285. *Reactions of α-Cyanoprene (1-Cyanobuta-1 : 3-diene). Part III. Dimers.*

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α-Cyanoprene (1-cyanobuta-1 : 3-diene), on storage at low temperatures in acetic acid, gives a dimer, *cis*-1-cyano-2-*trans*-2′-cyanovinyl*cyclo*hex-5-ene, the structure of which is confirmed by hydrogenation and hydrolysis to the known saturated diacid. When heated, this dimer is converted into the 2-*cis*-β-cyanovinyl isomer. On treatment with bases these isomers give another pair of isomers, 1-cyano-2-2′-cyanoethylidene*cyclo*hex-5-enes.

In recent publications, Synder and his co-workers (*J. Amer. Chem. Soc.*, 1949, **71**, 1055, 1057, 1395) reported the separation of the *cis*- and the *trans*-form of α-cyanoprene (1-cyanobuta-1 : 3-diene) and examined their reactions. One form, probably the *trans*-form, dimerised to give a 1-cyano-2-(2′-cyanovinyl)*cyclo*hexene. This structure was proved by bromination followed by dehydrohalogenation, the resulting nitrile being hydrolysed to the known β-(2-carboxyphenyl)-propionic acid. We also have investigated the properties of this dimer and have found its detailed structure by a different method. We find also that the dimer reported by Snyder—which will be referred to as dimer A—is readily converted into isomeric forms, dimers B, C, and D.

The carbon skeleton was elucidated by hydrogenating dimer A to its tetrahydro-derivative which was hydrolysed to give the known *cis*- and *trans*-β-(2-carboxy*cyclo*hexyl)propionic acids (Windaus, Hückel, and Reverey, *Ber.*, 1923, **56**, 91) : *cis*-diacid, m. p. 103—105° (dianilide, m. p. 179°), and *trans*-diacid, m. p. 143—145° (dianilide, m. p. 213°). Windaus *et al.* (*loc. cit.*) give m. p. 103° and 143° for the *cis*- and *trans*-β-(2-carboxy*cyclo*hexyl)propionic acids, and m. p. 159° and 212° for the *cis*- and *trans*-dianilides, respectively, though no method of preparation and no analysis is given for the *cis*-dianilide. In view of the alternative proof of structure of cyanoprene dimer given by Snyder and Poos, there can be no doubt that the diacids obtained are indeed β-(2-carboxy*cyclo*hexyl)propionic acids; Windaus's m. p. 159° instead of 179° for the *cis*-dianilide may be a typographical error.

Hückel (*Z. angew. Chem.*, 1926, **39**, 842) reported hydrolysis of esters of *cis*-β-(2-carboxy-*cyclo*hexyl)propionic acid with sodium ethoxide to the *trans*-acid. In agreement with this, the tetrahydro-nitrile with aqueous alkali gave complex mixtures, presumably of the *cis*- and *trans*-derivatives, from which the only diacid isolated was the *trans*-form; besides this, an acid amide was readily separated. Acid hydrolysis, on the other hand, gave simpler products and pure *cis*- and *trans*-acids were obtained in good yield by hydrolysing pure compounds (the dicyanide and the acid amide, respectively). It follows that under the conditions used (100°), hydrochloric acid does not rapidly convert one acid into the other and it is, therefore, probable that the tetrahydro-dimer is in the *cis*-configuration. At higher temperatures (180°) with hydrochloric acid, *cis*-β-(2-carboxy*cyclo*hexyl)propionic acid is known to be converted into the *trans*-acid (Windaus *et al.*, *loc. cit.*).

Our dimer A, obtained from aged acetic acid solutions of α-cyanoprene and crystallised from ether, had m. p. 53—54°, and was apparently identical with that of Snyder and Poos. Slow fractional distillation of the ethereal mother-liquors gave an unidentified colourless mobile liquid, b. p. 70—71°/15 mm. (presumably a constant-boiling mixture), and an oil which by crystallisation from ether gave dimer B, m. p. 51·5—53°. When, on the other hand, the total crude oil (after removal of α-cyanoprene) was slowly distilled, only dimer B was obtained, but rapid distillation gave a mixture of dimers A and B from which the pure products were separated with difficulty. Prolonged heating caused considerable formation of non-volatile resin. It therefore appears that dimer A is present in the crude α-cyanoprene residues and that it is converted by heat into dimer B.

