## 366. trans-cyclo*Heptane*-1 : 2-*dicarboxylic Acid and its Conversion into* trans-bicyclo[5 : 3 : 0]*Decan*-9-*one*.

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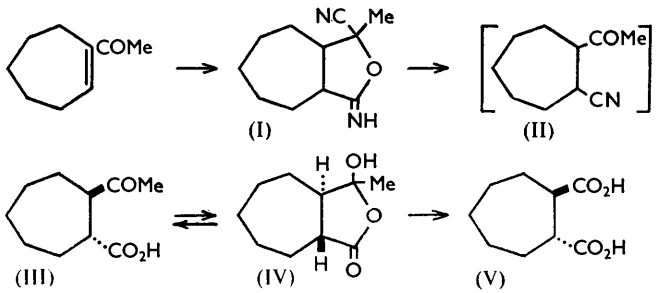
*cyclo*Heptane-1 : 2-dicarboxylic acid has been obtained from *cyclo*heptanone. Resolution by brucine has shown it to possess the *trans*-configuration and an independent stereospecific synthesis has been effected. Elaboration of the acid has produced *trans-bicyclo*[5 : 3 : 0]decan-9-one, obtained earlier by a sterically equivocal route.

It has been shown [1] that the catalytic and " chemical " reduction of *bicyclo*[5 : 3 : 0]dec-7-en-9-one lead stereoselectively to the two possible stereoisomers of *bicyclo*[5 : 3 : 0]decan-9-one, but no unambiguous assignment of configuration could be deduced. The key reference compounds for this task are the hitherto unknown *cis*- and *trans-cyclo*heptane-1 : 2-dicarboxylic acids and methods for the synthesis of the two acids were accordingly investigated.

As methods which were successful in the *cyclo*pentane and *cyclo*hexane series [2] proved abortive when applied to the corresponding *cyclo*heptane derivatives, a new method of approach was devised. *cyclo*Heptanone was converted into 1-ethynyl*cyclo*heptanol [3] which was transformed by the Meyer–Schuster rearrangement into acetyl*cyclo*heptene by Newman's technique.[4] The latter ketone with cold aqueous-alcoholic potassium cyanide furnished a crystalline substance, whose formula $C_{11}H_{16}ON_2$ corresponded to the




(Only one enantiomorph is shown throughout.)

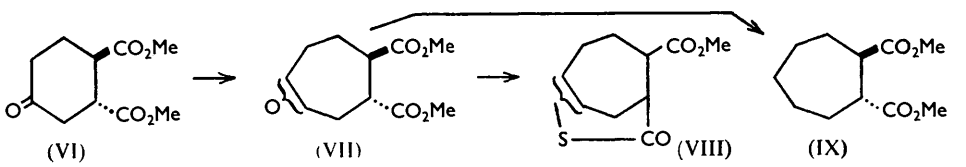
cyanohydrin of the expected cyano-ketone (II); similar behaviour has been reported for mesityl oxide.[5] The infrared characteristics of the product, however, indicated that a simple cyanohydrin structure was unlikely. No C≡N stretching frequency was present but bands appeared in the carbonyl region at 1710 and 1735 cm.$^{-1}$. A possible structure

[1] Islam and Raphael, *J.*, 1955, 3151.
[2] Raphael in Rodd's " Chemistry of Carbon Compounds," Elsevier, London, Vol. IIA, pp. 111, 235.
[3] Heilbron, Jones, Toogood, and Weedon, *J.*, 1949, 1827.
[4] Newman, *J. Amer. Chem. Soc.*, 1953, **75**, 4740.
[5] Lapworth, *J.*, 1904, **85**, 1214.

which corresponds to these findings is (I), in which the cyano- and the acetimidoyloxy-group are attached to the same carbon atom, so that the absence of the C≡N frequency may be rationalised since the band is absent in similar compounds with cyano- and acetoxy-groups on the same carbon atom.[6] Although higher in frequency than expected, the absorption in the carbonyl region may be regarded as the C=N stretching frequency of the imine. From results described in the sequel the rings in structure (I) are probably *trans*-fused.

Alkaline hydrolysis of compound (I) yielded the keto-acid (III), presumably by way of the cyano-ketone (II). The infrared spectrum (in $CCl_4$) of this acid showed it to be in equilibrium with the lactol (IV), with a band at 1780 cm.$^{-1}$ ($\gamma$-lactone): for the solid state (Nujol dispersion) a normal bonded-hydroxyl band appeared at 3300 cm.$^{-1}$, indicating a substantial proportion of the lactol.[7] With diazomethane the keto-acid yielded the normal ester corresponding to (III), while esterification [8] with methanol produced a mixture of this ester and the pseudo-ester corresponding to (IV). This mixture showed an absorption band at 1773 cm.$^{-1}$ ($\gamma$-lactone) in addition to the expected keto-ester bands at 1710 and 1727 cm.$^{-1}$. Both the pure normal ester and the ester mixture gave the 2 : 4-dinitrophenylhydrazone of the normal ester, the yield from the mixture being about 70%, which is presumably the content of normal ester in the mixture.

For large-scale working a substantially one-step conversion of acetyl*cyclo*heptene into the keto-acid (III) was devised, using aqueous glycol as solvent. Treatment of the acid with sodium hypochlorite [9] gave a homogeneous crystalline *cyclo*heptane-1 : 2-dicarboxylic acid (V) in an overall yield of 73% from *cyclo*heptanone. This product was shown to be the racemic *trans*-isomer by its resolution into two dibrucine salts. The less soluble salt crystallised from ethyl acetate; the more soluble one was purified by fractional precipitation from ethanol solution by ether. Regeneration of the free acids gave the two enantiomorphs of *trans-cyclo*heptane-1 : 2-dicarboxylic acid, m. p. 138—142°, $[\alpha]_D^{18}$ +3·3° (±0·3°), and m. p. 138—141°, $[\alpha]_D^{19}$ −4·7° (±0·5°). Although optically stable in ethanol solution over considerable periods both acids were racemised to a considerable extent by crystallisation from benzene or benzene–light petroleum. A *trans*-structure for the acid (V) is also in agreement with the dissociation constants. A potentiometric titration, kindly carried out by Dr. J. C. Speakman, showed the thermodynamic dissociation constants at 20° to be $pK_1$ 4·30, $pK_2$ 6·16, *i.e.*, $\Delta pK = 1{\cdot}86$ (±0·03). The corresponding differences for the *trans*-1 : 2-dicarboxylic acids in the *cyclo*pentane and *cyclo*hexane series are $\Delta pK$ = 1·95 and 1·75 respectively; for the *cis*-acids the values [10] are 2·14 and 2·40.



