abruptly, samples were taken for the determination of volatile acid.

Anal. Calcd. for $C_{26}H_{30}N_4O_5\cdot 2^1/_2\ HC_2H_3O_2$: weight loss, 23.88; volatile acid, 23.88. Found: weight loss at 100° (in vacuo), 23.4; volatile acid as acetic, 23.5.

The direction of vibration of the slower component was lengthwise of the crystal in crude I before washing and drying and also in I recrystallized from glacial acetic acid, but the direction of vibration of the slower component was crosswise of the crystal in I recrystallized from ethanol.

Attempted Formazan Formation.—Recrystallized I (from absolute ethanol) was recovered unchanged after attempted formazan formation,[2] as evidenced by comparison of elemental analyses, melting points, and X-ray powder patterns of the original and recovered osazones. Under the same conditions, sugar osazones having a phenylhydrazine group on C-1 underwent a marked color change to produce typical sugar formazans.

Acknowledgment.—We are greatly indebted to Dr. Nelson K. Richtmyer of the National Institutes of Health, Bethesda, Md., for a generous sample of pure D-mannoheptulose; to Dr. Francis T. Jones for microscopical observations; and to Mr. Dale R. Black for X-ray diffraction analyses.

Polyfunctional Aliphatic Compounds. I. The Preparation of 3-Hydroxyglutaronitriles

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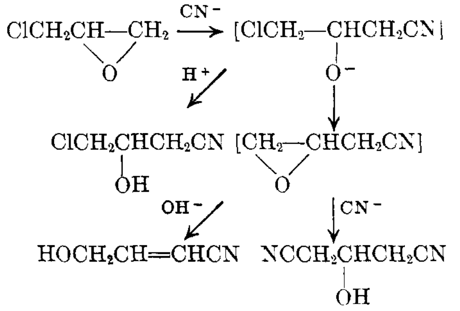
The necessity of obtaining large quantities of the base-sensitive 3-hydroxyglutaronitrile and related three-substituted homologs for cyclization studies has prompted us to re-examine the methods of preparation for these compounds. Previous syntheses of 3-hydroxyglutaronitrile itself have relied on the reaction of aqueous potassium cyanide with 1,3-dichloropropanol-2[1-4] and on the action of a concentrated solution of potassium cyanide on 4-chloro-3-hydroxybutyronitrile.[5,6] Of these only the latter appeared to merit any attention as a preparative method, but even here the reported yields were low (35–40%). This reaction proved to be highly exothermic and required careful control but when the operating temperature was kept around 40°, yields as high as 51.5% were obtained. Nevertheless on a large scale, the difficulties of manipulation and extraction prohibited the use of this method.

We now have found that the required 3-hydroxyglutaronitriles can be prepared by allowing an epichlorohydrin to react with an aqueous solution of potassium cyanide buffered by magnesium sulfate to a pH of approximately 9.5. The best yields were obtained by carrying out these mildly exothermic reactions at 10 to 11° followed by ethyl acetate extraction.

Epichlorohydrin, itself, in this reaction led to 3-hydroxyglutaronitrile in 60% yield accompanied by smaller amounts (18%) of 4-chloro-3-hydroxybutyronitrile and 4-hydroxycrotononitrile. The latter materials, being considerably more volatile, were easily separated by distillation. These two components were the only materials that could be isolated when magnesium sulfate was omitted from the reaction.[7] The various products probably arise according to the scheme shown below.



However, on no occasion did we isolate any 3,4-epoxybutyronitriles from our reaction products. Culvenor, Davies, and Haley[7] have commented on the instability to base of epoxy systems of this type, and it appears that they are attacked faster by nucleophiles than the corresponding chloro epoxides.

The use of 1,3-dichloropropanol-2 or 4-chloro-3-hydroxybutyronitrile in the buffered system led to poorer yields of 3-hydroxyglutaronitrile.

