data of III are compatible with structure VII. In view of the chemical shift (τ 7.01) reported for the C-4 hydrogen of 1,3-dimethyltricyclo[1.1.1.0^{4,5}]pentane,[11] the τ value 6.67 is in the region expected for the hydrogens directly attached to the tetrahedrane system. Since diphenyltricyclo[1.1.1.0^{4,5}]pentanol-2 showed a maximum at 269 mμ (ϵ 1.1 $\times$ 10^4)[12] the strong ultraviolet absorption of III, similar to that of diphenylacetylene but shifted toward shorter wave length, is reasonable. Thus, having eliminated all other possible structures, we must conclude that compound III possesses the tricyclo[1.1.0.0^{2,4}]butane system.

The thermal stability of the tetrahedrane is surprising. Although a crude sample decomposed readily, the analytically pure material has been stored under nitrogen without decomposition at least for a month. We plan to prepare a sufficient quantity of this compound for further investigation.

Acknowledgment. The authors are grateful to the National Research Council of Canada for financial support.

(11) G. L. Closs and R. B. Larrabee, *Tetrahedron Letters*, 287 (1965). It appears that the chemical shift of the C-1 hydrogen of the bicyclobutane system is very sensitive to the angle between the C–H bond and the plane of the cyclopropane. The bridging of C-2 and C-4 by a carbon chain, thus further distorting the bicyclobutane system, tends to shift the signal downfield.

(12) S. Masamune, unpublished results.

(13) A University of Alberta postdoctoral Fellow.

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6-Hemi-L-selenocystine-oxytocin and 1-Deamino-6-hemi-L-selenocystine-oxytocin, Highly Potent Isologs of Oxytocin and 1-Deamino-oxytocin[1]

Sir:

Considerable attention has been given to the study of selenium isologs of naturally occurring sulfur compounds. The present communication concerns the

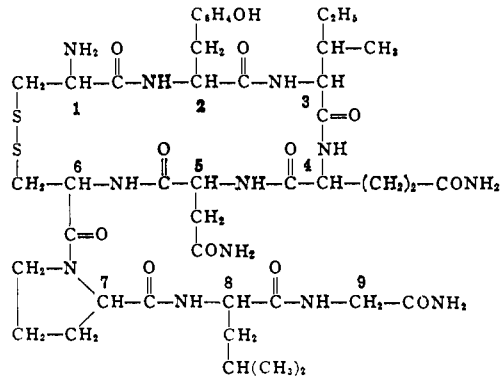

Figure 1. Structure of oxytocin.

syntheses of 6-hemi-L-selenocystine-oxytocin (6-seleno-oxytocin) and its deamino analog, two molecules which may be considered as being isosteric with oxytocin (Figure 1) and 1-deamino-oxytocin, respectively.

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The isologs have been synthesized by the stepwise *p*-nitrophenyl ester procedure earlier employed in this laboratory for the synthesis of oxytocin[2] and deamino-oxytocin.[3] The tripeptide, L-prolyl-L-leucyl-glycinamide,[4] was coupled with *p*-nitrophenyl N-carbobenzoxy-Se-benzyl-DL-selenocysteinate (m.p. 98–99°), prepared by condensation of *p*-nitrophenol with N-carbobenzoxy-Se-benzyl-DL-selenocysteine[5] in the presence of dicyclohexylcarbodiimide. *Anal.* Calcd. for $C_{24}H_{22}N_2O_6Se$: C, 56.1; H, 4.32; N, 5.45. Found: C, 56.2; H, 4.38; N, 5.41.

The protected tetrapeptide, N-carbobenzoxy-Se-benzyl-L-selenocysteinyl-L-prolyl-L-leucylglycinamide,[6] was separated from its diastereoisomer in 78% of the theoretical yield by crystallization from ethyl acetate followed by the slow addition of ethyl ether with the resulting ratio of 4:1.

After removal of the carbobenzoxy group by HBr–acetic acid the tetrapeptide was lengthened step by step as in the synthesis of oxytocin[2] and 1-deamino-oxytocin[3] to give the protected intermediates, N-carbobenzoxy-S-benzyl-L-cysteinyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparginyl-Se-benzyl-L-selenocysteinyl-L-prolyl-L-leucylglycinamide and S-benzyl-β-mercaptopropionyl-L-tyrosyl-L-isoleucyl-L-glutaminyl-L-asparaginyl-Se-benzyl-L-selenocysteinyl-L-prolyl-L-leucylcinamide.[7] The isologs were obtained after the cleavage of the protecting groups from these intermediates by sodium in liquid ammonia, followed by ring closure through air oxidation in aqueous solution at pH 6.8 and by treatment with ferricyanide until the solutions gave negative reactions to Ellman's reagent.[8] Subsequently, the ferrocyanide and ferricyanide ions were removed with the ion-exchange resin AG3X4 in the chloride form.

