formic acid is present in excess the rate of gas production is closer to that expected for formic acid alone, while excess trifluoroacetic acid leads to a rate of gas formation closer to that observed for trifluoroacetic acid alone. The observations can be rationalized by noting that trifluoroacetic acid is a much stronger acid than formic acid, resulting in a predominance of trifluoroacetate ions over formate ions, and that this predominance of trifluoroacetate ions could be sufficient to overcome the apparent difference in potentials for the two reactions.

The previously cited comparisons of discharge potentials[9-11] would place acetate discharge at a considerably lower potential than trifluoroacetate discharge. We have found, however, that trifluoroacetic acid is anodically oxidized to the virtual exclusion of acetic acid. This again can be explained by the much greater ionization of trifluoroacetic acid and it is entirely consistent with our observations in the formic acid–acetic acid and formic acid–trifluoroacetic acid mixtures.[12]

Registry No.—Formic acid, 64-18-6; acetic acid, 64-19-7; trifluoroacetic acid, 76-05-1; propionic acid, 79-09-4.

(12) A referee has suggested that voltammetric measurements (details not specified) should be reported for these systems. We have cited results of such measurements from the literature and have pointed out that conclusions based on these data do not explain our observations. The primary difficulty resides in the indeterminacy of liquid–liquid junction potentials (see Ives and Janz, "Reference Electrodes," Academic Press Inc., New York, N. Y., 1961, pp 50, 439). Measurements made in one acid simply cannot be related to data from another acid solvent. We might make measurements in solutions containing low concentrations of our acid anions in the presence of a high concentration of an indifferent electrolyte, thereby relating the anions to one another, but these data could not be translated to the systems that we have studied. Our work must be construed as a distinctly separate approach to which voltammetric data can be related crudely at best.

Ring-D-Bridged Steroid Analogs. III.[1] Hunsdiecker Reaction of *endo*-Norborn-5-ene-2-carboxylic Acids[2]

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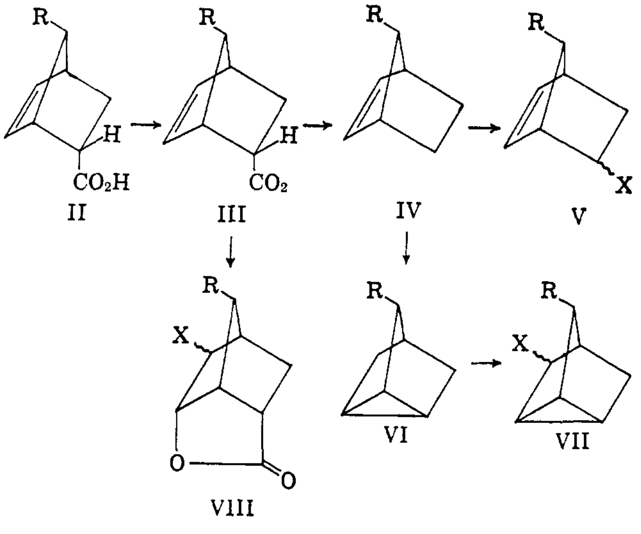
14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one acetate was found to undergo the Cristol modification of the Hunsdiecker reaction to afford a *cis*-iodo lactone. In contrast, under the same conditions, *endo*-norborn-5-ene-2-carboxylic acid formed a *trans*-iodo lactone. The differing steric nature of the products is attributed to steric hindrance, on the backside of the double bond, in the steroid.

We have been attempting to synthesize 14α,17α-etheno- (or ethano-) pregn-4-ene-3,20-dione in order to determine the effect of such a 14α,17α-hydrocarbon bridge on the biological activity of progesterone. We have therefore been investigating various possible approaches to the removal of the carboxylic acid moiety from 14α,17α-etheno-16α-carboxypregn-5-en-3β-ol-20-one (Ia). Lack of success, in attempts[4] to reduce selectively the ring-D double bond of the adducts[5] resulting from Diels–Alder addition of maleic anhydride or of 4-phenyl-1,2,4-triazoline-3,5-dione to 3β-acetoxy-17-cyano-5,14,16-androstatriene, discouraged us from attempting to reduce selectively the corresponding double bond of I. Therefore, we decided to subject compound Ib to the conditions of the Cristol–Firth[6] modification of the Hunsdiecker reaction.[7]