The action of the buffered potassium cyanide solution on 2-methyl-, 2-ethyl-, and 2-phenylepichlorohydrin was also examined. The latter two materials were prepared in high yield by the reaction of the appropriate Grignard reagent with 1,3-dichloroacetone at −60°, followed by treatment of the resultant 1,3-dichloroisopropanol with strong base. Under the conditions described above, 2-methyl-, and 2-ethylepichlorohydrin afforded exclusively the corresponding 3-hydroxy-3-alkylglutaronitriles in 71 and 77% yield. However, the reaction with 2-phenylepichlorohydrin did not proceed at any measurable rate. In this case modest yields of the crystalline 3-hydroxy-3-phenylglutaronitrile were realized by employing a mixture of potassium carbonate and bicarbonate (1:1 molar ratio) as the buffering agent.

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(1) M. Simpson, *Ann.*, **133**, 74 (1864).

(2) O. Morgenstern and E. Zerner, *Monatsh.*, **31**, 777 (1910).

(3) M. H. Dreifuss and C. K. Ingold, *J. Chem. Soc.*, **123**, 2964 (1923).

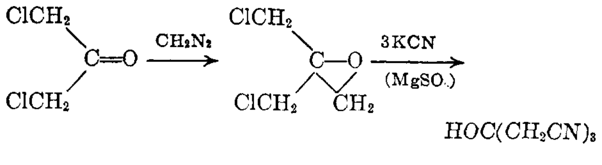
(4) G. Braun, *J. Am. Chem. Soc.*, **52**, 3167 (1930).

(5) R. Lespieau, *Bull. soc. chim. France*, [4] **33**, 725 (1923).

(6) R. Legrand, *Bull. soc. chim. Belges*, **53**, 166 (1944) [*Chem. Abstr.*, **40**, 4671 (1946)].

(7) C. C. J. Culvenor, W. Davies, and F. G. Haley, *J. Chem. Soc.*, 3123 (1950).

The ease with which these 3-hydroxyglutaronitriles were produced suggested that the reaction might be capable of extension to more complex system. Accordingly, 2 - chloromethylepichlorohydrin, most easily prepared by reaction of diazomethane on 1,3-dichloroacetone, was treated with three equivalents of potassium cyanide solution buffered by magnesium sulfate. After a mildly exothermic reaction, extraction of the mixture with ethyl acetate afforded a 60% yield of only one product, namely tris(cyanomethyl)carbinol.



1,4-Dichloro-2,3-epoxybutane was also treated under the same conditions with cyanide ion, but no product could be extracted from the reaction mixture.

All of the 3-hydroxyglutaronitriles prepared by the above methods showed both hydroxyl and nitrile absorptions in the infrared while bands that might be expected for a double bond or a carbonyl group were absent.

The results of cyclization studies on these materials will be presented in subsequent papers.

Experimental

Melting points were determined on a Fisher-Johns melting point block and are not corrected. Infrared spectra were recorded on a Baird spectrophotometer, Model No. 4-55, as films or as Nujol mulls. Epichlorohydrin as supplied by Eastman Kodak was used without further purification.

2-Ethylepichlorohydrin (1,2-Epoxy-2-chloromethylbutane).—1,3-dichloroacetone (84.6 g. 0.66 mole) was dissolved in anhydrous ether (600 ml.) and the solution cooled to −60°. While maintaining this temperature, a solution of ethylmagnesium bromide (0.66 mole) in ether (600 ml.) was added over a period of 2 hr. with vigorous mechanical stirring. Ten minutes after this addition was complete, the reaction mixture, which had remained heterogeneous throughout, was treated with acetic acid (64 g.) in ether (100 ml.) followed by water (50 ml.). With continued stirring the temperature was allowed to rise to 0° and the ether layer separated from the clear biphasic liquid. The aqueous phase was washed once with ether and the organic extract combined, washed with water, and evaporated down to small bulk. The crude 1-chloro-2-hydroxy-2-chloromethylbutane (101.3 g., 97% yield) thus obtained was not purified further but was added below the surface of a slurry of calcium hydroxide (200 g.) and water (500 ml.) during 20 min. During this period the reaction system was maintained at 57° and under a pressure of 160 mm. while the epoxide was distilled as its water azeotrope. The product was isolated *via* ether extraction and fractionally distilled at 40 mm. The fraction (42.4 g.) boiling at 65° was collected and constituted almost pure 1,2-epoxy-2-chloromethylbutane. A sample of this material redistilled at atmospheric pressure for analysis had a boiling point of 137°, $n^{25}D$ 1.4375.

