of the compound. It sintered at about 250° and foamed at about 300° (lit.[17] gives 260–300°); $\lambda_{max}^{H_2O}$ 262 mμ, ε 8.44 × 10^3.

Anal. Calcd. for $C_5H_6N_2O_3$: C, 42.25; H, 4.26. Found[29]: C, 40.58; H, 4.65.

Uracil-5-carboxylic Acid.—A suspension of 0.71 g. (0.005 mole) of 5-hydroxymethyluracil in 12 ml. of water was cooled and 1.9 ml. of concentrated sulfuric acid added slowly with stirring. A slurry of 1.47 g. (0.005 mole) of potassium dichromate in 3 ml. of water was added portionwise, care being taken that the temperature did not rise above 20°. At the conclusion of the addition, the solution was heated on the steam-bath for 5 minutes and filtered hot. The filtrate on standing in the cold overnight deposited 0.23 g. of greenish-white crystals. A second crop of 0.26 g. was obtained by concentrating the filtrate under vacuum. The total yield was 0.49 g. (63%) of off-white solid which melted at 278–279° (lit.[13] gives 278°) and did not depress a reference sample (identified lot 9501, Nutritional Biochemicals Corp.). The infrared spectra are also identical, with significant bands at 2.83 (OH), 6.2 and 8.43 μ which did not appear in the spectrum of uracil.[28]

5-Aminomethyluracil (IV) Hydrochloride.—A solution of 1.65 g. (0.01 mole) of 5-chloromethyluracil (V) and 1.55 g. (0.011 mole) of hexamethylenetetramine in 10 ml. of water was allowed to stand for 3 days. The solution was filtered to remove a small amount of solid and the filtrate diluted with alcohol and ether to precipitate 2.75 g. of the intermediate complex. The solid was suspended in 20 ml. of concentrated hydrochloric acid and 140 ml. of ethanol. After about 10 minutes of heating at reflux on the steam-bath, the solution cleared and after about one hour a white crystalline precipitate started to form. Refluxing was continued for a total of 6 hours and the reaction mixture cooled overnight in the ice-box. The 2.4 g. of solid was fractionally recrystallized from alcohol and water to remove the ammonium chloride. A total of 1.27 g. of product (72% yield) was obtained, m.p. 250–254°. The best sample obtained melted at 252–253° (lit.[14] gives 242–243°); $\lambda_{max}^{H_2O}$ 261.5 mμ, ε 6.3 × 10^3.

Anal. Calcd. for $C_6H_7N_3O_2 \cdot HCl$: Cl, 19.94. Found: Cl, 19.88.

5-Aminomethyluracil (IV) Sulfate.—A small quantity (0.2 g.) of the hydrochloride salt was dissolved in a minimum amount of warm water and a few drops of hot 12 *N* H_2SO_4 added. On cooling, white plates precipitated which, after three recrystallizations from alcohol and water, melted at 254–255° (lit.[14] gives 245–246° for the monohydrate).

Anal. Calcd. for $C_6H_7O_2N_3 \cdot {}^1/_2H_2SO_4 \cdot H_2O$: C, 28.86; H, 4.81. Found: C, 28.89; H, 4.71.

5-Chloro-6-ethoxyhydrothymine (VIII) from Thymine and N-Chlorosuccinimide.—The experiment of Barrett and West, who assigned a different structure (V) to the product,[8,20] was repeated. To a solution of 1.47 g. (0.011 mole) of N-chlorosuccinimide and 0.4 g. of benzoyl peroxide in 50 ml. of chloroform (Merck U.S.P.), 1.26 g. (0.01 mole) of thymine was added. The suspension was heated at reflux temperature for 10 hr. during which time the appearance of the suspended solid changed. The mixture was filtered to give 1.2 g. of white solid, m.p. 215–219°. Concentration of the filtrate and cooling yielded a further 1.2 g. of solid which, after treatment with cold water to remove succinimide, yielded an additional 0.25 g. of product; total crude yield 1.45 g. (72%). Recrystallization from hot water gave a first crop of crystalline VIII, m.p. 220–221° (lit.[8,20] gives 222–224° and erroneously assigns structure V). A mixed melting point with the product as prepared by Johnson and Sprague[23] showed no depression. The ultraviolet absorption spectrum of VIII in water showed a disappearance of the thymine peak at 266 mμ,[21] with only end absorption remaining[22]; $\lambda_{max}^{H_2O}$ 204 mμ, ε 8.19 × 10^3.

