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Stereospecific Syntheses of *cis*- and *trans*-1,2-Diaminocyclohexanes and Aliphatic Vicinal Diamines[1]

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Stereospecific syntheses of *cis*- and *trans*-1,2-diaminocyclohexanes (Scheme I), *erythro*- and *threo*-4-methyl-2,3-diaminopentanes (Schemes II and III), and *meso*- and *threo*-3,4-diaminohexanes (Scheme III) are described. An improved method of converting aziridines to vicinal diamines in high over-all yield has been developed; this involves ring opening with azide ion (with inversion) followed by hydrogenation. Solvolysis of *trans*-2-azidocyclohexyl tosylate with acetic acid gives a high yield (80%) of *trans*-2-azidocyclohexyl acetate; the over-all retention of configuration confirms the earlier conclusion of Streitwieser and Pulver. Several new vicinal diazides of known stereochemistry have also been prepared.

In a previous publication,[1] we described the stereospecific synthesis of *erythro*- and *threo*-9,10-diaminooctadecanoic acids and some derivatives. In a continuation of our investigations on the synthesis of vicinal diamines of known stereochemistry, we now describe the preparation of the isomeric *cis*- and *trans*-1,2-diaminocyclohexanes (Scheme I) and some aliphatic vicinal diamines (Schemes II and III).

Previous Work. Vicinal Diaminocycloalkanes.—1,2-Diaminocyclohexane was first reported in 1926 by Wieland, Schlichtung, and Langsdorf[3] who obtained it from hexahydrophthalic acid by conversion to the dihydrazide followed by a Curtius reaction. Although the melting point of their dihydrochloride (303°) is close to that of the now known *cis*-diamine (Scheme I, **5**, mp 312–314°), no positive statements can be made about the stereochemistry of the early product since that of the starting material was undefined. The product could have been a mixture of the *cis* and *trans* (Scheme I, **8**, mp 338°) isomers.

In 1936, Jaeger and Van Dijk[4] reported that *trans*-1,2-diaminocyclohexane [bp 80° (15 nm) and mp 14.8°, bisbenzenesulfonamide mp 153–155°] was the sole product of reduction of 1,2-dioximinocyclohexane with sodium in boiling ethanol. Proof of structure was that the product could be resolved into *d* and *l* forms with *d*-tartaric acid. The synthetic procedure was repeated recently by Broadbent and co-workers[5] who confirmed the boiling point reported earlier but noted that over-all yields were low (0–20%). It is not apparent why reduction of the vicinal dioxime should yield the *trans*-1,2-diamine exclusively.

In fact, in 1958 Yashunskii and Skchukina[6] had also tried to prepare *trans*-1,2-diaminocyclohexane by reduction of the vicinal dioxime with sodium in ethanol. Although they obtained a product that yielded a bisbenzenesulfonamide with the same melting point (153–155°) as that of the bisbenzenesulfonamide prepared earlier by Jaeger and Van Dijk,[4] the dihydrochloride had a melting point of 322–325°, halfway between the melting points of the now known *cis* and *trans* dihydrochlorides (Scheme I, **5** and **8**, present work).

To obtain the *cis*-1,2-diaminocyclohexane, Yashunskii and Skchukina[6] converted dimethyl *cis*-hexahydrophthalate to its dihydrazide by reaction with hydrazine at 135° for 24 hr followed by a Curtius reaction. The so-called *cis*-1,2-diamine, however, afforded a dihydrochloride whose melting point (323–326°) was the same as that of the dihydrochloride of their presumed *trans*-1,2-diamine.

Recognizing that stereospecificity had not been achieved, Yashunskii[7] repeated the preparation of the so-called *cis*-1,2-diaminocyclohexane, but he conducted the hydrazinolysis at room temperature for 1 week and then performed the Curtius reaction.[8] The 1,2-diaminocyclohexane now obtained gave a dihydrochloride, mp 307–310° (present work, 312–314°; Scheme I, **5**), and a bisbenzenesulfonamide, mp 165–166°. Apparently, high-temperature hydrazinolysis had caused isomerization (see other examples below) in the previous work, as

(1) Chemistry of Epoxy Compounds. XX. Paper XIX: G. Swift and D. Swern, *J. Org. Chem.*, **32**, 4226 (1966).

(2) Imperial Chemical Industries Ltd., Mond Division, Cheshire, England.

(3) H. Wieland, O. Schlichtung, and W. V. Langsdorf, *Z. Physiol. Chem.*, **161**, 74 (1926).

(4) F. M. Jaeger and J. A. Van Dijk, *Proc. Akad. Sci. Amsterdam*, **39**, 384 (1936); **40**, 12 (1937).

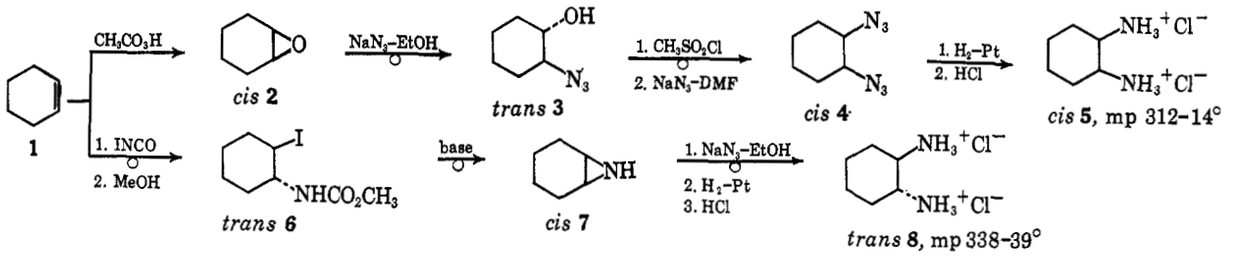
(5) H. S. Broadbent, E. L. Allred, L. Pendleton, and C. W. Whittle, *J. Am. Chem. Soc.*, **82**, 189 (1960); see A. T. Nielsen, *J. Org. Chem.*, **27**, 1998 (1962), who also prepared 1,2-diaminocyclohexane by reduction of the corresponding dinitro compound with iron and acetic acid.

(6) V. G. Yashunskii and M. N. Skchukina, *Zh. Obshch. Khim.*, **28**, 230 (1958).

