where B is a constant, ν is the frequency of the incident plane polarized light, and ν_0 is the frequency of the electronic transition making the dominant contribution. At Moffitt's suggestion, Doty and Yang[3] have measured the rotatory dispersion of PBG, confirming Equation (3). We wish to remark that our theory also predicts the same type of anomalous rotatory dispersion. Thus, the rotatory power is proportional to $\alpha_1^2\beta^2$ or $(\alpha_{||} - \alpha_\perp)^2$ where $\alpha_{||}$ and $\alpha_\perp$ are the residue polarizabilities parallel and perpendicular to the direction of the helix.[7] If the quantity $\alpha_1\beta$ can be represented by a single Drude dispersion term, $f_0/(\nu_0^2 - \nu^2)$, Equation (3) is at once obtained.

(7) J. G. Kirkwood, *J. Chem. Phys.*, **5**, 479 (1937).

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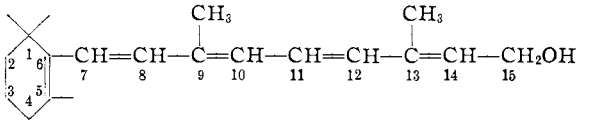
RECEIVED MAY 2, 1956

THE SYNTHESIS AND CONFIGURATION OF NEO-b VITAMIN A AND NEORETINENE b

Sir:

We wish to report that neo b vitamin A and neoretinene b have now been obtained by a synthetic route which establishes their configuration as 11-mono-*cis*.[1] A previously reported 11-*cis* vitamin A,[2] synthesized by the same route, has now been found to have the 11,13-di-*cis* configuration.



Allylic rearrangement of methylvinylethynylcarbinol with moderately strong acid at 80° yields a mixture of the two isomeric 3-methylpent-3-en-1-yn-5-ols.[5] The predominant isomer (**a**),[4] hitherto presumed *trans*,[3,5] showed after distillation through a 100-plate column: b.p. 65° (9.4 mm.), $n^{20}D$ 1.4820, λ_{max} 223 mμ (ϵ 11,000); C–O stretching band 9.92 μ (ϵ 139)[6] (*Anal.* Calcd. for C_6H_8O: C, 74.97; H, 8.39. Found: C, 75.13; H, 8.50); *p*-nitrobenzoate, m.p. 61–62°.

The other isomer (**b**),[4] purified through its *p*-nitrobenzoate, showed: b.p. 73° (9.4 mm.), $n^{20}D$ 1.4934, λ_{max} 224 mμ (ϵ 13,100); C–O stretching band 9.94 μ (ϵ 81) (*Anal.* Found: C, 75.11; H, 8.46). *p*-Nitrobenzoate, m.p. 63–64°; the mixed *p*-nitrobenzoates melted at 50–55°.

Catalytic semihydrogenation yielded the corresponding 3-methylpentadienols, which were acetylated at 25° with acetic anhydride in pyridine. The acetate from **a** *did not add* maleic anhydride at room temperature, while that from **b** gave a 60–70% yield of adduct under the same conditions (*Anal.* Calcd. for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.35; H, 6.01). *This establishes* **a** *as the cis isomer and* **b** *as the trans isomer, contrary to previous assumptions.*

The Grignard reagent from **a** condensed with the "C_{14} aldehyde" to yield the known corresponding glycol[7]; white crystals, m.p. 58°, λ_{max} 229 mμ (ϵ 14,800); C–O stretching band 10.00 μ (ϵ 242). In view of the configuration of **a**, this known glycol must have a 13-*cis* bond. Similarly, **b** was converted to the 13-*trans* isomer, an oil, purified and demonstrated as homogeneous by alumina chromatography: λ_{max} 230 mμ (ϵ 16,700), C–O stretching band at 9.93 μ (ϵ 196) (*Anal.* Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.42; H, 9.96).

