that its glucopyranoside rings exist in more than a single ring conformation. There are structural reasons for believing that two boat forms, B1 and 3B, may be the principal conformations involved. The conclusion is not entirely dependent upon the argument favoring these particular ring forms. It is recognized that other pairs of ring conformations might account for the behavior of amylose, provided one of the forms were reactive, the other unreactive with cuprammonium.

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NEW ORLEANS, LOUISIANA

[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY, OHIO STATE UNIVERSITY]

Attempted Syntheses of Nitrogen Analogs of Adamantane[1]

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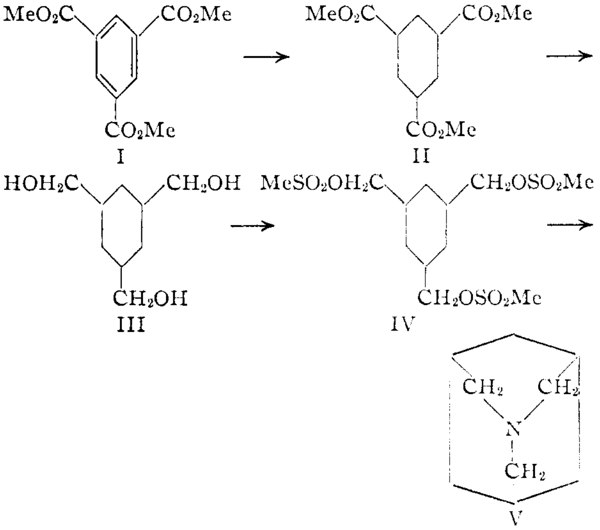
Attempts to prepare nitrogen analogs of adamantane from 1,3,5-trisubstituted cyclohexanes failed. A number of these cyclohexanes were related in configuration, postulated to be *cis*.

The interest shown in adamantane[3] and in quinuclidine[4] led us to seek a synthesis of the adamantane skeleton which could be modified to introduce a hetero atom at a bridgehead. The success of triple condensations for preparing bicyclic compounds[5] suggested the use of the *cis* isomers of 1,3,5-trisubstituted cyclohexanes for this synthesis. We therefore attempted the following sequence[6]



Trimethyl 1,3,5-cyclohexanetricarboxylate was prepared by reduction of trimethyl trimesate, and a predominant isomer, II, m.p. 48.0–49.0°, was separated.[7] Reduction by lithium aluminum hydride afforded an alcohol, III, which was converted to the trismethane sulfonate, IV, and treated with ammonia.

An amine hydrochloride XIII·HCl was obtained in very low yield (*ca.* 2%) from each of three runs along with large amounts of polymeric material. The analysis agreed with that calculated for V·HCl, but the compound was destroyed by alkaline permanganate,[8] and reacted with bromine to yield a monobromo derivative. Insufficient material forced us to abandon further work on the structure.

On hydrolysis, either the solid isomer, II, or the isomeric mixture of trimethyl 1,3,5-cyclohexanetricarboxylates gave only a single isomer, VI, of the parent acid, as found by earlier workers.[7b] Reaction of VI with diazomethane afforded II, which proves identical configurations. Since the lithium aluminum hydride reduction should not cause isomerization of II,[9] the alcohol, III, and its methanesulfonate, IV, should have the same configuration as II. VI, as the most stable isomer, should be of *cis* configuration[6c]; therefore, II, III and IV should also be *cis*. It thus seems likely that failure to obtain the tricyclic amine, V, was due to side reactions[6d] and an unfavorable conformation[6c] of the substituents of IV rather than to a *trans* configuration in IV.

The ready availability of the triacid, VI, prompted us to attempt the preparation of the tricyclic triamide, IX, since this compound would constitute a most unusual case of an amide involving a "bridgehead" nitrogen.[10]

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(1) Taken in part from the Ph.D. thesis of H. S. Lowrie, Ohio State University, 1952.

(2) Cincinnati Chemical Works Fellow, 1951–1952.

(3) C. Prelog and R. Seiwerth, *Ber.*, **74**, 1769 (1941), and references mentioned therein.

(4) H. C. Brown and N. R. Eldred, THIS JOURNAL, **71**, 445 (1949).

(5) V. Prelog, D. Kohlbach, E. Carkovnikov, A. Rezik and M. Piantanida, *Ann.*, **532**, 69 (1937).

