to wash out any solution entrained inside the resin beads for fear of hydrolysing the sorbed chloro-tin complexes, an approximate correction was made for entrained chloride by again equilibrating the resin sample with hydrochloric acid of the same normality as was used in the original experiment. The resin was then filtered off, and washed with 20 ml. of water under suction and then slowly with 250 ml. of water. The chloride in the latter washings gave the required correction, small compared with the total amount of chloride sorbed by the resin. The resin sample was finally eluted with *ca.* 250 ml. of 2N-nitric acid, the chloride in the eluate giving the capacity of the resin sample.

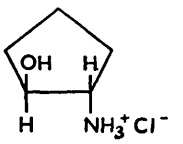
BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, September 18th*, 1956.]

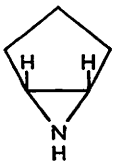
[4] Krauss and Moore, *J. Amer. Chem. Soc.*, 1951, **73**, 10.
[5] Gueron, *Compt. rend.*, 1933, **197**, 247; *Ann. Chim.* (*France*), 1935, **3**, 225.
[6] Everest, *J.*, 1951, 2903.

## 274. *Chemistry of Ethyleneimine. Part III.** cyclo*Penteneimine or* 6-*Aza*bicyclo[3 : 1 : 0]*hexane.*

By Paul E. Fanta.

In an earlier paper,[1] the stereochemistry associated with ring-closure and -opening of ethyleneimine was elucidated by a study of *cyclo*hexeneimine. These observations have now been extended to the homologous compound, *cyclo*penteneimine (II).

(I) 

(II)

*cyclo*Penteneimine (II) was prepared by the conventional Wenker procedure from (±)-*trans*-2-amino*cyclo*pentanol hydrochloride (I), and was obtained as a colourless liquid having a strong, unpleasant ammoniacal odour. It was characterized as the *N*-phenylthiocarbamoyl derivative.

Hydrolysis of *cyclo*penteneimine with aqueous perchloric acid gave (±)-*trans*-2-amino*cyclo*pentanol. Since the *cyclo*pentane and aziridine rings can be fused only in the *cis*-configuration, the ring-closure and -opening of *cyclo*penteneimine must occur with inversion at the carbon atom undergoing displacement.

*cyclo*Penteneimine is the first example of a stable, definitely characterized member of the 6-aza*bicyclo*[3 : 1 : 0]hexane system. This skeleton has previously been suggested, without conclusive evidence, for the product of a pyrolysis [2] and also, in the form of an unsaturated iminium derivative, as a possible intermediate in the reaction of 3 : 5-dibromo*cyclo*pentene with dimethylamine.[3]

*Experimental.*—(±)-*trans*-2-Amino*cyclo*pentanol hydrochloride (I) was prepared as previously described.[4] Hydrogenation of *cyclo*pentanone was accomplished in 99% yield by using freshly prepared Raney nickel without solvent at 60—110° and a hydrogen pressure of 30—120 atm.

(±)-trans-2-*Amino*cyclo*pentyl hydrogen sulphate.* A solution of the hydrochloride (0·289 g.) and sulphuric acid (0·210 g.) in water (2 ml.) was gently heated in an evacuated vessel until the residue solidified. The hard, brown solid was recrystallized from ethanol–water (50%, then 70%) (charcoal) to give fine crystals of (±)-trans-2-*amino*cyclo*pentyl hydrogen sulphate*, m. p. >280° (vigorous decomp.) (Found: C, 33·0; H, 6·2. $C_5H_{11}O_4NS$ requires C, 33·1; H, 6·1%).

