Tetrahedron, 1963, Vol. 19, pp. 1195 to 1200. Pergamon Press Ltd. Printed in Northern Ireland

SYNTHESES OF 2,6-DICHLOROBENZONITRILE FROM CYCLOHEXANOL

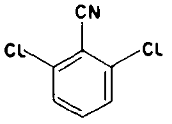
G. I. FRAY
Research Laboratory, Shell Chemical Company Ltd., Egham, Surrey

(*Received* 19 *March* 1963)

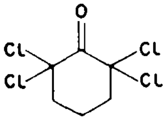
Abstract—A new synthetic approach to 2,6-dichlorobenzonitrile has been found, starting from cyclohexanol and proceeding *via* 2,2,6,6-tetrachlorocyclohexanone.

2,6-DICHLOROBENZONITRILE (I) is a herbicide; it is particularly effective in inhibiting the germination of seeds, and has a low mammalian toxicity.[1] Hitherto all known syntheses of I have depended on the preparation or availability of suitable 1,2,3-trisubstituted benzenes, which are not easy to obtain in the quantities required for large-scale production.

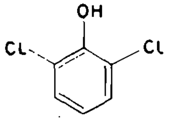
It was considered that a new synthetic approach to 2,6-dichlorobenzonitrile (I) could be made from cyclohexanol, which is cheap and readily available. Treatment of cyclohexanol with chlorine is known to afford 2,2,6,6-tetrachlorocyclohexanone (II)[2–4]; this compound loses hydrogen chloride on heating, with the formation of 2,6-dichlorophenol (III).[2,3] This suggested that some derivatives of the tetrachloroketone (II), containing an actual or potential cyano-group in the appropriate position, might be found to give the required 2,6-dichlorobenzonitrile (I) on pyrolysis.



I

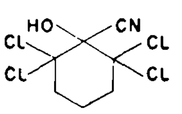


II

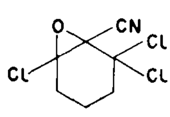


III

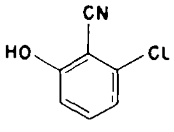
The first step in the proposed scheme was accomplished by the conversion of the tetrachloro-ketone (II) into the cyanohydrin (IV), in 78 per cent yield, by the action of hydrogen cyanide (from potassium cyanide and glacial acetic acid). With an excess of potassium cyanide, the cyanohydrin (IV) reacted further to afford an 80 per cent yield of a compound formulated as the epoxy-nitrile (V). This structure was based on elemental analysis and the I.R. spectrum, which showed no $\mathrm{O{-}H}$, $\mathrm{C{=}C}$, or $\mathrm{C{=}O}$ bands; confirmatory evidence was obtained from certain reactions described below.



IV



V



VI

---

* Present address: Chemistry Dept., University of Reading.

[1] H. Koopman and J. Daams, *Nature*, **186**, 89 (1960).

[2] O. Hassel and K. Lunde, *Acta Chem. Scand.* **4**, 200 (1950).

[3] R. Riemschneider and H. Rübner, *Z. Naturforsch.* **8b**, 161 (1953); R. Riemschneider, *Monatsh.* **85**, 417 (1954).

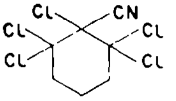
[4] W. Gündel and W. Scherff, German Patent 823, 449/1951.

These two compounds, the cyanohydrin (IV) and the epoxy-nitrile (V), were the materials on which the following investigations were based.

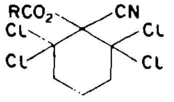
As was expected, the cyanohydrin itself decomposed on heating with loss of hydrogen cyanide, resulting in the formation of the tetrachloro-ketone (II). Ways of preventing the elimination of hydrogen cyanide by modification of the cyanohydrin molecule were therefore investigated.

The product of one such modification, the epoxy-nitrile (V), was already in hand. Its pyrolysis, however, did not afford any 2,6-dichlorobenzonitrile, but gave (in very poor yield) a phenol, most probably the 2-chloro-1-cyano-compound (VI).

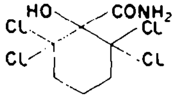
Replacement of the hydroxyl group of the cyanohydrin (IV) was then considered. The chloro-group was an obvious choice for the replacement, since it could eventually be eliminated (on pyrolysis) as hydrogen chloride, and the next objective was therefore the pentachloro-nitrile (VII). Attempts to form VII by treatment of the cyanohydrin (IV) with hydrogen chloride (either alone or in the presence of zinc chloride), or with the phosphorus chlorides, were unsuccessful. The required compound was obtained, however, in 38 per cent yield by the action of thionyl chloride in the presence of a catalytic amount of pyridine. Pyrolysis of the pentachloro-nitrile (VII) then afforded a 67 per cent yield of 2,6-dichlorobenzonitrile (I). This was very promising, but repeated attempts failed to improve the preparation of VII. Hence the examination of other routes to the benzonitrile (I) was undertaken.