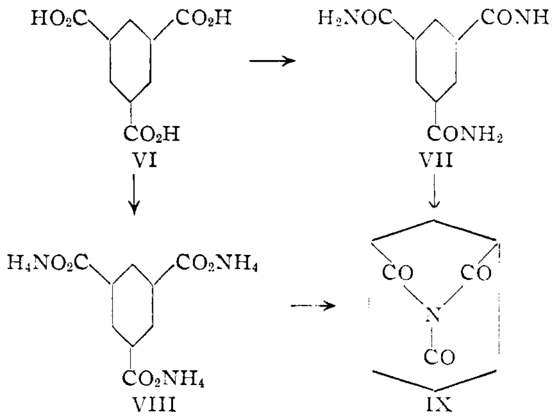
(6) The preparation of predominantly the *cis* isomer by the reduction of mesitylene (a) and evidence that this was the more stable of the pair (b) made us expect, when this work was begun in 1949, that the isomeric mixture obtained by the reduction of trimethyl trimesate (I) would consist mainly of the *cis* form. Later work (c) has substantiated these beliefs, but has indicated that even though the substituents are in the necessary *cis* configuration, they are bound by equatorial bonds and are thus widely separated, favoring side-reactions (e) from the trismethanesulfonate, IV, rather than the intramolecular condensation desired. (a) C. E. Bowers, M. S. Thesis, Ohio State University, 1949; (b) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947); (c) E. M. Fry, *ibid.*, **76**, 284 (1954), and references mentioned therein; (d) D. D. Reynolds and W. O. Kenyon, *ibid.*, **72**, 1597 (1950), and references therein.

(7) (a) R. C. Fuson and C. H. McKeever, *ibid.*, **62**, 2088 (1940), give m.p. 42–44° for II; (b) J. M. Van der Zanden and G. DeVries, *Rec. trav. Chim.*, **67**, 998 (1948), found m.p. ranges between 43–47° for II.

(8) Both adamantane[1] and quinuclidine (a) are stable to these conditions; by analogy, V should be. (a) K. Löffler and F. Stiezel, *Ber.*, **42**, 124 (1909).

(9) W. G. Brown in R. Adams, "Organic Reactions," Vol. 6, J. Wiley and Sons, Inc., New York, N. Y., 1951, p. 469.

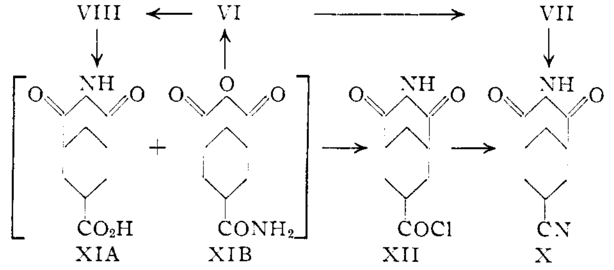
(10) The attempts to prepare this type of compound, and the properties expected of it have been reviewed recently. (a) F. S. Fawcett, *Chem. Revs.*, **47**, 219 (1950); see also Y. J. Topper, Ph.D. Dissertation, Harvard, 1946; S. M. McElvain and L. W. Bannister, THIS JOURNAL, **76**, 1126 (1954).



VI was converted *via* the triacid chloride to the triamide, VII, which was pyrolyzed to give a crystalline solid for which the structure X is advanced because of the following data: (a) Analysis indicated the formula $C_9H_{10}O_2N_2$; monomeric because of ready sublimation and solubility. (b) The compound was neutral and could be recrystallized from boiling water, thus ruling out an imino ester structure. (c) Sharp absorption at 4.6 μ in the infrared indicated a cyanide group. (d) Otherwise, the absorption between 3 and 10 μ was almost identical to that of the product of pyrolysis of the ammonium salt (VIII) of VI, which was converted to X, and yielded VI upon hydrolysis (see below).

An alternative attempt to prepare the triamide IX involving pyrolysis of VIII led to the isolation of a mixture consisting mainly of XIA and XIB as indicated by the following information: (a) The analysis, although varying slightly with the run chosen, agreed best with the requirements of $C_9H_{11}O_4N$; ready sublimation and solubility indicated a monomeric formula. (b) Hydrolysis afforded the starting acid VI. (c) A solution of the mixture was acid. Titration gave an initial neutralization equivalent of about 300,[11] which gradually fell, on addition of excess base, to an equilibrium value of about 110. Such behavior would be expected of a mixture of an imide-acid, XIA, and an amide-anhydride, XIB. (d) A lack of absorption peaks between 4 and 5μ indicated that no cyanide group was present.

