added. The mixture was heated at reflux for one hour, and the reaction mixture concentrated to dryness. The residue was taken up in 50 ml. of 1.2 *M* hydrochloric acid and heated on a water-bath at 40–50° for 15 minutes. The mixture was concentrated to dryness under reduced pressure in a water-bath at 50°. The residue was dispersed in 30 ml. of water, and the insoluble phthalylhydrazide removed by filtration. The aqueous solution, on dilution with 75 ml. of 95% ethyl alcohol, precipitated 2.9 g. of carnosine hydrochloride as an amorphous, hygroscopic solid. It was converted to carnosine by passing an aqueous solution of the hydrochloride through an ion exchange column containing Deacidite. The aqueous eluate was concentrated to dryness and the residue was recrystallized from aqueous alcohol to give 0.6 g. of carnosine.

Anal. Calcd. for $C_9H_{14}O_3N_4$: N, 24.7. Found: N, 24.5.

(**Method B**).—The procedure was a modification of that described by Shuman and Boissonnas.[4d] To 1.78 g. of phthalylcarnosine (0.005 mole), there was added 25 ml. of 95% ethyl alcohol, 0.5 g. of triethylamine and 1.55 g. of phenylhydrazine. The mixture was refluxed for three hours on a water-bath. At the completion of the heating period, the clear yellow solution was cooled, and acidified with 1 g. of glacial acetic acid, and the mixture poured into 80 ml. of methyl ethyl ketone. An amorphous precipitate was obtained which was dissolved in 5 ml. of water and reprecipitated by the addition of 75 ml. of 95% ethyl alcohol. The dried product weighed 0.63 g., and after recrystallization from aqueous ethyl alcohol, 0.41 g. of carnosine was obtained.

DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY
YALE UNIVERSITY SCHOOL OF MEDICINE
NEW HAVEN, CONNECTICUT

Stereochemistry of 1,4-Addition. II. The Bromination of Butadiene

BY KURT MISLOW

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A recent paper[1] reports the 1,4-adduct of bromine and butadiene, 1,4-dibromo-2-butene (m.p. 53°), to have the *cis* configuration. This claim rests on the observed Raman frequency of 1655 cm.$^{-1}$, associated with *cis*-ethylenic double bonds,[2] and is the basis for the assumption that butadiene enters into reaction with bromine in the "bent" or s-*cis* form.

It has been shown that a frontal transition state cannot be of any appreciable importance in the 1,4-addition of chlorine to butadiene[3]; the implied claim that this argument does not apply in the case of bromine addition would therefore be of considerable interest. The following observations may however be marshaled as convincing evidence in favor of the identity of 1,4-dibromo-2-butene (m.p. 53°), I, with *trans*-1,4-dibromo-2-butene. (a) The infrared spectrum of I exhibits a pronounced and characteristic[4] *trans* peak near 10.3 μ, absent in the saturated analog.[5]

(b) Lithium aluminum hydride reduction of I affords *trans*-2-butene, as evidenced by conversion to *meso*-2,3-dibromobutane.[6] The present author has repeated this experiment and obtained *meso*-2,3-dibromobutane, b.p. 46° (14 mm.), $n^{25}D$ 1.5088 (repd.[7] $n^{25}D$ 1.5091).

(c) The dipole moment of I, 1.63 *D*, is similar to that of *trans*-1,4-dibromo-2,3-dimethyl-2-butene, 1.72 *D*, but smaller than that of the *cis*-isomer 2.49 *D*.[8]

(d) A *cis*-1,4-dibromo-2-butene (II), prepared from authentic *cis*-2-butene-1,4-diol,[9] differs from I in a manner characteristic[4a] of the relative properties of *cis* and *trans* isomers. Thus, the melting point of I is higher than that of II, II is thermally unstable with respect to I, and I and II give different 1,2,3,4-tetrabromobutanes, m.p. 116 and 39°, respectively.

