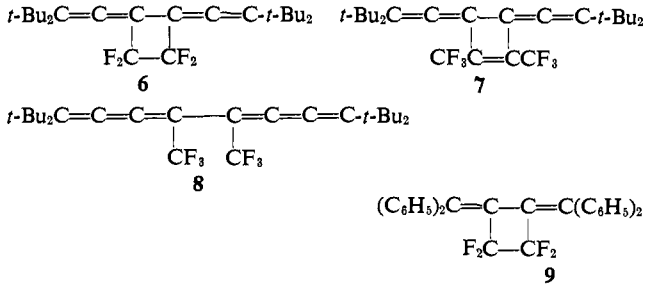
70% yield. With hexafluoro-2-butyne, **4** gave the cycloadduct **7** as well as its valence bond isomer **8**. It was shown that **7** isomerized to **8** at this temperature (200°).

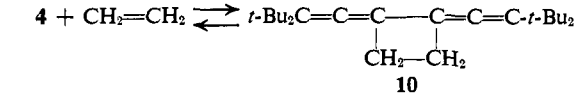


6 **7**

8

9

The reaction of **4** with ethylene in ethyl acetate at 200° returned **4** even though the cumulene in ethyl acetate dimerized rapidly at 200°. A possible explanation for the preservation of **4** in the presence of ethylene is that the cycloadduct **10** is formed but reverts to starting materials. Opening of **10** to 1,1-di-*t*-butylbutatriene is not observed, and such a reaction of **10** would be expected to be energetically less favorable than the return to starting materials.



10

Although we were unable to isolate the dimer of tetraphenylbutatriene from its thermal reactions, this cumulene also gave cycloadditions. With tetrafluoroethylene at 200°, a low yield of the adduct **9** was obtained.

The symmetry of the cycloadducts **6–9** was determined by single, unsplit absorption signals in both the fluorine and proton nmr.

In all cases where cycloaddition to cumulenes has been observed, addition has occurred at the central bond. This is to be expected if the triplet states of the cumulenes are intermediates.

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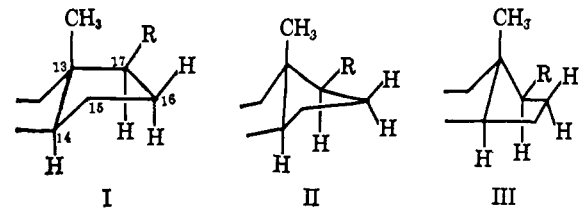
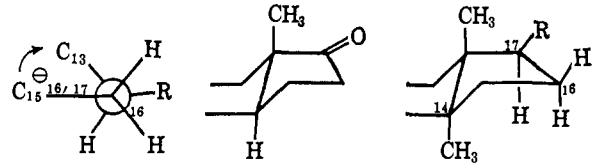
Steroid Ring D Torsional Angles and Conformations from X-Ray Data

Sir:

One of the subtlest problems extant in molecular geometry is that of determining the conformations adopted by ring D of the steroids. Thus, for the three symmetrical conformations (I, II, and III),[1] the C_{16},C_{17} torsional angle ($\theta_{16,17}$, IV) only varies from 0° in I to about −30° in III.[2] This is approximately one-half the staggered (60°) to eclipsed (0°) value normally found in cyclohexane conformations.[3,4] While important ring D data have been obtained by some physical methods[1,5–9] it has become apparent that the precision of X-ray crystallography would be definitive here. In particular scrutiny of the five torsional angles of ring D would readily reveal the subtlest aspects of its symmetry.[10] Unfortunately it is the present X-ray practice to report bond angles (ω_a) and bond lengths (d_{ab}) but not the vitally necessary torsional angles.



I II III



IV V VIII

In this communication, the requisite torsional angles have been calculated[11] from all accurate reported fractional atomic coordinate data of steroids,[12–17] and these values were used to solve the ring D conformational problem.

In Table I, the value of $\theta_{16,17}$ of 1° 52′ calculated from the excellent Norton, Kartha, and Lu data[12] on 4-bromoestrone (V) is significant since a value of 0° means that C_{13}, C_{15}, C_{16}, and C_{17} are in one plane and ring D is α envelope. Since 1° 52′ is within experimental error of zero,[18] the biologically important estrone type prefers the α envelope (V). Presumably the angle strain for the ketone at C_{17} is minimized in this conformation. The reduction product of V, however, 4-bromoestradiol (VI), has undergone a ring D conformational change since $\theta_{15,16}$ derived from

(1) F. V. Brutcher, Jr., and W. Bauer, *J. Am. Chem. Soc.*, **84**, 2233, 2236 (1962). Conformation I is termed the α envelope since the C_{14} atom is below the plane of C_{13}, C_{15}, C_{16}, C_{17}. III then represents the β envelope, while II is the half-chair.

(2) In IV, from the nearer to the farther ring valence bond the motion is clockwise and as in a standard mathematics handbook, the torsional angle ($\theta_{16,17}$) is defined as a negative angle.