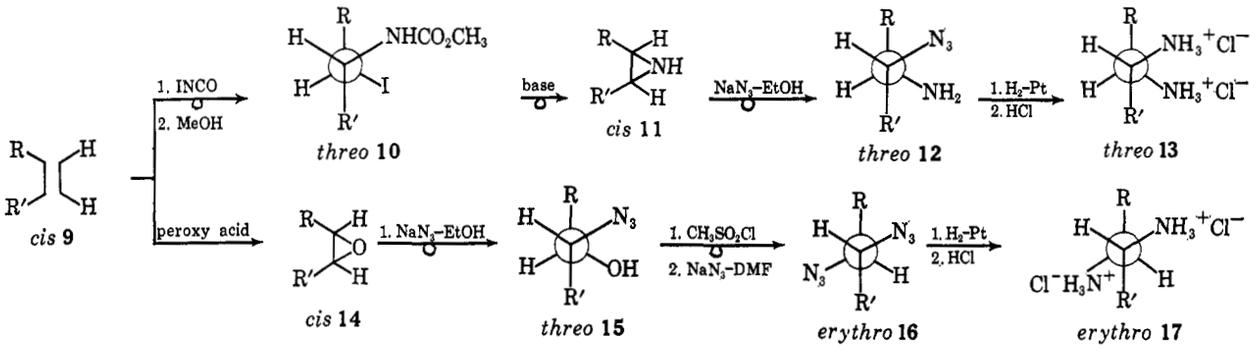
(7) V. G. Yashunskii, *ibid.*, **28**, 1361 (1958).

(8) The Crutius reaction is stereospecific: L. W. Jones and E. S. Wallace, *J. Am. Chem. Soc.*, **48**, 169 (1926).

SCHEME I

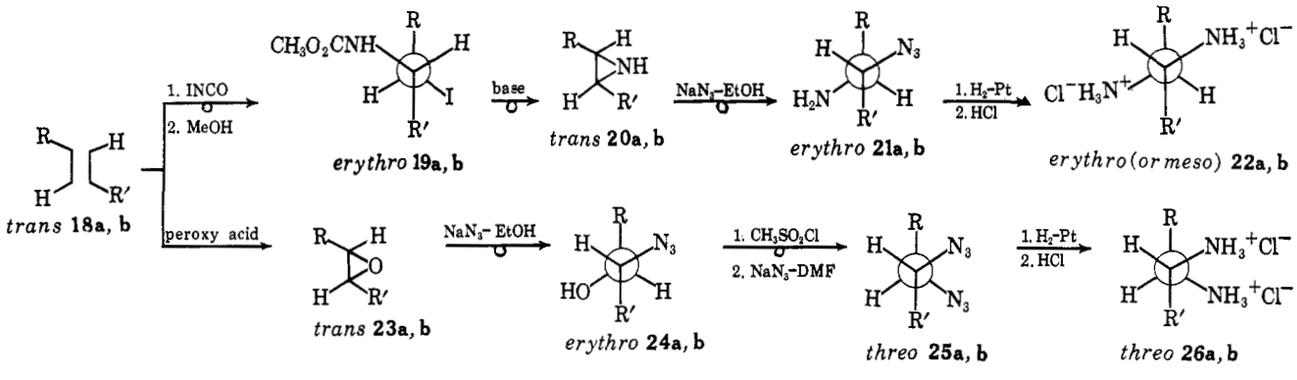


SCHEME II



R = $(CH_3)_2CH$; R′ = CH_3

SCHEME III



a, R = $(CH_3)_2CH$; R′ = CH_3
b, R = R′ = C_2H_5

Yashunskii himself realized. We believe that Yashunskii had, in fact, isolated authentic *cis*-1,2-diaminocyclohexane in his later investigation.

Two other preparations of the 1,2-diaminocyclohexanes are described in the literature. Simons[9] claimed to have obtained the *cis* isomer by reaction of α-chlorocyclohexanone with urea followed by hydrogenation of the resulting imidazolone to the imidazolidone which was then hydrolyzed to the diamine. No proof of stereochemistry or preparation of derivatives was reported. Winternitz, Mousseron, and Dennilauler[10] treated 7-azabicyclo[4.1.0]heptane (1,2-iminocyclohexane) with ammonia and obtained a diamine, bp 85–86° (25 mm). Although no derivatives were prepared, they had undoubtedly obtained *trans*-1,2-diaminocyclohexane. We have repeated this ring-opening reaction and find that poor yields of *trans*-1,2-diamine are obtained. (Later in this paper we shall describe an improved technique for obtaining the *trans*-1,2-diamine that involves opening of the aziridine ring with azide ion followed by reduction.)

The preparation of *cis*- and *trans*-1,2-diaminocyclobutanes was attempted by Buchman and co-workers in 1942.[11] They started with the dimethyl esters of *cis*- and *trans*-cyclobutane-1,2-dicarboxylic acids and converted them to dihydrazides by high-temperature (130°) hydrazinolysis, being unaware at the time that such a reaction is not stereospecific. The diamines obtained had boiling points of 141 and 151°, and were written as *cis* and *trans*, respectively; the stereochemistry was assumed to correspond to that of the starting materials.

Subsequently, Mueller and co-workers[12] used a similar procedure to prepare *cis*-1,2-dihydrazidocyclopen-

(9) C. Simons, U. S. Patent 2,850,532 (1958).
(10) F. Winternitz, M. Mousseron, and R. Dennilauler, *Bull. Soc. Chim. France*, 382 (1956).
(11) E. R. Buchman, A. O. Reims, T. Skei, and M. G. Schlatter, *J. Am. Chem. Soc.*, **64**, 2696 (1942).
(12) J. H. Mueller, M. N. Donir, W. E. Behrke, and K. Hofmann, *ibid.*, **73**, 2487 (1951).

tane by reaction by diethyl *cis*-cyclopentane-1,2-dicarboxylate with hydrazine at 160–170° but indicated that the reaction product was mainly *trans*-dihydrazide contaminated with the *cis* isomer.

Other examples of isomerization during high-temperature hydrazinolysis of vicinal diesters are known. Both *cis*- and *trans*-3,4-dicarbomethoxy-2-*n*-propyltetrahydrothiophenes[13] yield *trans*-1,2-diamine on hydrazinolysis at 100° followed by a Curtius reaction. Even with the *n*-propyl substituent absent, high-temperature hydrazinolysis occurs with isomerization.[14]

Aliphatic Vicinal Diamines.—Aside from our previous publication,[1] no work could be found on the stereospecific synthesis of vicinal diamines. It would be anticipated that these compounds could be prepared by the reaction of vicinal dihalides with ammonia. In only a few reported instances, however, has this been successfully accomplished, and the dihalides used were simple dihalides, such as 1,2-dichloroethane[15] and 1,2-dibromopropane.[16] Ammonolysis of the next higher homolog, 2,3-dibromobutane, yielded 2-bromo-2-butene principally and a small quantity of 2,3-diaminobutane.[17] The stereochemistry of the diamine was not reported.

Other methods for preparing vicinal diamines are known but again details of the stereochemistry are lacking. 2,3-Diaminobutane was obtained in 60% yield by hydrogenation of 2,3-iminonitrobutane with a platinum catalyst.[18] 3,4-Diaminohexane was obtained similarly in 46% yield from the corresponding iminonitro compound. Heath and Rose[19] reduced 1-nitro-2-aminopropane and 2-nitro-3-aminobutane with Raney nickel in absolute methanol to obtain 1,2-diaminopropane and 2,3-diaminobutane in 52 and 40% yields, respectively. The reduction of 2,3-dioximinobutane with sodium in ethanol is reported to yield 2,3-diaminobutane as the sole product.[20]

By the very nature of the reactions employed by previous workers to obtain vicinal diamines, it is highly probable that mixtures of stereoisomers were obtained in all cases where stereoisomerism is possible. In no previous case, with the exception noted,[1] was stereochemistry proven.