cyclo*Penteneimine* (II). A solution of the hydrochloride (I) (13·7 g.) and sulphuric acid (10·0 g.) in water (30 ml.) was evaporated to dryness and gently heated at about 10 mm. for several minutes. Cold aqueous sodium hydroxide (40 g. in 50 ml.) was added and distillation conducted until the residue was nearly solid. The distillate was cooled, saturated with sodium hydroxide, and extracted with ether (15 ml.). The ether solution was dried (Na) and distilled (from Na) to give the imine (5·1 g., 61%), b. p. 115—135°. The middle fraction (2·0 g.) of pure cyclo*penteneimine* had b. p. 122—123°, $n_D^{22}$ 1·4700 (Found: N, 16·6. $C_5H_9N$ requires N, 16·8%). The N-*phenylthiocarbamoyl* derivative, m. p. 167—168° (Found: C, 66·5; H, 6·7; N, 12·8. $C_{12}H_{14}N_2S$ requires C, 66·0; H, 6·5; N, 12·8%), was obtained by treating the imine with phenyl *iso*thiocyanate in light petroleum (b. p. 40—60°)

* Part II, *J. Org. Chem.*, 1956, **21**, 892.

[1] Paris and Fanta, *J. Amer. Chem. Soc.*, 1951, **74**, 3007.
[2] Wolff, *Annalen*, 1913, **399**, 294.
[3] DeWolfe and Young, *Chem. Rev.*, 1956, **56**, 851.
[4] McCasland and Smith, *J. Amer. Chem. Soc.*, 1950, **72**, 2190.

*Hydrolysis of* cyclo*penteneimine*. A solution of *cyclo*penteneimine (0·83 g.) and 60% perchloric acid (1 ml.) in water (3·0 ml.) was refluxed for 30 min. Excess of sodium hydroxide solution and a few drops of benzoyl chloride were added. Warming and shaking followed by cooling gave a white solid, which was recrystallized from methanol–water to give the ON-*dibenzoyl* derivative, m. p. 115·5—116° (Found: N, 4·5. $C_{19}H_{19}O_3N$ requires N, 4·5%). An authentic sample which had an identical m. p. and mixed m. p. was prepared by benzoylation of an aqueous solution of (±)-*trans*-2-amino*cyclo*pentanol hydrochloride as described above for the hydrolysis product.

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## 275. *Preparation of β-3-Indolylacrylic Acid.*

By J. S. Moffatt.

β-3-Indolylacrylic acid, first prepared by Bauguess and Berg,[1] has been studied as an inhibitor of growth of certain micro-organisms.[2] In our hands, the earlier methods [1,3] gave low and variable yields of a red-brown acid. The indolylacrylic acid was prepared more conveniently and in improved yield (48%) by condensation of 1-acetyl-3-formylindole [4] with malonic acid at 80° and deacetylation of the crude product; the acrylic acid was then obtained as pale-yellow plates. Condensation at 36—40° afforded,[1] in addition to β-3-indolylacrylic acid, mainly (3-indolylmethylene)malonic acid.

*Experimental.—Interaction of* 1-*acetyl*-3-*formylindole and malonic acid at* 40°. The acetylaldehyde [4] (560 mg.) and malonic acid (936 mg.) were heated in pyridine (4·5 ml.), containing piperidine (3 drops), at 36—40° for 24 hr. The mixture was poured into water and then acidified with 5N-hydrochloric acid. The precipitate was dissolved in 0·5N-sodium hydroxide (18 ml.), and the solution set aside for 1 hr. and then acidified with hydrochloric acid. The resulting yellow precipitate (450 mg.) was extracted with cold ether (30 ml.). The insoluble portion (210 mg.), on repeated crystallisation from methanol, formed minute, yellow needles, m. p. 208—209° (decomp.), of (3-*indolylmethylene*)*malonic acid* (Found: C, 61·7; H, 3·7; N, 6·2%; equiv., 108. $C_{12}H_9O_4N$ requires C, 62·3; H, 3·9; N, 6·1%; equiv., 115). The soluble portion, on fractional crystallisation from ether–light petroleum (b. p. 40—60°), afforded some β-3-indolylacrylic acid (52 mg.).

