trans-1-bromo-2-butene to equilibrate at room temperature. The mixture had a refractive index of n_D^{25} 1.4690. This refractive index indicated a mixture containing 46% 1-bromo-2-butene and 54% 3-bromo-1-butene.[10] The infrared spectrum of the mixture indicated the presence of only these two isomers.

1-Bromo-2-butene. 1-Bromo-2-butene (crotyl bromide) was purchased from Columbia Organic Chemicals, Inc., and used without further purification. n_D^{25} 1.4788. Lit.[10] n_D^{25} 1.4794.

Lithium aluminum hydride reductions. The lithium aluminum hydride reduction procedure was similar to that previously described.[5] Tetrahydrofuran was the solvent for both the halide and the hydride. After the addition of the lithium aluminum hydride at room temperature, the reaction mixture was refluxed (67°) for 1 hr. The reaction products distilled into a cold trap (dry-ice acetone) as formed and were weighed and analyzed by gas-liquid partition chromatography. In nearly every reaction the material balance was approximately 100%.

Anal. The chromatography equipment consisted of a 10 ft. by 1/4 in. copper tube containing dinonyl phthalate (30%) on 40–60 mesh fire brick (70%) as packing. The detector was a Gow-Mac thermal conductivity cell, helium was the carrier gas and the temperature was 30°. 3,4-Dichloro-1-butene: 100% *trans*-2-butene. 3-Chloro-1-butene: 5% *cis*-2-butene; 8% butadiene; 18% *trans*-2-butene; 69% 1-butene. 3-Bromo-1-butene (69%) and *trans*-1-bromo-2-butene: 26% *cis*-2-butene; 44% *trans*-2-butene; 30% 1-butene. 1,4-Dichloro-2-butene (purchased): 71% *cis*-2-butene; 29% *trans*-2-butene. 1,4-Dichloro-2-butene: (from butadiene): 100% *trans*-2-butene. *trans*-1-Chloro-2-butene: 100% *trans*-2-butene. *trans*-1-Bromo-2-butene: 100% *trans*-2-butene.

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DL-1,2-Diketo-*myo*-inositol Phenylosotriazole and 2-Phenyl-2,1,3-triazole-4,5-dicarboxaldehyde

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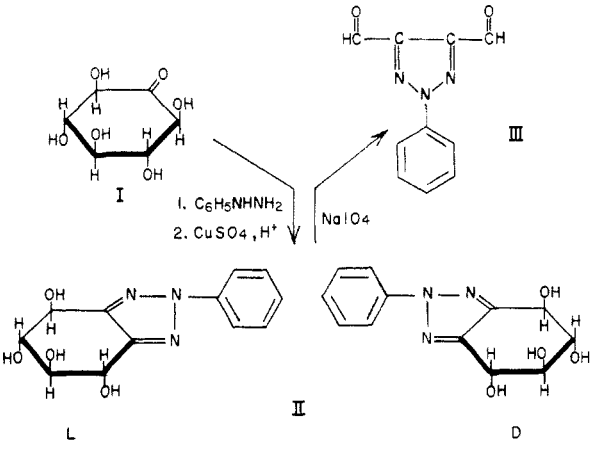
An interest in procedures for the carbon-by-carbon degradation of *myo*-inositol[2] prompted us to study osotriazole formation[3] with the racemic phenylosazone obtained by treating *myo*-inosose-2 (I) with excess phenylhydrazine.[4] Magasanik and Chargaff[5] had reported that they were unable to obtain the osotriazole from one of the optically active forms of this osazone, D(+)-1,2-diketo-*myo*-inositol bisphenylhydrazone. However, we found that the racemic osazone could be converted to the osotriazole II, albeit in poor yield, by the usual treatment with acidic copper sulfate. The osotriazole was degraded to the hitherto unknown 2 - phenyl - 2,1,3 - triazole - 4,5 - dicarboxaldehyde (III).



EXPERIMENTAL[6]

DL-*1,2-Diketo-myo-inositol phenylosotriazole (II).* Thirteen g. of crude DL-1,2-diketo-*myo*-inositol bisphenylhydrazone[4] was refluxed for 2 hr. with 940 ml. of acidic copper sulfate solution (33 g. $CuSO_4 \cdot 5H_2O$ per liter of 0.01 *N* H_2SO_4) and 625 ml. of isopropanol.[7] The osazone gradually went into solution. After the solution had cooled, the copper was precipitated with hydrogen sulfide and removed by filtration, and the filtrate, after treatment with charcoal, was concentrated under vacuum to less than 200 ml. On standing 3 hr. at room temperature, the concentrate deposited 1.2 g. (12%) of light brown solid. Several recrystallizations of this from pyridine-benzene, pyridine-ether, and water gave colorless prisms melting at 278–282° (dec.). Losses of material in the recrystallizations were moderate.

Anal. Calcd. for $C_{12}H_{13}O_4N_3$ (263.35): C, 54.8; H, 5.0. Found: C, 53.8; H, 5.3.

Attempts to isolate additional quantities of the osotriazole by concentrating the reaction liquors were fruitless, as were efforts to improve the yield by varying the proportions of the reactants, and by using methanol, 2-methoxyethanol and acetone as solvents.

*Tetra-O-acetyl-*DL-*1,2-diketo-myo-inositol phenylosotriazole* was obtained by treating the free osotriazole with acetic anhydride and pyridine on the steam bath. After recrystallization from warm acetone, the tetraacetate melted at 194–195°.