Anal. Calcd. for C_5H_9OCl: C, 49.80; H, 7.52; Cl 29.40. Found: C, 49.6; H, 7.5; Cl, 29.5.

1,3-Dichloro-2-phenylpropanol-2.—To 1,3-dichloroacetone (63.5 g., 0.5 mole) in ether (680 ml.) at −60° there was added phenylmagnesium bromide (0.55 mole) in ether solution (500 ml.) during 1.5 hr. After a further 10 min. glacial acetic acid (53 g.) in ether (80 ml.) was added slowly and the temperature of the reaction mixture allowed to rise to 4°. Water (200 cc.) was run into the flask and the product isolated in the usual way. The viscous oil thus obtained was fractionally distilled and that portion (78.9 g.) boiling at 80–85° (0.1 mm.) collected. This was suitable for further reaction. A sample, distilled at 0.5 mm., had b.p. 102° and $n^{25}D$ 1.4568. The infrared showed a strong band at 2.82 with a shoulder at 2.87 μ.

Anal. Calcd. for $C_6H_{10}Cl_2O$: C, 52.71; H, 4.92; Cl, 34.58. Found: C, 52.6; H, 4.8; Cl, 34.8.

2-Phenylepichlorohydrin.—With rapid stirring *N* sodium hydroxide solution (575 ml.) was added dropwise over a period of 1 hr. to 1,3-dichloro-2-phenylpropanol-2 (102.6 g., 0.5 mole). Stirring was continued for 2.5 hr. and the biphasic liquid extracted with ether (4 × 150 ml.). The product (82.6 g.) isolated in the usual way afforded, after fractional distillation, pure 2-phenylepichlorohydrin (81.3 g.); b.p. 109–109.5° (6 mm.), $n^{25}D$ 1.5461.

Anal. Calcd. for C_9H_9ClO: C, 64.10; H, 5.38; Cl, 21.03. Found: C, 64.4; H, 5.5; Cl, 20.8.

This epoxide has been prepared previously by Adamson and Kenner[8] who recorded b.p. 135–137° (17 mm.).

2-Chloromethylepichlorohydrin.—To a solution of diazomethane prepared from "Diazald" (280 g.), in ether (4 l.) was added a solution of 1,3-dichloroacetone (80 g., 0.63 mole). The mixture was then kept at 5° for 5 days. A small amount of polymethylene was separated by filtration and the solvent then removed by evaporation. The residual light brown oil (97 g.) on fractional distillation afforded a colorless liquid (67.8 g.), b.p. 60–62° (8 mm.), whose infrared spectrum indicated the presence of ketonic material (band at 5.75 μ). To remove this the distilled liquid was dissolved in ether (350 ml.) and the solution stirred vigorously with 1 *M* sodium hydrogen sulfite (165 ml.) for 1.5 hr. After reisolation of the pale yellow product (54 g.) from the ether solution, distillation afforded 2-chloromethylepichlorohydrin (45.4 g., 51% yield); b.p. 78° (23 mm.), $n^{25}D$ 1.4688. [Reported,[9] b.p. 89.5 (31 mm.)].

Anal. Calcd. for $C_4H_6Cl_2O$: C, 34.07; H, 4.29; Cl, 50.29. Found: C, 34.0; H, 4.3; Cl, 50.5.