*Interaction at* 80°: *preparation of* β-3-*indolylacrylic acid*. The acetylaldehyde (3 g.) and malonic acid (2·52 g.) were heated in pyridine (15 ml.) containing piperidine (0·3 ml.) at 78—80° for 3 hr. The solution was poured into ice-cold water (300 ml.), and the mixture acidified with 5N-hydrochloric acid. After the mixture had been stored in the refrigerator overnight, the yellow precipitate was washed with water and then dissolved in 0·5N-sodium hydroxide (75 ml.). The solution was stored for 1 hr., filtered, and then acidified. The yellow precipitate (1·95 g.) was then dissolved in ether (300 ml.). The solution was filtered, concentrated (to half-volume), and then treated with light petroleum (b. p. 40—60°; 150 ml.). The resulting pale-yellow precipitate on recrystallisation from ethyl acetate afforded 3 crops of the indolylacrylic acid: (i) pale yellow plates (920 mg.), m. p. 192—193° (decomp.) (Found: C, 70·5; H, 5·1; N, 7·6. Calc. for $C_{11}H_9O_2N$: C, 70·6; H, 4·85; N, 7·5%), (ii) pale tan-coloured plates (302 mg.), m. p. 192—193° (decomp.), and (iii) pale tan-coloured plates (234 mg.), m. p. 191—193° (decomp.)

[1] Bauguess and Berg, *J. Biol. Chem.*, 1934, **104**, 675.
[2] Fildes, *Brit. J. Exp. Path.*, 1945, **26**, 416; Marnay, *Bull. Soc. Chim. biol.*, 1951, **33**, 174.
[3] Furst, Harper, Seiwald, Morris, and Nevé, *Arch. Biochem. Biophys.*, 1951, **31**, 190.
[4] Majima and Kotake, *Ber.*, 1925, **58**, 2037.

[total yield 48%; Bauguess and Berg [1] reported a yield of 34% (from 3-formylindole) of reddish-brown rhombic platelets, m. p. 195—196°].

The author is indebted to Messrs. W. Brown and A. G. Olney for the microanalyses.

AKERS RESEARCH LABORATORIES,
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[*Received, November 14th*, 1956.]

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## 276. *The Preparation of 2-Hydroxyglyoxalines from α-Amino-acids.*

By ALEXANDER LAWSON.

ALTHOUGH 2-hydroxyglyoxaline has been synthesised by the action of cyanate on α-amino-acetaldehyde acetal,[1, 2a] the use of α-amino-aldehydes for the preparation of the 4(5)-substituted homologous 2-hydroxyglyoxalines has not been reported, the 4(5)-methyl,[2b] ethyl,[2a, 3] and phenyl compounds [4] having been obtained from the appropriate amino-methyl ketones. Akabori and Numano [5] prepared a number of 2-mercaptoglyoxalines by the action of thiocyanate on the solutions of amino-aldehydes obtained by the reduction of α-amino-acid esters with sodium amalgam, but did not mention the ring closure with cyanate to give the corresponding oxygen analogues. Owing to the ready accessibility of the α-amino-acids and the improved technique available for the Akabori reduction [5] it seemed of interest to attempt the preparation of some 4(5)-substituted 2-hydroxy-glyoxalines by this route.

The method previously adopted for the condensation of amino-aldehydes with thio-cyanate [6] cannot be used for the condensation with cyanate, presumably because of the relatively lower stability of cyanic acid. It was found (as with amino-acetaldehyde diethylacetal [2a]) that the temperature had to be kept well below 0° in the initial stages and the pH adjusted to about 7·0. Under these conditions, the yields were satisfactory.

The reaction between cyanate and secondary amino-acetals also takes place readily, as shown by the preparation of 2-hydroxy-1-methylglyoxaline from α-methylaminoacet-aldehyde diethyl acetal.