The evidence here adduced compels us to maintain that as yet no satisfactory experimental basis exists for the view of frontal attack in the 1,4-addition of halogen to butadienes.[10] Equally, the tetrabromides, m.p. 116 and 39°, must be assigned the *meso* and racemic configurations, respectively, the claim[1] to the contrary notwithstanding.

(1) Ya. M. Slobodin and S. A. Zaboev, *Zhur. Obshchei Khim.* (*J. Gen. Chem., U. S. S. R.*), **22**, 603 (1952).

(2) *E. g.*, N. Sheppard and D. M. Simpson, *Quart. Revs.*, **6**, 1 (1952).

(3) K. Mislow and H. M. Hellman, THIS JOURNAL, **73**, 244 (1951).

(4) *E.g.* (a) L. Crombie, *Quart. Revs.*, **6**, 101 (1952); (b) L. Crombie, *J. Chem. Soc.*, 2997 (1952); (c) F. Sondheimer, THIS JOURNAL, **74**, 4040 (1952); (d) K. Mislow, *ibid.*, **74**, 5155 (1952).

(5) A Baird Model B instrument with 0.1-mm. cells was employed. In this connection, the assistance afforded by correspondence with Dr. Ralph Nusbaum and his staff, Spectroscopy Section, Atomic Energy Project, U. C. L. A., Los Angeles, Calif., is gratefully acknowledged.

(6) L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949).

(7) R. T. Dillon, W. G. Young and H. J. Lucas, *ibid.*, **52**, 1953 (1930).

(8) O. J. Sweeting and J. R. Johnson, *ibid.*, **68**, 1057 (1946).

(9) A. Valette, *Ann. chim.*, [12] **3**, 644 (1948).

(10) Some recent developments pertaining to this concept as originally expressed (ref. 3): the 1,4-addition of sulfur dioxide to terminally substituted butadienes involves the s-*cis* form of butadiene (O. Grummitt and J. Splitter, THIS JOURNAL, **74**, 3924 (1952)); halonium ions can be incorporated in a stable symmetrical 5-membered ring as part of a diphenyl system (R. B. Sandin and A. S. Hay, *ibid.*, **74**, 274 (1952)); the argentation constants of monoargentated *cis*-1,2-diiodoethylene and *o*-diiodobenzene are indicative of the existence of symmetrical 5-membered onium rings (L. J. Andrews and R. M. Keefer, *ibid.*, **73**, 5733 (1951)).

DEPARTMENT OF CHEMISTRY
NEW YORK UNIVERSITY
NEW YORK, N. Y.

D-Glucuronolactone Isonicotinyl Hydrazone

BY PETER P. T. SAH

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D-Glucuronolactone isonicotinyl hydrazone, a new compound with comparatively low toxicity and very high antitubercular activity *in vitro* as well as *in vivo*,[1] may be prepared easily by the following procedure.

D-Glucuronolactone (Eastman Kodak Co., 88 g.) was placed in a 3-l. round-bottomed flask and covered with 1.5 liters of methyl alcohol (acetone-free). The mixture was boiled gently on the steam-bath for 10 minutes when a clear solution was obtained. To the hot solution, isonicotinic acid hydrazide (Pfizer, 70 g.) was added all at once. The mixture was boiled vigorously for 10 minutes and the clear solution filtered without suction through a piece of lens paper into a 2-l. erlenmeyer flask. After standing for 24 hours at room temperature, the beautiful crystals (white rods and narrow plates) were filtered off with suction, washed with a small amount of methyl alcohol, and sucked completely to dryness. The product was dried in a vacuum desiccator for 3 days; yield 148 g. The product thus ob-

(1) Biological tests were performed by W. B. Sutton of the Lilly Research Laboratories, Indianapolis, Indiana, and the results later confirmed by Dr. E. G. Roberts of Stanford University School of Medicine. The new drug is now undergoing clinical trial. Results will be reported elsewhere.