Attempts were made to add 2-nitropropane to each of the dimers, using methyltriethylammonium hydroxide as catalyst, though it was known that alkali alone caused their rapid polymerisation. The only products isolated were isomers of the starting materials, dimer A giving dimer C, m. p. 70—71°, and dimer B giving dimer D, m. p. 86—88°. The same isomerisation was effected with morpholine and is presumably promoted by basic catalysts. An attempt was made to convert dimer C into dimer D by heating it at 150°, but from the resinous product no pure component was isolated. The inter-relations of the dimers are summarised below :

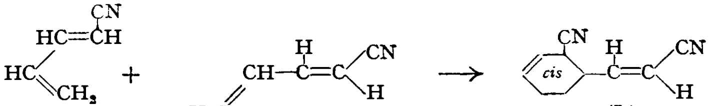
$$\underset{\text{m.p. }70\text{—}71^\circ.}{\text{Dimer C,}} \xleftarrow{\text{base}} \underset{\text{m.p. }53\text{—}54^\circ.}{\text{Dimer A,}} \xrightarrow{\text{heat}} \underset{\text{m.p. }51{\cdot}5\text{—}53{\cdot}5^\circ.}{\text{Dimer B,}} \xrightarrow{\text{base}} \underset{\text{m.p. }86\text{—}88^\circ.}{\text{Dimer D,}}$$

Hydrogenation of the four dimers gave the respective tetrahydro-derivatives, all of which gave the same acid-amide after hydrolysis with sodium hydroxide, so that all are 1-cyano-2-2′-cyanoethyl*cyclo*hexanes. Dimers A and B gave the same tetrahydro-derivative in quantitative yield and free from stereoisomers; thus it is probable that the double bonds were all of the type $-CH{:}CH-$. Acid hydrolysis of tetrahydro-dimer AB, under conditions milder than those known to cause conversion of *cis*-β-(2-carboxy*cyclo*hexyl)propionic acid into its *trans*-isomer (cf. Windaus *et al., loc. cit.*), gave the *cis*-diacid in good yield, thus showing that tetrahydro-dimer AB has the *cis*-configuration. Hence, if hydrogenation had affected only bonds of the type $-CH{:}CH-$, dimers A and B must also have the *cis*-configuration about the *cyclo*hexane ring. Hydrogenation of dimers C and D, on the other hand, gave a mixture of tetrahydro-derivatives, presumably *cis* and *trans* with respect to the *cyclo*hexane ring. It is therefore probable that dimers C and D differ from A and B by the shift of a double bond from $-CH{:}CH{\cdot}CH<$ to $-CH_2{\cdot}CH{:}C<$, in which the quaternary carbon atom is part of the *cyclo*hexane ring.

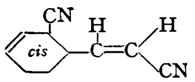
The position of the double bonds was then investigated. The ultra-violet absorption spectra showed only end absorption, down to 210 mμ. ($E^{1\%}_{1\,cm.}$ 750—900), whereas α-cyanoprene itself had a maximum at 241 mμ. ($E^{1\%}_{1\,cm.}$ 2260); therefore, none of the dimers has conjugated double-bonds. Linstead and his co-workers (*J.*, 1927, 2566; 1929, 2139; 1932, 443) have shown that a compound with a double bond βγ to a cyano-group adds iodine chloride more readily than does the isomer with the double bond in the αβ-position; a typical result is 56% addition to a βγ-double bond compared with 3% to an αβ-double bond. Titrations of the four dimers with iodine chloride under standard conditions gave the following mole-% absorption: A 74, B 57, C 105, D 99%. This indicated that a double bond which is αβ to the cyano-group in dimers A and B has migrated to the βγ-position in dimers C and D; it is also probable that the other double bond is βγ to a cyano-group in all four isomers, though the γδ-position is not excluded. The only cyanopropenes which are mainly in the βγ-form on equilibration under alkaline conditions are those which are γγ-dialkyl-substituted (cf. Linstead's table quoted in Gilman's "Organic Chemistry," 2nd edn., p. 1042). It follows then that the conversion of dimers A and B under basic conditions into dimers C and D involves the change $>CH{\cdot}CH{:}CH{\cdot}CN$ to $>C{:}CH{\cdot}CH_2{\cdot}CN$. This cyano-group must be that on the side chain; if it were that on the ring, dimers A and B, as substituted 1-cyano*cyclo*hexenes, would not be expected to give the single isomer on hydrogenation.

