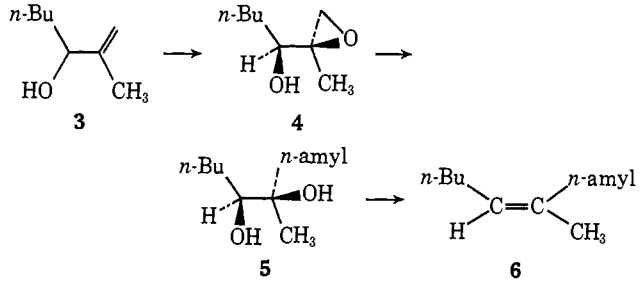
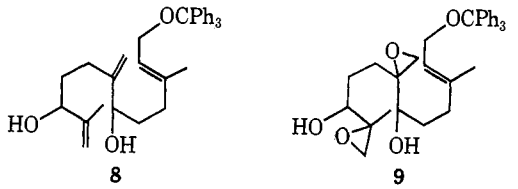
was heated in acetic anhydride at 130° for 2.5 hr to produce (*Z*)-6-methyl-5-undecene (**6**, 70% yield from **5**):



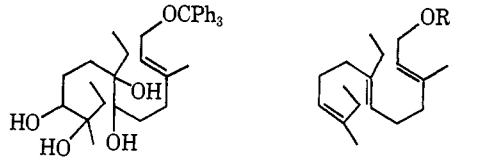
3 **4** **5** **6**

nmr (CCl_4, TMS) δ 1.65 (s, 3 H, $=CCH_3$), 5.03 (bt, 1 H, J = 7 Hz, =CH); >97% pure by glpc analysis.

The synthesis of hormone **1** begins with the known diol **8** (previously prepared from farnesol (**2**) by van Tamelen and McCormick[1]) and employs a series of reactions which parallel those described above for the stereoselective generation of olefin **6**. The bisallylic alcohol **8** was transformed to the bisepoxy alcohol **9** by reaction with vanadium acetylacetonate–*tert*-butyl hydroperoxide in benzene at 25° for 2 hr. After removal of the benzene, the crude product was subjected to the action of 8 equiv of ethereal lithium dimethylcopper at 0° for 12 hr. The tetraol trityl ether **10**, isolated by thin-layer chromatography (58% yield based on **8**), was homogeneous by silica gel tlc analysis using ethyl acetate as eluent (R_f = 0.60). Treatment of the tetraol **10** with excess *N*,*N*-dimethylformamide dimethyl acetal at 25° for 12 hr afforded the bisdioxolane derivative, which was subsequently heated at 130° with acetic anhydride to furnish the triene trityl ether **11** in 33% yield, homogeneous by tlc: nmr (100 MHz, $CDCl_3$, TMS) δ 0.94 and 0.86 (t, 3 H each), 1.46 (s, 3 H), 1.66 (s, 3 H), 3.61 (d, 2 H), 5.08 (bt, 2 H), 5.44 (bt, 1 H). Removal of the trityl group by 5% perchloric acid in tetrahydrofuran at 0° for 1.5 hr followed by chromatography on silica gel led to the desired bishomofarnesol **12** in essentially quantitative yield. Alcohol **12** exhibited appropriate spectral properties[9-11] and was identified, following acetylation, by tlc and glpc comparison with an authentic sample of acetate **13**.[12,13]



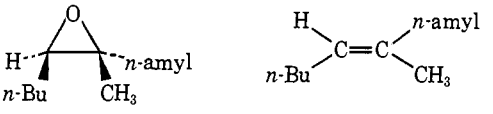
8 **9**



10 **11**, R = CPh_3; **12**, R = H; **13**, R = Ac

This completes the formal synthesis of C_{18} juvenile hormone **1** since Corey has already converted alcohol **12** to the natural product.[9]

The stereochemical control and the flexibility inherent in this approach to the construction of trisubstituted olefins is further demonstrated by the following experiments. The vicinal diol **5** on successive treatment with *n*-butyllithium (2 equiv) and *p*-toluenesulfonyl chloride (1 equiv) at 25° for 2 hr was converted to epoxide **14** in 73% yield. The oxirane moiety in **14** was stereospecifically reduced to the corresponding olefin by the procedure of Cornforth[14,15] producing (*E*)-6-methyl-5-undecene (**15**) in 80% yield: nmr (CCl_4, TMS) δ 1.59 (s, 3 H, $=CCH_3$), 5.05 (bt, 1 H, J = 7 Hz, =CH).[16] Thus, taken together with the aforementioned results, these processes allow the synthesis of either olefinic isomer with high stereospecificity and in good yield.



