At present, we are not aware of any evidence in solvolyses of simple secondary substrates that requires postulating hidden return of large magnitude.[35-37] All kinetic data for nonanchimerically assisted substrates can be quantitatively explained, within a small rate factor, by varying degrees of nucleophilic solvent assistance. Such nucleophilic assistance is reduced in weakly nucleophilic solvents and sterically hindered substrates;[38] in these situations, the carbonium ion character of the transition state is greater and inductive/hyperconjugative effects are larger in magnitude.[12,16]

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(35) This comment applies to k_s solvolyses of unactivated secondary substrates. There are good indications that solvolysis of *tert*-butyl chloride in trifluoroethanol involves some hidden return.[30e,36,37]

(36) J. M. Harris, D. J. Raber, R. E. Hall, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **92**, 5729 (1970).

(37) T. W. Bentley, unpublished results.

(38) T. W. Bentley, F. L. Schadt, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **94**, 992 (1972).

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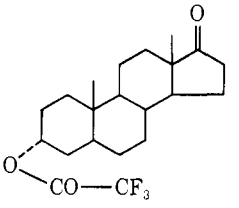
Selective Steroid Halogenations Directed by Proximity and Substituent Effects

Sir:

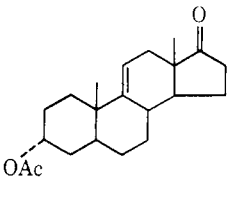
We have reported[1] that certain free radical halogenating reagents, and in particular phenyliodine dichloride, are sufficiently selective that in a random attack on a steroid nucleus halogenation occurs to an appreciable extent only at carbons 5, 9, and 14. Furthermore, our previous work indicated that the proportion of attack among these three positions could be influenced by substituents on the steroid skeleton. Halogenation at C-9 allows easy introduction of the 9(11) double bond which permits entry into the corticosteroids; our procedure has also been utilized by Djerassi[2] in the synthesis of a starfish sterol. Halogenation at C-14, and subsequent introduction of the Δ14 double bond in a steroid, is of interest with respect to the synthesis of cardiac-active steroids.

Although in the previously described procedure appropriate substituents could suppress attack at C-5 and allow the production of various proportions of Δ9(11) and Δ14 steroids, it would clearly be desirable to be able to direct exclusively the introduction of one or the other of these functionalities. We now wish to report that with appropriate substituent effects we can direct the halogenation to the introduction of a 9(11) double bond in an attractive corticosteroid precursor.[3] Alternatively, by the application of intramolecular orientation procedures to this halogenation, we have been able to direct it to the selective introduction of the Δ14 double bond or the 9(11) double bond.

Although bulky substituents at C-17 have some effect in suppressing the halogenation at C-14, the most convenient and effective group is simply the C-17 carbonyl, which deactivates C-14 to halogenation presumably by a combination of polar and conformational effects. As we have indicated earlier, C-5 halogenation can be diminished by attachment of an electron-withdrawing group at C-3, and particularly effective is a 3α substituent which is thus 1,3-diaxial with the C-5 hydrogen. Commercially available androsterone was converted to its trifluoroacetate (I), mp 123.5–124°,[4]



I



II

and 1.0 g was halogenated with 1 equiv of $C_6H_5ICl_2$ in benzene at 10^{-2} *M* by irradiation with a sun lamp for 10–15 min. The product was then dehydrochlorinated and saponified with methanolic KOH, acetylated, and chromatographed. Unfunctionalized androsterone acetate (25%) was separated from 3α-acetoxy-5α-androst-9(11)-en-17-one (II), mp 187.5–189°.[4] (41%) and *ca.* 5% of the corresponding Δ5 isomer. The remaining 25% of more polar material, containing chlorine, was formed by further halogenation.[5] With 2 equiv of $C_6H_5ICl_2$ conversion was 95%, with 49% of II being isolated. Again the only other products detected are a trace of the Δ5 isomer, and 34% of polar products of further reaction.

Selective functionalization at C-14 was obtained by applying our principle of remote oxidation to this halogenation process. We have described selective functionalization of steroids by attached benzophenone[6,7] or nitrite ester derivatives,[7] but it was problematical whether internal attack by a rigid attached reagent far from the attachment point could also be applied in a radical chain reaction. In a chain process there must be both an intramolecular hydrogen transfer in the attack on the substrate and an intermolecular halogen transfer to carry the chain. For the former, low concentrations are required to suppress competing intermolecular hydrogen abstractions, and under these conditions it is not necessarily clear that the chain transfer steps would be possible. However, it turns out that halogenation by $C_6H_5ICl_2$ can indeed be turned into a

(1) R. Breslow, J. A. Dale, P. Kalicky, S. Y. Liu, and W. N. Washburn, *J. Amer. Chem. Soc.*, **94**, 3276 (1972).