Summarising, we see that (i) the four isomers have the same carbon skeleton, (ii) dimers A and B have the same configuration (*cis*) on the *cyclo*hexene ring, (iii) none of the isomers contains conjugated double bonds, (iv) dimers A and B probably have one double bond αβ and the other βγ to cyano-groups, whereas dimers C and D probably have both double bonds βγ to cyano-groups, and (v) the conversion of dimers A and B into dimers C and D under basic conditions involves isomerisation in the side chain of $>CH{\cdot}CH{:}CH{\cdot}CN$ to $>C{:}CH{\cdot}CH_2{\cdot}CN$.

Snyder *et al.* (*loc. cit.*) showed that of the *cis*- and *trans*-forms of α-cyanoprene, one underwent the Diels–Alder reaction, and also dimerised, much more easily than the other, and that from steric considerations the *trans*-isomer would be the more active. The simplest dimer obtained by a Diels–Alder reaction of *trans*-α-cyanoprene with the γδ-bond of a second molecule would be 1-cyano-2-*trans*-2′-cyanovinyl*cyclo*hex-5-ene. As dimer A gives a *cis*(ring)-tetrahydro-derivative, dimer A is probably cis-1-*cyano*-2-trans-2′-*cyanovinyl*cyclo*hex*-5-*ene* (I), which agrees with its known properties.



(I.)



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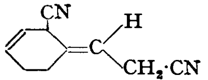
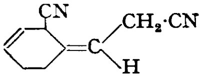


(III.)



(IV.)

The conversion of dimer A into dimer B by heat does not involve a change in orientation on the *cyclo*hexene ring as these dimers give the same *cis*-tetrahydro-derivative. Nor is it likely to involve migration of double bonds, for Letch and Linstead (*J.*, 1932, 443) have shown that the αβ- and βγ-forms of olefinic cyanides are not equilibrated by heat in the absence of a catalyst. The most probable difference between dimers A and B is, therefore, the geometrical configuration in the side-chain double bond, so that dimer B is cis-1-*cyano*-2-cis-2′-*cyanovinyl*cyclo*hex-5-ene* (II).

In confirmation of this, the dipole moments of dimers A and B were measured by Mr. G. F. Longster, who also calculated the moments of structures (I) and (II). It will be appreciated that the calculated values are only approximate and have to span the values allowing both for the four possible ways in which a *cyclo*hexene ring can crumple and for the free rotation about the single bonds in the side chain. In (I), the cyano-groups tend to reinforce one another, giving a dipole moment of about 5·5 D.; in (II), the groups are to some extent in opposition so that a total moment below that of a single cyano-vector (3·2 D.) is probable. The dipole moments found for dimers A and B were 5·8 and 2·9 D., respectively.

From the discussion above, it is clear that dimers C and D are (III) and (IV), respectively. If this is so, the geometrical configuration of the αβ-unsaturated form governs, to some extent at least, the configuration of the βγ-isomer derived from it. So far as we are aware, this point does not appear to have been examined in the classical studies of cyanopropene tautomerism. Dipole moment measurements and calculations, although in agreement with the proposed formulæ, do not make it possible to decide which dimer is (III), and which (IV).

In conclusion, we should point out that the four dimers obtained in this work were those most easily isolated from reactions under particular conditions and it may well be that in each case other isomers were also present.

EXPERIMENTAL.

Isolation of Dimer A.—The material used was a 50% solution in acetic acid of α-cyanoprene prepared by pyrolysis of the acetate of crotonaldehyde cyanohydrin (Gudgeon and Hill, B.P. 515,737). The solution was stabilised with quinol and had been kept in an ice-house for 6 years.