VII



VIII



IX

Esterification of the hydroxyl group of the cyanohydrin (IV), leading to compounds of the structure VIII, was found to be possible. The acetoxy-nitrile (VIII, R = CH_3) was obtained by prolonged treatment of the cyanohydrin with acetyl chloride or acetic anhydride in the presence of pyridine, but on pyrolysis gave only a small yield of I. The benzoyloxy-nitrile (VIII, R = Ph) was also prepared, using benzoyl chloride, but in very poor yield.

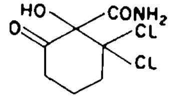
Modification of the cyano-group of the cyanohydrin (IV) could be effected by hydrolysis, which occurred very readily with concentrated sulphuric acid, affording an 84 per cent yield of the hydroxy-amide (IX). This compound was also obtained by similar treatment of the pentachloro-nitrile (VII), hydrogen chloride being evolved. The hydroxy-amide (IX) decomposed on heating, better in the presence of phosphorus pentoxide, to give a low yield of the benzonitrile (I).

An attempt to convert the hydroxy-amide (IX) into the pentachloro-nitrile (VII) by means of thionyl chloride, which can effect dehydration of amides,[5] was not successful. Reaction of the hydroxy-amide (IX) with nitrous acid (from sodium nitrite and concentrated sulphuric acid), which normally converts an amide into the parent carboxylic acid,[6] in this case led directly to the tetrachloro-ketone (II).

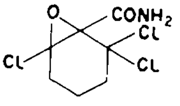
[5] R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry* p. 596. John Wiley New York (1953).

[6] *Idem, ibid.* p. 416.

Attention then turned from the reactions of the cyanohydrin (IV) to those of the epoxy-nitrile (V). Treatment of the epoxy-nitrile with cold concentrated sulphuric acid effected hydrolysis of both the cyano-group and the epoxide ring; hydrogen chloride was evolved, and the product was a hydroxy-keto-amide, formulated as X, which formed a 2,4-dinitrophenylhydrazone. Alkaline hydrolysis of the epoxy-nitrile (V), however, furnished an 82 per cent yield of the epoxy-amide (XI). This compound was also obtained by treatment of the hydroxy-amide (IX) with alkali. These reactions provided confirmation of the structure of the epoxy-nitrile (V).

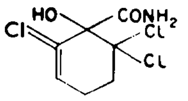


X

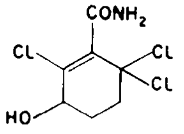


XI

The epoxy-amide (XI) dissolved in hot 50 per cent sulphuric acid with the formation, in 60 per cent yield, of an isomeric amide. The structure of this compound was not established with certainty, but the most likely possibilities were considered to be XII, and the structure derived from it by an allylic rearrangement, XIII. In order to distinguish between these alternatives, the amide was treated with nitrous acid, as described above for the hydroxy-amide (IX). The product, though not obtained pure, was undoubtedly an unsaturated carboxylic acid. This result seemed to eliminate the possible structure XII, since this compound would be expected to afford a ketone under the conditions of the reaction, by analogy with the hydroxy-amide (IX) above. The isomer of the epoxy-amide (XI) was therefore formulated as XIII. Pyrolysis of this compound in the presence of phosphorus pentoxide furnished 2,6-dichlorobenzonitrile in 37 per cent yield.



XII



XIII

EXPERIMENTAL

Unless stated otherwise, light petroleum refers to the fraction of b.p. 40–60°. I.R. spectra were determined for Nujol mulls.

2,2,6,6-*Tetrachlorocyclohexanone* (II)

The tetrachloro-ketone was prepared from cyclohexanol according to the directions given by Riemschneider.[3]

2,2,6,6-*Tetrachloro*-1-*hydroxycyclohexanecarbonitrile* (IV)

To a stirred suspension of potassium cyanide (25 g) in ethanol (250 cc) at 0° was gradually added, first glacial acetic acid (22 cc), and then the tetrachloro-ketone (20 g) in ethanol (250 cc). The resulting mixture was kept overnight at room temp, then made strongly acid by the addition of dil. sulphuric acid, and finally diluted with a large vol of water. The product was extracted with ether, and the extract washed with water, dried ($MgSO_4$), and evaporated. The residual oil (22 g) crystallized, on prolonged chilling, and was recrystallized from ether-light petroleum at 0° to afford the *cyanohydrin* as needles (12 g). The m.p. of the product was diffuse and variable, even after repeated recrystallization; analytically pure material was completely molten at temps ranging from ca.