A free-radical mechanism has been suggested for the Hunsdiecker reaction and apparently also pertains to the Cristol–Firth modification.[8] This mechanism leads to the prediction that the reaction of an *endo*-norborn-5-ene-2-carboxylic acid (II) should proceed by way of carboxy radical III. Decarboxylation of III should lead to alkyl radical IV which can either halogenate to give the normal Hunsdiecker product V[9] or yield, *via* the rearranged radical VI, the nortricyclyl halide VII.[10] Alternatively, the carboxy radical III could add to the double bond to afford halo lactone VIII. A concerted attack on the double bond should lead to *trans* addition, giving a product identical with that expected to be derived from a Prevost reaction[7] of the starting material. Nonconcerted addition



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(1) Part II: A. J. Solo and Baldev Singh, *J. Med. Chem.*, **9**, 179 (1966).

(2) This work was supported in part by Grants AM-06900-03 and AM-06900-04 from the National Institutes of Arthritis and Metabolic Diseases, The National Institutes of Health, U. S. Public Health Service.

(3) To whom inquiries regarding this work should be addressed.

(4) Unpublished results from this laboratory.

(5) A. J. Solo, H. S. Sachdev, and S. S. H. Gilani, *J. Org. Chem.*, **30**, 769 (1965).

(6) (a) S. J. Cristol and W. C. Firth, *ibid.*, **26**, 280 (1961); (b) S. J. Cristol, L. K. Gaston, and T. Tiedman, *ibid.*, **29**, 1279 (1964); (c) J. A. Davis, J. Herynk, S. Carrol, J. Bunds, and D. Johnson, *ibid.*, **30**, 415 (1965).

(7) (a) C. V. Wilson, *Org. Reactions*, **9**, 335 (1957); (b) R. G. Johnson and R. K. Ingham, *Chem. Rev.*, **56**, 219 (1956).

(8) F. W. Baker, H. D. Holtz, and L. M. Stock, *J. Org. Chem.*, **28**, 514 (1963).

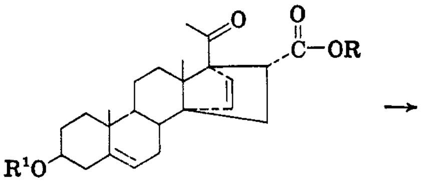
(9) S. J. Cristol, J. R. Douglass, W. C. Firth, and R. E. Kroll, *ibid.*, **27**, 2711 (1962).

(10) M. M. Martin and D. C. DeJongh, *J. Am. Chem. Soc.*, **84**, 3526 (1962), and references therein.

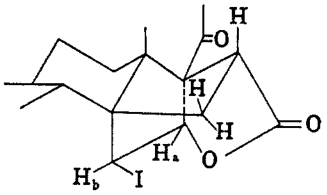
of the carboxy radical to the double bond would also be expected to lead to predominantly *exo* halide, unless substitution of that face of the system should make such a position sterically hindered.

Dreiding molecular models indicate that in I the side of the ring-D double bond, away from the carboxyl group, is severely hindered. This hindrance is confirmed by the failure of Ia or Ic to form lactones when treated with strong acid, and by the failure of Ib to form an iodo lactone when treated with iodine in carbon tetrachloride solution or in aqueous bicarbonate solution. It was hoped that this hindrance would cause Ib to afford normal products rather than halolactones under Hunsdiecker conditions.[11]

The major product resulting from treatment of Ib with mercuric oxide and iodine in refluxing carbon tetrachloride proved to be iodo lactone IX. The 100-Mc nmr spectrum of IX showed[12] that H_a and H_b were coupled with $J_{ab} = 7.7$ cps, thus establishing the *cis* nature of the iodo lactone.[13]