(2) J. E. Gurst, Y. M. Sheikh, and C. Djerassi, *J. Amer. Chem. Soc.*, **95**, 628 (1973).

(3) Introduction of the appropriate side chain, conversion of a Δ9(11) double bond to an 11-oxy substituent, and modification of ring A to a Δ4-3-one system are all well-known processes.

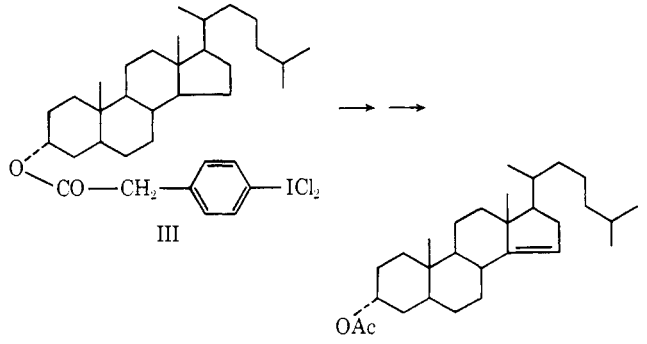
(4) Characterized by mass and pmr spectra.

(5) Apparently some of the olefin is formed directly and reacts further during halogenation. Treatment of II with $C_6H_5ICl_2$ in the *dark*, followed by our standard work-up, afforded similar polar material.

(6) R. Breslow, S. Baldwin, T. Flechtner, P. Kalicky, S. Liu, and W. Washburn, *J. Amer. Chem. Soc.*, **95**, 3251 (1973), and references therein.

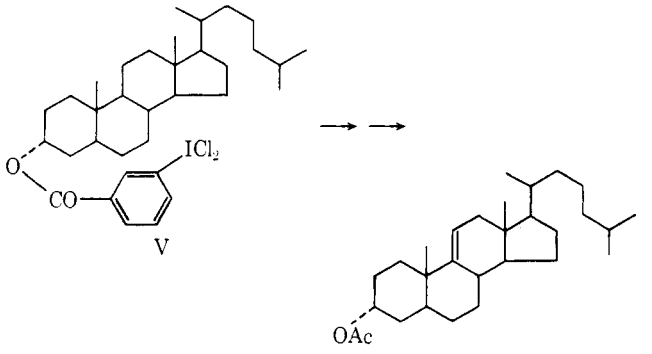
(7) R. Breslow, *Chem. Soc. Rev.*, **1**, 553 (1972).

predominantly intramolecular remote functionalization. The *p*-iodophenylacetic ester,[8] mp 95–97°, of 3α-cholestanol was converted with Cl_2 to the corresponding dichloride III. Irradiation of a 0.33×10^{-3} *M* solution



of ester III in chlorobenzene at −25° with a sun lamp, followed by hydrolysis and work-up as above, yielded 20% of recovered cholestanol (acetate) and 53% of Δ14-cholestenyl 3α-acetate (IV) identical with authentic material.[6] In addition only 5% of the Δ9(11) isomer and 0.8% of the Δ5 isomer were detected, along with polar and unidentifiable material. These other isomers must have been formed in a competing *inter*molecular process, since 0.33×10^{-3} *M* androstane included in the reaction mixture as a control was converted to 9% of the expected mixture of androstenes. The *intra*molecular process is apparently completely selective for C-14; more intermolecular, randomized, halogenation is seen at room temperature or with higher concentrations.

Remote oxidation by benzophenone esters attached to 3α occurs at C-14 with some para derivatives but in ring B with the corresponding meta esters.[7] This proves to be true for attached $PhICl_2$ as well. Thus 3α-cholestanyl *m*-iodobenzoate,[8] mp 89.5–90.5°, was converted to the dichloride V and irradiated in benzene at



1.0×10^{-3} *M* and room temperature. After hydrolysis, etc., 35% of 3α-cholestanol (acetate) was recovered, and 43% of Δ9(11)-cholestenyl 3α-acetate (VI) was isolated, mp 80.5–82°, which was hydrolyzed to the known[6] Δ9(11)-3α-cholestenol. Only 9% of the Δ14 isomer was formed and 2% of the Δ5 olefin. In a control reaction, androstane at 1.0×10^{-3} *M* was 20% functionalized, so the *inter*molecular process has not been completely suppressed. The yield of VI and conversion of V are even higher for reaction in CH_2Cl_2.