100–110° (Found: C, 32·1; H, 2·8; Cl, 53·6; N, 5·2. $C_7H_7Cl_4NO$ requires: C, 32·0; H, 2·7; Cl, 53·9; N, 5·3%). The I.R. spectrum showed a band at 2·87 μ (O—H).

The mother-liquors from the first recrystallization were evaporated and the residue was crystallized from carbon tetrachloride to yield a further quantity (5·4 g) of the cyanohydrin (total yield 78%).

2,6,6-*Trichloro*-1,2-*epoxycyclohexanecarbonitrile* (V)

(a) *From the tetrachloro-ketone directly.* An experiment similar to the previous one was carried out using potassium cyanide (30 g) in ethanol (300 cc), glacial acetic acid (15 cc), and the tetrachloro-ketone (25 g) in ethanol (300 cc), the mixture being allowed to stand for 1 week at the normal temp. Working up as above then yielded an oil (22 g), which crystallized on standing in the refrigerator. Recrystallization from ether-light petroleum at 0° furnished the *epoxy-nitrile* as prisms (13 g), m.p. 44–45°, raised to 45–46° on further recrystallization (Found: C, 37·0; H, 2·7; Cl, 47·4; N, 6·5. $C_7H_6Cl_3NO$ requires: C, 37·1; H, 2·7; Cl, 47·0; N, 6·2%). The I.R. spectrum showed no O—H, C=O, or C=C bands, but exhibited a very weak band at 4·41 μ (C≡N).

A second crop of the epoxy-nitrile (6·3 g), m.p. 39·5–43·5°, was obtained from the mother-liquors of the above recrystallization (total yield 80%).

(b) *From the cyanohydrin and potassium cyanide.* A mixture of the cyanohydrin (1·6 g), potassium cyanide (1·6 g), and ethanol (15 cc) was kept at room temp for 2 days. Working up as above then gave an almost quantitative yield of the epoxy-nitrile, m.p. and mixed m.p. 45–46°.

Pyrolysis of the cyanohydrin (IV). Heating the cyanohydrin (1·0 g) at 190–200° for 15 min afforded an almost theoretical yield of the tetrachloro-ketone, m.p. and mixed m.p. 82·5–83·5° after recrystallization from light petroleum (b.p. 30–40°).

Pyrolysis of the epoxy-nitrile (V). The epoxy-nitrile (6·0 g) was kept at 200–205° for 1 hr (hydrogen chloride was evolved), and then the product was collected by flash-distillation. The resulting *phenol* (0·35 g, 9%) was obtained as clusters of needles, m.p. 158–159°, after recrystallization from ether-light petroleum (Found: C, 54·1; H, 2·8; Cl, 23·1; N, 9·4. C_7H_4ClNO requires: C, 54·7; N, 2·6; Cl, 23·1; N, 9·1%). The I.R. spectrum exhibited a broad band at ca. 3·0–3·1 (O—H) and other bands at 4·46 (C≡N) and 6·26 μ (C=C). The compound gave a violet colour with ferric chloride solution.

1,2,2,6,6-*Pentachlorocyclohexanecarbonitrile* (VII)

A mixture of the cyanohydrin (7·9 g), thionyl chloride (25 cc), and pyridine (3 drops) was refluxed for 6 hr. The excess thionyl chloride was removed under red. press., and benzene was distilled from the residue, which was then treated with methanol. The resulting crystalline *pentachloro-nitrile* (3·2 g, 38%) was obtained from ether-chloroform as elongated prisms, m.p. 182–183° (Found:* C, 29·7; H, 2·2; N, 5·1. $C_7H_6Cl_5N$ requires: C, 29·9; H, 2·1; N, 5·0%). The I.R. spectrum showed a very weak band at ca. 4·43 μ (C≡N).