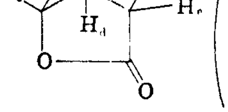


Ia, R = R¹ = H
b, R = H; R¹ = Ac
c, R = CH₃; R¹ = Ac

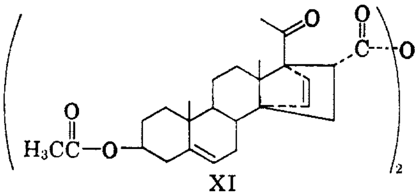


IX

To confirm that the *cis* attack on the ring-D double bond of I is the result of steric hindrance to *trans* attack on the bond and that it is not the result of any inherent tendency of norbornenes to undergo *cis* attack under Hunsdiecker conditions,[14] *endo*-2-norbornene-5-carboxylic acid was cyclized under conditions similar to those employed in the formation of IX. The resulting iodo lactone X proved to be identical with the compound[15] formed by normal iodo lactonization[16] of II. The 60-Mc nmr spectrum of X confirms the *trans* nature of the iodo lactone in that $J_{ab} = 0$. The lack of the 2.2–2.9-cps coupling usually associated[13a] with *trans*-2,3-disubstituted norbornanes is probably caused by a decrease, toward 90°, of the vicinal angle between H_a and H_b. Dreiding-type molecular models clearly indicate that lactone formation causes such an angular distortion and further show a small reduction of the acute vicinal angle between H_a and H_d. The latter change causes J_{ad} to increase from its usual value of approximately 3.5 cps[13a] to 4.9 cps. The doublet attributed to H_a is broadened, probably as a result of weak coupling to H_e. H_b appears as a sharp doublet with J = 2.2 cps, presumably reflecting coupling with H_j.[13]



X



XI

Experimental Section[17]

Total Hydrolysis of 14α,17α-Etheno-16α-carbomethoxypregn-5-en-3β-ol-20-one Acetate (Ic).—A mixture of 785 mg of Ic,[1] 2.5 g of potassium hydroxide, 3 ml of water, and 25 ml of ethanol was stirred at room temperature for 40 hr. The mixture was then concentrated under reduced pressure. The residue was partitioned between water and chloroform. The aqueous phase was acidified with hydrochloric acid. The resulting precipitate was collected by filtration, washed with water, and crystallized from acetone to give 14α,17α-ethano-16α-carboxypregn-5-en-3β-ol-20-one (Ia),[1] mp 233–234°, in a yield of 640 mg (93%).

14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one Acetate (Ib).—After a solution of 335 mg of Ia in 1.5 ml of pyridine plus 1.5 ml of acetic anhydride had been allowed to stand at room temperature for 24 hr, it was poured on ice. The precipitate which resulted was collected by filtration and then washed with hot water until free of pyridine. Recrystallization from ethanol gave Ib in a yield of 346 mg (93%) as white needles: mp 202–205°; ν^{Nujol} 3316, 1749, 1733, 1672 cm^{-1}.

Anal. Calcd for $C_{26}H_{34}O_5$: C, 73.21; H, 8.03. Found: C, 73.05; H, 7.79.

Attempted Lactonization of 14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one (Ia).—After a solution of 150 mg of Ia in 1.0 ml of trifluoroacetic acid had been kept overnight at room temperature, it was diluted with ethyl ether, washed several times with water, dried over magnesium sulfate, filtered, and then concentrated under vacuum to afford 145 mg of crude starting material. The nmr spectrum of the crude acid showed no sign of lactonization. Recrystallization of the crude acid from acetone–methanol produced Ia, mp 231–233°, in a yield of 111 mg.

Attempted Lactonization of 14α,17α-Etheno-16α-carbomethoxypregn-5-en-3β-ol-20-one Acetate (Ic).—A solution of 200 mg of Ic in 20 ml of methanol was saturated with anhydrous hydrogen chloride and then heated under reflux overnight. Standard work-up gave a crude product which, on the basis of its nmr spectrum, appeared to consist solely of starting material and of the alcohol derived from transesterification of the 3β-acetyl group of Ie. Crystallization led to the isolation of 167 mg of pure starting material.

Attempted Iodo Lactonization of 14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one Acetate (Ib). A.—A solution of 100 mg of Ib plus 60 mg of iodine in 40 ml of carbon tetrachloride was heated under reflux for 3 hr and then left at room temperature overnight. Standard work-up afforded only unchanged starting material, in a yield of 72 mg. A run in which an excess of finely powdered sodium bicarbonate was added to the reaction mixture also led only to recovery of Ib (72% recovery).

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[11] It has been established that, under some conditions, the *endo*-norborn-5-ene-2-carboxylate radical (III) gives products resulting from decarboxylation in preference to products resulting from lactonization. See ref 10.

[12] Nmr assignments were confirmed by spin-decoupling experiments.

[13] (a) J. C. Davis, Jr., and T. V. Van Aukin, *J. Am. Chem. Soc.*, **87**, 3900 (1965); (b) P. M. Subramanian, M. T. Emerson, and N. A. LeBel, *J. Org. Chem.*, **30**, 2625 (1965); (c) references cited in a and b.

[14] It has been pointed out by a referee that our compounds could have reacted by mechanisms other than those considered, for example by intramolecular addition of a mixed mercury salt.