The selective attack at C-14 in III, and C-9 in V, is consistent with predictions from molecular models assuming that hydrogen abstraction is done by the chlorine atom in the [Ar–I–Cl]· intermediate.[9] The chlorine atom in the intermediate derived from III is in fact in essentially the same place as is the abstracting oxygen in the *p*-benzophenoneacetic ester of 3α-cholestanol, whose photolysis also produced a Δ14-3α-cholestanol derivative.[6] The present work not only furnishes alternative and convenient approaches to this olefin and to the important Δ9(11) unsaturation but it also demonstrates that the principles we have developed in connection with intramolecular benzophenone photochemistry can be extended to impose orientation factors on radical chain processes.[10]

(8) Characterized by analysis and pmr spectrum.

(9) D. D. Tanner and P. B. van Bostelen, *J. Org. Chem.*, **32**, 1517 (1967), suggest abstraction by iodine to form an unstable tricovalent iodine derivative which then loses HCl. Such a mechanism looks energetically unfavorable and is not geometrically possible for III.

(10) Financial support of this work by the National Institutes of Health and an NSF predoctoral fellowship to R. C. are gratefully acknowledged.

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Stereochemistry of the Di-π-methane Rearrangement at the Methane Carbon. Mechanistic and Exploratory Organic Photochemistry[1]

Sir:

In our earlier studies on the di-π-methane rearrangement,[1-4] we found that retention of configuration is the preferred stereochemistry at carbons 1 and 5 of the 1,4-pentadiene system. We did encounter some evidence in constrained systems[5] pointing toward a preference for inversion of configuration at the one other stereochemical center, namely the methane carbon (*i.e.*, C-3). Mariano in his elegant studies has attacked the problem from another perspective and demonstrated that in constrained di-π-methane systems it is possible to enforce either retention or inversion of configuration.[6]

The present research aimed at determination of the preferred C-3 stereochemistry in an unconstrained, acyclic system. For this we selected 3-ethyl-3,5-dimethyl-1,1-diphenyl-1,4-hexadiene (**1**). It was found that the di-π-methane rearrangement of ethylmethyldiene **1** led to *cis*- and *trans*-3-ethyl-3-methyl-2-(2′-methylpropenyl)-1,1-diphenylcyclopropane (**2a** and **b**) with a quantum yield of 0.11. Optically active ethylmethyldiene **1** was prepared as were optically active *cis*- and *trans*-vinylcyclopropanes **2a** and **2b**.[7] The con-

(1) Paper LXXXV of the series. For the previous paper note H. E. Zimmerman, P. Baeckstrom, T. Johnson, and D. W. Kurtz, *J. Amer. Chem. Soc.*, **96**, 1459 (1974).

(2) S. S. Hixson, P. S. Mariano, and H. E. Zimmerman, *Chem. Rev.* **73**, 531 (1973).

(3) H. E. Zimmerman and A. C. Pratt, *J. Amer. Chem. Soc.*, **92**, 6267 (1970).

(4) H. E. Zimmerman, P. Baeckstrom, T. Johnson, and D. W. Kurtz, *J. Amer. Chem. Soc.*, **94**, 5504 (1972).

(5) (a) H. E. Zimmerman and G. A. Epling, *J. Amer. Chem. Soc.*, **92**, 1411 (1970); (b) *ibid.*, **94**, 8749 (1972); (c) H. E. Zimmerman and G. E. Samuelson, *ibid.*, **89**, 5971 (1967); (d) *ibid.*, **91**, 5307 (1969); (e) H. E. Zimmerman, P. Hackett, D. F. Juers, J. M. McCall, and B. Schröder, *ibid.*, **93**, 3653 (1971).

(6) (a) P. S. Mariano and J. Ko, *J. Amer. Chem. Soc.*, **94**, 1766 (1972); (b) P. S. Mariano and R. B. Steitle, *ibid.*, **95**, 6114 (1973).

(7) All compounds gave satisfactory elemental analyses. Complete synthetic and experimental details will be given in our full paper.