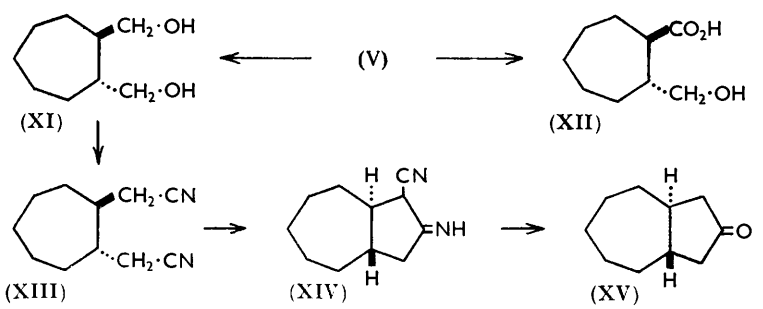

Further, we have effected a stereoselective synthesis of the *trans*-acid (V). Dimethyl 4-oxo*cyclo*hexane-*trans*-1 : 2-dicarboxylate (VI) was prepared by a Diels–Alder reaction involving 2-ethoxybuta-1 : 3-diene and fumaroyl chloride, followed by treatment of the crude product with dry methanol. The hydrogen chloride liberated in the latter reaction was neutralised with solid sodium hydrogen carbonate, and one of two products was obtained depending on the speed of this operation. Gradual addition of the alkali allowed hydrolysis of the intermediate enol ether to the crystalline free keto-diester (VI); rapid addition gave a product containing some of this ester (VI) but consisting mainly of the

[6] Kitson and Griffith, *Analyt. Chem.*, 1952, **24**, 334.
[7] Grove and Willis, *J.*, 1951, 879.
[8] Clinton and Laskowski, *J. Amer. Chem. Soc.*, 1948, **70**, 3135.
[9] Smith, Prichard, and Spillane, *Org. Synth., Coll. Vol.* III, 1955, p. 302.
[10] Speakman, *J.*, 1941, 491.

corresponding dimethyl ketal. The keto-diester and the ketal show similar absorption at 1740 cm.$^{-1}$ but in the ketal an additional triplet appears at 1169, 1127, 1096 cm.$^{-1}$ characteristic of this function.[11] Alkaline hydrolysis of the keto-diester (VI) gave the crystalline *trans*-diketo-acid, m. p. 188°, from which the ester was regenerated by diazomethane. A keto-diacid of this structure, but with m. p. 161°, was prepared by Newman and Lloyd [12] by alkaline hydrolysis of the adduct from 2-methoxybutadiene and maleic anhydride. As their compound gave *trans-cyclo*hexane-1 : 2-dicarboxylic acid by Huang-Minlon reduction,[13] the American authors assigned the *trans*-structure to their keto-diacid. In view of the discrepant melting points, however, it is highly probable that Newman and Lloyd's acid is the *cis*-isomer, inversion having taken place during the drastic alkaline treatment entailed in Huang-Minlon reduction.

The keto-diester (VI) with diazomethane generated *in situ* from methylnitrosourethane gave a mixture of the required dimethyl *trans-cyclo*heptanone-1 : 2-dicarboxylate (VII) and unchanged starting material. The latter was removed by selective treatment with semicarbazide acetate in methanol; crystallisation then yielded the ester (VII), m. p. 60—64°. This product was probably a mixture of the theoretically possible 4- and 5-keto-compounds, with one of them predominating. Reaction of the product (VII) with ethanethiol followed by treatment of the crude thioketal with Raney nickel [14] gave as sole product a sulphur-containing liquid of formula $C_{10}H_{14}O_3S$. When ethanedithiol was used the predominant product was the same compound, but in addition dimethyl *trans-cyclo*heptane-1 : 2-dicarboxylate (IX) was obtained. Mild alkaline hydrolysis of the latter gave the free acid (V), identical with the acid obtained previously from *cyclo*heptanone.

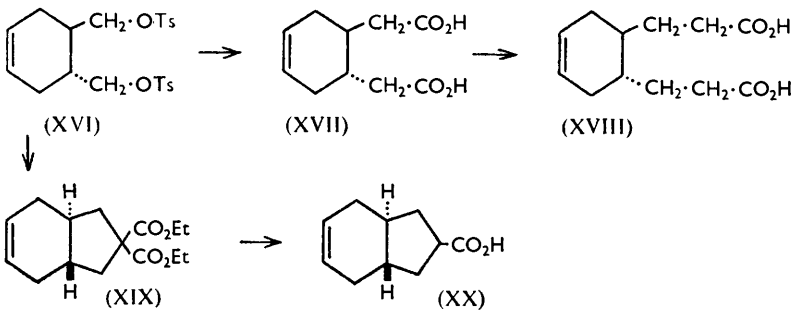
The Raney nickel used in the desulphurisation was rich in hydrogen [15] and isolation of a sulphur-containing product in these circumstances is unusual. Owen and Peto obtained a sulphide by a desulphurisation [16] and considered that this was due to its insolubility in the medium but this explanation cannot apply in the present case as the product was wholly soluble. The molecular formula and general characteristics of the compound point to a thiolactone structure of type (VIII), and this was confirmed when the compound was converted into *trans-cyclo*heptane-1 : 2-dicarboxylic acid (V) by alkaline hydrolysis followed by treatment with Raney nickel.




The *trans*-acid (V) was converted into *trans-bicyclo*[5 : 3 : 0]decan-9-one (XV) by the following route: Reduction of the dimethyl or the diethyl ester with lithium aluminium hydride gave *trans*-1 : 2-di(hydroxymethyl)*cyclo*heptane (XI). Direct reduction of the acid, even under forcing conditions, furnished *trans*-2-hydroxymethyl*cyclo*heptane-1-carboxylic acid (XII) as the predominant product. The ditoluene-*p*-sulphonate of the

[11] Bergmann and Pinchas, *Rec. Trav. chim.*, 1952, **71**, 161.
[12] Newman and Lloyd, *J. Org. Chem.*, 1952, **17**, 577.
[13] Huang-Minlon, *J. Amer. Chem. Soc.*, 1946, **68**, 2487.
[14] Wolfrom and Karabinos, *ibid.*, 1944, **66**, 909.
[15] Hauptmann and Wladislaw, *ibid.*, 1950, **72**, 707, 710.
[16] Owen and Peto, *J.*, 1955, 2383.

diol (XI) was readily obtained by Owen and Smith's method,[17] but did not yield the dinitrile (XIII) on reaction with potassium cyanide. Treatment of the diol (XI) with gaseous hydrogen bromide and of the resulting dibromide with aqueous-alcoholic potassium cyanide furnished the required dinitrile (XIII). Thorpe cyclisation of the dinitrile was effected by sodium in ethylene glycol, and the resulting imino-nitrile (XIV) was hydrolysed




and decarboxylated by sulphuric–acetic acid. The semicarbazone and 2 : 4-dinitrophenylhydrazone of the ketone (XV) thus obtained were identical with those of the ketone obtained by the lithium–ammonia reduction of *bicyclo*[5 : 3 : 0]dec-7-en-9-one;[1] this saturated ketone must therefore be the *trans*-isomer. As this method of reduction usually gives the thermodynamically more stable isomer[18] this result seems to indicate that in simple systems the *trans*-fusion of a seven-membered and a five-membered ring is the more stable arrangement.

So far neither the *cis-cyclo*heptane-1 : 2-dicarboxylic acid nor any derivative of it has been obtained in this work. Hot acetic anhydride converted the *trans*-acid into the crystalline *trans*-anhydride, which was transformed back into the parent acid by mild aqueous hydrolysis. The *trans*-configuration of the anhydride was confirmed by reduction to the crystalline *trans*-diol (XI) by lithium aluminium hydride. Pyrolysis of the *trans*-acid at 240° furnished a liquid anhydride which differed significantly in infrared absorption characteristics from the solid anhydride. Reduction gave a non-crystalline diol whose ditoluene-*p*-sulphonate melted over a 10° range. Thus pyrolysis gave a mixture of anhydrides in which the *trans*-isomer probably predominated.