Monoacetylation of each glycol, followed by dehydration (tosic acid in benzene), mild hydrolysis, and alumina chromatography, gave in 40–50% over-all yield the corresponding isomer of 11-dehydrovitamin A, a deep yellow oil. In each case only one stereoisomer was produced: 13-*cis:* λ_{max} 317 mμ (ϵ 32,000), C–O stretching band 10.04 μ (ϵ 183), *trans* —CH=CH— band 10.35 μ (ϵ 176) (*Anal.* Calcd. for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.47; H, 10.06). β-Anthraquinonecarboxylate (cream-white) m.p. 111–112°, $\lambda\lambda_{max}^{cyclohex}$ 256 mμ (ϵ 62,700), 321 mμ (ϵ 38,100). 13-*trans:* λ_{max} 317 mμ (ϵ 34,500), C–O stretching band 9.95 μ (ϵ 112), *trans* —CH=CH— band 10.36 μ (ϵ 182) (*Anal.* Found: C, 84.33; H, 10.21). β-Anthraquinonecarboxylate (deep golden-yellow), m.p. 113.5–115°, $\lambda\lambda_{max}^{cyclohex}$ 256 mμ (ϵ 63,000), 321.5 mμ (ϵ 40,500). A mixture of the two anthraquinonecarboxylates melted at 90–95°.

Catalytic semihydrogenation of 11-dehydro-13-*cis*-vitamin A gave 11,13-di-*cis* vitamin A, the 311-mμ isomer reported previously.[2] The yield of chromatographically purified product, a viscous golden-yellow oil, was 50%; λ_{max} 311 mμ (ϵ 26,000); C–O stretching band 10.03 μ (ϵ 158); *trans* —CH=CH— bond 10.34 μ (ϵ 180) (*Anal.* Calcd. for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 83.72; H, 10.62.) First-order rate constant with excess maleic anhydride in ether at 25°: 0.0054/hr. *p*-Phenylazobenzoate, m.p. 99°. Iodine isomerization in the dark produced all-*trans* vitamin A, λ_{max} 325 mμ.[8] Oxidation with manganese dioxide gave the aldehyde, which showed no capacity to produce rhodopsin when treated in the dark with opsin.

Catalytic semihydrogenation of 11-dehydro-13-*trans*-vitamin A gave 11-mono-*cis* vitamin A. The yield of chromatographically purified product, a viscous yellow oil, was 40%; λ_{max} 321 mμ (ϵ 32,500); C–O stretching band 10.08 μ (ϵ 110); *trans* —CH=CH— band 10.35 μ (ϵ 191) (*Anal.* Found: C, 83.22; H, 10.67). First-order rate constant with excess maleic anhydride, same conditions as above: 0.03/hr. *p*-Phenylazobenzoate, m.p. 67°. Iodine isomerization in the dark produced all-*trans* vitamin A, λ_{max} 325 mμ.[8] The ultraviolet and infrared absorption curves of 11-mono-*cis* vitamin A were identical with those of an authentic specimen of neo b vitamin A.[9]

(1) The numbering system used here corresponds to that officially adopted for carotenoids: *Chem. and Eng. News*, **24**, 1235 (1946).

(2) G. Wald, P. K. Brown, R. Hubbard and W. Oroshnik, *Proc. Nat. Acad. Sci.*, **41** (7), 438 (1955).

(3) L. J. Ferrari, Thesis, Newark College of Engineering, 1955. Personal communication, Dr. D. F. Hinkley of Merck and Co.

(4) The author is indebted to Dr. D. F. Hinkley of Merck and Co. for a supply of pure **a** and crude **b**.

(5) G. W. H. Cheeseman, I. M. Heilbron, E. R. H. Jones, F. Sondheimer and B. C. L. Weedon, *J. Chem. Soc.*, 2031 (1949).

(6) Ultraviolet and infrared data were obtained on ethanolic and carbon bisulfide solutions, respectively, unless otherwise specified

(7) O. Isler, A. Ronco, W. Guex, N. C. Hindley, W. Huber, K. Dialer and M. Kofler, *Helv. Chim. Acta*, **32**, 489 (1949).