14 **15**

Acknowledgment. This collaborative work grew out of an exchange of ideas between H. Y. and K. B. S. at the first U. S.–Japan Seminar on Natural Product Synthesis (NSF sponsored, Tokyo, 1972). One of us (K. B. S.) thanks the National Science Foundation (GP-30485X), Chevron Research Co., and Mobil Foundation for support of the research at M.I.T. J. D. C. is grateful to the National Science Foundation for a Graduate Fellowship (1973–1975).

(9) E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, and B. W. Erickson, *J. Amer. Chem. Soc.*, 90, 5618 (1968).
(10) J. A. Katzenellenbogen, Ph.D. Thesis, Harvard University, 1969.
(11) E. J. Corey and J. Yamamoto, *J. Amer. Chem. Soc.*, 92, 6636 (1970).
(12) We thank Dr. K. Kondo and associates for a generous comparison sample of the acetate **13**.
(13) Our product is contaminated with a maximum of 7% of unidentified impurities.
(14) J. W. Cornforth, R. H. Cornforth, and K. K. Mathes, *J. Chem. Soc.*, 112 (1959).
(15) The epoxide **14** was also converted to (*Z*)-olefin **6** by treatment with lithium diphenylphosphide followed by methyl iodide (30% yield): E. Vedejs and P. L. Fuchs, *J. Amer. Chem. Soc.*, 95, 822 (1973).
(16) For stereochemical assignments of **6** and **13**, see G. D. Abrams, W. R. Bartlett, V. A. Fung, and W. S. Johnson, *Bioorg. Chem.*, 1, 243 (1971).

Shin Tanaka, Hisashi Yamamoto, Hitosi Nozaki
Department of Chemistry, Kyoto University
Yoshida, Kyoto 606, Japan

K. B. Sharpless,* R. C. Michaelson, J. D. Cutting
Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received March 25, 1974

Electrochemical Synthesis and Structure of a New Cyclic Barbiturate

Sir:

The synthesis of heterocyclic oligomers has been accomplished by a variety of conventional chemical methods as well as by photochemical and thermochemical techniques.[1] Of the various oxidative methods, however, the use of electrochemical techniques for the preparation of heterocyclic oligomers has been virtually ignored although Bobbit and coworkers[2-4]

(1) A. Albert and H. Yamamoto, *Advan. Heterocycl. Chem.*, 15, 1 (1973).
(2) J. M. Bobbit, K. H. Weisgraber, A. S. Steinfeld, and S. G. Weiss, *J. Org. Chem.*, 35, 2884 (1970).
(3) J. M. Bobbit, H. Yagi, S. Shibuyu, and J. T. Stock, *J. Org. Chem.*, 36, 3006 (1971).
(4) J. M. Bobbit, J. F. Colarutolo, and S. J. Huang, *J. Electrochem. Soc.*, 120, 773 (1973).

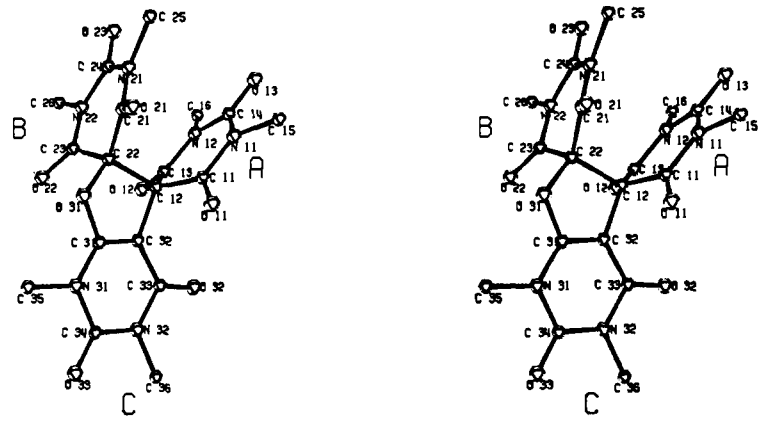


Figure 1.