Another route to the *trans-bicyclo*decanone (XV) was explored but not completed. Reduction of diethyl *trans-cyclo*hex-4-ene-1 : 2-carboxylate by lithium aluminium hydride gave the corresponding *trans*-diol which was converted into the crystalline ditoluene-*p*-sulphonate (XVI). This derivative was treated with potassium cyanide, and the resulting dinitrile was hydrolysed to the *trans*-diacetic acid (XVII). A double Arndt–Eistert homologation furnished the crystalline *trans*-dipropionic acid (XVIII). An attempt to prepare this acid from the ditoluene-*p*-sulphonate (XVI) and diethyl sodiomalonate was unsuccessful, the sole product being the reduced *trans*-indane diester (XIX), readily converted into the crystalline monocarboxylic acid (XX) by hydrolysis and decarboxylation.

## Experimental

1-*Ethynyl*cyclo*heptanol*.—This was prepared from *cyclo*heptanone (191 g.) by the method of Heilbron *et al.*,[3] yielding 1-ethynyl*cyclo*heptan-1-ol (216 g., 91%), b. p. 97—100°/20 mm., $n_D^{25}$ 1·4868. A sample, crystallised from pentane, had m. p. 24·5—26°.

1-*Acetyl*cyclo*heptene*.—1-Ethynyl*cyclo*heptanol (216 g.), on treatment with Dowex 50 resin (14 g.) in glacial acetic acid (220 ml.),[4] gave 1-acetyl*cyclo*heptene (189·5 g., 88%), b. p. 99—102°/20 mm., $n_D^{25}$ 1·4924.

[17] Owen and Smith, *J.*, 1952, 4029.
[18] Barton and Robinson, *J.*, 1954, 3045.

*Reaction of* 1-*Acetyl*cyclo*heptene with Hydrogen Cyanide.*—The ketone (3·5 g., 0·025 mole) in alcohol (16 ml.) was added to a solution of potassium cyanide (3·25 g., 0·05 mole) in water (7·5 ml.). The solution was seeded with crystals of m. p. 131—135° obtained in a small-scale experiment and left at room temperature for 24 hr. The crystalline *product* (I) (2·05 g.) was obtained as needles, m. p. 150·5—152°, from aqueous alcohol (Found: C, 69·1; H, 8·0; N, 14·7. $C_{11}H_{16}ON_2$ requires C, 68·7; H, 8·4; N, 14·6%), $\nu_{max.}$ (in $CCl_4$) 3400, 3175 (bonded NH or OH), 1710, 1735 cm.$^{-1}$ (C=N?).

This product (0·75 g., 0·0039 mole) was refluxed with 2N-sodium hydroxide (6 ml.) for 5 hr., evolution of ammonia having by then ceased. The cooled solution was acidified with sulphuric acid, and the separated oil extracted into ether (2 × 10 ml.). Evaporation of the dry ethereal solution ($MgSO_4$) gave a thick oil (0·43 g., 67%) which crystallised on trituration with light petroleum (b. p. 40—60°). Recrystallisation from light petroleum–benzene gave 2-*acetyl*-cyclo*heptanecarboxylic acid*, m. p. 67—68·5° (Found: C, 65·1; H, 8·9. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·75%), $\nu_{max.}$ (dil. soln. in $CCl_4$) 3570 (free OH), 3350 (associated OH), 1780 (γ-lactone), 1705 cm.$^{-1}$ (ketone C=O).

*Large-scale Preparation of* 2-*Acetyl*cyclo*heptanecarboxylic Acid.*—1-Acetyl*cyclo*heptene (103·8 g., 0·75 mole) was added to a solution of potassium cyanide (107·5 g.) in water (200 ml.), and this was diluted with ethylene glycol (750 ml.). The mixture was not homogeneous but gave a clear solution after being stirred at room temperature for an hour. After a further hour's stirring potassium hydroxide (70 g.) in water (100 ml.) was added and the solution refluxed for 6 hr. The cool solution was extracted with ether (3 × 200 ml.), and the combined extracts were washed with water (50 ml.). Evaporation of the dry ethereal solution, and trituration in light petroleum (b. p. 40—60°), gave a neutral product (16·7 g.), m. p. 50—55°. As this material contained nitrogen and gave a high yield of the acid on further treatment with alkaline glycol it was probably a mixture of the intermediate 1-acetyl-2-cyano*cyclo*heptane and the corresponding amide.

The alkaline liquor was acidified with concentrated hydrochloric acid (270 ml.), and extracted with ether (4 × 200 ml.). The combined extracts were washed with water (30 ml.), dried ($MgSO_4$), and evaporated. The product (102·7 g., 74%) crystallised on being seeded with 2-acetyl*cyclo*heptanecarboxylic acid.

In another experiment acetyl*cyclo*heptene (23·0 g.) was converted into 2-acetyl*cyclo*heptane-carboxylic acid (29·4 g., 96%), by increasing the time of reflux to 22 hr.

*Esterification of* 2-*Acetyl*cyclo*heptane*-1-*carboxylic Acid.*—(*a*) The acid (4·5 g., 0·024 mole) was refluxed for 15 hr. in ethylene dichloride (13·0 ml.)–methanol (4·0 ml.) containing toluene-*p*-sulphonic acid (80 mg.). The solution was evaporated and the residue dissolved in ether (20 ml.), washed with 10% sodium carbonate solution (2 × 12 ml.) and water (5 ml.), and dried ($MgSO_4$). Distillation gave a mixture of the *pseudo*- (V) and normal ester (1·98 g., 51% after allowance for 0·86 g. of recovered acid), b. p. 80°/0·4 mm., $n_D^{25}$ 1·4702 (Found: C, 66·7; H, 9·25. Calc. for $C_{11}H_{18}O_3$: C, 66·6; H, 9·15%), $\nu_{max.}$ (liquid film) 1773 (γ-lactone), 1727, 1712 cm.$^{-1}$ (keto-ester).

(*b*) The acid (2·9 g., 0·016 mole), treated with diazomethane in ether in the usual way, gave the normal ester (2·08 g., 67%), b. p. 77°/0·3 mm., $n_D^{25}$ 1·4660, $\nu_{max.}$ (liquid film) 1726, 1712 cm.$^{-1}$ (keto-ester).

With Brady's reagent the normal ester gave an orange 2 : 4-*dinitrophenylhydrazone* in 95% yield. After chromatography on alumina (eluant, benzene containing 5% of ethyl acetate) the derivative crystallised from methanol, and had m. p. 100·5—102° (Found: C, 54·2; H, 5·8; N, 14·7. $C_{17}H_{22}O_6N_4$ requires C, 54·0; H, 5·9; N, 14·8%).

Under the same conditions the Clinton–Laskowski product gave the same 2 : 4-dinitrophenylhydrazone (mixed m. p.) in 72% yield.