In the case of 6-seleno-oxytocin the solution containing the crude material was concentrated to a small volume and subjected to countercurrent distribution in the system 1-butanol–1-propanol–0.5% aqueous acetic acid containing 0.1% pyridine (4:1:5). The desired isolog was found to have an approximate *K* value of 0.52 as detected by determination of the Folin–Lowry color values,[9] and the material representing this peak was isolated by lyophilization; $[\alpha]^{20.5}D$ −10.5° (*c* 0.5, 1 *N* acetic acid). *Anal.* Calcd. for $C_{43}H_{66}N_{12}O_{12}SSe$: N, 15.9. Found: N, 15.6. The 6-seleno-oxytocin was indistinguishable from oxytocin upon thin-layer chromatography on silica gel G in the upper phase of the solvent system 1-butanol–acetic acid–water (4:1:5, ascending) and gel filtration (Sephadex G-25) in 0.2 *N* acetic acid.

The 1-deamino-6-hemi-L-selenocystine-oxytocin (deamino-6-seleno-oxytocin) was isolated by countercurrent distribution in a 1-butanol–benzene–0.05%

(2) M. Bodanszky and V. du Vigneaud, *J. Am. Chem. Soc.*, 81, 5688 (1959).

(3) V. du Vigneaud, G. Winestock, V. V. S. Murti, D. B. Hope, and R. D. Kimbrough, Jr., *J. Biol. Chem.*, 235, PC 64 (1960); D. B. Hope, V. V. S. Murti, and V. du Vigneaud, *ibid.*, 237, 1563 (1962).

(4) C. Ressler and V. du Vigneaud, *J. Am. Chem. Soc.*, 76, 3107 (1954).

(5) J. Janicki, J. Skupin, and B. Zagalak, *Roczniki Chem.*, 36, 353 (1962).

(6) W. Frank, *Hoppe-Seylers Z. Physiol. Chem.*, 339, 222 (1964).

(7) All intermediate peptides showed correct C, H, and N analyses, which were carried out by Galbraith Laboratories, Knoxville, Tenn.

(8) G. L. Ellman, *Arch. Biochem. Biophys.*, 82, 70 (1959).

(9) O. H. Lowry, N. J. Rosebrough, A. L. Farr, and R. J. Randall, *J. Biol. Chem.*, 193, 265 (1951).

acetic acid system (3:2:5) at an approximate K value of 1.04; $[\alpha]^{21}D$ −54.0° (c 1, 1 N acetic acid). *Anal.* Calcd. for $C_{43}H_{65}N_{11}O_{12}SSe$: C, 49.7; H, 6.31; N, 14.8. Found: C, 49.6; H, 6.50; N, 14.6. The deamino-6-seleno-oxytocin was indistinguishable from deamino-oxytocin[3] upon thin-layer chromatography and gel filtration under the conditions described for 6-seleno-oxytocin.

Upon bioassay 6-seleno-oxytocin was found to possess approximately 420 units/mg. of oxytocic activity,[10] 400 units/mg. of avian vasodepressor activity,[11] 400 units/mg. of milk-ejecting activity,[12] and 4 units/mg. of pressor activity.[13] The deamino-6-seleno-oxytocin was found to possess approximately 500 units/mg. of oxytocic activity, 620 units/mg. of avian vasodepressor activity, 400 units/mg. of milk-ejecting activity, and 1 unit/mg. of pressor activity. Thus the replacement of sulfur by selenium in the 6 position yields highly potent isologs of oxytocin and deamino-oxytocin although they are somewhat lower in potency than the hormone itself and its comparable deamino analog. The results also show that with 6-seleno-oxytocin, which is practically isosteric with oxytocin, the replacement of the free amino group by hydrogen enhances the oxytocic and avian vasodepressor activities and lowers the pressor activity as it does in the case of oxytocin.[14]

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(10) Oxytocic assays were performed according to the method of Holton (*Brit. J. Pharmacol.*, **3**, 328 (1948)) on uteri from rats in natural estrus with the use of magnesium-free van Dyke–Hastings solution as employed by Munsick (*Endocrinology*, **66**, 451 (1960)).

(11) R. A. Munsick, W. H. Sawyer, and H. B. van Dyke, *ibid.*, **66**, 860 (1960).

(12) H. B. van Dyke, K. Adamsons, Jr., and S. L. Engel, *Recent Progr. Hormone Res.*, **11**, 1 (1955); W. Y. Chan, *J. Pharmacol.*, **147**, 48 (1965).

(13) "The Pharmacopeia of the United States of America," 16th Revision, Mack Printing Co., Easton, Pa., 1960, p. 793.

(14) W. Y. Chan and V. du Vigneaud, *Endocrinology*, **71**, 977 (1962).