*Experimental.—Preparation of 2-hydroxyglyoxalines from amino-acids.* The amino-acid (0·05 mole) was heated with ethanol (100 ml.) saturated with dry hydrogen chloride and the solvent removed by distillation under reduced pressure after addition of benzene (50 ml.). The residue of amino-ester hydrochloride was dissolved in ice-cold water (100 ml.), and 2·3% sodium amalgam (200 g.) added slowly with stirring, the pH being maintained between 2 and 3 by the addition of 5N-hydrochloric acid and the temperature held between 0° and −5° by the addition of powdered solid carbon dioxide. The resulting solution was then filtered, cooled to −15° by the addition of carbon dioxide, and brought to pH 4·0 by the addition of sodium hydrogen carbon-ate, and a cold aqueous solution of potassium cyanate (0·05 mole) added. The pH was then about 7·0. After 30 min. the solution was warmed on the steam-bath for a further 30 min. and finally boiled for several minutes. In the cases of 4(5)-*iso*butyl-, -*n*-butyl-, -*n*-hexyl-, -benzyl-, -*p*-hydroxybenzyl-, and -phenyl-substituted 2-hydroxyglyoxalines the product crystallised from the hot solution. In other cases the product was extracted with ethanol from the solid left after evaporation of the solution under reduced pressure. The m. p., yields, and analyses are shown in Table 1. The monoacetyl derivatives of the hydroxyglyoxalines were prepared on the steam-bath with acetic anhydride–sodium acetate. The analytical

[1] Marckwald, *Ber.*, 1892, **25**, 2354.
[2] Duschinsky and Dolan, *J. Amer. Chem. Soc.*, (*a*) 1946, **68**, 2350; (*b*) 1945, **67**, 2079.
[3] Kolshorn, *Ber.*, 1904, **37**, 2474.
[4] Rupe, *Ber.*, 1895, **28**, 251.
[5] Akabori and Numano, *Ber.*, 1933, **66**, 151, 159.
[6] Bullerwell and Lawson, *J.*, 1951, 2223.

values and m. p. are in Table 2. A *monobenzoyl derivative* of 2-hydroxy-4(5)-*p*-hydroxybenzylglyoxaline (from tyrosine) had m. p. 242°, prisms from ethanol (Found : C, 69·1; H, 4·9. $C_{17}H_{14}O_3N_2$ requires C, 69·4; H, 4·8%).

*2-Hydroxy-1-methylglyoxaline.* To a solution of methylaminoacetaldehyde diethyl acetal (7·8 g.) in water (11 ml.) cooled to −15° with solid carbon dioxide, cold 3N-hydrochloric acid

TABLE 1. *4(5)-Substituted 2-hydroxyglyoxalines.*

| Parent Amino-acid | 4-Subst. | Form [a] | Yield † (%) | M. p. | Formula | Found (%) C | Found (%) H | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|---|---|
| Glycine ..... | H | [a] | 27 | 250° | $C_3H_4ON_2$ | — | — | — | — |
| Alanine ..... | Me | [a] | 42 | 202 | $C_4H_6ON_2$ | 48·6 | 6·1 | 48·9 | 6·1 |
| α-Aminobutyric | Et | Plates | 37 | 192 | $C_5H_8ON_2$ | 53·3 | 7·0 | 53·5 | 7·1 |
| Norvaline ..... | $Pr^n$ | Prisms | 43 | 194 | $C_6H_{10}ON_2$ | 56·8 | 7·9 | 57·1 | 7·9 |
| Valine ..... | $Pr^i$ | Needles | 44 | 223 | $C_6H_{10}ON_2$ | 57·3 | 7·9 | 57·1 | 7·9 |
| Norleucine ..... | $Bu^n$ | Prisms | 48 | 191 | $C_7H_{12}ON_2$ | 59·6 | 8·6 | 60·0 | 8·6 |
| Leucine ..... | $Bu^i$ | ,, | 29 | 245 | $C_7H_{12}ON_2$ | 59·9 | 8·6 | 60·0 | 8·6 |
| Aspartic ..... | $CH_2{\cdot}CO_2Et$ | Plates | 56 | 213 | $C_7H_{10}O_3N_2$ | 49·7 | 6·1 | 49·4 | 5·9 |
| Glutamic ..... | $[CH_2]_2{\cdot}CO_2Et$ | Prisms [b] | 45 | 140 | $C_9H_{12}O_3N_2$ | 52·3 | 6·4 | 52·1 | 6·5 |
| Glutamic ..... | $[CH_2]_2{\cdot}CO_2H$ | ,, | — | 246 ‡ | $C_6H_8O_3N_2$ | 45·9 | 5·3 | 46·1 | 5·1 |
| 2-Amino-octanoic ..... | $C_6H_{13}$ | ,, | 32 | 183 | $C_9H_{16}ON_2$ | 63·9 | 9·3 | 64·2 | 9·5 |
| α-Phenylglycine | Ph | Plates [c] | 57 | 325 ‡ | $C_9H_8ON_2$ | 67·3 | 4·9 | 67·5 | 5·0 |
| Phenylalanine... | $CH_2Ph$ | Needles | 32 | 238 | $C_{10}H_{10}ON_2$ | 68·9 | 5·9 | 69·0 | 5·8 |
| Tyrosine ..... | $CH_2{\cdot}C_6H_4{\cdot}OH$ | Plates | 50 | 254 | $C_{10}H_{10}O_2N_2$ | 62·9 | 5·5 | 63·2 | 5·3 |