The 2 : 4-dinitrophenylhydrazone of the parent 2-acetyl*cyclo*heptanecarboxylic acid (0·29 g.) was prepared by addition of a hot solution in methanol (2 ml.)–water (10 ml.) to 2 : 4-dinitrophenylhydrazine hydrochloride (0·5 g.) in hot water (15 ml.). The product was purified by chromatography on bentonite–kieselguhr (eluant, benzene containing 20% of chloroform). It was freely soluble in methanol and crystallised from carbon tetrachloride in orange needles, m. p. 183—184°. The sample retained solvent tenaciously, giving a positive reaction for chlorine in the Lassaigne test even after several hours' drying at 20°/3 × $10^{-3}$ mm. A loss of 10% occurred when the temperature was raised to 110° (Found: C, 52·1; H, 5·35; N, 14·6. Calc. for $C_{16}H_{20}O_6N_4$: C, 52·7; H, 5·5; N, 15·4%).

trans-cyclo*Heptane*-1 : 2-*dicarboxylic Acid*.—2-Acetyl*cyclo*heptanecarboxylic acid (32·0 g., 0·18 mole) was stirred with sodium hypochlorite solution [9] (490 ml.; 10—14% of available chlorine); emulsification and refluxing of chloroform were noted after 45 min. After a further 5 hours' stirring the mixture had regained room temperature and excess of hypochlorite was reduced by the addition of sodium pyrosulphite (18 g.) in water. The product was acidified by sulphuric acid (30 g.) in water (50 ml.), and the oil obtained was separated by ether (100 ml.) and combined with the ether-extract (4 × 200 ml.) of the aqueous liquor. Evaporation of the dried ($MgSO_4$) extract gave the *dicarboxylic acid* as a white solid (30·5 g., 95%). After one crystallisation from benzene–light petroleum it had m. p. 142—146°. The analytical sample had m. p. 145—147° (Found: C, 58·0; H, 7·6. $C_9H_{14}O_4$ requires C, 58·0; H, 7·6%).

*Resolution of the Acid as the Brucine Salts.—trans-cyclo*Heptane-1 : 2-dicarboxylic acid (1·97 g., 0·011 mole; m. p. 142—146°) and anhydrous brucine (8·3 g.; m. p. 167—171°) were dissolved in hot ethyl acetate (30 ml.). The brucine salt began to separate from the warm solution almost immediately; it was filtered off after 48 hours. The white solid product (8·25 g., 80% of total) was extracted with boiling ethyl acetate (30 ml.) for 45 min. and the mixture filtered. In 24 hr. the filtrate deposited a crystalline product (*salt A*; 3·8 g., 37%), m. p. 129—132°, $\alpha$ −0·44°, $[\alpha]_D^{19}$ −15·2° ± 0·7° (*c* 2·9 in EtOH) unchanged in rotation by further crystallisation (Found: C, 62·6; H, 6·7; N, 5·7. $C_{55}H_{66}O_{12}N_4,4H_2O$ requires C, 63·0; H, 7·1; N, 5·35%).

Evaporation of the original ethyl acetate liquor gave a thick oil (*salt B*; 1·1 g.) which solidified when rubbed in ether, and then had $\alpha$ −0·68°, $[\alpha]_D^{20}$ −39·5° ± 0·7° (*c* 1·7 in EtOH). Evaporation of the liquor from the first crystallisation of salt A gave more of salt B (3·7 g.), $\alpha$ −0·38°, $[\alpha]_D^{20}$ −38° ± 1·0° (*c* 2·0 in EtOH, *l* 0·5 dm.). This did not crystallise; purified by precipitation from alcohol by ether, it had m. p. 101—108°, $[\alpha]_D^{19}$ −46·0° ± 1·0° (Found: C, 62·6; H, 6·9; N, 5·5%). The salts probably became hydrated on exposure to the atmosphere. There was no weight loss at 76°/0·05 mm., and a loss of only 1% after 3 hr. at 110°/$10^{-3}$ mm.

The brucine salts A and B (3·8 g.), $[\alpha]_D^{19}$ −15·2° and $[\alpha]_D^{20}$ −39·5°, were separately decomposed by stirring them with 2N-hydrochloric acid (25 ml.) for 4 min. at 0°. The acid solution was ether-extracted (3 × 20 ml.), and the combined extracts were washed with water (2 × 5 ml.), dried ($MgSO_4$), and evaporated below room temperature. Salt A gave an acid, m. p. 138—142°, $\alpha$ +0·41°, $[\alpha]_D^{19}$ +3·4° (±0·3°) (*c* 12·5 in EtOH). After one crystallisation from benzene this had m. p. 142—145°, $[\alpha]_D^{19}$ +1·6° (±0·4°). Partial racemisation also occurred during crystallisation from benzene–light petroleum (b. p. 60—80°). Salt B gave an acid, m. p. 138—141°, $\alpha$ −0·19°, $[\alpha]_D^{18}$ −4·7° (±0·5°) (*c* 8·2 in EtOH, *l* 0·5 dm.). The rotation of this sample was unchanged when the ethanolic solution was kept overnight at room temperature, but after crystallisation from benzene the material had $[\alpha]_D^{19}$ −1·0° (±0·2°). The time interval between the commencement of the acid treatment and the first reading of the polarimeter was 50 min. for the (+)-acid and 56 min. for the (−)-acid.

*Dimethyl* trans-cyclo*Heptane*-1 : 2-*dicarboxylate*.—The dicarboxylic acid (1·18 g., 0·006 mole) was treated with diazomethane in ether and worked up after being kept overnight. The *product* (1·10 g., 81%) boiled at 74—81°/0·5 mm.; redistillation gave pure material, b. p. 78°/0·5 mm., $n_D^{26}$ 1·4602 (Found: C, 61·85; H, 8·5. $C_{11}H_{18}O_4$ requires C, 61·7; H, 8·5%).

*Diethyl* trans-cyclo*Heptane*-1 : 2-*dicarboxylate*.—The dicarboxylic acid (5·7 g., 0·03 mole) was converted by Cope and Herrick's method [19] into the *diethyl ester* (6·6 g., 89%), b. p. 80°/0·2 mm., $n_D^{25}$ 1·4556 (Found: C, 64·6; H, 8·9. $C_{13}H_{22}O_4$ requires C, 64·4; H, 9·15%).

*Attempted Inversion of Diethyl* trans-cyclo*Heptane*-1 : 2-*dicarboxylate*.—The diethyl ester (6·25 g., 0·026 mole) was refluxed in ethanol (20 ml.) containing sodium (1·0 g.) for 3 hr.; after 16 hr. water (10 ml.) was added and the solution evaporated under reduced pressure. The residue (4·6 g.) was taken up in 2N-sodium hydroxide (30 ml.), extracted with ether (2 × 15 ml.), acidified with sulphuric acid, and again ether-extracted (3 × 20 ml.). The last extracts were dried and evaporated, to give an acid (3·0 g.) which crystallised under light petroleum. Crystallisation from benzene raised the m. p. to 145—147·5°, not depressed on admixture with the starting acid.

*Reactions of the Diethyl Ester with Bases*.—There was no apparent reaction between the ester and ammonia solution (*d* 0·88) during several days' shaking at room temperature.