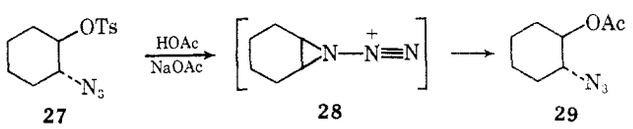
Present Work.—Our approach to the problem was to employ starting materials of known stereochemistry and, by the use of high-yield stereospecific reactions and control over the number of inversions in the synthetic pathways, prepare *cis*- and *trans*-1,2-diaminocyclohexanes (Scheme I), *threo*- and *erythro*-4-methyl-2,3-diaminopentanes (two methods, Schemes II and III), and *threo*- and *meso*-3,4-diaminohexanes (Scheme III).

1,2-Diaminocyclohexanes.—The sequence finally used to prepare the *cis*- and *trans*-1,2-diaminocyclohexanes is summarized in Scheme I. Cyclohexene (**1**) was converted to the *cis* epoxide (**2**) by epoxidation with peroxyacetic acid.[21] The epoxide (**2**) was ring opened, with inversion, to the *trans*-azido alcohol (**3**, 70–75% yield) by reaction with sodium azide in ethanol, followed by mesylation with methanesulfonyl chloride in pyridine to yield (80%) *trans*-2-azidocyclohexyl methanesulfonate. It was treated with sodium azide in dimethylformamide to displace the methanesulfonate function, with inversion (see later discussion), to yield (73%) *cis*-1,2-diazidocyclohexane (**4**), a readily distillable liquid.[22] The vicinal diazide (**4**) was then hydrogenated at room temperature over Adams catalyst to yield (79%) *cis*-1,2-diaminocyclohexane, isolated by distillation. It reacted so readily with carbon dioxide that it was immediately converted (97% yield) to the dihydrochloride (**5**), mp 312–314°.

The *trans* isomer was prepared by a sequence involving three inversions in contrast with the preparation of the *cis* isomer that involved only two. Iodine isocyanate, generated *in situ* from silver cyanate and iodine,[23] was added to cyclohexene (**1**) and the crude vicinal *trans*-iodoisocyanate was immediately converted to methyl *trans*-1,2-iodocyclohexylcarbamate (88%, **6**). Reaction of **6** with methanolic potassium hydroxide converted it, with inversion, to 7-azabicyclo[4.1.0]-heptane (**7**, 60% yield). The aziridine (**7**) was converted to the *trans*-diamine by ring opening with sodium azide in ethanol followed by hydrogenation over Adams catalyst at room temperature. The diamine was immediately converted to the crystalline *trans*-dihydrochloride (**8**, 60% over-all from aziridine), mp 338–339°. A mixture melting point determination of approximately equal weights of **5** and **8** showed considerable depression, mp 290–296°.

The two-step sequence (azide ring opening and hydrogenation) for converting an aziridine to a vicinal diamine is preferred to the usual literature method[10] of one-step reaction with ammonia. Work-up is easier, over-all yields are higher, and gummy polymeric products are not obtained. This improved technique was used in all subsequent work. Identical *trans* dihydrochlorides, mp 338°, were obtained from 7-azabicyclo-[4.1.0]heptane by either method.

Although the number of inversions in each sequence shown in Scheme I is now unequivocal and the stereochemistry of the final products is known, two interesting stereochemical side issues developed and were resolved during the course of the work. The first concerned the question of whether an over-all inversion had occurred during the transformation of **3** → **4** in the displacement of a methanesulfonate function vicinal to an already present azide group by sodium azide in dimethylformamide. Streitwieser and Pulver[24] had reported that acetolysis of *trans*-2-azidocyclohexyl tosylate (**27**) gave the product of retention of configuration,



27 **28** **29**

(13) B. R. Baker, M. V. Querry, S. R. Safir, and S. Bernstein, *J. Org. Chem.*, **12**, 138 (1947).

(14) G. B. Brown, B. R. Baker, S. Bernstein, and S. R. Safir, *ibid.*, **12**, 155 (1947).

(15) H. Kraut, *Ann.*, **212**, 253 (1882).

(16) H. Strache, *Ber.*, **21**, 2359 (1888).

(17) G. F. Morgan and W. J. Hickinbottom, *J. Soc. Chem. Ind.*, **43**, 3107 (1924).

(18) L. B. Clapp, J. F. Brown, Jr., and L. Zeftel, *J. Org. Chem.*, **15**, 1043 (1950).

(19) R. L. Heath and J. B. Rose, *J. Chem. Soc.*, 1486 (1947).

(20) A. Angell, *Ber.*, **23**, 1357 (1890).

(21) D. Swern, G. N. Billen, and J. T. Scanlan, *J. Am. Chem. Soc.*, **68**, 1504 (1946).

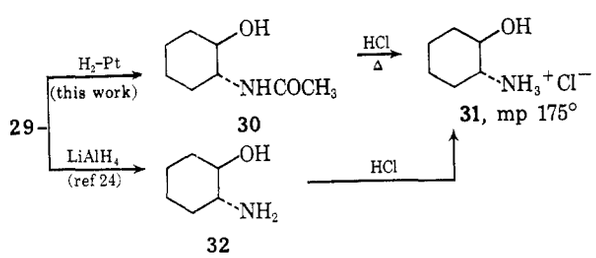
(22) We have distilled several vicinal diazides under high vacuum without incident even though the azide nitrogen content exceeded 50% of the total molecular weight of the molecule. The maximum quantity distilled was 5 g but usually less; the apparatus was completely surrounded by safety shields. A water bath, *not* a heating mantle, was employed.

(23) A. Hassner and C. Heathcock, *Tetrahedron*, **20**, 1037 (1964).

(24) A. Streitwieser and S. Pulver, *J. Am. Chem. Soc.*, **86**, 1587 (1964).

trans-2-azidocyclohexyl acetate (**29**), in 37% yield. To rationalize this result, an "azidonium" intermediate (**28**) was proposed thus providing for two inversions, instead of the anticipated one inversion, and consequently over-all retention of configuration. From our results (Scheme I), it is apparent that only one inversion had occurred in proceeding from **3** → **4** and we concluded, as did Guthrie and Murphy,[25a] that the "azidonium" intermediate does not exist in the basic medium employed. Since Streitwieser and Pulver[24] had reported a yield of **29** of only 37%, it seemed desirable to repeat their solvolysis work.