(1) Published with the approval of the Director of the Wisconsin Agricultural Experiment Station. Supported in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Alumni Research Foundation.

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(6) All crystalline compounds were recrystallized to constant melting point. Melting points were determined in capillary tubes. The thermometer used has been calibrated against Anschütz thermometers calibrated by the National Bureau of Standards. Microanalyses by the Micro-Tech Laboratories, Skokie, Illinois.

Anal. Calcd. for $C_{20}H_{21}O_8N_3$ (431.39): C, 55.7; H, 4.9. Found: C, 55.6; H, 5.0.

2-Phenyl-2,1,3-triazole-4,5-dicarboxaldehyde (III). II (288 mg., 1.1 mmole) was shaken at room temperature with 10 ml. of aqueous sodium metaperiodate (755 mg., 3.55 mmole). During 24 hr., the silky needles of osotriazole changed to shorter, thicker crystals. The product, obtained by filtration, was cream white and had a perfume-like odor. (2-Phenyl-2,1,3-triazole-4-carboxaldehyde smells like geraniol.[7]) After two recrystallizations from ethanol-water, it weighed 164 mg. (75% yield) and melted at 145–147°. The compound sublimes readily.

Titration of aliquots of the original filtrate showed that slightly over 3 molar equivalents of periodate had been consumed with the production of exactly 2 molar equivalents of acid, as required for the removal of 2 carbon atoms from II to give a triazole dialdehyde.

The aldehyde gave a 2,4-dinitrophenylhydrazone (presumably the bis derivative) melting at 304–307° (dec.). Final identification of the aldehyde was made by oxidizing it with neutral permanganate to an acid which, after recrystallization from 30% acetic acid containing a few drops of conc. HCl, had the properties of the known *2-phenyl-2,1,3-triazole-4,5-dicarboxylic acid.* [Found: Neutral equivalent[8]; 126; m.p., 259–261° (dec.). Lit.:[9] Neutral equivalent, 116.5, m.p., 255–256° (dec.).]

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Some Reactions Leading to 8-Aminocaffeine

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8-Aminocaffeine is an important intermediate in the preparation of certain pharmacologically useful compounds. It has been prepared previously by three different methods and each method has certain disadvantages. The earliest and still most widely used method is due to Fischer,[1] who prepared this compound by heating 8-bromocaffeine with ammonia under pressure. Yields are excellent, but the method is not convenient for the laboratory preparation of moderate amounts of compound. Two other reports exist in the literature for the preparation of 8-aminocaffeine. The second is by Brooks and Rudner,[2] who reported that caffeine reacts with chloramine to give a low yield of a product which was thought to be 8-aminocaffeine; and the third is by Burgison and Wilson,[3] who obtained 8-aminocaffeine by reducing 8-nitrotheophylline to 8-aminotheophylline. Methylation of this compound yielded 8-aminocaffeine. The over-all yield for this latter method has not been reported.

We have prepared 8-aminocaffeine by two different routes. The first was by a Gabriel synthesis from 8-bromocaffeine using dimethylformamide as a solvent. This, in itself, would not be an improvement over the Fischer synthesis of this compound, as, generally, the *N*-substituted phthalimides have to be hydrolyzed in a sealed tube. In this case, however, hydrolysis was effected very easily by heating the *N*-(8-caffeinyl)phthalimide for a short period of time with dilute acid at atmospheric pressure. The second method consisted in heating 8-caffeinylhydrazine in either phenol or dimethylformamide solution. This latter reaction was discovered when an attempt to prepare 1,6-di(8-caffeinyl)-1,2,5,6-tetrazahexane from the reaction of 8-caffeinylhydrazine with ethylene bromide led unexpectedly to the formation of 8-aminocaffeine.

Although the yields in these reactions are not high, they do represent relatively simple laboratory methods of preparing 8-aminocaffeine. The second method is considered preferable since 8-caffeinylhydrazine can be obtained in quantitative yield from the reaction of 8-bromocaffeine with hydrazine hydrate and 8-caffeinylhydrazine can be converted to 8-aminocaffeine in 40–43% yield while the Gabriel synthesis resulted in only a 24% yield of 8-aminocaffeine.

EXPERIMENTAL

Microanalyses are by A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck Institut, Mulheim/Ruhr, Germany.

Gabriel Reaction. A mixture of 82 g. of 8-bromocaffeine (0.3 m.), 88 g. of phthalimide (0.6 m.). 56 g. of potassium carbonate and 500 ml. of dimethylformamide was refluxed for 18 hr. During this time the mixture became red and a yellow precipitate formed. The yellow precipitate was then dissolved in dilute hydrochloric acid and the solution refluxed for 15 min. After cooling and making the solution basic a white precipitate was obtained which was recrystallized from an ethanol-acetic acid mixture. The yield was 15 g. (24%) of white powder, m.p. >320°.

Anal. Calcd. for $C_8H_{11}N_5O_2$: C, 45.93; H, 5.30. Found: C, 45.95; H, 5.55.

Reaction of 8-caffeinylhydrazine in dimethylformamide. A solution of 3.5 g. of 8-caffeinylhydrazine in 100 ml. of dimethylformamide was refluxed for 14 hr. The solution became dark red in color. After cooling to −20°, 1.3 g. of a green precipitate were collected which after recrystallization from an ethanol-acetic acid mixture gave 0.7 g. of a tan product, m.p. >320°. This compound was identified as 8-aminocaffeine by the characteristic triplet peak it exhibited in the N—H region of the infrared and conversion to the known 8-diacetamidocaffeine. The yield was 40% before recrystallization.

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