The ester (0·72 g., 0·003 mole) dissolved in 100% hydrazine hydrate (3 ml.) during 1·5 hours'

[19] Cope and Herrick, *Org. Synth.*, 1950, **30**, 29.

refluxing; the cooled solution deposited the *dihydrazide* as needles, m. p. 150—155°. Desiccation over sulphuric acid gave crude material (0·65 g., 100%); pure material had m. p. 156—157° (from *tert.*-butyl alcohol) (Found: C, 50·6; H, 8·4; N, 25·9. $C_9H_{18}O_2N_4$ requires C, 50·45; H, 8·5; N, 26·15%).

trans-cyclo*Heptane*-1 : 2-*dicarboxylic Anhydride*.—The *trans*-acid (800 mg.) was refluxed in acetic anhydride for 2 hr. Excess of acetic anhydride was removed under a vacuum and the residue distilled, to give the *anhydride* (557 mg., 77%), b. p. 94°/0·25 mm., $n_D^{25}$ 1·4920, which solidified and, crystallised from hexane–ether, had m. p. 43—45° (Found: C, 63·2; H, 7·1. $C_9H_{12}O_3$ requires C, 64·3; H, 7·2%. The carbon analyses were consistently low), $\nu_{max.}$ (in $CCl_4$) 1785, 1870 cm.$^{-1}$ (C=O of 5-ring anhydride).

The anhydride (45 mg.) dissolved in boiling water (0·3 ml.) in 2 min., and the cooled solution deposited crystals of the *trans*-dicarboxylic acid (33 mg.), m. p. and mixed m. p. 145—146·5°.

Reduction of this anhydride (557 mg.) by lithium aluminium hydride (600 mg.) in refluxing ether for 3 hr. gave the *trans*-glycol (491 mg., 94%), m. p. 55—57° undepressed by authentic material (see below).

*Mixed Anhydrides of* cyclo*Heptane*-1 : 2-*dicarboxylic Acid*.—The *trans*-acid (400 mg.) was added in small amounts to a small flask maintained at 240° (bath). Addition was complete in 5 min. and after a further 5 minutes' heating the residual anhydride was distilled (b. p. 98°/0·2 mm.; $n_D^{23}$ 1·4928; 258 mg., 71%) but did not crystallise (Found: C, 64·5; H, 6·7. Calc. for $C_9H_{12}O_3$: C, 64·3; H, 7·2%): it had infrared max. in $CCl_4$ at 1783 and 1868 cm.$^{-1}$ (C=O of 5-ring anhydride).

Reduction (of 258 mg.) by lithium aluminium hydride was carried out as for the pure *trans*-anhydride; the glycol obtained (227 mg., 93%) did not crystallise, but gave a ditoluene-*p*-sulphonate, m. p. 75—83° (from methanol), under conditions described below. A mixture with the authentic *trans*-ditoluene-*p*-sulphonate (m. p. 89—90°; see below) had m. p. 80—90°.

trans-1 : 2-*Di*(*hydroxymethyl*)cyclo*heptane*.—(*a*) *trans-cyclo*Heptane-1 : 2-dicarboxylic acid (0·80 g., 0·004 mole) in ether (10 ml.) was added to lithium aluminium hydride (0·40 g., 66% excess) in ether (15 ml.) during 15 min. with ice-cooling. The mixture was stirred at room temperature for 2 hr. and the excess of hydride then destroyed with ethyl acetate. After acidification with sulphuric acid (4 g. in 10 ml. of water) the ether layer was separated and extracted with water (3 × 10 ml.). Continuous ether-extraction of the combined aqueous liquors yielded a residue (0·15 g., 22%) which crystallised under light petroleum (b. p. 40—60°). This material was the required *diol* which crystallised from hexane–ether in prisms, m. p. 56—57° (Found: C, 68·6; H, 11·2. $C_9H_{18}O_2$ requires C, 68·3; H, 11·5%).

Evaporation of the original ether layer yielded a residue of trans-2-*hydroxymethyl*cyclo*heptanecarboxylic acid* (0·48 g., 65%) which solidified under light petroleum (b. p. 40—60°) to a crystalline mass, m. p. 64—70°, raised to 77—79° on crystallisation from benzene–light petroleum (b. p. 40—60°) [Found: C, 62·9; H, 9·6. $C_9H_{16}O_3$ requires C, 62·8; H, 9·4%) and had $\nu_{max.}$ in $CHCl_3$ at 2400—3640 (chelated OH) and 1710 cm.$^{-1}$ (C=O of acid). Under more forcing conditions, *i.e.*, 4 hours' refluxing with a five-fold excess of lithium aluminium hydride, the dicarboxylic acid (1·02 g.) was converted into a mixture of the same two products, diol (0·35 g., 40%) and hydroxy-acid (0·45 g., 48%).

(*b*) Diethyl *trans*-1 : 2-*cyclo*heptanedicarboxylate (13·6 g., 0·056 mole) was refluxed for 2 hr. with lithium aluminium hydride (5·5 g., 80% excess) in ether. The mixture was worked up as usual and gave only the diol (8·1 g., 90%), m. p. 53—56°.

*Ditoluene*-p-*sulphonate of* trans-1 : 2-*Di*(*hydroxymethyl*)cyclo*heptane*.—This was prepared from the diol (1·80 g., 0·0011 mole) by Owen and Smith's method [17] and worked up after 45 hr. at 0°, to yield a crude *ester*, m. p. 80—85° (3·94 g., 74%), which crystallised from methanol as needles, m. p. 89—90° (Found: C, 59·3; H, 6·5. $C_{23}H_{30}O_6S_2$ requires C, 59·2; H, 6·45%).

*Reaction with potassium cyanide*. The ditoluene-*p*-sulphonate (2·93 g.) was refluxed for 1 hr. in ethylene glycol (18 ml.) containing potassium cyanide (1·25 g. in 2 ml. of water). The cooled liquor was extracted with ether (4 × 15 ml.), and the dried extract was evaporated to a clear oil (0·91 g.). The bulk of this material was undistillable but a small fraction (0·18 g.) of b. p. 44°/0·7 mm. was obtained. This material was soluble in light petroleum (b. p. 40—60°), contained neither nitrogen nor sulphur, and rapidly decolorised bromine in carbon tetrachloride.

trans-1 : 2-*Di*(*bromomethyl*)cyclo*heptane*.—A stream of dry hydrogen bromide was passed into *trans*-1 : 2-di(hydroxymethyl)*cyclo*heptane (3·55 g., 0·022 mole) at 110° (bath). Uptake of hydrogen bromide had almost ceased after 15 min., but passage of the gas was continued for

a further 15 min. at 110°. The cooled residue was stirred with 10% potassium carbonate solution (20 ml.), the insoluble oil taken up in light petroleum (20 ml., b. p. 60—80°), and this solution dried over potassium carbonate. Distillation yielded the *dibromo-compound* (3·1 g., 53%), b. p. 84°/0·3 mm., $n_D^{27}$ 1·5378 (Found: C, 38·1; H, 5·85; Br, 56·3. $C_9H_{16}Br_2$ requires C, 38·0; H, 5·7; Br, 56·3%).