(3) M. Hanack, "Conformation Theory," Academic Press, New York, N. Y., 1965.

(4) E. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," John Wiley and Sons, Inc., New York, N. Y., 1965.

(5) J. Fishman and C. Djerassi, *Experientia*, **16**, 138 (1960).

(6) A. D. Cross and P. Crabbé, *J. Am. Chem. Soc.*, **86**, 1221 (1964).

(7) A. D. Cross and C. Beard, *ibid.*, **86**, 5317 (1964).

(8) J. Fishman, *ibid.*, **87**, 3455 (1965).

(9) W. Klyne, *Bull. Soc. Chim. France*, 1396 (1960).

(10) While inspection of the stacking diagram may rule out the other envelope, it does not differentiate between a particular envelope, a distorted envelope, or a half-chair.

(11) This involves proper multiplication of the fractional atomic coordinates by the dimensions of the unit cell. These atomic coordinates lead to the relevant C–C bond vectors. Derivation of the proper θ's is standard (see E. B. Wilson, "Vector Analysis," Dover Publications, Inc., New York, N. Y., 1901, and also E. J. Corey and R. Sneen, *J. Am. Chem. Soc.*, 77, 2505 (1954)). By recalculating ω and d to avoid round-off and using our θ's we have shown that these internal coordinates lead to mathematically closed five-membered rings.

(12) D. A. Norton, G. Kartha, and C. T. Lu, *Acta Cryst.*, **16**, 89 (1963).

(13) D. A. Norton, G. Kartha, and C. T. Lu, *ibid.*, **17**, 77 (1964).

(14) H. Bürki and W. Nowacki, *Z. Krist.*, **108**, 206 (1956).

(15) J. Fridrichsons and A. McL. Mathieson, *J. Chem. Soc.*, 2159 (1953).

(16) H. J. Geise, C. Romers, and E. W. M. Rutten, *Acta Cryst.*, 20, 249 (1966). We calculate that the 2α,3β-dibromo- and the 2α,3β-dichloro-5α-cholestanes reported by H. J. Geise and C. Romers (*ibid.*, 20, 257 (1966)) have smaller $\theta_{15,16}$'s of −7° 35′ and −8° 18′. They are not included in Table I.

(17) C. Romers, B. Hesper, E. VanHeijkoop, and H. J. Geise, *ibid.*, 20, 363 (1966).

(18) In Table I, $\Delta\theta$ is the column average of the probable error in each θ calculated by propagation of the standard deviations of the atomic coordinates where reported (see L. G. Parratt, "Probability and Experimental Errors in Science," John Wiley and Sons, Inc., New York, N. Y., 1961).

Table I

	V	VI	VII	VIII	IX	X
$\theta_{13,14}$(D)[a]	−39° 50′	−49° 34′	−45° 16′	−37° 41′	−47° 57′	−46° 17′
$\theta_{14,15}$	+41° 51′	+34° 40′	+26° 40′	+37° 25′	+36° 10′	+38° 25′
$\theta_{15,16}$	−25° 04′	−6° 7′	+1° 19′	−15° 26′	−10° 45′	−13° 12′
$\theta_{16,17}$	+1° 52′	−24° 13′	−28° 25′	−5° 30′	−18° 2′	−15° 44′
$\theta_{13,17}$	+23° 33′	+44° 42′	+45° 31′	+22° 49′	+39° 3′	+37° 42′
$\theta_{13,14}$(C)[b]	+69° 36′	+64° 15′	+69° 35′	+51° 11′	+60° 2′	+62° 9′
$\Delta\theta$[18]	±3° 12′	±1° 25′	...	...	±2° 1′	±2° 41′

[a] Calculated using C_{15}, C_{14}, C_{13}, and C_{17}. [b] Calculated using C_8, C_{14}, C_{13}, and C_{12}.

the Norton, Kartha, and Lu coordinates[13] is −6° 7′. For the first time one can distinguish this slightly deformed β envelope (III) from the corresponding half-chair (II)[19] since for VI $\theta_{16,17}$ is −24° 13′, only slightly less than $\theta_{16,17}$ for 3β-chloro-7α-bromo-$\Delta^{5,6}$-cholestene (VII).[14]

The favoring of III for VI is not unexpected conformationally;[1] however, for lanostenyl iodoacetate (VIII),[15] the fact that $\theta_{16,17}$ is −5° 30′ and that a slightly deformed α envelope is preferred is unexpected since the C_{17}-β-side chain is driven into near eclipse with the C_{16}-β-hydrogen. Apparently the severity of the steric compression between the axial 14α-methyl and 17α-hydrogen forces this.