The solution (5 l.) was shaken with crushed ice and sufficient 16% aqueous sodium hydroxide for neutralisation (about 3 l.). Brine was added and the aqueous layer discarded. The oil was washed twice with water, dried, and distilled under nitrogen (bath-temperature, <80°), to give α-cyanoprene (940 g.), b. p. 36—37°/14 mm. The residual oil (1600 g.) in ether (1 l.) was cooled to −70°; the solid was collected and recrystallised from ether with good cooling to give *dimer A*, cis-1-*cyano*-2-trans-2′-*cyanovinyl*cyclo*hex-5-ene* (I) (360 g.). Repeated crystallisation raised the m. p. to 53—54° (Found: C, 75·9; H, 6·1; N, 18·0%; *M*, 164. $C_{10}H_{10}N_2$ requires C, 76·0; H, 6·3; N, 17·7%; *M*, 158).

Dimer B.—The first ethereal mother-liquors from dimer A were slowly fractionated through a good column to give fractions: (*a*) b. p. 38—71°/17 mm. (95 g.), (*b*) b. p. 70—72°/17 mm. (232 g.), (*c*) b. p. 32—118°/0·2 mm. (101 g.), (*d*) b. p. 118—130°/0·13 mm. (262 g.), (*e*) b. p. 130—144°/0·2 mm. (150 g.), and a considerable amount of resin.

Fraction (*b*) was refractionated to give a colourless mobile oil, probably a constant-boiling mixture, b. p. 70—71°/15 mm., n_D^{20} 1·4240 (Found: C, 54·2, 53·8; H, 5·2, 5·2; N, 13·8, 14·2, 14·4%; *M*, 161).

Fraction (*d*) partly solidified on cooling and was twice crystallised from ether to give *dimer B*, cis-1-*cyano*-2-cis-2′-*cyanovinyl*cyclo*hex-5-ene*, m. p. 51·5—53·5° (mixed m. p. with dimer A, 26—39°) (Found: C, 75·7; H, 6·35; N, 17·7%; *M*, 156).

Fraction (*e*) had m. p. about 10° and analysed for a cyanoprene polymer (Found: C, 76·2; H, 6·4; N, 18·05%).

In another experiment, the total crude oil after fractionation of the cyanoprene was distilled rapidly under nitrogen. The amount of residual tar was much higher, indicating further polymerisation. The fraction of b. p. 115—130°/0·1 mm. was crystallised from ether to give a solid, m. p. 33—40°, from which dimers A and B were isolated by repeated crystallisations from ether. Slow distillation of the total crude oil through a good column increased the resin formation considerably, but from the distillate pure dimer B was readily isolated and there was no evidence of the presence of dimer A.

Dimer C.—(*a*) A solution of dimer A (16 g.) in dioxan (25 c.c.) was added slowly to a mixture of 2-nitropropane (8·6 g.), 35% aqueous methyltriethylammonium hydroxide (6 c.c.), and dioxan (20 c.c.) at 40°. After being heated for 1 hour at 70°, the cooled mixture was acidified with 2N-hydrochloric acid and extracted with ether. The extract was dried, the solvent removed, and the residue crystallised from alcohol with good cooling (−10°), to give *dimer C* (1-*cyano*-2-2′-*cyanoethylidene*cyclo*hex-5-ene*) m. p. 70—71° (Found: C, 75·8; H, 6·2; N, 17·75%; *M*, 164). When the 2-nitropropane was omitted in this reaction, only viscous polymers were obtained.

(*b*) A solution of dimer A (2·0 g.) and morpholine (2·0 c.c.) in alcohol (8 c.c.) was kept for 4 days, poured into water, and acidified with 2N-hydrochloric acid. The oil was extracted with ether and dried, the solvent removed, and the residue crystallised from alcohol, to give dimer C, m.p. and mixed with that obtained by (*a*), 70—71°.

Dimer D.—(*a*) Dimer B was treated with 2-nitropropane in the same way as dimer *A* (see previous section) to give *dimer D* (1-*cyano*-2-2′-*cyanoethylidene*cyclo*hex-5-ene*), m. p. 86—88° (from alcohol) (Found: C, 75·6; H, 6·4; N, 17·3%; *M*, 161). (*b*) Dimer B was treated with morpholine in the same way as dimer A (see previous section) to give dimer D, m. p. and mixed m. p. with product obtained above, 86—88°.