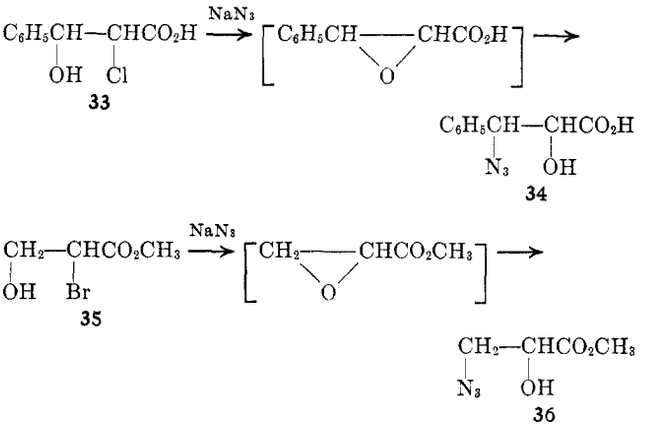
Acetolysis of **27** was carried out by the published procedure;[24] the yield of acetate (**29**) was increased to about 80%, however. The acetate was, in fact, the product with retention of configuration as Streitwieser and Pulver had concluded. Proof of stereochemistry was conducted as shown below (**29** → **30** → **31**) rather than by the published technique (**29** → **32** → **31**). The final product in both sequences was the same, *trans*-2-hydroxycyclohexylamine hydrochloride, mp 175–176°.[24,26] If an "azidonium" intermediate occurs at all it is restricted to an acidic medium.[25b]



The second interesting side issue was concerned with the original plan for obtaining *trans*-1,2-diaminocyclohexane and/or its dihydrochloride from cyclohexene by introducing an additional inversion into the top sequence of Scheme I. After preparing cyclohexene epoxide (**2**), a portion of it was converted to the *trans*-iodohydrin[27] which was then treated with sodium azide in ethanol to yield the presumed *cis* isomer of **3**. When this presumed *cis* isomer was put through the remainder of the sequence, the dihydrochloride obtained was identical with that obtained from the *trans*-azidohydrin (**3**), namely, *cis*-1,2-diaminocyclohexane dihydrochloride (**5**), mp 312–314°.

The presumed *cis* isomer of **3** was therefore studied in greater detail; it and **3** had identical infrared spectra and melting points (28.5–29.5°). They showed no depression of melting point on admixture and yielded identical products on tosylation (*trans*-2-azidocyclohexyl tosylate, mp and mmp 58–59°)[24] and on reduction with lithium aluminum hydride (*trans*-2-hydroxycyclohexylamine hydrochloride, mp and mmp 175–176°).[26] The two compounds were clearly identical.

The most probable conclusion is that the *trans*-iodohydrin was reconverted to cyclohexene oxide (**2**) under the alkaline conditions of reaction with sodium azide in refluxing ethanol, and the oxirane ring was then reopened by azide ion, with inversion, to yield **3**, the *trans* compound. There is precedent in the literature for ring closure to reoccur on attempting to displace halide vicinal to a hydroxyl group by azide ion. Thus, β-azido-α-hydroxycinnamic acid (**34**) is the product of reaction of sodium azide with α-chloro-β-hydroxycinnamic acid (**33**)[28] and methyl β-azido-α-hydroxypropionate (**36**) is obtained from methyl α-bromo-β-hydroxypropionate (**35**).[29] The oxiranes (not isolated) are the intermediates.



Aliphatic Vicinal Diamines.—The successful reaction sequences shown in Scheme I were then applied to the preparation of vicinal diamines from *cis*- and *trans*-4-methyl-2-pentene (Schemes II and III). Since both isomeric olefins (**9** and **18a**) were available in pure form, both sequences of Scheme I were applied to them. In this way an internal check could be obtained on the cleanness of the chemical operations and separations and, at the final stage, we could compare the properties of the purified dihydrochlorides of the *erythro*- and *threo*-4-methyl-2,3-diaminopentanes obtained from both olefinic isomers. Without discussing the procedures again in detail (see the Experimental Section), the dihydrochlorides of the *erythro* isomer (**17** or **22a**), obtained from either *cis*- or *trans*-4-methyl-2-pentene, were identical in every respect (infrared spectra, melting point, and mixture melting point, 226–227°). Likewise, the dihydrochlorides of the *threo* isomer (**13** or **26a**), prepared from either olefin, were also identical (mp and mmp 240–242°).

To check the generality of the methods, *trans*-3-hexene was converted to the dihydrochlorides of *meso*-3,4-diaminohexane (**22b**, mp 263–266°) and its *threo* isomer (**26b**, mp 298–300°) (Scheme III).

Finally, a comment is in order concerning the iodine isocyanate route to aziridines *via* the intermediate iodocarbamates. Although the sequence is stereospecific, over-all yields of aziridine from short-chain aliphatic olefins are not always high. Ketones may be formed as by-products, often in good yield, by the elimination–

(25) (a) R. D. Guthrie and D. Murphy, *J. Chem. Soc.*, 6956 (1965). While our work was in progress these investigators, working in the carbohydrate field, reported a single inversion in displacing a methanesulfonate function adjacent to an azide group using sodium azide in dimethylformamide. (b) We have been concerned that the proposed anchimeric involvement of the azide group[24] gives little or no rate acceleration on solvolysis of *trans*-2-azidocyclohexyl tosylate in acetic acid–sodium acetate medium. An alternative mechanism for retention of configuration without involving the unprecedented "azidonium" intermediate involves elimination of toluenesulfonic acid thermally or by β elimination (in which sodium acetate serves as the base) to yield 1-azidocyclohexene, immediately converted to **29** by *trans* addition of acetic acid to the double bond.

(26) G. E. McCasland, R. K. Clarke, Jr., and H. E. Carter, *J. Am. Chem. Soc.*, **71**, 637 (1949).

(27) S. Winstein, E. Grunwald, R. E. Buckles, and C. Hanson, *ibid.*, **70**, 820 (1948).

(28) P. A. Levine and A. Schormüller, *J. Biol. Chem.*, **105**, 547 (1934).

(29) M. Oesterlin, *Metallbörse*, **19**, 1237 (1929); *Chem. Abstr.*, **23**, 4684 (1929); M. O. Forster and J. H. Schaeppi, *J. Chem. Soc.*, 2595 (1922); M. O. Forster and K. A. N. Rao, *ibid.*, 1943 (1926).

hydrolysis mechanism described by Hassner and Heathcock.[23] Product losses also occur because of the water solubility and volatility of the aziridines. Also, reaction of *erythro*-iodocarbamates with base to yield aziridines by ring closure requires long reaction periods and yields of *trans*-aziridines may be low. In general, yields of *cis*-aziridines are higher from *threo*-iodocarbamates.[30] Yields of *trans*-aziridines can be improved by using aqueous methanol as the solvent for the base, rather than anhydrous methanol.