*Reaction with potassium cyanide.* The dibromo-compound (3·0 g., 0·01 mole) was gently refluxed in ethylene glycol (18 ml.) containing potassium cyanide (2·6 g.) for 10 min. The cooled product (discoloured) was extracted with ether (3 × 15 ml.), and the ether layer washed with water (4 ml.). Evaporation of the dried extract gave an oil (1·56 g.) which was bromine-free; this was distilled, giving the *dinitrile* (1·07 g., 57%), b. p. mainly 106°/0·1 mm. Redistilled material had b. p. 112°/0·6 mm., $n_D^{21}$ 1·4950 (Found: C, 75·2; H, 9·0; N, 15·4. $C_{11}H_{16}N_2$ requires C, 74·95; H, 9·15; N, 15·9%), $\nu_{max.}$ (liquid film) 2258 cm.$^{-1}$ (C≡N).

When the time of refluxing in glycol was increased to 30 min. the material obtained by ether-extraction was partly crystalline. Needles, m. p. 152—158°, were separated from the dinitrile by crystallisation from aqueous methanol and represented 31% of the total yield. Crystallisation from methanol gave pure material, m. p. 160·5—162°, identical with the product from Thorpe cyclisation of the dinitrile (see below).

The dibromo-compound (2·9 g., 0·01 mole) was also treated with potassium cyanide (2·6 g.) in ethanol (25 ml. containing 4 ml. of water) and refluxed for 1·5 hr., the yield of dinitrile being 62%.

*Thorpe Cyclisation of* trans-1 : 2-*Di*(*cyanomethyl*)cyclo*heptane*.—(*a*) The dinitrile (231 mg.) was refluxed in absolute alcohol (1 ml.) containing sodium (10 mg.) for 1 hr. Dilution with water (3 ml.) led to the separation of an oil which did not crystallise on being seeded and was presumed to be starting material. (*b*) The nitrile (973 mg.) was refluxed in ethylene glycol (5 ml.) containing sodium (120 mg.) for 45 min.; dilution with water (8 ml.) precipitated crystals (730 mg., 75%), m. p. 153—157°. The pure trans-8-*cyano*-9-*imino*bicyclo[5 : 3 : 0]*decane* (XIV) had m. p. 161—162° (methanol) (Found: C, 75·1; H, 8·7; N, 15·9. $C_{11}H_{16}N_2$ requires C, 74·95; H, 9·15; N, 15·9%), $\nu_{max.}$ (in $CHCl_3$) 3487, 3387 (NH), 2187 (C≡N), 1644, 1610 cm.$^{-1}$ (C=N). Unchanged nitrile (98 mg., 10% recovery) was obtained by ether-extraction of the liquor. Cyclisation did not take place when the concentration of sodium glycoside was one-third of that shown above.

trans-bicyclo[5 : 3 : 0]*Decan*-9-*one*.—(*a*) The imino-nitrile (XVI) (215 mg.) from the Thorpe cyclisation was hydrolysed, with decarboxylation, by Ziegler's method.[20] After 3·5 hours' refluxing, steam-distillation and ether-extraction of the distillate yielded *trans-bicyclo*[5 : 3 : 0]-decan-9-one (24 mg. 13%). (*b*) The imino-nitrile (73 mg.) was treated as above, but with continuous steam-distillation. A good yield (45·5 mg.) of material was isolated from the distillate, but reaction was incomplete, since the product contained nitrogen and gave only a small quantity of semicarbazone on being treated with semicarbazide acetate in methanol. (*c*) The imino-nitrile (116 mg.) was treated as in (*a*) but in a solution made homogeneous by the addition of glacial acetic acid. Steam-distillation and ether-extraction of the distillate (dried with sodium carbonate) yielded the ketone (52 mg., 51%).

The ketone gave a high yield of the semicarbazone, m. p. 214—216·5° (Islam and Raphael [1] give 221—223°), which with 2 : 4-dinitrophenylhydrazine sulphate yielded an orange 2 : 4-dinitrophenylhydrazone, m. p. 136—138°, undepressed by the material obtained by Islam and Raphael (m. p. 138°).

*Dimethyl* trans-1 : 2-4-*Oxo*cyclo*hexanedicarboxylate*.—Fumaroyl chloride (4·75 g., 0·03 mole) in dry ether (10 ml.) was added with stirring and ice cooling, during 20 min., to 2-ethoxybuta-1 : 3-diene [21] (3·5 g., 0·036 mole) in ether (10 ml.). The yellow solution was stirred for a further 2·5 hr. at room temperature and was then added, with stirring, to dry methanol (40 ml.). Stirring was continued for 1 hr. and the solution neutralised by the gradual addition of solid sodium hydrogen carbonate. The mixture was filtered, dried ($MgSO_4$), and evaporated, and the oil obtained was distilled; it had b. p. 110—114°/0·6 mm., $n_D^{27}$ 1·4724 (3·70 g., 56%). The *keto-diester* crystallised: from ether–light petroleum (b. p. 40—60°), had m. p. 53—54° (Found: C, 56·0; H, 6·6. $C_{10}H_{14}O_5$ requires C, 56·1; H, 6·6%), $\nu_{max.}$ (in $CCl_4$) 1748 cm.$^{-1}$ (combined ester and ketone C=O). The *semicarbazone*, obtained with semicarbazide acetate in boiling

[20] Ziegler in " Methoden der Organischen Chemie," Georg Thieme, Stuttgart, 1955, Vol. IV, Part 2, p. 758.

[21] Braude, Jones, Sondheimer, and Toogood, *J.*, 1949, 613.

methanol, had m. p. 171—172° (from methanol) (Found: C, 48·5; H, 6·25; N, 15·3. $C_{11}H_{17}O_5N_3$ requires C, 48·7; H, 6·3; N, 15·5%).

When this experiment was repeated (scale, 0·1 mole) and the product neutralised by *rapid* addition of solid sodium hydrogen carbonate, a mixture was obtained. One component, the *dimethyl ketal* (6·0 g.) of the keto-ester separated as prisms, m. p. 60—65°, on being stirred in ether and a further quantity (12·5 g., overall yield 70%) was obtained by evaporating the liquor and stirring the residue in light petroleum (b. p. 40—60°). Recrystallisation from benzene–light petroleum (b. p. 40—60°) raised the m. p. to 75·5—76·5° (Found: C, 55·3; H, 7·4. $C_{12}H_{20}O_6$ requires C, 55·4; H, 7·75%). Infrared absorption was at 1742 (ester C=O), 1169, 1127, 1096 cm.$^{-1}$ (C·O·C of ketal). Evaporation of the petroleum washings yielded the second component (3·85 g., 17%), the keto-diester described above.

The ketal (13·3 g., 0·05 mole) was shaken for 1 hr. in 2N-hydrochloric acid (40 ml.), whence ether-extraction yielded the keto-diester (9·9 g., 89%), m. p. 39—45°, undepressed by pure material.

trans-4-*Oxo*cyclo*hexane*-1 : 2-*dicarboxylic Acid.*—The dimethyl ester (3·20 g., 0·015 mole) was refluxed with potassium hydroxide (3·0 g.) in water (12 ml.) for 1 hr., and the cooled solution was acidified with concentrated hydrochloric acid (4 ml.) and evaporated to dryness under reduced pressure. The residue (9·2 g.) was extracted with dry acetone in a Soxhlet extractor; extraction was complete in 1·5 hr. Evaporation of the acetone gave a residue, m. p. 162—168° (2·80 g., 100%), raised to 186—188° by crystallisation from acetic acid (Found: C, 51·7; H, 5·3. $C_8H_{10}O_5$ requires C, 51·6; H, 5·4%). The pure *acid* was almost insoluble in acetone and in subsequent extractions, in the presence of seed crystals, it was necessary to use dioxan as solvent.