1-*Acetoxy*-2,2,6,6-*tetrachlorocyclohexanecarbonitrile* (VIII, R = CH_3)

A mixture of the cyanohydrin (5·8 g), acetyl chloride (25 cc), and pyridine (3 drops) was refluxed for 65 hr. The excess of acetyl chloride was removed under red. press., and the crystalline residue washed with methanol to afford the *acetoxy-nitrile* (2·5 g, 37%), m.p. 189·5–190·5° after recrystallization from chloroform (Found: C, 35·3; H, 3·1; Cl, 46·3; N, 4·6. $C_9H_9Cl_4NO_2$ requires: C, 35·4; H, 3·0; Cl, 46·5; N, 4·6%). The I.R. spectrum exhibited a band at 5·54 μ (C=O).

A somewhat higher yield (52%) was obtained using acetic anhydride at 120–130° (bath) for 5 days.

1-*Benzoyloxy*-2,2,6,6-*tetrachlorocyclohexanecarbonitrile* (VIII, R = Ph)

Treatment of the cyanohydrin with benzoyl chloride at 120–130° (bath) for 5 days afforded a 7 per cent yield of the *benzoyloxy-nitrile*, m.p. 167·5–168° after recrystallization from chloroform-methanol (Found:* C, 46·3; H, 2·9; N, 3·8. $C_{14}H_{11}Cl_4NO_2$ requires: C, 45·8; H, 3·0; N, 3·8%). The I.R. spectrum showed a band at 5·66 μ (C=O).

2,2,6,6-*Tetrachloro*-1-*hydroxycyclohexanecarbonamide* (IX)

(a) *From the cyanohydrin* (IV). A solution of the cyanohydrin (5·1 g) in conc. sulphuric acid (10 cc) was warmed on the steam-bath for ½ hr, and then poured into ice-water. The crystalline product was

---

* Low Cl values were obtained in repeated analyses.

collected, washed with cold water, and dried, furnishing the *hydroxy-amide* (4·6 g, 84%), which was obtained as needles of m.p. 202–203° from benzene (Found: C, 30·0; H, 3·1; Cl, 50·0; N, 5·0. $C_7H_9Cl_4NO_2$ requires: C, 29·9; H, 3·2; Cl, 50·5; N, 5·0%). The I.R. spectrum showed bands at 2·82 and 2·92 (O—H and N—H), 5·81 (C=O), and 6·35 μ (Amide II).

(b) *From the pentachloro-nitrile* (VII). The pentachloro-nitrile (0·82 g) dissolved in warm conc. sulphuric acid (2 cc) with evolution of hydrogen chloride. The resulting solution was worked up as above to yield the hydroxy-amide (0·64 g, 78%), m.p. and mixed m.p. 202–203° after recrystallization from ether-light petroleum.

Reaction of the hydroxy-amide (IX) *with nitrous acid*

An ice-cold solution of sodium nitrite (3·0 g) in water (5 cc) was added slowly to a solution of the hydroxy-amide (2·9 g) in conc sulphuric acid (10 cc) at 0°. The resulting mixture was warmed on the steam bath for ½ hr, and then poured into ice-water. The crystalline product was collected, washed with water, and dried, affording 2,2,6,6-tetrachlorocyclohexanone (2·2 g, 75%), m.p. and mixed m.p. 82–83° after recrystallization from light petroleum (b.p. 30–40°)

6,6-*Dichloro*-1-*hydroxy*-2-*oxocyclohexanecarbonamide* (X)

The epoxy-nitrile (V) (5·3 g) dissolved in ice-cold conc. sulphuric acid (10 cc) with evolution of hydrogen chloride. The resulting solution was allowed to stand at room temp. for ½ hr, and was then poured into ice-water. The crystalline product was collected, washed with water, and dried, giving the *hydroxy-keto-amide* (2·1 g, 40%), obtained as prisms of m.p. 174·5–175·5° after recrystallization from ether-methanol (Found:* C, 37·7; H, 4·3; N, 6·0. $C_7H_9Cl_2NO_3$ requires: C, 37·2; H, 4·0; N, 6·2%). The I.R. spectrum showed bands at 2·86, 3·01 (shoulder), and 3·10 (O—H) and N—H), and at 5·74 (ketone C=O), 5·88 (amide C=O), and 6·25 μ (Amide II).

The 2,4-*dinitrophenylhydrazone* formed yellow needles, m.p. 255–256° (dec.) (rapid heating), from glacial acetic acid (Found†: C, 38·6; H, 3·2. $C_{13}H_{13}Cl_2N_5O_6$ requires: C, 38·4; H, 3·2%).