Experimental Section

Cyclohexene, *cis*- and *trans*-4-methyl-2-pentene, and *trans*-3-hexene were the purest available grades; they gave a single peak on glpc. Peroxyacetic acid (40%) in acetic acid was the standard commercial material. Silver cyanate used for the generation of iodine isocyanate was prepared from silver nitrate and potassium cyanate. Iodine was the resublimed grade. All other reagents were the purest and dryest available. Infrared spectra were determined with an Infracord 137B. Boiling and melting points are uncorrected. Microanalyses were performed by Micro-Analysis, Inc., Wilmington, Del.

1,2-Epoxycyclohexane (**2**).—This was prepared in the conventional way from **1** and peroxyacetic acid containing sodium acetate to neutralize sulfuric acid present.[21]

***trans*-2-Azidocyclohexanol** (**3**).—1,2-Epoxycyclohexane (**2**, 29.4 g, 0.3 mole), dissolved in 80% ethanol (500 ml), was refluxed for 24 hr with sodium azide (26.0 g, 0.4 mole) and ammonium chloride (21.4 g, 0.4 mole). The reaction mixture was poured into water (500 ml) and the oil that separated was extracted with ether. The ether solution was washed several times with water and dried and the ether was evaporated in a rotary evaporator to yield a pale yellow oil (35 g). Vacuum distillation yielded 30 g of colorless *trans*-2-azidocyclohexanol: bp 62–64° (0.05 mm), 56–60° (0.01 mm); mp 28.5–29.5°. The yield of distilled product ranged from 70 to 75%; infrared showed 3300 (OH) and 2090 and 1245 cm^{-1} (N_3).

***cis*-1,2-Diazidocyclohexane** (**4**).—The *trans*-azidohydrin (**3**, 10.0 g, 0.071 mole) dissolved in pyridine (50 ml) at 0–5° was treated with methanesulfonyl chloride (10.0 g, 0.088 mole) with stirring. After 3 hr the ice bath was removed and stirring was continued for 1 more hr. The solution was poured into water and extracted with ether and the ether layer was washed several times with water. After drying, the ether was evaporated and the residue was distilled under vacuum: bp 123–125° (0.005 mm). The yield was 13.0 g (83%) of *trans*-2-azidocyclohexyl methanesulfonate, an unstable colorless oil; infrared showed 2090 and 1258 (N_3) and 1175 cm^{-1} (SO_3CH_3).

Anal. Calcd for $C_7H_{13}N_3O_3S$: C, 38.35; H, 5.97; N, 19.16; S, 14.62. Found: C, 37.23; H, 5.95; N, 18.39; S, 15,63.

The somewhat impure azidomethanesulfonate (4.4 g, 0.025 mole), dissolved in dimethylformamide (30 ml) and water (5 ml), was refluxed for 5 hr with sodium azide (2.6 g, 0.04 mole). The solution was poured into water and extracted with ether and the solute was isolated in the usual way. The crude diazide was distilled under vacuum from a water bath, yielding 2.4 g (73%) of pure **4**, a colorless oil, bp 54–55° (0.005 mm). The yield of distilled diazide ranged from 73 to 77%; infrared showed 2075 and 1245 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{10}N_6$: C, 43.37; H, 6.07; N, 50.57. Found: C, 43.57; H, 6.12; N, 50.31.

***cis*-1,2-Diaminocyclohexane Dihydrochloride** (**5**).—The *cis*-diazide (**4**) (4.8 g, 0.02 mole) was dissolved in absolute ethanol and hydrogenated at room temperature and 800 psi for 24 hr using Adams catalyst. No change in pressure was observed; the volume of hydrogen absorbed exactly balanced the nitrogen liberated. The solution was filtered and the ethanol was evaporated in a rotary evaporator. The residue was vacuum distilled yielding *cis*-1,2-diaminocyclohexane (2.6 g, 79%), bp 36–38° (0.05 mm), as a colorless oil. It absorbed carbon dioxide rapidly on exposure to the atmosphere as indicated by immediate formation of solid on the surface. It was dissolved in ether and a stream of dry hydrogen chloride gas was passed into the solution. A white solid precipitated immediately (3.7 g, 97%). It was recrystallized from a large volume of 95% ethanol to yield pure **5**: 3.3 g, 95%; mp 312–314°; infrared showed (free diamine) 3250, 1575, and 1085 cm^{-1}, and (**5**) 1580 and 1520 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{16}Cl_2N_2$: C, 38.52; H, 8.62; Cl, 37.89; N, 14.97. Found C, 38.65; H, 8.82; Cl, 37.87; N, 15.35.

Methyl 2-Iodocyclohexylcarbamate (**6**).—Cyclohexene (24.6 g, 0.3 mole) and iodine (76.2 g, 0.3 mole) were dissolved in dry ether (500 ml) at 0–5° and silver cyanate (45.0 g, 0.3 mole) was added in one portion. The mixture was stirred for 24 hr and filtered. The precipitate was washed with cold ether and the washings were combined with the main filtrate. The ether was evaporated and the oily residue was refluxed for 3 hr with absolute methanol (500 ml). The solution was concentrated to 100 ml and then poured into water (2 l.) to precipitate **6**: 745 g, 88%; mp 130–131° (lit.[23] mp 135°). This was pure enough for the ring-closure step.

7-Azabicyclo[4.1.0]heptane (**7**).—To **6** (50 g, 0.18 mole) in methanol (500 ml), a solution of potassium hydroxide (50.0 g of 85%) in water (100 ml) was added and the reaction mixture was refluxed for 4 hr. The methanol was evaporated, water was added, and the oil was extracted with ether and worked up in the usual way. Vacuum distillation yielded pure **7**: 10 g, 60%; bp 61° (20 mm); infrared showed 3250 (>NH) and 882 cm^{-1} (aziridine ring).

***trans*-1,2-Diaminocyclohexane Dihydrochloride** (**8**).—A solution of **7** (3.6 g, 0.037 mole), sodium azide (9.75 g, 0.15 mole), and ammonium chloride (8.0 g, 0.15 mole) in ethanol (150 ml) and water (50 ml) was refluxed for 18 hr. The solute was isolated in the usual way by dilution and extraction with ether, yielding 5 g. Vacuum distillation yielded *trans*-2-azidocyclohexylamine as a colorless liquid: 3.0 g, 60%; bp 50° (0.125 mm); infrared showed 2080 and 1250 (N_3) and 3300 and 1575 cm^{-1} (NH_2). A small quantity was converted to the phenylurea derivative, mp 155–157.5°, by reaction with phenyl isocyanate in hexane.

Anal. Calcd for $C_{13}H_{16}N_5O$: C, 60.21; H, 6.61; N, 27.01. Found: C, 60.12; H, 6.46; N, 26.68.