(8) The absence of iodine-stable 9-*cis*-vitamin A in the isomerate proves the absence of this configuration in the original compound.

(9) Prepared by the potassium borohydride-reduction of neoretinene b (*cf.* J. M. Dieterle and C. D. Robeson, *Science*, **120**, 219 (1954).

Manganese-dioxide oxidation of the synthetic 11-mono-*cis* isomer yielded the corresponding aldehyde. The product of this reaction was identified as neoretinene b by Prof. George Wald[10] through its condensation with opsin to yield rhodopsin.

(10) Biological Laboratories, Harvard University, Cambridge, Mass.

ORGANIC CHEMISTRY DIVISION
ORTHO RESEARCH FOUNDATION WILLIAM OROSHNIK
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RECEIVED MARCH 23, 1956

A NEW INOSAMINE FROM AN ANTIBIOTIC

Sir:

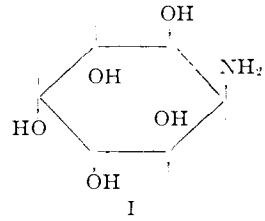
The occurrence of non-synthetic amino analogs of inositol ("inosamines")[1] has been reported only in the case of the streptomycin[2] and neomycin[3] families of antibiotics; in each case the compound was a diamine.

We have isolated a *mono*-inosamine having a configuration unprecedented in natural inositols. By hydrolysis of a new antibiotic (designated in these laboratories as 1703–18B[4]) with concentrated hydrochloric acid, we obtained a compound, m.p. 217–221[6] (dec.) (*Anal.* Calcd. for $C_6H_{13}NO_5 \cdot HCl$ (215.6): C, 33.42; H, 6.54; N, 6.50; Cl, 16.44. Found: C, 33.54; H, 6.83; N (Dumas), 6.20; N (Van Slyke), 6.52; Cl, 16.37) which yielded a free base, m.p. 238–240° (dec.) (*Anal.* Calcd. for $C_6H_{13}NO_5$ (179.2): C, 40.22; H, 7.31; N, 7.82. Found: C, 40.40; H, 7.30; N, 7.87).

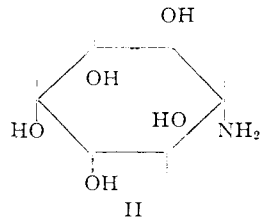
The base consumed 6.14 moles of periodate (inositol, 6.20) with no formaldehyde formation. The optical rotation of the base in water or in aqueous ammonium molybdate[7] was zero; the hexa-acetate, m.p. 277.5–278.5° (*Anal.* Calcd. for $C_{18}H_{25}NO_{11}$ (431.4): C, 50.11; H, 5.84; N, 3.25; acetyl, 59.85. Found: C, 49.88; H, 6.00; N, 3.32; acetyl 58.61) in chloroform was also optically inactive, and the inactive base was recovered from its nicely crystalline salt (m.p. 230–232°) with *d*-camphorsulfonic acid.

The above data show the compound to be a meso-inosamine. Three of the eight possible meso-inosamines have been reported[1,8,9]; the physical properties of the new inosamine do not correspond to those of any of them.

Under the conditions described by Angyal and MacDonald[10] the phthalimido derivative,[11] m.p. 255–261° (dec.) (*Anal.* Calcd. for $C_{14}H_{15}NO_7$ (309.3): C, 54.37; H, 4.89; N, 4.53. Found: C, 54.03; H, 5.08; N, 4.86) of the inosamine furnished a single, racemic *mono*-acetonide, m.p. 210–212° (*Anal.* Calcd. for $C_{17}H_{19}NO_7$: C, 58.45; H, 5.48; N, 4.01. Found: C, 58.23; H, 5.84; N, 3.92) which took up one mole of periodate. Only two structures, I and II, are thus possible for the inosamine.