[15] C. D. Ver Nooy and C. S. Rondestvedt, Jr., *J. Am. Chem. Soc.*, **77**, 3583 (1955).

[16] E. E. van Tamelen and M. Shamma, *ibid.*, **76**, 2315 (1954).

[17] Melting points were determined in capillary tubes on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. The infrared spectra were determined on Perkin-Elmer Infracord Models 137 or 237. Nmr spectra, unless otherwise noted, were determined in $CDCl_3$ on a Varian A-60 spectrometer and are reported in parts per million downfield from a tetramethylsilane internal standard.

B.—Attempted iodo lactonization of Ib with iodine in aqueous bicarbonate solution[15] also resulted only in recovery of 88% of the starting material.

Hunsdiecker Reaction[6b] of 14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one Acetate (Ib).—A slurry of 210 mg of Ib and 203 mg of mercuric oxide in 25 ml of carbon tetrachloride was stirred and heated to reflux for 1 hr in the dark. Then 132 mg of solid iodine was added and stirring and heating were continued for an additional 105 min. The mixture was then cooled and filtered. The filtrate was extracted with aqueous sodium bicarbonate (9 mg of Ib was recovered on work-up of the aqueous phase). The organic phase was washed with aqueous sodium thiosulfate, dried over anhydrous magnesium sulfate, and evaporated to dryness under reduced pressure to give 251 mg of crude product. Crystallization from acetone–hexane gave iodo lactone IX in a yield of 142 mg (54.5%) as white crystals: mp 227–228°; ν^{Najol} 1789, 1733, 1704 cm^{-1}; the nmr spectrum (100 Mc) showed singlets at 1.05 (18-CH_3 and 19-CH_3), 2.03 (acetate), and 2.29 (21-CH_3) quartets at 4.73 (CH bearing O of lactone) and 5.14 (CH bearing iodine), and multiplets at 3.17 (CH bearing of C═O lactone), and 5.40 (C-6—H).

Anal. Calcd for $C_{26}H_{33}IO_5$: C, 56.53; H, 6.02. Found: C, 56.80; H, 6.04.

The mother liquors on tlc examination (25% ethyl acetate in benzene on silica gel plates) showed two main components and trace amounts of two other substances. The major components on the basis of their R_f values seemed to be IX and the anhydride XI, described below. As the fastest moving spot was that of the anhydride, the presence of normal Hunsdiecker products was precluded. The infrared and nmr spectra of the mother liquors were consistent with their being a mixture of IX and anhydride XI, the composition estimated by nmr being three parts of IX to one part of XI. Attempted chromatogaphy of the mother liquors on silica gel led to detection of iodine color in the first eluted fractions. The column was therefore rapidly eluted with ethyl acetate and the eluate was partitioned between aqueous sodium bicarbonate and ethyl acetate. The aqueous layr afforded 33.5 mg of impure starting acid (nmr) while the neutral fraction consisted mainly of a 2:1 mixture of the iodo lactone IX to anhydride XI (nmr and tlc). Chromatography was again attempted on the recovered neutral fraction with similar results, 17.5 mg of acid and 39 mg of neutral fraction being recovered. It was subsequently demonstrated that stirring pure iodo lactone IX with silica gel in ethyl acetate leads to slow partial decomposition to form a carboxylic acid.

Anhydride of 14α,17α-Etheno-16α-carboxypregn-5-en-3β-ol-20-one Acetate (XI).—After a solution of 0.54 g of Ib in 2.0 ml of acetic anhydride had been left at room temperature overnight, the acetic anhydride was distilled under reduced pressure. The residue was crystallized twice from acetone to give XI, in a yield of 255 mg: mp 211–213°; ν^{Nujol} 1820, 1745 (sh), 1735, 1690 cm^{-1}; the nmr spectrum showed singlets at 2.03 (methyl of acetate) and 2.23 (21-CH_3), a quartet at 3.88 (CH bearing anhydride), a multiplet at 5.46 (vinyl hydrogen at C-6), and a pair of doublets at 6.22 and 6.34 ($J = 6.3$ cps, vinyl hydrogens at C-15 and C-16).

Anal. Calcd for $C_{52}H_{60}O_9$: C, 74.71; H, 7.89. Found: C, 74.52; H. 7.93.