Hydrogenation of Dimers.—(*a*) Dimer A (4 g.) in methyl alcohol (20 c.c.) was hydrogenated at room temperature and pressure over a pre-reduced catalyst from 0·15 g. of 7·8% palladium-on-calcium-carbonate in methyl alcohol (10 c.c.). Hydrogen absorption was 1160 c.c. (Calc. for 2 double bonds in $C_{10}H_{10}N_2$, 1134 c.c.) The rate of absorption fell rapidly after 600 c.c. had been absorbed. The mixture was filtered and the bulk of the solvent distilled off. The residue was poured into water and extracted with ether, the extract dried, and the solvent removed, to give *tetrahydro-dimer AB*, cis-1-*cyano*-2-2′-

*cyanoethyl*cyclo*hexane*, m. p. 32—33·5° (m. p. not raised by crystallisation from methyl alcohol) (Found : C, 74·1; H, 8·7; N, 16·95. $C_{10}H_{14}N_2$ requires C, 74·1; H, 8·6; N, 17·3%).

(*b*) Dimer B was hydrogenated under the same conditions to give tetrahydro-dimer AB, m. p. 32—33·5°, identical with that from dimer A.

(*c*) Dimer C was hydrogenated under the same conditions (hydrogen absorbed : 1115 c.c.) to give *tetrahydro-dimer C* (a mixture of cis- and trans-1-*cyano*-2-2′-*cyanoethyl*cyclo*hexane*) as a viscous oil, b. p. 112—119°/0·2 mm., which partly solidified on strong cooling (Found : C, 74·2; H, 8·4%).

(*d*) Dimer D was hydrogenated under the same conditions (hydrogen absorption : 1120 c.c.) to give *tetrahydro-dimer D* as a viscous oil, b. p. 103—110°/0·075 mm., which partly solidified on strong cooling (Found : C, 74·3; H, 8·0%).

The curves for the rates of hydrogenation for dimers B, C, and D were almost identical : for dimer A, the uptake of the first mole of hydrogen was more rapid.

Hydrolysis of Tetrahydro-dimer AB.—(a) *With acid.* The tetrahydro-dimer (11·2 g.) was refluxed for 20 hours with a mixture of 35% hydrochloric acid (25 c.c.) and water (25 c.c.), a further 22 c.c. of acid being added after 3 hours' heating. After cooling, crystals separated and were collected (m. p. 86—94°). Repeated crystallisation from water gave *cis*-*β*-(2-carboxy*cyclo*hexyl)propionic acid, m. p. 103—104° (Found : C, 59·85; H, 8·15%; equiv., 100·7. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%; equiv., 100). The acid (1 g.) in thionyl chloride (0·8 c.c.) was kept overnight. After removal of excess of thionyl chloride at 30°/15 mm., ether (5 c.c.) was added and the solution treated with aniline (2·5 c.c.) in ether (5 c.c.). The mixture was stirred with water and acidified with hydrochloric acid. The solid was collected, washed with dilute sodium hydroxide (m. p. 176—177°), and repeatedly crystallised from methyl alcohol to give the *cis*-dianilide, m. p. 179—180° (Found : C, 75·6; H, 7·35; N, 8·5. $C_{22}H_{26}O_2N_2$ requires C, 75·4; H, 7·4; N, 8·0%). When the acid chloride was prepared by heating the acid with excess of thionyl chloride, only the *trans*-anilide (see below), m. p. 213—214°, was obtained. The methyl ester of the *cis*-acid (prepared by using diazomethane) did not react with aniline below 60°.