2,6,6-*Trichloro*-1,2-*epoxycyclohexanecarbonamide* (XI)

(a) *From the epoxy nitrile* (V). A mixture of the epoxy-nitrile (4·5 g), potassium hydroxide (5·0 g), ethanol (45 cc), and water (5 cc) was kept overnight at room temp. The dark solution was poured into water, and the resulting crystals were collected, washed with a little water, and dried to give the *epoxy-amide* (2·5 g), m.p. 145–146°; recrystallization from benzene afforded needles m.p. 145·5–146·5° (Found: C, 34·7; H, 3·6; Cl, 43·1; N, 5·6. $C_7H_8Cl_3NO_2$ requires: C, 34·4; H, 3·3; Cl, 43·5; N, 5·7%). The I.R. spectrum exhibited bands at 2·89, 2·99, and 3·09 (N—H), and at 5·96 (C=O) and 6·18 μ (Amide II).

A further quantity (1·5 g) of the epoxy-amide was obtained from the original filtrate by saturating it with sodium chloride (total yield 82%).

(b) *From the hydroxy-amide* (IX). A mixture of the hydroxy-amide (1·0 g), potassium hydroxide (2·0 g), ethanol (10 cc), and water (10 cc) was warmed on the steam-bath for 75 min. Addition of brine then precipitated the epoxy-amide (0·66 g, 76%), m.p. and mixed m.p. 145–146°.

Reaction of the epoxy-amide (XI) *with* 50% *sulphuric acid*

The epoxy-amide (9·8 g) was dissolved in hot 50% sulphuric acid (70 cc), and the solution cooled and diluted with water. The resulting crystals were collected and washed with water, affording an isomeric *amide* (5·3 g, 60%), m.p. 195–196° (with frothing) after recrystallization from methanol (Found: C, 34·4; H, 3·4; Cl, 43·2; N, 5·8. $C_7H_8Cl_3NO_2$ requires: C, 34·4; H, 3·3; Cl, 43·5; N, 5·7%). The I.R. spectrum showed bands at 2·84, 2·94, and ca. 3·1 (O—H and N—H), and at 5·94 (C=O) and 6·38 μ (Amide II); there was an indication of an unresolved band in the region characteristic of C=C.

The above amide (0·62 g) in conc sulphuric acid (5 cc) was allowed to react with sodium nitrite (0·70 g) in water (3 cc) at 0°, as described above for the hydroxy-amide (IX). The mixture was then heated on the steam-bath for 15 min and poured into water. The oily product (0·51 g), collected by

---

* Low Cl values were obtained in repeated analyses.

† Correct analyses could not be obtained for Cl or N.

ether-extraction, could not be induced to crystallize. It dissolved in sodium hydrogen carbonate solution with effervescence, and its I.R. spectrum showed bands at ca. 2·9 (O—H), 5·82 (C=O), and 6·22 μ (C=C).

2,6-*Dichlorobenzonitrile* (I)

(a) *From the pentachloro-nitrile* (VII). The pentachloro-nitrile (1·1 g) was kept at 225–235° (bath for 1 hr; hydrogen chloride was evolved. The resulting tar was extracted repeatedly with boiling light petroleum, and the combined extracts were evaporated. The residue was then kept at 90–100°/20 mm in a sublimation apparatus, yielding a sublimate of 2,6-dichlorobenzonitrile (0·45 g, 67%), m.p. and mixed m.p. 145–146° after recrystallization from light petroleum; the I.R. spectrum was identical with that of an authentic sample.*

(b) *From the acetoxy-nitrile* (VIII, R = CH_3). A similar experiment carried out with the acetoxy-nitrile (1·1 g) at 260–270° (bath) for ½ hr furnished 0·11 g (19%) of crude 2,6-dichlorobenzonitrile, identified by its I.R. spectrum.

(c) *From the hydroxy-amide* (IX). A mixture of the hydroxy-amide (2·5 g) and phosphorus pentoxide (1·0 g) was kept at 250–260° (bath) for ½ hr. The product was collected in boiling ether, and then sublimed to afford crude 2,6-dichlorobenzonitrile (0·29 g, 19%), identified by its I.R. spectrum.

(d) *From the compound obtained by the action of* 50% *sulphuric acid on the epoxy-amide* (XI). A mixture of the compound (1·0 g) and phosphorus pentoxide (1·0 g) was kept at 220–230° (bath) for 1 hr. Working up as in (c) above then afforded 2,6-dichlorobenzonitrile (0·26 g, 37%), m.p. 145·5.–146·5° after recrystallization from ether-light petroleum; the I.R. spectrum was identical with that of an authentic specimen.

Acknowledgement—The author is indebted to Sir Robert Robinson for his interest and encouragement.

---

* Kindly supplied by Woodstock Agricultural Research Centre.