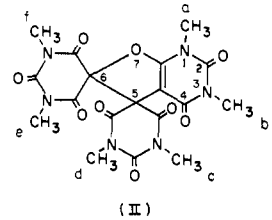
I

have recently described the electrochemical synthesis of a number of dimeric and trimeric derivatives of 1,2,3,4-tetrahydroisoquinolines.

During a series of investigations of the electrochemistry of a variety of barbituric acid derivatives, we discovered a very simple method for the synthesis of a new cyclic barbiturate, 5,6-dihydro-1,3-dimethyl-5,6-di[1′,-3′-dimethyl-2′,4′,6′-trioxopyrimid(5′,5′)yl]furo[2,3-*d*]-uracil, which is a trimeric form of 1,3-dimethylbarbituric acid. Reported here is a very simple, single-step, high yield electrochemical synthesis of this trimeric species and an outline of the structure elucidation.

Electrolyses were carried out in a two-compartment cell. The working electrode compartment had a capacity of *ca.* 200 ml and was separated from the counter electrode compartment (capacity *ca.* 150 ml) by a fine sintered glass disk and an agar-saturated KCl salt bridge. A large cylindrical platinum gauze electrode immersed in 1 *M* acetic acid served as the counter electrode. The working electrode consisted of six pyrolytic graphite plates (5 × 1.5 × 0.2 cm thick) (Super Temp Co., Santa Fe Springs, Calif.) connected in series and suspended in the electrolysis solution in the working electrode compartment. The reference electrode was a Coleman fiber-tip sce inserted into the solution in the working electrode compartment. With continuous stirring under nitrogen, 1,3-dimethylbarbituric acid[5] (700 mg, 4.482 mmol) was electrolyzed in 1 *M* acetic acid (150 ml) at +1.00 V *vs.* sce at the pyrolytic graphite electrode. Complete electrolysis (*ca.* 48 hr) involved transfer of close to 2.5 faradays/mol. After electrolysis a considerable quantity of white precipitate was present in the solution which was filtered. The solid material adhering to the graphite electrodes was removed by dissolving in hot acetonitrile. The filtered solid was also dissolved in hot acetonitrile (200 ml). The latter two solutions were combined and again filtered to separate the product from small amounts of carbon that flake off the electrodes. Evaporation of the acetonitrile yielded a white solid (322 mg, 0.696 mmol as the trimer, yield 46.6%[6]) which was recrystallized from acetonitrile (40 ml) to give fine needles (204 mg), mp 370–373° dec. *Anal.* Calcd for $C_{18}H_{18}N_6O_6$ (462.37): C, 46.75; H, 3.92; N, 18.18. Found: C, 46.59; H, 3.94; N, 18.44. The structure was established by X-ray crystallography. For such studies a suitable crystal was obtained by further recrystallization of the trimer from methanol. The space group is P_{bca} (no. 61) with unit cell dimensions a = 13.236 (1), b = 15.931 (1), and c = 19.584 (2) Å. The 3705 intensities of all reflections with $2\theta < 135°$ were measured using Cu Kα radiation (λ(Cu Kα) 1.5418 Å). Only the intensities for which $I > 2\sigma(I)$ were used in the structure determination and refinement. The final R value for these 3285 reflections was 0.043. The standard deviations for the bond distances are between 0.002 and 0.003 Å. A stereoscopic view of one molecule (I) is shown in Figure 1. Two of the three dimethylbarbituric acid molecules form spiro linkages while the third contributes one oxygen to form a central five-membered ring. This central ring is not planar and contains one double bond (C(31)–C(32), 1.337 Å). The two C–O bonds in this ring are not equivalent: C(31)–O(31) is 1.353 Å and C(22)–O(31) is 1.425 Å. The bond C(12)–C(22) between the two spiro carbons is extremely long (1.612 Å) while the C(12)–C(32) bond has a normal length of 1.501 Å. Ring C is planar but rings A and B are not and are bent toward each other. The C=O distances in rings A and B vary between 1.201 and 1.207 Å and only the C(33)–O(32) bond in ring C is somewhat lengthened (1.223 Å). All six N–CH_3 distances are the same ranging between 1.468 and 1.474 Å.