The mixture was treated with thionyl chloride to give a product presumed to have the structure XII,[12] which then reacted with ammonia and was sublimed to yield X (the product from pyrolysis of the triamide, VII). The sequence is outlined below.



Experimental[13]

Trimethyl 1,3,5-Cyclohexanetricarboxylate (II).—Trimethyl trimesate (I),[7b] was distilled at reduced pressure, then recrystallized twice from methanol, to yield white needles, m.p. 145–146°. Reduction[7a] and distillation afforded trimethyl 1,3,5-cyclohexanetricarboxylate as a semicrystalline, isomeric mixture which was recrystallized three times from ether at −70°. In the best of several runs, 33.3 g. of the mixture gave 20.6 g. (62%) of the solid isomer II, m.p. 48.0–49.0°.[7] Additional crops could be obtained from the mother liquors.

1,3,5-Cyclohexanetrimethanol (III).—Reduction of 30.0 g. of the solid isomer II was carried out with a slurry of lithium aluminum hydride in ether.[9] The reaction mixture was acidified with dilute sulfuric acid, saturated with sodium sulfate, and continuously extracted with ether for 12 days. The extracts were diluted with methanol to dissolve the yellow oil which had separated, and passed through a column of alumina to remove traces of acid. Removal of the solvents gave 14.6 g. of an oily yellow solid. Three recrystallizations of a portion from acetone gave white rods, III, m.p. 101.0–102.0°. *Anal.* Calcd. for $C_9H_{18}O_3$: C, 62.0; H, 10.4. Found[g]: C, 62.1; H, 10.6.

Reduction of 43.8 g. of the isomeric mixture of trimethyl 1,3,5-cyclohexanetricarboxylates was carried out in the same way to give 32.5 g. of an oily solid. Recrystallization from acetone furnished 8.4 g. (28%) of III, m.p. 97–100°. The mother liquor was evaporated to dryness, and the oil remaining was refluxed with dilute sodium hydroxide to hydrolyze any unreacted ester. The solution was saturated with sodium sulfate and extracted as before, to yield 10.6 g. (36%) of III, m.p. 95–100°. Two recrystallizations from acetone furnished pure material.

1,3,5-Cyclohexanetrimethanol Trimethanesulfonate (IV).—In the best of several runs, 2.10 g. of III was dissolved in dry pyridine and treated with methanesulfonyl chloride at −5–0° for three hours.[14] Working up in the cold gave a yellow solid which was dissolved in acetone and passed through activated charcoal (Norit A). Removal of the solvent with air yielded 4.4 g. (89%) of white crystals, m.p. 125.5–126.5°. Two recrystallizations of a portion from acetone–ether (without heating) raised the m.p. of IV to 126.8–127.4°. *Anal.* Calcd. for $C_{12}H_{14}O_9S_3$: C, 35.3; H, 5.9; S, 23.6. Found[g]: C, 35.5; H, 5.9; S, 23.5. The material turned yellow when warmed in acetone.

Attempted Preparation of 1-Azatricyclo(3,3,1,$1^{3,7}$)decane (V).—In the best of the three runs 35 g. of crude IV, m.p. 108–118°, was placed in a steel bomb with 500 ml. of dioxane, and 0.6 mole (100% excess) of dry ammonia added. After shaking overnight, the bomb was heated slowly to 85° for 24 hours, cooled, 0.2 mole of ammonia added, and then heated at 95° for 24 hours. After cooling, the contents were poured into dilute sulfuric acid and distilled with the aid of steam to remove the dioxane. The solution was made strongly basic with potassium hydroxide and distilled as before until the distillate, which was collected in excess dilute hydrochloric acid, was no longer basic. Evaporation of the distillate gave a yellow-white solid which was dried thoroughly, extracted once with acetone to remove the yellow color, and three times with chloroform.[15] Evaporation of the chloroform solution furnished 0.42 g. (2.8%) of a white powder. One recrystallization from ethanol–toluene gave white crystals of XIII·HCl which had an X-ray powder photograph identical to that of the product from an earlier run which had been analyzed. *Anal.* Calcd. for $C_9H_{16}NCl$: C, 62.2; H, 9.3; N, 8.1. Found[g]: C, 62.1; H, 9.1; N, 8.1, 8.1.