Anal. Calcd. for $C_7H_{11}ClN_2O_3$: C, 40.70; H, 5.36; Cl, 17.15; N, 13.56. Found: C, 40.73; H, 5.26; Cl, 17.04; N, 13.58.

A second crop of crystals was obtained, m.p. 227.5°. Admixture with first crop product depressed the melting point. Recrystallization from hot water gave needles, m.p. 227.5°.

Anal. Found: C, 41.05; H, 5.08.

Upon further recrystallization or standing for several weeks, the product was converted to the lower melting form, m.p. 223–224°.

An attempt to effect a reaction between the lower melting form of VIII and silver carbonate resulted in a recovery of unchanged material, m.p. 221–222°. It did not depress the melting point of starting material but did depress that of the 227.5° compound.

Anal. Found: C, 41.16; H, 5.32.

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(29) Agrees with the presence of about one-third mole of water. Because of the ready decomposition of the substance to give water, a water determination would probably be valueless.

COMMUNICATIONS TO THE EDITOR

THE CONFIGURATION OF DEUTERIO-L-MALIC ACID PRODUCED ENZYMATICALLY. SYNTHESIS OF *THREO*-3-DEUTERIO-DL-MALIC ACID

Sir:

The recent extensive work of Alberty and his co-workers[1-3] has established that the hydration of fumaric acid in deuterium oxide, catalyzed by fumarase, proceeds stereospecifically to give a single deuterio-L-malic acid (I). From a broad-line n.m.r. study[2] of the crystalline acid the *threo*

(1) R. A. Alberty and P. Bender, THIS JOURNAL, **81**, 542 (1959).

(2) T. C. Farrar, H. S. Gutowsky, R. A. Alberty and W. G. Miller, *ibid.*, **79**, 3978 (1957).

(3) H. F. Fisher, C. Frieden, J. S. McKinley McKee and R. A. Alberty, *ibid.*, **77**, 4436 (1955).

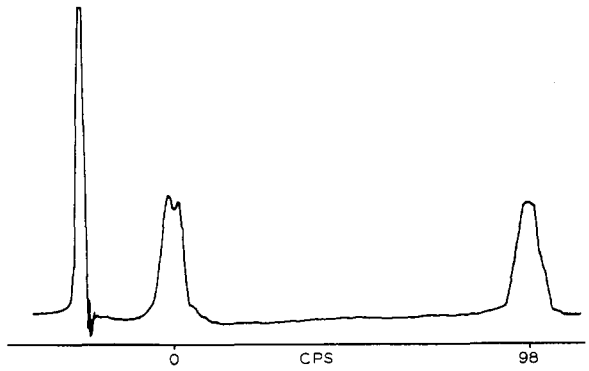

Fig. 1.—Proton nuclear magnetic resonance spectrum of 1.5 *M* dipotassium *threo*-3-deuterio-DL-malate in D_2O at 60 Mc. The magnetic field increases from left to right. The intense line on the left is due to H_2O in the D_2O.

configuration was assigned to I. In further work,[1] the high-resolution n.m.r. spectra of I, malic acid and their salts were examined in D_2O solution. The above assignment of configuration was accepted, and the results showed that either the relative magnitude of coupling constants of hydrogens on adjacent carbons were in the reverse order to those found by Lemieux, *et al.*[4] ($J_{trans} > J_{gauche}$), and recently confirmed,[5-9] or the two carboxyl groups of malic acid in solution were *gauche* to one another. As neither of these possibilities was attractive, it seemed more plausible that the original assignment[2] of configuration to I was incorrect, especially as the assumption was made that the two carboxyl groups of *crystalline* I were *trans*.[10]

We now report an unambiguous synthesis of *threo*-3-deuterio-DL-malic acid (II). This is shown *not* to be the DL-form of I. I must therefore have the *erythro* and not the *threo* configuration previously assigned.