A sample of the vicinal azidoamine (5.0 g, 0.036 mole) was dissolved in ethanol (50 ml) and hydrogenated at 800 psi and room temperature for 2 days over Adams catalyst. Filtration and evaporation of the solvent yielded a pale yellow oil that was immediately dissolved in ether and converted to the dihydrochloride by bubbling a stream of dry hydrogen chloride through the solution. The white solid that precipitated weighed 6.5 g, mp 334–336°. Crystallization from 95% ethanol in which it was very soluble, as distinguished from **5**, yielded pure **8**: mp 338–339°; 5.5 g, 76%; infrared showed 1600, 1560, and 1525 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{16}Cl_2N_2$: C, 38.52; H, 8.62; Cl, 37.89; N, 14.97. Found: C, 38.43; H, 8.49; Cl, 38.10; N, 15.03.

A mixture melting point of **5** and **8** was 290–296°.

***trans*-2-Azidocyclohexyl Tosylate** (**27**).—*trans*-2-Azidocyclohexanol (**3**, mp 28.5–29.5°, 35.0 g, 0.25 mole) dissolved in pyridine (175 ml) was stirred at 0–5° with *p*-toluenesulfonyl chloride (65 g, 0.34 mole) for 3 hr and then for 1 hr with the ice bath removed. The reaction mixture was poured into a large excess of ice water and the solid product was filtered, washed several times with water, and dried (59 g, 80% yield). Recrystallization from hexane yielded pure **27**: mp 58–59° (lit.[24] mp 56.5–57°); infrared showed 2080 and 1258 (N_3) and 1590 cm^{-1} (aromatic).

***trans*-2-Azidocyclohexyl Acetate** (**29**).—A solution of **27** (13.6 g, 0.046 mole) in acetic acid (100 ml) containing sodium acetate (3.6 g) was refluxed for 5 days. The black reaction mixture was poured into water and extracted with low-boiling petroleum ether. The petroleum ether solution was washed several times with water and the solvent was evaporated. The crude, oily product was vacuum distilled to yield **29**: 7.0 g, 83%; bp 83–85° (0.35 mm); infrared showed 2100 and 1240 (N_3), 1740 (carbonyl), and 1215 cm^{-1} (ester).

***trans*-2-Hydroxycyclohexylamine Hydrochloride** (**31**).—Compound **29** (3.0 g, 0.067 mole) in absolute ethanol (50 ml) was hydrogenated at room temperature and 800 psi for 2 days over Adams catalyst. After the usual work-up *trans*-2-acetamidocyclohexanol (**30**) was isolated as a crude oil; infrared showed 3300 (broad, NH and OH), 1645 (carbonyl), and 1550 cm^{-1} (amide). Without further purification, **30** was refluxed with 25% hydrochloric acid (100 ml) for 2 hr followed by evaporation to dryness in a rotary evaporator. The crude, crystalline residue was crystallized twice from ethanol–ether to yield **31**: 1.9 g, 76%; mp 175–176° (lit.[24,26] mp 175–176°); infrared showed

(30) C. G. Gebelein, C. Swift, and D. Swern, unpublished results.

3350 and 3200 (OH), and 2800, 2000, 1920, 1600, and 1575 cm^{-1} (NH_3^+).

trans-**2-Iodocyclohexanol** (**37**).—To a solution of **2** (9.8 g, 0.1 mole) in ether (60 ml) at 0°, constant boiling hydriodic acid (25.6 ml containing 12.8 g hydriodic acid) was slowly added and the reaction mixture was held at this temperature for 2 hr with occasional agitation. The lower aqueous acid layer was separated and aqueous sodium bisulfite solution was added to decolorize the red ethereal solution. The ether solution was dried and evaporated to dryness yielding a white solid. Recrystallization from low-boiling petroleum ether yielded the pure iodohydrin: 18–20 g, 80–88%; mp 41.5–43 (lit.[27] mp 41.5–42.5°).

Reaction of Sodium Azide with 37. (Preparation of 3).—A solution of **37** (13.2 g, 0.06 mole) and sodium azide (8.5 g, 0.13 mole) in ethanol (250 ml) was refluxed for 24 hr. The usual work-up afforded the presumed *cis* isomer of **3**: 6.5 g, 81%; bp 63–65° (0.03 mm); mp 28.5–29.5° (tosylate mp 58–59°). That the presumed *cis* isomer of **3** was in fact **3** was shown as follows: a mixture melting point was undepressed, (b) their infrared spectra were identical, and (c) they yielded identical tosylates, mp and mmp 58–59°. Chemical confirmation was obtained by lithium aluminum hydride reduction followed by reaction of the reduction product with hydrogen chloride gas in ether solution. The white solid obtained (2.5 g, 76% yield), mp 175–176°, was identical in all respects (melting point, mixture melting point, and infrared spectrum) with **31**.

cis-**2-Methyl-3-isopropylaziridine** (**11**).—*cis*-4-Methyl-2-pentene (**9**, 16.8 g, 0.2 mole), silver cyanate (30 g, 0.2 mole), and iodine (51 g, 0.2 mole) were stirred in ether (500 ml) at 0–5° for 24 hr. The intermediate iodoisocyanate, isolated by filtration and evaporation of ether, was stirred in methanol (500 ml) for 24 hr at room temperature followed by addition of a solution of potassium hydroxide (28 g, 0.5 mole) in water (50 ml), without isolation of **10**. The reaction mixture was refluxed for 24 hr, the methanol was evaporated, water was added, and the aziridine was extracted with ether. Distillation yielded **11**: 6.5 g, 33%; bp 38–39° (30 mm) and 30–32° (17 mm); infrared showed 3200 (>NH) and 856 cm^{-1} (*cis*-aziridine).

Anal. Calcd for $C_6H_{13}N$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.71; H, 12.99; N, 13.95.

The phenylurea and α-naphthylurea derivatives were prepared in the conventional way from **11** and phenylisocyanate and α-naphthylisocyanate, respectively, in hexane solution. The phenylurea of **11** had mp 76–77°.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.35; H, 8.19; N, 12.99.

The α-naphthylurea of **11** had mp 98.5–99°.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 75.82; H, 7.60; N, 10.56. Found: C, 75.94; H, 7.57; N, 10.59.

threo-**4-Methyl-2,3(3,2)azidoaminopentane** (**12**).—The aziridine (**11**, 2.0 g, 0.02 mole), sodium azide (6.5 g, 0.1 mole), and ammonium chloride (5.35 g, 0.1 mole) dissolved in ethanol (200 ml) and water (50 ml) were refluxed for 24 hr. After the usual isolation procedure followed by vacuum distillation, **12** [1.8 g, 71%, bp 90° (34 mm)], was obtained as a colorless liquid; infrared showed 3300, 1600 (NH_2) and 2100 and 1250 cm^{-1} (N_3). It was analyzed as the phenylurea derivative: mp 130–133°; infrared showed 3350 (>NH) and 2110 and 1260 cm^{-1} (N_3).