(b) *With alkali.* Tetrahydro-dimer AB (50 g.) was refluxed for 16 hours with 10% aqueous sodium hydroxide (370 c.c.). The solution, after treatment with carbon, was acidified with hydrochloric acid and the solid collected (43 g.); it had m. p. 160—175°. [The aqueous filtrates were extracted with ether, to yield a viscous oil (13·5 g.) from which no pure product was isolated.] This solid was washed well with ether (for working up of ethereal washings, see below) and repeatedly crystallised from water to give a *half-amide* of *trans*-*β*-(2-carboxy*cyclo*hexyl)propionic acid (23 g.), m. p. 206—207° (Found : C, 60·45; H, 8·6; N, 6·8. $C_{10}H_{17}O_3N$ requires C, 60·3; H, 8·5; N, 7·0%). The acid amide (1 g.) was refluxed with acetyl chloride (5 c.c.) for 3 hours. The product was washed well with water and crystallised from a large bulk of ether to give the *imide*, m. p. 160—161° (Found : C, 66·25; H, 7·95; N, 7·75. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3; N, 7·7%). The ethereal washings of the crude acid from the hydrolysis were evaporated to small bulk and a little more acid amide was collected. The rest of the ether was then removed and the oily product repeatedly crystallised from benzene to a m. p. of 137—140°. This was not depressed on admixture with the pure *trans*-acid (m. p. 143—145° obtained below).

Hydrolysis of Acid Amide.—(a) *With acid.* The acid amide (1·5 g.) was refluxed with 17% hydrochloric acid (10 c.c.) for 17 hours. After cooling, *trans*-*β*-(2-carboxy*cyclo*hexyl)propionic acid was collected, having m. p. 143—145°, not altered by repeated crystallisation from water (Found : C, 60·2; H, 8·3. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%). The acid (0·5 g.) in aniline (1 c.c.) was refluxed for 2 hours, cooled, and diluted with ether; the solid was collected, washed with aqueous sodium hydroxide, and crystallised from methyl alcohol, to give the *trans*-anilide, m. p. 213—214° (Found : N, 8·4. Calc. for $C_{22}H_{26}O_2N_2$: N, 8·0%).

(b) *With alkali.* The acid amide (1·5 g.) was refluxed with 15% sodium hydroxide (10 c.c.) for 17 hours. The solution, after clarification with carbon, was acidified with hydrochloric acid and extracted with ether. Evaporation of the ether left a mixture of acids, m. p. 105—120°, from which after repeated crystallisation from benzene, a sample of impure *trans*-acid, m. p. 136—138° (clear at 140°), was obtained.

Hydrolysis of Tetrahydro-dimer C.—This tetrahydro-dimer was hydrolysed with sodium hydroxide as described for tetrahydro-dimer AB. The products isolated were the solid amide, m. p. 203—206° (mixed m. p. with authentic sample, 203—207°), and a crude *trans*-diacid, m. p. 136—139° (mixed m. p. with authentic *trans*-diacid, 137—142°).

Hydrolysis of Tetrahydro-dimer D.—This was carried out with sodium hydroxide as described for tetrahydro-dimer AB; the products isolated were the acid amide, m. p. 202—205° (mixed m. p. with authentic sample, 202—206°), and the crude *trans*-diacid, m. p. 135—138° (mixed with authentic *trans*-diacid, 136—140°).

Iodine Chloride Titrations.—The estimations were carried out as described by Letch and Linstead (*J.*, 1932, 443). To obtain reasonable absorption of iodine chloride, the solution of dimer (1/300 mol.) in chloroform was mixed with the alcoholic iodine chloride and kept in the dark for 48 hours. The solution was then poured into aqueous potassium iodide and titrated with 0·1N-sodium thiosulphate. In all cases, a control experiment was done, omitting the addition of the dimer. The results (expressed as % double bond for dimers A, B, C, and D were 74, 57, 105, and 99, respectively.

Dipole Moments (Mr. G. F. LONGSTER).—The dipole moments were determined in benzene as solvent at 25°. The results obtained for dimers A, B, C, and D were 5·8, 2·9, 5·1, and 5·6 D., respectively.

Rough estimates of the dipole moments of structures (I), (II), (III), and (IV) were made by examining molecular models and allowing, so far as possible, for the four crumpled forms of the *cyclo*hexene ring and for the free rotation in the side chain. The results obtained for (I), (II), (III) and (IV) were 5·5, $<3·2$, $>4·2$, and 1—5·6 D., respectively.

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