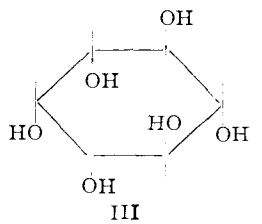


I

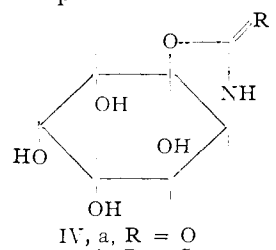


II

Nitrous acid deamination of the inosamine produced the known "meso" inositol III. In the inosamine series this reaction is known to proceed with inversion[12]; therefore, our compound is I.



III



IV, a, R = O
b, R = S

Reaction of the inosamine with carbobenzyloxy chloride provides further evidence for structure I; under appropriate conditions the chief product is the cyclic carbamate IVa, m.p. 203–205° (*Anal.* Calcd. for $C_7H_{11}NO_6$ (205.2): C, 40.97; H, 5.40; N, 6.83. Found: C, 41.20; H, 5.56; N, 6.81). The carbamate consumed 2.92 moles of periodate (mannitol standard, 5.00), as required for structure IVa. Similarly, the thiocarbamate IVb, m.p. 245° (dec.) is produced by reaction of I with phenyl isothiocyanate.[8b,13] (*Anal.* Calcd. for $C_7H_{11}NSO_5$ (221.2): C, 37.99; H, 5.01; N, 6.33; S, 14.49. Found: C, 38.16; H, 5.23; N, 6.37; S, 14.68).

We believe that this constitutes the first occurrence of a mono-inosamine and of a cyclitol of this configuration. The structure of antibiotic 1703–18B will be the subject of a future publication.

(1) H. E. Carter, R. K. Clarke, B. Lytle and G. E. McCasland, *J. Biol. Chem.*, **175**, 683 (1943).

(2) (a) H. E. Carter, *et al.*, *Science*, **103**, 53 (1946); (b) J. Fried, A. Boyak and O. Wintersteiner, *J. Biol. Chem.*, **162**, 393 (1946); (c) R. L. Peck, *et al.*, THIS JOURNAL, **68**, 776 (1946).

(3) F. A. Kuehl, M. N. Bishop and K. Folkers, *ibid.*, **73**, 881 (1951).

(4) On the basis of published data[5] it appears that this antibiotic is similar to hygromycin, although not identical with it.

(5) R. L. Mann, R. M. Gale and F. R. van Abeele, *Antibiotics and Chemotherapy*, **3**, 1279 (1953).

(6) All melting points were determined on the Kofler hot stage and are corrected.

(7) W. W. Pigman and R. M. Goepp, Jr., "Chemistry of the Carbohydrates," Academic Press, New York, N. Y., 1948, p. 248.

(8) (a) L. Anderson and H. A. Lardy, THIS JOURNAL, **72**, 3141 (1950); (b) G. E. McCasland, *ibid.*, **73**, 2295 (1951).

(9) (a) J. M. Grosheintz and H. O. L. Fischer, *ibid.*, **70**, 1479 (1948); (b) H. D. Orloff, *Chem. Revs.*, **54**, 347 (1954).

(10) S. J. Angyal and C. G. MacDonald, *J. Chem. Soc.*, 686 (1952).

(11) We are indebted to Dr. B. R. Baker for suggesting this derivative for the purpose.

(12) (a) T. Posternak, *Helv. Chim. Acta*, **33**, 1597 (1950); (b) H. Straube-Rieke, H. A. Lardy and L. Anderson, THIS JOURNAL, **75**, 694 (1953).

(13) M. Roux, *Ann. Chim.*, [8] **1**, 112 (1904). The question of tautomeric forms is immaterial to our argument.

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RECEIVED MAY 2, 1956

IDENTIFICATION OF ENZYMATICALLY ACTIVE SULFATE AS ADENOSINE-3′-PHOSPHATE-5′-PHOSPHOSULFATE[1]

Sir:

DeMeio's pioneering work has shown that enzymatic sulfate activation is an ATP-linked reac-

(1) This investigation was supported by research grants from the Cancer Institute of the National Institutes of Health, Public Health Service, and the Life Insurance Medical Research Fund.