The structure, as determined (I and II), is compatible



(II)

with the spectral data: nmr spectrum (60 MHz) (δ, CF_3COOH) 3.64 (s, 3 H, H_a or H_b), 3.43 (s, 3 H, H_a or H_b), 3.33, and 3.31 (both s, 12 H the sum of both peaks), H c, d, e, f); ir (KBr pellet) 2940 cm^{-1} (CH_3), 1740–1640 cm^{-1} (broad and strong, C=O and C=O conjugated to C=C); mass spectrum (*m/e*, 70 eV, 160°) 462 (M^+, 100%), 348 ($M^+ - 2CH_3NCO$, 23%), 320 ($M^+ - 2CH_3NCOCO$, 73%); uv λ_{max} in CH_3CN, 246 nm (ϵ_{max} 2000 l. mol^{-1} cm^{-1}).

(5) H. Blitz and H Wittek, *Chem. Ber.*, **54**, 1035 (1921).

(6) The other major product of the reaction, dimethylalloxan (191 mg, 1.123 mmol, yield 25%), was isolated from the analyte, after freeze drying, by sublimation and identified by comparison with an authentic sample. E. Biilmann and N. Berg, *Chem. Ber.*, **63**, 2188 (1930).

The pharmacological properties of this compound are currently being investigated as is the detailed mechanism of the electrode reaction and the possibility of electrochemical synthesis of a variety of related pyrimidine oligomers.

Acknowledgments. The authors would like to thank the National Science Foundation and the Faculty Research Committee of the University of Oklahoma for financial support of this work. One of us (D. v. d. H.) was supported by a National Institutes of Health Development Award 5-K4-GM-42572.

Supplementary Material Available. A listing of the structure factor amplitudes will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche, referring to code number JACS-74-5255.

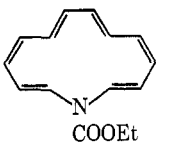
Shozo Kato, M. Poling
D. van der Helm, Glenn Dryhurst*
Department of Chemistry, University of Oklahoma
Norman, Oklahoma 73069
Received March 27, 1974

1*H*-Aza[13]annulene and Derivatives[1]

Sir:

The hetero[13]annulene system was recently described by Schröder and coworkers in the form of urethane, **1**, which apparently lacks aromatic character.[2] Nonetheless, the basic question as to whether an *unrestricted* (as opposed to bridged) hetero[13]annulene is capable of realizing its 14π aromatic potential has remained largely unanswered because of two undesirable structural features of **1**: (i) the molecule incorporates a strongly electron-withdrawing N substitutent and one known to prevent the development of aromatic character in the related hetero[9]annulene (heteronin) frame[3] and (ii) serious pairwise interference of the four "inner" protons (Dreiding molecular model) in the planar form needed for π delocalization. Bearing these two points in mind and having ourselves recently prepared[4] a potential photoprecursor, **2**, of the general aza[13]annulene frame, we resolved to examine the question of aromaticity in this intriguing heteromonocycle. We now relate our findings and conclusions on the subject.

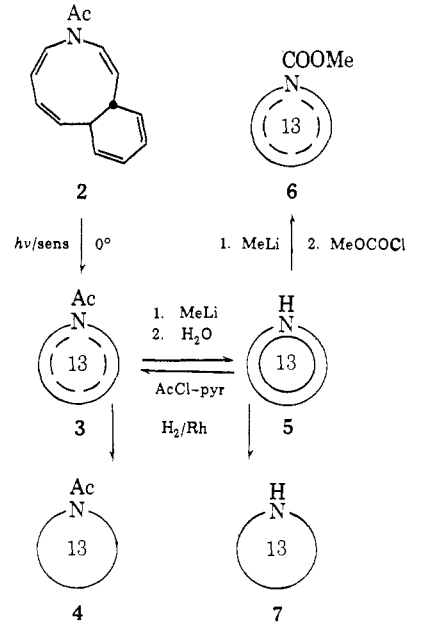
Brief (*ca.* 80 min) sensitized irradiation of **2** in acetone, at 0°, yields a mixture of three identifiable bicyclic[5] (*ca.* 50%) and one monocyclic (*ca.* 20%) isomers. These were separated by chromatography on alumina at *ca.* −15°, and the desired monocycle, **3**, was obtained pure