XIII·HCl was unchanged by aqueous nitrous acid at 95° for 12 hours. It sublimed at 180–200° before melting in an open tube, and melted above 400° in a sealed tube. An alkaline solution of potassium permanganate was immediately discolored by addition of 0.10 g. of XIII·HCl dissolved in base. Sufficient permanganate was added to restore the

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(11) Calculated for XIA: 197. This indicates about 70% of XIA in the mixture.

(12) While a diacid chloride, $C_6H_9(CONH_2)(COCl)_2$, is possible from XIB of the mixture, the composition given in ref. 11, and the similarity of the infrared absorption of the product with the starting material, indicated XII as the predominant structure.

(13) (a) All melting points are corrected. (b) Analyses marked *g* by Galbraith Microanalytical Laboratories, Knoxville, Tenn.; *e* by Elek Microanalytical Laboratories, Los Angeles, Calif.; *h* by Huffman Microanalytical Laboratories, Wheatridge, Col.

(14) Compare R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

(15) An earlier run had shown that the hydrochloride desired was insoluble in acetone, but readily soluble in chloroform, which was used, therefore, to separate it from the principal contaminant, ammonium chloride.

purple color, the solution was refluxed for one hour, then distilled as above. The distillate gave less than 5 mg. of white powder, identified by its X-ray powder photograph as ammonium chloride.

A solution of bromine in carbon tetrachloride was dropped into 80 mg. of XIII·HCl dissolved in chloroform. The first drops were decolorized rapidly, but addition was continued until the bromine color persisted. The solvents were removed with air, the orange solid was taken up in absolute ethanol and precipitated with petroleum ether (b.p. 90–97°). The yellow precipitate was washed with a small quantity of acetone, which removed the color, and then recrystallized from boiling acetone. Two crystal forms were deposited and were separated manually, washed with cold acetone, and dried for analysis: XIV, 20 mg. of long needles, fairly soluble in acetone. Calcd. for $C_9H_{15}NBr_2$: C, 36.4; H, 5.1; Br, 53.8. Found[g]: C, 37.4; H, 5.2; Br, 52.9. XV, 15 mg. of small cubes, rather insoluble in acetone. Calcd. for $C_9H_{16}NBr$: C, 49.6; H, 7.4; Br, 36.6. Found[g]: C, 48.8; H, 7.0; Br, 36.7. A small quantity of XIII·HCl was dissolved in hydrobromic acid and the solution was evaporated to dryness. The solid obtained had an identical X-ray powder photograph to that of XV, which was thus shown to be XIII·HBr.

1,3,5-Cyclohexanetricarboxylic Acid (VI).—II, 20.5 g., was dissolved by refluxing with dilute sodium hydroxide (2–3 hr.).[7b] The solution was concentrated, acidified with sulfuric acid, saturated with sodium sulfate, and extracted continuously with ether for 12 hours. Removal of the ether gave 18.0 g. (93% for $VI\cdot 1^1/_2H_2O$[7b]) of a white, powdery solid, m.p. 208–213°. Three recrystallizations from acetone–benzene gave white needles of VI, m.p. 215–218°.[7b]

Esterification of 1.30 g. of VI with diazomethane yielded 1.22 g. of solid, m.p. 43–47°. Distillation and recrystallization from ether at −70° gave fine needles, m.p. 48–49°, not depressed by II. The infrared absorption spectrum was identical to that of II.

1,3,5-Cyclohexanetricarboxamide (VII).—Using thionyl chloride, VI was converted to the acid chloride[7a] which was dissolved in benzene and added to 28% ammonium hydroxide. The aqueous layer was cooled, filtered and the solid recrystallized twice from water to yield white crystals of VII which softened at 283.5°, melted at 287.5–288.5° dec. *Anal.* Calcd. for $C_9H_{15}O_3N_3$: C, 50.7; H, 7.1; N, 19.7. Found[g]: C, 50.5; H, 7.0; N, 19.8.

Pyrolysis of 1,3,5-Cyclohexanetricarboxamide (VII).—VII, 1.24 g., was placed in a sublimation apparatus and heated slowly on a Woods metal-bath to 285°, causing the solid to turn dark and melt, and a white solid to sublime. The odor of ammonia was strong, and moisture collected high on the cold finger. In six hours various fractions were collected which, after drying *in vacuo*, melted in 20° ranges between 210 and 240°, and totaled 0.81 g. (78%). This material was boiled with absolute ethanol but proved rather insoluble. The ethanol was removed, and the solid was recrystallized twice from acetone to give white crystals of X which softened at 230–231° and melted at 239–243° with darkening. *Anal.* Calcd. for $C_9H_{10}O_2N_2$: C, 60.7; H, 5.7; N, 15.7. Found[g]: C, 60.3; H, 5.3; N, 15.6.