Anal. Calcd for $C_{13}H_{19}N_5O$: C, 59.75; H, 7.33; N, 26.80. Found: C, 59.76; H, 7.28; N, 26.83.

threo-**4-Methyl-2,3-diaminopentane Dihydrochloride** (**13**).—The *threo*-azidoamine (**12**, 1.4 g) dissolved in absolute ethanol (50 ml) was hydrogenated at room temperature and 600 psi with Adams catalyst for 2 days. After filtration of the solution concentrated hydrochloric acid (10 ml) was added to the filtrate and it was evaporated to dryness in a rotary evaporator. The residue, a crystalline mass, was recrystallized from 95% ethanol to yield pure **13**: 1.1 g, 59%; mp 240–242°; infrared showed 2800, 2000, 1580, 1505, and 1550 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.25; H, 9.35; Cl, 37.43; N, 14.88.

This compound was identical with **26a** obtained *via* the epoxide route from the *trans* olefin.

cis-**4-Methyl-2,3-epoxypentane** (**14**).—This was prepared in the usual way from **9** and peroxyacetic acid containing sodium acetate.[21]

threo-**4-Methyl-2,3(3,2)-azidohydroxypentane** (**15**).—This was prepared in the same way as **3**, already described. From **14** (5 g, 0.05 mole), **15** was obtained in pure form by vacuum distillation: 4.9 g, 70% yield; bp 38° (0.15 mm) (colorless liquid); infrared showed 3450 (OH) and 2110 and 1260 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{13}N_3O$: C, 50.32; H, 9.15; N, 29.34. Found: C, 50.54; H, 9.16; N, 29.04.

erythro-**4-Methyl-2,3-diazidopentane** (**16**).—The azidohydrin (**15**, 4.9 g) was mesylated in the same way as **3** and the crude product [infrared showed ν_{max} 2110 and 1270 (N_3) and 1190 cm^{-1} (SO_3CH_3)] was used without purification. It was dissolved in dimethylformamide (50 ml) and stirred for 24 hr at 100° with a suspension of sodium azide (4.2 g, 0.065 mole). The usual work-up yielded **16**: 3.8 g, 65%; bp 61–63° (0.02 mm) (colorless liquid); infrared showed 2100 and 1260 cm^{-1} (N_3). This compound was unstable.

Anal. Calcd for $C_6H_{12}N_6$: C, 42.64; H, 7.61; N, 49.52. Found: C, 43.16; H, 7.17; N, exploded.

erythro-**4-Methyl-2,3-diaminopentane Dihydrochloride** (**17**).—The *erythro*-diazide (**16**, 2.5 g) was hydrogenated over Adams catalyst in the usual way and the resulting diamine was converted directly to the dihydrochloride **17**: 1.8 g, 62% yield; mp 226–227° (from ethanol–ethyl acetate); infrared showed 2800, 2000, 1610, 1580, and 1525 cm^{-1} (NH_3^+). The compound was identical in every respect (melting point, mixture melting point, and infrared spectrum) with the *erythro* dihydrochloride (**22a**) obtained *via* the aziridine route starting with *trans*-4-methyl-2-pentene.

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.38; H, 9.49; Cl, 37.55; N, 14.83.

trans-**2-Methyl-3-isopropylaziridine** (**20a**).—This was prepared as described for the *cis* isomer (**11**) from *trans*-4-methyl-2-pentene (**18a**, 16.8 g, 0.2 mole), silver cyanate (30 g, 0.2 mole), and iodine (51 g, 0.2 mole), followed by reaction of the intermediate iodoisocyanate successively with methanol (to obtain **19a**) and then with base. The pure aziridine (**20a**) was isolated as a colorless liquid by vacuum distillation: 6.3 g, 32%; bp 36° (30 mm); infrared showed 3210 (>NH) and 862 cm^{-1} (*trans*-aziridine).

Anal. Calcd for $C_6H_{13}N$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.61; H, 13.05; N, 13.92.

The phenylurea of **20a** had mp 78–79°.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.72; H, 8.34; N, 13.02.

The α-naphthylurea of **20a** had mp 120–121°.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 75.82; H, 7.60; N, 10.56. Found: C, 75.90; H, 7.44; N, 10.46.

erythro-**4-Methyl-2,3(3,2)-azidoaminopentane** (**21a**).—Compound **21a** was prepared in the same way as **12** but from **20a** (3.0 g). The pure azidoamine (**21a**) was isolated as a colorless liquid by vacuum distillation: 2.5 g, 58%; bp 95° (39 mm) and 34° (0.1 mm); infrared showed 3320 and 1610 (NH_2), and 2100 and 1260 cm^{-1} (N_3). It was analyzed as the phenylurea derivative: mp 144–147°; infrared showed 3300 (>NH), and 2100 and 1260 cm^{-1} (N_3).

Anal. Calcd for $C_{13}H_{19}N_5O$: C, 59.75; H, 7.33; N, 26.80; O, 6.12. Found: C, 59.90; H, 7.42; N, 26.52; O, 6.16.

erythro-**4-Methyl-2,3-diaminopentane Dihydrochloride** (**22a**).—The azidoamine (**21a**, 2.0 g) was reduced as described for the *threo* isomer (**12**) and the diamine was converted directly to the dihydrochloride (**22a**): 1.8 g, 60% yield; mp 226–227° (ethanol). It was identical in every way with **17**.

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.28; H, 9.57; Cl, 37.43; N, 14.71.

trans-**4-Methyl-2,3-epoxypentane** (**23a**).—This was prepared in the usual way from **18a** and peroxyacetic acid containing sodium acetate.[21]

erythro-**4-Methyl-2,3(3,2)-azidohydroxypentane** (**24a**).—This was prepared in the same way as **3** and **15**. From **23a** (8.0 g, 0.08 mole), **24a** was obtained in pure form as a colorless liquid by vacuum distillation: 8.9 g, 40% yield; bp 60–63° (0.05 mm); infrared showed 3450 (OH) and 2110 and 1260 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{13}N_3O$: C, 50.32; H, 9.15; N, 29.34. Found: C, 50.19; H, 9.15; N, 29.01.

threo-**4-Methyl-2,3-diazidopentane** (**25a**).—The azidohydrin (**24a**, 8.9 g) was mesylated in the same way as **3** and **15** and the crude product was dissolved in dimethylformamide (50 ml) and stirred for 24 hr at 100° with a suspension of sodium azide (10.4 g, 0.16 mole). The usual work-up yielded **25a**: 7.6 g, 81%; bp 40–41° (0.01 mm) (colorless liquid); infrared showed 2110 and 1260 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{12}N_6$: C, 42.64; H, 7.61; N, 49.52. Found: C, 42.80; H, 7.32; N, 49.67.

threo-**4-Methyl-2,3-diaminopentane Dihydrochloride (26a).**—Hydrogenation of the diazide (**25a**, 5.0 g) as described yielded the free diamine, a colorless oil, that was immediately converted to the dihydrochloride in ether solution from which it immediately precipitated: 4.0 g, 71% yield; mp 239–242° (ethanol); infrared showed 2800, 2000, 1580, 1505, and 1550 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.05; H, 9.27; Cl, 37.42; N, 14.68.