1

by successive low-temperature recrystallization. It is a bright yellow crystalline solid, mp 40–42°, displaying the following spectral characteristics: ν_{CO}^{KBr} 1670 cm^{-1}, $\lambda_{max}^{C_6H_{14}}$ 238 nm (ϵ 27,400), 260 (32,000), and 350 (4,000); nmr (100 MHz, $CDCl_3$) multiplets at τ 2.5–3.0 (2 H) and 3.3–4.2 (10 H), and a sharp singlet at τ 7.80 (3 H); *m/e* 213 (P^+, 26%). Chemically, the monocyclic frame of **3** was established by catalytic hydrogenation (Rh/C) to the perhydro counterpart **4** (ν_{CO}^{neat} 1645 cm^{-1}, *m/e* 225 (P^+, 51%)). Exposure of **3** to methyllithium in THF at *ca.* −70° followed by protonation (methanol at −70° then water at 0°) yielded the key amine **5**. When pure (sublimation) this substance is a bright yellow, air-sensitive solid characterized by $\lambda_{max}^{C_6H_{14}}$ 297 and 360 nm in a ratio of *ca.* 7.5[6]; nmr (100 MHz, acetone-d_6, −6°) τ 0.6 (br, s, N–H), 2.8–3.2 (5 H, m), 3.86 (1 H, t, J = 10.0 Hz), 4.1–4.5 (2 H, m), 4.88 (1 H, dd, J = 16.0, 6.0 Hz), 5.99 (1 H, dd, J = 16.0, 10.0 Hz), 6.52 (1 H, dd, J = 16.0, 8.0 Hz), 7.22 (1 H, dd, J = 14.5, 11.5 Hz; "inner" α proton coupled to N–H); *m/e* 171 (P^+, 15%). Chemically, the presence of a monocyclic frame in this substance was demonstrated by the following transformations: (i) conversion to the methoxycarbonyl derivative **6** (yellow crystals mp 51–52.5°; ν_{CO}^{KBr} 1710 cm^{-1}, $\lambda_{max}^{C_6H_{14}}$ 231 nm (ϵ 23,500), 263 (21,350), and 335 (4,500); nmr (100 MHz, $CDCl_3$) multiplets at 2.9–3.4 (2 H) and 3.6–4.2 (10 H) and a sharp singlet at τ 6.20 (3 H); *m/e* 229 (P^+, 88%)) on successive low-temperature treatment with methyllithium and methyl chloroformate in THF, (ii) reversion to **3** (nmr) on exposure to acetyl chloride–pyridine, and (iii) catalytic hydrogenation (Rh/C) to the perhydro analog **7** (*m/e* 183; P^+, 22%).

Scheme I



(1) Early portions of this work were presented Oct 15, 1973 at the Symposium on Organic Synthesis, 5th Northeast Regional Meeting of the American Chemical Society, Rochester, N. Y.

(2) G. Schröder, G. Frank, and J. F. M. Oth, *Angew. Chem.*, **85**, 353 (1973); *Angew. Chem., Int. Ed. Engl.*, **12**, 328 (1973), and private communication from Professor Schröder.

(3) For recent reviews on the subject see A. G. Anastassiou, *Accounts Chem. Res.*, **5**, 281 (1972); A. G. Anastassiou in "Topics in Nonbenzenoid Aromatic Chemistry," T. Nozoe, R. Breslow, K. Hafner, S. Ito, and I. Murata, Ed., Hirokawa Publishing Company, Tokyo, 1973, pp 1–27.

(4) A. G. Anastassiou, E. Reichmanis, and R. L. Elliott, *Tetrahedron Lett.*, 3805 (1973).

(5) This portion of the work will be described in a later report.

(6) The intense air sensitivity of the substance precluded a quantitative determination of extinction coefficients at this early stage.