3-Hydroxyglutaronitrile.—A 12-l. three-necked flask was fitted with a mechanical stirrer, an adapter incorporating a reflux condenser, and a thermometer, and an addition funnel of 500-ml. capacity. The reaction flask was placed in an acetone–Dry Ice cooling bath, and the atmosphere in the flask replaced by pure nitrogen. Magnesium sulfate heptahydrate (4930 g. 20 moles) was dissolved in tap water (7 l.) and the solution filtered into the reaction flask. This liquid was cooled to 10° and potassium cyanide (1430 g., 22 moles) then added with stirring and allowed to dissolve during 45 min. At this point the mixture had an opaque milky white appearance due to the precipitation of a little magnesium hydroxide. With continued stirring and cooling, epichlorohydrin (1018 g., 11 moles) was added over a period of 5.5 hr., the temperature of the reaction mixture being maintained at 10–11° throughout this period. After the addition was complete, stirring was continued for a further 48 hr. at room temperature. The reaction mixture which at this point had a dark red-brown color was extracted continuously with ethyl acetate (5 l.) for a period of 48 hr. The extract was dried over anhydrous magnesium sulfate and the solvent

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[8] D. W. Adamson and J. Kenner, *J. Chem. Soc.*, 181 (1939).

[9] G. Hearne and H. W. deJong, *Ind. Eng. Chem.*, **33**, 940 (1941).

removed under vacuum on a steam bath. The residual dark brown oil (950 g.) was then subjected to fractional distillation at reduced pressure. A forerun (207 g.) consisting essentially of 4-chloro-3-hydroxybutyronitrile and 4-hydroxycrotononitrile was collected from 90–115° at 0.4 mm. Pure 3-hydroxyglutaronitrile (723 g.) then distilled at 155–160° at the same pressure (yield 60%). A sample (12 g.) of the dinitrile was purified by fractional distillation through a 6-in. column and the portion boiling at 156° (0.22 mm.) collected (10 g.). $n^{23}\mathrm{D}$ 1.4632 (Reported,[5] b.p. 202° (11 mm.) $n^{22}\mathrm{D}$ 1.4805). The infrared spectrum of the material showed bands at 2.91 and 4.41 μ.

Anal. Calcd. for $C_5H_6N_2O$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.3; H, 5.5; N, 25.4.

3-Hydroxy-3-methylglutaronitrile.—Magnesium sulfate heptahydrate (112 g., 0.45 mole) and potassium cyanide (32.5 g., 0.5 mole) were dissolved in water (160 ml.). This solution was cooled to 5° and over a period of 1.25 hr. there was added 1-chloro-2,3-epoxy-2-methylpropane (26.6 g., 0.25 mole) dropwise. After 24 hr., the product was isolated as in the above experiment. The resulting dark brown liquid was distilled at 0.09 mm. and the main fraction (23 g.) consisting of almost pure 3-hydroxy-3-methylglutaronitrile, collected at 128–130°; yield 71%. A sample of this material redistilled for analysis boiled at 131° and 0.07 mm., $n^{25}\mathrm{D}$ 1.4596.

Anal. Calcd. for $C_6H_8ON_2$: C, 58.05; H, 6.50; N, 22.57. Found: C, 58.0; H, 6.5; N, 22.3.

The infrared spectrum of the pure material showed bands at 2.91 and 4.41 μ characteristic of hydroxyl and saturated nitrile groups, respectively.

3-Hydroxy-3-ethylglutaronitrile.—This was prepared in exactly the same way as the methyl homolog. From 2-ethylepichlorohydrin (20.1 g., 0.167 mole) and a solution of potassium cyanide (2.17 g., 0.334 mole) and magnesium sulfate heptahydrate (73.8 g., 0.30 mole) there was obtained pure 3-hydroxy-3-ethylglutaronitrile (17.71 g., 77% yield) b.p. 134–137° (0.3 mm.), $n^{25}\mathrm{D}$ 1.4658. A sample was redistilled for analysis b.p. 135° (0.35 mm.).

Anal. Calcd. for $C_7H_{10}N_2O$: C, 60.85; H, 7.3; N, 20.28. Found: C, 60.8; H, 7.4; N, 20.5.