Reduction of 3,4-epoxy-2,5-dimethoxytetrahydrofuran[11] with lithium aluminum deuteride gave 4-deuterio-3-hydroxy-2,5-dimethoxytetrahydrofuran (III), which had the same retention time on gas chromatography as undeuterated III.[11] Since $LiAlH_4$ is known to open epoxides in a *trans* fashion,[12] III should have the deuterium atom *trans* to the hydroxyl group.[13] Hydrolysis of III with 0.1*N* HCl and then oxidation with bromine in the presence of calcium carbonate gave II, initially isolated as the calcium salt, m.p. 125–126°, mixed m.p. with DL-malic acid, 125–126° [*Anal.* Calcd. for $C_4H_5DO_5$: C, 35.56; H and D, 5.22. Found: C 35.86, H and D (1 D assumed), 4.94].

The n.m.r. spectrum (60 Mc.) of the dipotassium salt of I in D_2O is shown in Fig. 1. It is different[14] from the spectrum[1] of the dipotassium salt of I. Hence I is the *erythro* isomer, and the addition of water to fumaric acid is *trans*, and not *cis*, as had been deduced previously.[2] The spectrum in Fig. 1 is that expected if the two carboxylate groups of the di-anion of II are *trans* and the coupling constants have their normal values.[4-9] Work is at present under way to synthesize the DL-form of I.

(4) R. U. Lemieux, R. K. Kullnig, H. G. Bernstein and W. G. Schneider, *ibid.*, **79**, 1005 (1957); **80**, 6098 (1958).

(5) A. D. Cohen, N. Sheppard and J. J. Turner, *Proc. Chem. Soc.*, 118 (1958).

(6) R. U. Lemieux, R. K. Kullnig and R. Y. Moir, THIS JOURNAL, **80**, 2237 (1958).

(7) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(8) C. N. Banwell, A. D. Cohen, N. Sheppard and J. J. Turner, *Proc. Chem. Soc.*, 266 (1959).

(9) F. A. L. Anet, *ibid.*, 327 (1959).

(10) The *gauche* conformation cannot be ruled out because of the strong lattice forces present in the solid state.

(11) J. C. Sheehan and B. M. Bloom, THIS JOURNAL, **74**, 3825 (1952).

(12) E. L. Eliel, "Steric Effects in Organic Chemistry," M. S. Newman, Editor, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 61.

(13) The configuration at C_2 and C_5, which is immaterial for the present purpose, will be discussed in a future publication.

(14) After correction for the fact that the spectrum given in ref. (1) was taken at 40 Mc. The n.m.r. spectra of the L and DL forms of the same diastereoisomer would be expected to be identical in solution. The spectrum in Fig. 1 is exactly that predicted for the *erythro* isomer on the basis of the (incorrect) assignments of ref. 1, both as regards chemical shifts and coupling constants. The assignments in ref. 1 become correct if, in the terminology used in that paper, H_b and H_c are interchanged.

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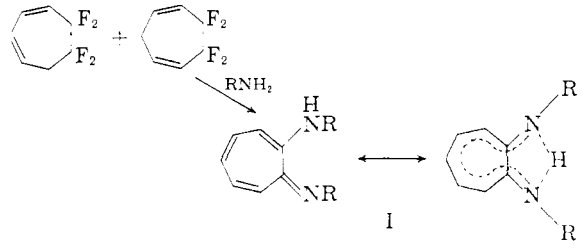
RECEIVED DECEMBER 31, 1959

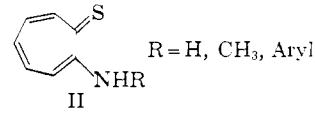
NOVEL ANALOGS OF TROPOLONE

Sir:

An attractive synthesis of tropolone by hydrolysis of the tetrafluorocycloheptadienes accessible from cyclopentadiene and tetrafluoroethylene was reported recently from this Laboratory.[1] It has now been found that the tetrafluorocycloheptadienes also serve as intermediates to the little-studied 1-amino-7-imino-1,3,5-cycloheptatrienes I, the nitrogen analogs of tropolone.



The N,N′-dialkyl and -diaryl derivatives are stable, highly colored compounds that exhibit aromatic-like reactivity similar to that of tropolone. Furthermore, the aminoimines I are convertible by reaction with hydrogen sulfide to the previously unreported 1-amino-7-thioxo-1,3,5-cycloheptatrienes II.



Reported examples of 1-amino-7-imino-1,3,5-cycloheptatrienes include the compounds III and IV.

(1) J. J. Drysdale, W. W. Gilbert, H. K. Sinclair and W. H. Sharkey, THIS JOURNAL, **80**, 3672 (1958).