This compound was identical in every respect with **13** obtained *via* the aziridine route from the *cis* olefin.

trans-**2,3-Diethylaziridine (20b).**—Compound **20b** was prepared as previously described but from *trans*-3-hexene (**18b**, 8.4 g, 0.1 mole), silver cyanate (15 g, 0.1 mole), and iodine (25.4 g, 0.1 mole) in dry ether (250 ml) followed by successive reaction of the intermediate iodoisocyanate with methanol (200 ml) and then with potassium hydroxide (8.4 g) dissolved in water (30 ml), without separate isolation of **19b**. The pure aziridine (**20b**) was isolated as a colorless liquid by vacuum distillation: 2.3 g, 45%; bp 45° (32 mm) and 26–29° (15 mm); infrared showed 3200 (>NH) and 875 cm^{-1} (*trans*-aziridine).

Anal. Calcd for $C_6H_{13}N$: C, 72.66; H, 13.21; N, 14.12. Found: C, 72.67; H, 13.08; N, 14.05.

The phenylurea of **20b** had mp 85–86°.

Anal. Calcd for $C_{13}H_{18}N_2O$: C, 71.53; H, 8.31; N, 12.83. Found: C, 71.71; H, 8.48; N, 12.74.

The α-naphthylurea of **20b** had mp 114–115°.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 75.82; H, 7.60; N, 10.56. Found: C, 75.94; H, 7.42; N, 10.71.

erythro-**3,4-Azidoaminohexane (21b).**—Compound **21b** was prepared in the same way as **12** and **21a** but from **20b** (3.5 g). The pure azidoamine (**21b**) was isolated as a colorless liquid by vacuum distillation: 2.7 g, 56%; bp 78–79° (18 mm); infrared showed 3350 and 1610 (NH_2) and 2100 and 1275 cm^{-1} (N_3).

Anal. Calcd for $C_6H_{14}N_4$: C, 50.67; H, 9.93; N, 39.43. Found: C, 50.68; H, 9.91; N, 39.05.

meso-**3,4-Diaminohexane Dihydrochloride (22b).**—The azidoamine (**21b**, 2.0 g) was hydrogenated as described for **12** and **21a**, and the resulting diamine was converted directly to the dihydrochloride in the ethanol solution followed by evaporation to dryness. Recrystallization of the residue from ethanol yielded pure **22b**: 1.7 g, 72%; mp 263–266°; infrared showed 2800, 2000, 1600, and 1515 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 38.22; H, 9.60; Cl, 37.39; N, 14.74.

trans-**3,4-Epoxyhexane (23b).**—This was prepared in the usual way from **18b** and peroxyacetic acid containing sodium acetate.[21]

threo-**3,4-Diaminohexane Dihydrochloride (26b).**—By procedures already described the *trans* epoxide (**23b**, 6.0 g) was converted to the azidohydrin (**24b**) [infrared showed 3375 (OH) and 2100 and 1270 cm^{-1} (N_3)], which was then converted to the *threo*-3,4-diazidohexane (**25b**) *via* the intermediate azidomesylate. The usual reduction procedure over Adams catalyst yielded the diamine from **25b** which was converted to its dihydrochloride (**26b**) in ether solution. The precipitate of crude **26b** was recrystallized from ethanol to yield the pure compound: 4.0 g (35% from epoxide); mp 298–300°; infrared showed 2800, 2000, 1620, and 1520 cm^{-1} (NH_3^+).

Anal. Calcd for $C_6H_{18}Cl_2N_2$: C, 38.10; H, 9.59; Cl, 37.49; N, 14.81. Found: C, 37.98; H, 9.23; Cl, 37.01; N, 14.95.

Registry No.—**3,** 10027-78-8; *trans*-2-azidocyclohexyl methanesulfonate, 10043-43-3; **4,** 10027-79-9; **5,** 10027-80-2; **6,** 1199-15-1; **7,** 10027-82-4; **8,** 10027-83-5; *trans*-2-azidocyclohexylamine, 10043-36-4; **27,** 10027-84-6; **29,** 10027-85-7; **31,** 5456-63-3; **37,** 10039-14-2; *cis* isomer of **3,** 10027-87-9; **11,** 10027-88-0; phenylurea of **11,** 10027-89-1; 2-naphthylurea of **11,** 10039-15-3; phenylurea of **12,** 10027-90-4; **13,** 10027-91-5; **15,** 10027-92-6; **16,** 10027-93-7; **17,** 10027-94-8; **20a,** 10027-95-9; phenylurea of **20a,** 10027-96-0; 2-naphthylurea of **20a,** 10027-97-1; phenylurea of **21a,** 10027-98-2; **26b,** 10027-99-3; **24a,** 10028-00-9; **25a,** 10028-01-0; **20b,** 10028-02-1; phenylurea of **20b,** 10028-03-2; 2-naphthylurea of **20b,** 10028-04-3; **21b,** 10028-05-4; **22b,** 10028-06-5.

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A Study of the Acid-Catalyzed Cyclization of Some Condensed Cyclohexenone and Cyclohexanone Aliphatic Acids

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Condensed cyclohexenone aliphatic acids of type **5** can be cyclized under acid-catalyzed conditions to bicycloalkenediones of type **6**, when n = 1–3. The corresponding cyclization of some saturated keto acids of type **7** appears to proceed preferentially toward the more substituted α-carbonyl position, or, in the absence of substitution, toward the direction of preferred enolization of the ketone group. The unusual spectroscopic properties of some of the bridged-ring compounds obtained have been noted.

In a synthesis of (±)-gibberone (**1**), a degradation product of gibberellic acid, formation of the bicyclo[3.2.1]octane system was achieved by the acid-catalyzed cyclization of unsaturated keto acid **3**, which gave in high yield diketone **2**.[2] A similar approach was followed in a total synthesis of (±)-gibberic acid (**4**).[3] The object of the present work was to try to evaluate this type of carbon–carbon bond formation more fully as applicable in particular to the formation of a bridged-ring system.[4,5] This involved determining (a) the generality of the cyclization of a cycloalkenone aliphatic acid of type **5** to give a bicyclo[3.n.1]alkenedione of type **6**, and (b) whether the same type of cyclization could be applied to the corresponding saturated keto acid of type **7**, and, if so, which of the two possible bicycloalkanediones (**8** or **9**) would be formed depending on the nature of the substituents R and R′ (see Scheme I).

Hydrophenanthrone 10a-aliphatic acids, as exemplified by structures **17–19**, **23** and **25**, and **30–32**, appeared very suitable as model keto acids, both because of their potential synthetic relationship to some of the tetra-

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