Standard ethereal diazomethane (23 ml. containing 2 equivs.) was added dropwise to a stirred suspension of the acid (0·49 g., 0·0026 mole) in ether (8 ml.). Rapid evolution of nitrogen occurred and a clear solution was obtained in 15 min. This ethereal solution (diluted to 50 ml.) was washed with saturated sodium hydrogen carbonate solution (5 ml.), dried ($MgSO_4$), and evaporated. The semisolid residue was distilled (b. p. 100—103°/0·35 mm.; 0·47 g., 82%) and when stirred in light petroleum (b. p. 40—60°) gave crystals of dimethyl *trans*-4-oxo*cyclo*hexane-1 : 2-dicarboxylate, m. p. 46—49° undepressed on admixture with material obtained in the Diels–Alder reaction.

*Dimethyl* trans-*Oxo*cyclo*heptane*-1 : 2-*dicarboxylate.*—The preceding ester (4·95 g., 0·023 mole) was diluted with methanol (5 ml.); a little sodium carbonate (0·4 g.) was added and the solution stirred in a bath at 60°. After addition of a small portion of methylnitrosourethane there was an induction period of about 15 min. As soon as evolution of nitrogen began, the remainder of the urethane (2·60 g. in all, 0·020 mole; b. p. 32—34°/1 mm.) was added as quickly as possible and the reaction proceeded rapidly. The crude product contained up to 15% of starting material, which was removed by selective reaction with semicarbazide acetate in methanol. After filtration from the semicarbazone the solution was evaporated, the residue stirred with ether, and the ether-soluble material was distilled (b. p. 94—96°/3 × $10^{-3}$ mm., $n_D^{23}$ 1·4718). The product (3·19 g., 72%) crystallised; recrystallised from pentane, it had m. p. 60—64° but satisfactory analyses could not be obtained (Found: C, 58·9; H, 7·6. Calc. for $C_{11}H_{16}O_5$: C, 57·9; H, 7·1%). Infrared absorption (in $CCl_4$) occurred at 1742 cm.$^{-1}$ (combined ester and ketone C=O).

*Reactions of Dimethyl* trans-*Oxo*cyclo*heptane*-1 : 2-*dicarboxylate with Thiols, followed by Raney Nickel.*—(*a*) The keto-ester (2·40 g., 0·011 mole) in dry ether (2 ml.) was added to ethanethiol (1·34 g., 10% excess) in ether (4 ml.), containing freshly fused zinc chloride (2·0 g.) and sodium sulphate (2·0 g.). The mixture was cooled in ice during the 10 min required for the addition, and was shaken at room temperature for a further 1·5 hr. before being poured on ice-water–ether (5 ml. of ether). The ether layer was separated and the aqueous layer extracted with ether (10 ml.). The combined ether layers were washed with 5% sodium hydroxide solution (5 ml.), dried ($MgSO_4$), and evaporated, to give a sulphur-containing residue (2·20 g.) which did not crystallise.

The oil from the thiol condensation was dissolved in ethanol (25 ml.) and refluxed with Raney nickel (8 g.) for 40 min.; evolution of gas had then ceased. The mixture was filtered, the filtrate evaporated, and the product freed from a trace of inorganic material by dissolution in ether and filtration. Evaporation of ether gave a residue (1·09 g.) which was distilled, to give a sulphur-containing product, b. p. 110—114°/0·5 mm. [0·78 g. corresponding to a yield

of 35% of (VIII)]. Analytical *thiolactone* (VIII) had b. p. 111°/0·35 mm., $n_D^{25}$ 1·4872 (Found: C, 56·2; H, 6·7; S, 14·85. $C_{10}H_{14}O_3S$ requires C, 56·1; H, 6·6; S, 14·9%), $\nu_{max.}$ (in $CCl_4$) 1738 (C=O), 1445, 1330, 1275, 1205, 1175, 1020 cm.$^{-1}$.

(*b*) The keto-ester (2·40 g.) was condensed with ethanedithiol (1·5 g.) under the conditions described above, and the product worked up in the same way except that organic material was extracted into benzene, not ether. Evaporation of benzene gave a sulphur-containing oil (2·67 g.) which was treated with Raney nickel (8 g.) in ethanol (25 ml.) as above. The oil (1·37 g.) obtained was distilled, giving fractions (i) b. p. 84—87°/0·8 mm. (0·34 g.), $n_D^{25}$ 1·4611 and (ii) b. p. 124—128°/1·0 mm. (0·84 g.), $n_D^{25}$ 1·4820. A portion of fraction (i) (66 mg.) was hydrolysed in boiling 15% sodium hydroxide solution and yielded *trans-cyclo*heptane-1 : 2-dicarboxylic acid (44 mg., 78%), m. p. 141—144° (benzene), undepressed on admixture with the acid obtained as above (m. p. 145—147°). A portion (111 mg.) was reduced with lithium aluminium hydride in ether to the *trans*-diol (43 mg., 60%), a thick oil which was converted into the ditoluene-*p*-sulphonate, m. p. and mixed m. p. 89—90°. Fraction (ii) was redistilled and identified as thiolactone (VIII) by its infrared spectrum.

*Reactions of the Thiolactone* (VIII).—The thiolactone (VIII) (207 mg.) was refluxed in 15% sodium hydroxide solution (12 ml.) for 2 hr. and the cooled product extracted with ether (10 ml.) to remove a little insoluble material. The aqueous layer was acidified with concentrated hydrochloric acid (5 ml.) and extracted with ether (3 × 10 ml.). Evaporation of the dried ($MgSO_4$) extract gave a thick oil (132 mg.) containing sulphur. This was refluxed in ethanol (8 ml.) containing Raney nickel (1 g.) for 1 hr. Filtration and evaporation of the filtrate yielded a pale green solid, insoluble in ether and having m. p. 220°. This was presumably a nickel salt; it was dissolved in 2N-hydrochloric acid (5 ml.) and extracted with ether (3 × 5 ml.). Evaporation of the dry extract gave an oil (50 mg.) which crystallised under light petroleum (b. p. 60—80°) to a solid with m. p. 127—135°. Recrystallisation from benzene–light petroleum (b. p. 60—80°) raised the m. p. to 144—146°, undepressed on admixture with authentic *trans-cyclo*heptane-1 : 2-dicarboxylic acid, m. p. 145—147° (overall yield from thiolactone, 28%).