3-Hydroxy-3-phenylglutaronitrile.—A solution of potassium cyanide (19.5 g., 0.3 mole), potassium carbonate (17 g.), and potassium bicarbonate (17 g.) in water (120 ml.) was stirred vigorously with 2-phenylepichlorohydrin (25 g., 0.15 mole) for 1 week at room temperature. The semisolid organic phase was then diluted with a small amount of a 50–50 mixture of ether and petroleum-ether (b.p. 30–60°) and the solid removed by filtration. The filtrate contained mainly unchanged epoxide. Recrystallization of the solid from ethanol gave almost pure 3-hydroxy-3-phenylglutaronitrile (7.8 g.) as feathery white needles, m.p. 117–118°. A sample recrystallized for analysis had m.p. 118–120°.

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.9; H, 5.6; N, 15.1.

Tris(cyanomethyl)carbinol.—2-(Chloromethyl)epichlorohydrin (14.1 g., 0.1 mole) was added dropwise over a period of 15 min. to a cooled solution of potassium cyanide (20.4 g., 0.314 mole) and magnesium sulfate heptahydrate (74 g., 0.3 mole) in water (200 ml.). Isolation of the product in the usual way afforded a somewhat oily crystalline solid (10.5 g.). One recrystallization of this material from ethanol afforded tris(cyanomethyl)carbinol (8.0 g., yield 53.5%) m.p. 106–108°, raised to 109° from the same solvent. The infrared spectrum showed hydroxyl absorption at 2.99 μ and a split band at 4.37 and 4.41 μ for nitrile.

Anal. Calcd. for $C_7H_7N_4O$: C, 56.37; H, 4.73; N, 28.18. Found: C, 56.5; H, 4.8; N, 28.0.

Acknowledgment.—We are much indebted to Dr. C. K. Fitz who carried out all microanalyses.

Polycyclic Studies. II. The Ultraviolet Spectra of Some Diels-Alder Adducts[1]

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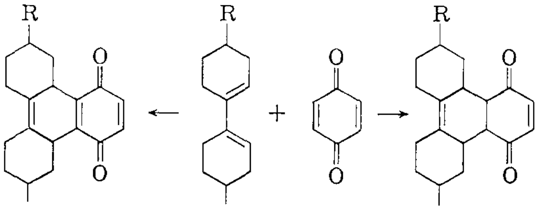
The bicyclohexenyl-*p*-benzoquinone Diels-Alder adducts I and II have been recently employed[1] as intermediates in the synthesis of triphenylenes.

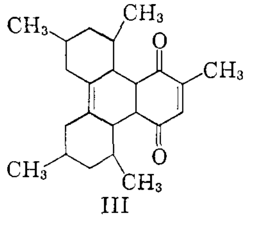


II

Ia. R = H
b. R = CH_3
c. R = OCH_3

Ia. R = H
b. R = CH_3
c. R = OCH_3

The difference in the ultraviolet absorption spectra between adducts I and II is one of the criteria[1] by which these two types of compounds can be distinguished. Whereas the quinones II show the expected maximum at 258–259 mμ (log ε 4.1–4.2), the adducts I do not show a definite maximum in the region 220–230 mμ, as would be expected from the data for enediones summarized in Table I. On the other hand, substituted enediones have been shown to exhibit an absorption maximum in the region 235–250 mμ (Table II). Indeed, of the compounds investigated by us, only one, 2,5,7,10,12 pentamethyl-$\Delta^{2,14}$-tetradecahydrotriphenylene-1,4-dione, III, showed such a maximum ($\lambda_{\max}^{\text{ethanol}}$ 242 mμ, ε 11,500).



III

This apparent lack of a maximum has been observed also in other similar unsubstituted Diels-Alder adducts investigated in this laboratory.[3]

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[1] Part I. A. Mandelbaum and Michael Cais, *J. Org. Chem.*, **26**, 2633 (1961).

[2] American Chemical Society–Petroleum Research Fund Fellow, 1959–1961.

[3] Yanina Altman and David Ginsburg, *J. Chem. Soc.*, 1498 (1961).