In interpreting X-ray crystallographic results some caution must be observed since these represent solid-state data and the packing forces of crystallization operating especially on the C_{17} side chain might deform ring D[20] whose α and β envelope energy differences are small and about 2–3 kcal/mole in magnitude.[1] Possible evidence on this point is seen in comparing $\theta_{15,16}$ calculated for VII ($\theta_{15,16}$ = +1° 19′)[14] and 2β,3α-dichloro-5-α-cholestane[16] (IX, $\theta_{15,16}$ = −10° 45′). Both have the long cholesterol side chain and differ conformationally only in rings A and B, yet VII is an envelope within experimental error while IX is a distorted half-chair. Another possible case in point is X, 4-bromo-9β,10α-pregna 4,6-diene-3,20-dione.[17] Since $\theta_{15,16}$ = $\theta_{16,17}$, ring D with a C_{17}-β-acetyl side chain is half-chair. In contrast to the others, however, X has a *cis* B/C junction and a C_{19}-α-methyl group.

Torsional angle data solve thoroughly the problem of the extent of puckering of ring D. $\theta_{13,14}$(D) varies between −38° (VIII) and −50° (VI) and averages out to −45°, a value close to the equilibrium value reported for cyclopentane itself by Pitzer and Donath.[21] Since ring D does not reach a maximally puckered value of $\theta_{13,14}$(D) equal to −60°, ring C must be detectably deformed. For VI, we calculate that $\theta_{13,14}$(C) is +64° 15′, $\theta_{12,13}$ is −55° 19′, $\theta_{11,12}$ is +53° 56′, $\theta_{9,11}$ is −56° 48′, $\theta_{8,9}$ is + 60° 18′, and $\theta_{8,14}$ is −65° 49′. Since all θ's for a perfect cyclohexane chair should be ±60°, ring C in VI is a slightly deformed chair.

Table I represents solid-state data; hence it is necessary to use the excellent nmr, infrared, ORD, and dipole moment data of Fishman, Djerassi, Brutcher, and Cross and their co-workers[1,5–8] to show that there is, as yet, for substituted 17-keto and 17β-hydroxy steroids no evidence that ring D conformational changes occur on solution. Solution data on VII and IX are not readily obtainable, but based on Table I a conformation between II and III might be anticipated.

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Received February 19, 1966

(19) In the half-chair, $\theta_{15,16}$ will equal $\theta_{16,17}$ and be approximately −16°.

(20) Ethylene carbonate is nonplanar (half-chair) in the solid state (X-ray, C. J. Brown, *Acta Cryst.*, 7, 92 (1954)) and also in the vapor phase (microwave, I. Wang, C. O. Britt, and J. E. Boggs, *J. Am. Chem. Soc.*, 87, 4950 (1965).

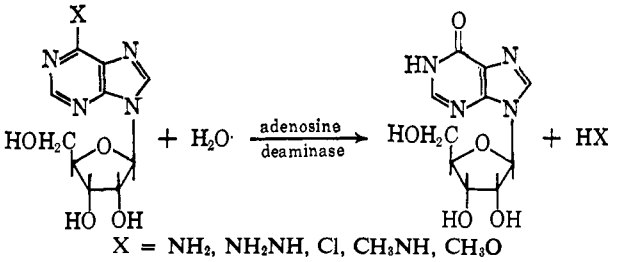
(21) K. S. Pitzer and W. Donath, *ibid.*, **81**, 3213 (1959).

Enzymatic Hydrolysis of 6-Substituents on Purine Ribosides[1]

Sir:

The insensitivity of the adenosine deaminase of *Aspergillus oryzae* to carbonyl group reagents and to dialysis suggests the absence of groups appropriate for Schiff base formation with the substrate.[2] Enzymatic deamination of nucleosides may thus differ sharply in mechanism from the deamination of amino acids.[3] Alternative mechanisms, involving specific enzymatic protonation of the nucleoside at N_1 or N_3 to force it over to a potentially hydrolyzable 6-imino tautomer, are rendered doubtful by the fact that 3-β-(D-ribofuranosyl)adenine is also a substrate.[2]

Prompted by recent findings that mammalian adenosine deaminase preparations catalyze rather slow hydrolysis of chloride ion from 6-chloropurine riboside,[4] we have tested the enzyme from *Aspergillus* on a variety of substrates. We wish to report that this enzyme, which has been purified approximately 5000-fold,[5] catalyzes hydrolysis of 6-hydrazinopurine riboside, 6-chloropurine riboside, 6-methylaminopurine riboside, and 6-methoxypurine riboside, at limiting veloci-



X = NH_2, NH_2NH, Cl, CH_3NH, CH_3O

(1) This work was supported by Research Grant USPHS-GM-12725 from the National Institutes of Health, U. S. Public Health Service.

(2) R. Wolfenden, T. K. Sharpless, I. S. Ragade, and N. J. Leonard, *J. Am. Chem. Soc.*, **88**, 185 (1966).

(3) *Cf.* A. E. Braunstein, *Enzymes*, **2**, 113 (1960).

(4) J. G. Cory and R. J. Suhadolnik, *Biochemistry*, **4**, 1733 (1965); S. Frederiksen, *Arch. Biochem. Biophys.*, **113**, 383 (1966); H. P. Baer, G. T. Drummond, and E. L. Duncan, *Federation Proc.*, **25**, 786 (1966).

(5) T. K. Sharpless and R. Wolfenden, *Methods Enzymol.*, **8**, in press.