*Diethyl* trans-cyclo*Hex*-4-*ene*-1 : 2-*dicarboxylate*.—The corresponding *cis*-ester was prepared in 89% yield by Cope and Herrick's method [19] and was inverted by sodium ethoxide in boiling ethanol, to give the *trans*-acid, m. p. 170—171°.[22] This acid was converted into the diethyl ester by Cope and Herrick's method.[19] The product (68% yield) had b. p. 74—78°/0·1 mm., $n_D^{25}$ 1·4673 (Petrov and Sopov [23] give b. p. 150·5—151·5°, $n_D^{20}$ 1·4592).

trans-4 : 5-*Di*(*hydroxymethyl*)cyclo*hexene*.—Diethyl *trans-cyclo*hex-4-ene-1 : 2-dicarboxylate (31·6 g., 0·14 mole) was reduced with lithium aluminium hydride (8·3 g., 50% excess) and, after being stirred overnight, was worked up as usual. The *diol* (15·3 g., 77%), m. p. 39—40° (from hexane–ether), had b. p. 101—102°/0·15 mm., $n_D^{25}$ 1·5048 (Found: C, 67·4; H, 9·5. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). The corresponding *cis*-diol [24, 25] has m. p. 34·5°.

The diol (15·3 g., 0·11 mole) was treated with toluene-*p*-sulphonyl chloride (41·3 g.) as described by Owen and Smith.[17] The mixture was worked up after 48 hr. at 0° to give the *ditoluene*-p-*sulphonate* (44·4 g., 92% yield) as plates, m. p. 94—95·5°, from methanol (Found: C, 58·7; H, 5·8. $C_{22}H_{26}O_6S_2$ requires C, 58·6; H, 5·8%). The *cis*-derivative [25] has m. p. 97·5°.

*Reaction between the Ditoluene*-p-*sulphonate and Diethyl Sodiomalonate*.—The sodio-derivative was prepared by the addition of a solution of sodium (1·06 g., 0·046 g.-atom) in dry ethanol (100 ml.) to diethyl malonate (32 g., 0·2 mole). Sodium iodide (2·0 g.) was dissolved in dry ethanol (35 ml.), half the solvent was distilled off in a dry atmosphere, and the residue added to the solution of diethyl sodiomalonate. The ditoluene-*p*-sulphonate (9·0 g., 0·02 mole) in benzene (50 ml.) was added during 2·75 hr. to the vigorously stirred solution, which was refluxed during the addition and for a further 18 hr. The cooled solution was filtered from insoluble sodium toluene-*p*-sulphonate and evaporated under reduced pressure. The sodio-derivative was decomposed by shaking the residue with benzene (80 ml.)–water (40 ml.), and the residue obtained on evaporation of the benzene layer was distilled, to give diethyl *trans-bicyclo*[4 : 3 : 0]non-3-ene-8 : 8-dicarboxylate (4·6 g., 87%), b. p. 90—92°/3 × $10^{-3}$ mm., $n_D^{25}$ 1·4718.

This diethyl ester was hydrolysed under reflux for 6 hr. in methanol (35 ml.) containing

[22] Alder *et al.*, *Annalen*, 1950, **570**, 244; 1949, **564**, 103.
[23] Petrov and Sopov, *Sbornik Statei po obshchei Khim.*, 1953, **2**, 853; *Chem. Abs.*, 1955, **49**, 5329.
[24] Eliel and Pillar, *J. Amer. Chem. Soc.*, 1955, **77**, 3600.
[25] Braude, personal communication.

potassium hydroxide (15 g. in a little water). Methanol was removed in steam, and the aqueous solution remaining was extracted with ether (25 ml.); this extract was discarded and the aqueous solution acidified with 30% sulphuric acid; trans-bicyclo[4 : 3 : 0]*non-3-ene*-8 : 8-*dicarboxylic acid* (2·92 g., 81%) separated, having m. p. 181—183°, raised to 184—186° by crystallisation from hot water (Found: C, 63·0; H, 6·6. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%).

trans-bicyclo[4 : 3 : 0]*Non-3-ene-8-carboxylic Acid.*—The dicarboxylic acid (2·25 g., 0·017 mole) was decarboxylated at 185—205°. The crystalline residue of *monocarboxylic acid* (1·75 g., 100%) sublimed at 90—110° (bath)/$10^{-4}$ mm., and then had m. p. 53—55° (Found: C, 72·4; H, 8·4. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·5%).

trans-4 : 5-*Di*(*cyanomethyl*)cyclo*hexene.*—The ditoluene-*p*-sulphonate (16·4 g., 0·033 mole) was dissolved in hot ethylene glycol (100 ml.) containing potassium cyanide (6·9 g., 1·5 equiv.) and water (8 ml.). Heating under reflux was continued for 2 hr. and the cooled alkaline solution extracted with ether (4 × 75 ml.). Evaporation of the dried extracts yielded the *dinitrile* (4·65 g., 59%) which crystallised from aqueous methanol in needles, m. p. 79·5—80·5° (Found: C, 74·8; H, 7·3. $C_{10}H_{12}N_2$ requires C, 75·0; H, 7·55%). Ether-extraction of the acidified liquors yielded the diacetic acid (1·4 g., 20%; see below). The *cis*-dinitrile [25] has m. p. 50°.

trans-cyclo*Hex-4-ene*-1 : 2-*diacetic Acid.*—The dinitrile (1·00 g., 0·006 mole) was refluxed with 33% potassium hydroxide solution (7 ml.) for 4 hr.; evolution of ammonia had then almost ceased. The cooled liquor was extracted with ether (8 ml.) and acidified with concentrated hydrochloric acid (3 ml.), and the precipitated *acid* (1·14 g., 92%) was filtered off as needles, m. p. 194—197°, raised to 199—200° by crystallisation from hot water (Found: C, 60·5; H, 7·0. $C_{10}H_{14}O_4$ requires C, 60·6; H, 7·1%). The *cis*-diacetic acid [25] has m. p. 157°.

trans-4 : 4-*Di*-(2-*carboxyethyl*)cyclo*hexene.*—The diacetic acid (1·00 g.; 0·005 mole) was added to excess of thionyl chloride (4 ml.), and the mixture refluxed for 10 min. Excess of thionyl chloride was removed under reduced pressure. The residue crystallised when stirred in ether and was added as a slurry in ether–benzene to diazomethane (from 3·3 g. of methylnitrosourea) in benzene. During the 30 min. taken for the addition the mixture was stirred at −10°, and afterwards for 1·5 hr. at room temperature. The mixture was kept for a further 36 hr. at 0° and the solvent was evaporated below 30°. The residue (1·05 g.) was dissolved in benzyl alcohol (5 ml.)–γ-collidine (5 ml.) and heated rapidly to 170° by immersion in a preheated oil bath; [26] rapid evolution of nitrogen occurred, which ceased after 8 min. The cooled residue was taken up in ether (40 ml.), filtered from insoluble material, washed with 2N-hydrochloric acid and water, dried, and evaporated, to give the crude dibenzyl ester (3·1 g.).

The ester was hydrolysed for 3·5 hr. in refluxing methanol (10 ml.) and 45% aqueous potassium hydroxide (10 ml.). The mixture was evaporated, and the residue taken up in water (15 ml.) and ether-extracted (2 × 20 ml.); the extracts were rejected. Acidifying the aqueous layer with concentrated hydrochloric acid (9 ml.) precipitated a solid which was extracted into ether (3 × 15 ml.). Drying and evaporation furnished a crystalline residue of the *dipropionic acid* (0·43 g., 43%), m. p. 166—172°. Analytical material crystallised from hot water in prisms, m. p. 172—172·5° (Found: C, 63·8; H, 7·85. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%).

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[26] Wilds and Meader, *J. Org. Chem.*, 1948, **13**, 763.