[a] From aq. EtOH. [b] From $H_2O$. [c] From aq. EtOH.
[d] From EtOH unless otherwise stated. † Based on the amino-acid used. ‡ With decomp.

TABLE 2. *Monoacetyl derivatives of 4(5)-substituted 2-hydroxyglyoxalines.*

| 4-Subst. | Form [a] | M. p. | Formula | Found (%) C | Found (%) H | Required (%) C | Required (%) H |
|---|---|---|---|---|---|---|---|
| Me ..... | Needles | 190° [a] | $C_6H_6O_3N_2$ | 51·4 | 5·8 | 51·4 | 5·7 |
| Et ..... | ,, | 170 | $C_7H_{10}O_3N_2$ | 54·5 | 6·4 | 54·5 | 6·5 |
| $Pr^n$ ..... | ,, | 124 | $C_8H_{12}O_3N_2$ | 56·8 | 6·8 | 57·1 | 7·1 |
| $Pr^i$ ..... | ,, | 129 | $C_8H_{12}O_3N_2$ | 57·0 | 6·9 | 57·1 | 7·1 |
| $Bu^n$ ..... | ,, | 120 | $C_9H_{14}O_3N_2$ | 59·5 | 7·8 | 59·3 | 7·7 |
| $CH_2{\cdot}CO_2Et$ ..... | ,, | 95 | $C_8H_{12}O_4N_2$ | 51·0 | 5·6 | 51·0 | 5·7 |
| $[CH_2]_2{\cdot}CO_2Et$ ..... | Plates | 48 | $C_{10}H_{14}O_4N_2$ | 53·1 | 6·1 | 53·1 | 6·2 |
| $[CH_2]_5{\cdot}CH_3$ ..... | Needles | 109 | $C_{11}H_{18}O_3N_2$ | 63·2 | 8·7 | 62·9 | 8·6 |
| Ph ..... | Plates | 238 [b] | $C_{11}H_{10}O_3N_2$ | 65·5 | 4·9 | 65·4 | 4·9 |
| $CH_2Ph$ ..... | ,, | 178 | $C_{12}H_{12}O_3N_2$ | 66·6 | 5·6 | 66·7 | 5·6 |

[a] Duschinsky and Dolan [25] gave m. p. 175°. [b] Rupe [4] gave m. p. 157°. [a] From EtOH.

(17·5 ml.) and a cold solution of potassium cyanate (6·4 g.) in water (14 ml.) were added. The pH was about 7·0. The mixture, after 30 min. at −15°, was warmed on the steam-bath for 1½ hr.; then after addition of 3N-hydrochloric acid (5 ml.) it was diluted to 100 ml. and heating continued for 2½ hr. The residue left on evaporation under reduced pressure was extracted with hot ethanol, and the *product* (71%) crystallised as prismatic needles, m. p. 219°, after concentration and addition of water (Found : C, 41·0; H, 6·9. $C_4H_6ON_2,H_2O$ requires C, 41·3; H, 6·9%). The *monoacetyl derivative*, needles from ethanol, had m. p. 230° (Found : C, 51·1; H, 5·7. $C_6H_8O_2N$ requires C, 51·4; H, 5·7%).

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