A portion of these crystals was dissolved in hot water and boiled for five minutes; the solution remained neutral to litmus. On cooling, crystals were deposited whose melting point, X-ray powder photograph, and infrared spectrum were identical to those of X.

Pyrolysis of Triammonium 1,3,5-Cyclohexanetricarboxylate (VIII).—In a typical preparation, 1.3 g. of VI was placed in 5 ml. of 28% ammonium hydroxide, evaporated to dryness, and pyrolyzed at 270–300° as in the previous preparation. The white solid, which sublimed along with moisture and ammonia, was dried *in vacuo* giving 0.90 g. (76%) which softened at 190–220° and melted at 230–250° with decomposition. Two recrystallizations from ethanol–toluene gave white, poorly formed crystals which softened at 240–244° and melted at 244–247° dec. *Anal.* Calcd. for $C_9H_{11}O_4N$: C, 54.8; H, 5.6; N, 7.1. Found[g]: C, 55.6; H, 5.7; N, 7.1.

The preparation was repeated with 6.1 g. of VI and gave 4.2 g. (76%) of material in various fractions which melted in the same range as the sublimate above. One fraction was resublimed at 195° (0.1 mm.) to give white, powdery crystals that softened at 204°, melted at 215–233° dec. and were sealed against moisture for analysis. Calcd. for $C_9H_{11}O_4N$: C, 54.8; H, 5.6; N, 7.1. Found[g,16]: C, 55.1; H, 5.4; N, 8.3. Another fraction was recrystallized twice from ethanol–toluene, then sublimed at 195° (0.1 mm.) to give a white powder which softened at 223° and melted at 227–254° dec. *Anal.* Calcd. for $C_9H_{11}O_4N$: C, 54.8; H, 5.6; N, 7.1. Found[16]: C,[e] 55.9; H, 5.8; N,[h] 8.5, 8.4.

The neutral equivalents of the various fractions were initially 280–300 but dropped steadily when excess base was added to final equilibrium values of 108–114.[16] A portion of the material upon which the neutralization equivalent had been taken was boiled with dilute sodium hydroxide, acidified with dilute hydrochloric acid and evaporated to dryness. Evaporation of an acetone extract of the residue afforded a white solid which was recrystallized from ethanol–toluene to yield white needles, m.p. 211–215°, not depressed by VI. The infrared spectrum was identical to that of VI. The material was treated with diazomethane and worked up as before, giving clear needles, m.p. 48–49°, not depressed by II.

The pyrolysis was repeated with 10.8 g. of VI and gave 6.6 g. (67%) of a product having the same melting point range and infrared spectrogram as the sublimates above. Three grams was added to thionyl chloride, allowed to stand two days, and refluxed a short time. The solvent was removed *in vacuo*, and the solid remaining sublimed at 35 mm. to give 0.9 g. (27%) of white needles, XII, m.p. 170–180° on rapid heating. The infrared spectrum was identical to that of the starting material between 3 and 9 μ except for an additional peak at 5.6 μ (characteristic of a carbonyl in an acid chloride). Elemental analysis showed nitrogen and chlorine present, sulfur absent.

XII, 0.3 g., was partially dissolved in chloroform which had been saturated with ammonia. The suspension was allowed to stand one hour, then filtered and evaporated to dryness. The solid was sublimed as in the preparation of X. The sublimate was recrystallized from acetone–benzene giving 0.05 g. of tan crystals, m.p. 260–265°. On evaporation of the mother liquor white crystals were obtained, m.p. 207–220°, whose X-ray powder photograph and infrared diagram were identical to those of X.

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[16] High values for nitrogen, and for the neutralization equivalent at equilibrium (see below), could be caused by the impurity 5-carbamoyl-1,3-cyclohexanedicarboximide (XIA, where $-CO_2H = -CONH_2$) which would cause no appreciable change in the carbon–hydrogen analysis, (calcd. for $C_9H_{12}O_3N_2$: C, 55.1; H, 6.2; N, 14.3) or in the infrared absorption. The infrared absorptions of the analytical samples were found to be identical.