Hunsdiecker Reaction[6b] of 2-Norbornene-5-carboxylic Acids.—A mixture of *endo*- and *exo*-2-norbornene-5-carboxylic acids (Aldrich Chemical Co.) was analyzed by nmr spectroscopy and found to consist of 69% *endo* isomer and 31% *exo*. Iodo lactonization[14,15] led to the isolation of 26% *exo* acid and of iodo lactone corresponding to the presence of 67% *endo* acid.

A slurry of *endo*-2-norbornene-5-carboxylic acid (regenerated[18] from the iodo lactone prepared above[15,16]) and 483 mg of mercuric oxide in 20 ml of carbon tetrachloride was stirred and refluxed for 45 min in the dark. Then 584 mg of solid iodine was added to the mixture and refluxing was resumed for 1 hr. After the reaction mixture had cooled, it was filtered, and the filtrate was extracted with cold, aqueous sodium bicarbonate. (Work-up of the aqueous extract failed to reveal the presence of any carboxylic acid.) The carbon tetrachloride solution was washed with aqueous sodium thiosulfate, dried over anhydrous magnesium sulfate, filtered, and then evaporated to dryness under reduced pressure to afford 583 mg of crude iodo lactone X. Crystallization from ether–hexane solution gave X, identical with the iodo lactone prepared above, in a yield of 384 mg (64%): mp 56–58°; ν^{CHCl_3} 1790 cm^{-1}; the nmr spectrum showed a doublet at 3.94 (CH bearing I), and a broad doublet at 5.08 (CH bearing O of lactone).[19]

The nmr spectrum of the mother liquors (186 mg) indicated that at least 80% of this material was also iodo lactone X.

Registry No.—Ia, 5498-14-6; Ib, 7732-49-2; IX, 7732-47-0; X, 7732-50-5; XI, 7771-28-0.

Acknowledgments.—We are deeply grateful to Dr. J. Colson of the Hooker Chemical Co. for the 100-Mc nmr spectra and spin decoupling experiments.

(18) J. A. Berson and D. A. Ben-Efraim, *J. Am. Chem. Soc.*, **81**, 4083 (1959).

(19) Note Added in Proof.—After this manuscript was submitted, a detailed study of the nmr spectrum of X was published. See R. M. Moriarty, H. Gopal, H. G. Walsh, K. C. Ramey, and D. C. Lini, *Tetrahedron Letters*, 4555 (1966).

Carbonium Ion Reactions of 3-Nortricyclylcarbinyl Systems

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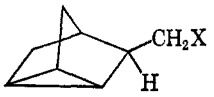
Received September 19, 1966

Products of several carbonium ion reactions of 3-nortricyclylcarbinyl systems have been examined. In all cases, *exo,exo*-tricyclo[3.2.1.0^{2,4}]octan-6-ol was a major product, along with unrearranged nortricyclylcarbinol and bicyclo[3.2.1]oct-2-en-7-ol. Experiments bearing on these interconversions are reported.

As an outgrowth of our studies on ring-expansion reactions of polycyclic systems[1] and as a result of an inherent interest in the chemistry of cyclopropylethyl systems,[2] we initiated studies of reactions involving cationic intermediates in the 3-nortricyclylcarbinyl system (1).[3,4] In addition to the many interesting possibilities for rearrangements in this system, this study offered promise of providing information concerning the stereoelectronic requirements involved in participation of cyclopropyl groups in solvolysis reactions of β-cyclopropylethyl systems.[5] At the inception of



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(1) (a) R. R. Sauers and J. A. Beisler, *J. Org. Chem.*, **29**, 210 (1964); (b) R. R. Sauers and R. J. Tucker, *ibid.*, **28**, 876 (1963); (c) R. R. Sauers, *Tetrahedron Letters*, 146 (1961); (d) R. R. Sauers, R. A. Parent, and H. M. How, *Tetrahedron*, **21**, 2907 (1965).

(2) R. R. Sauers and R. Ubersax, *J. Org. Chem.*, **31**, 495 (1966).

(3) Preliminary results were reported earlier; see R. R. Sauers and J. A. Beisler, *Tetrahedron Letters*, 2181 (1964).

(4) K. B. Wiberg and G. Wenzinger [*J. Org. Chem.*, **30**, 2278 (1965)] have published some related results.

(5) For a recent review, see P. G. Gassman and F. V. Zalar, *J. Am. Chem. Soc.*, **88**, 2252 (1966). See also M. Hanack and H. M. Ensslin, *Tetrahedron Letters*, 4445 (1966).