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The Vibrational State of Hydroxyl Radicals Produced by Flash Photolysis of a Water–Ozone–Argon Mixture

Sir:

A number of gas phase reactions of the general type[1]

$$A + BCD \longrightarrow AB + CD + \Delta H \qquad (1)$$

are known in which the products are formed with excess vibrational energy. The generalization has been made that "the molecule AB with the newly formed bond, may take a high proportion of the exothermic energy of reaction in the form of unequilibrated vibrational energy."[1] Only two experiments have been performed in which the state of the CD molecule was observed.

(1) R. G. W. Norrish, *Inst. Intern. Chim. Solvay, Conseil Chim.*, **12**, 99 (1964).

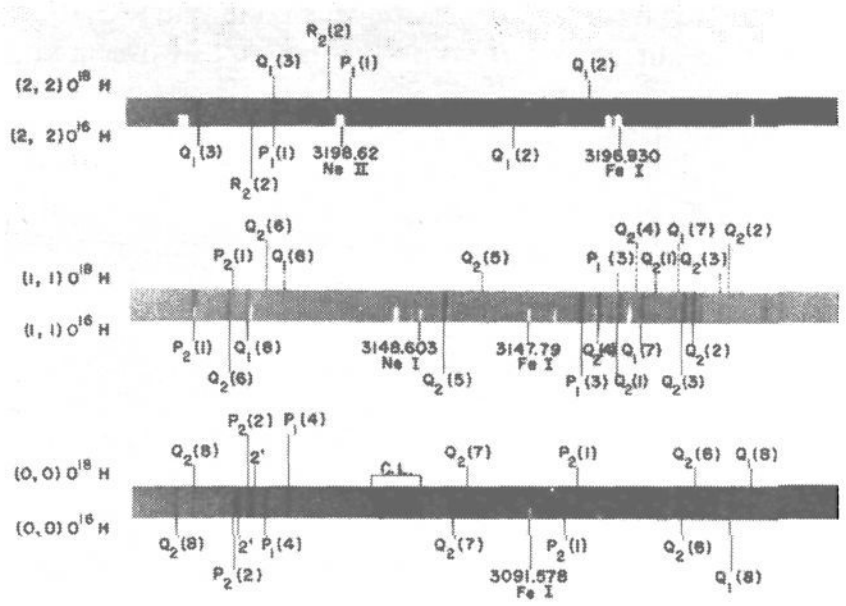

Figure 1. Absorption spectra from flash photolysis of ozone–water(O^{18})–argon mixture.

A study of reaction 2[2] by flash photolysis and absorption

$$Cl + ClNO \longrightarrow Cl_2 + NO + 20 \text{ kcal.} \qquad (2)$$

spectroscopy has shown the absence of vibrationally excited NO, but no attempt was made to observe excited Cl_2. An infrared emission experiment in the flow system

$$H + ClNO \longrightarrow HCl + NO + 65 \text{ kcal.} \qquad (3)$$

has shown the presence of vibrationally excited HCl, but the concentration of excited NO was below the limit of detectability.[3]

This communication deals with the reaction[4]

$$O(^1D) + H_2O \longrightarrow OH + OH + 29 \text{ kcal.} \qquad (4)$$

in which the products are identical and the new bond must be distinguished by isotopic labeling. It is also unlike reactions 2 and 3 in that it must involve conversion of electronic energy of a reactant to vibrational energy of a product, since reaction 4 with ground-state $O(^3P)$ atoms is endothermic by 16 kcal. The $O(^1D)$ was generated by the flash photolysis of ozone in the ultraviolet. The water vapor mixed with the ozone was highly enriched in O^{18}. The OH was observed in the near-ultraviolet band system and the small isotope shift was used to distinguish between the old and the new OH bonds.

The annular flash photolysis system used here will be described in a later publication. The 1000-joule photolysis flash lamp gave a light pulse of about 10-μsec. duration. The effective path length through the photolyzed gas was 180 cm. Absorption spectra were obtained with a quartz capillary flash lamp. The plane grating vacuum spectrograph used here[5] has a resolution greater than 300,000 and a reciprocal dispersion of 0.15 Å./mm.

(2) N. Basco and R. G. W. Norrish, *Proc. Roy. Soc.* (London), **A268**, 291 (1962).

(3) J. K. Cashion and J. C. Polanyi, *J. Chem. Phys.*, **35**, 600 (1961); P. E. Charters, B. N. Khare, and J. C. Polanyi, *Discussions Faraday Soc.*, **33**, 276 (1962).

(4) W. D. McGrath and R. G. W. Norrish, *Proc. Roy. Soc.* (London), **A254**, 317 (1960); N. Basco and R. G. W. Norrish, *ibid.*, **A260**, 293 (1961).

(5) P. E. Rouse, Jr., D. L. Upham, R. Engleman, Jr., and H. M. Peek, to be published.