NHR
A
C=O
O—Fe^III
O
NH
CHO
A

NHR NHR
C=O O C
O∶Fe^III O
NH   NH
CHO   CHO
B

R =

Figure 2. Proposed structure of antimycin A_3–Fe(III) chelates: A, 1:1 chelate; B, 2:1 chelate. The suggested structure, B, is not intended to exclude other possible stereochemical arrangements of the ligands around the Fe atom. The other coordination positions, presumably occupied by water or other solvent molecules, are not included in the structure.

chelates with the results observed with antimycin A_3 confirmed these similarities (Table II). In further support of this type of ring formation Loomans[23] noted that the infrared spectrum of the ferric chloride–antimycin coordination compound was identical with that of antimycin except for a marked decrease in the 1-carbonyl peak at 6.01 μ.[24] Finally, Pfeiffer[25] reported that six-membered ring chelates are favored when one or more double bonds are present in the ring. The aromatic carbons of the benzene ring would contribute this double bond character in the case of antimycin.

The above evidence taken together strongly indicates that antimycin forms a chelate with iron(III) which contains a six-membered ring formed by coordination

between the 1-carboxamide carbonyl and the 2-hydroxyl group. The proposed structures of the 1:1 and 2:1 complexes are given in Figure 2. In contrast, Folkers[26] has proposed a π-type 2:1 coenzyme Q–Fe(III) complex for the nonheme iron associated with the flavoproteins of succinic dehydrogenase and DPNH dehydrogenase.

Application to Electron Ttransport in Vivo. Extrapolation of the above results concerning the nature of the ferric–antimycin chelate to the intact reduced coenzyme Q–cytochrome c reductase particle as it occurs *in vivo* would be of doubtful validity. Whether or not antimycin will bind nonheme iron in the lipoprotein environment must depend very greatly on the accessibility of the bidentate ligands to the six coordination sites of iron(III). Clarification of this point must await further knowledge of the lipoprotein-bound iron. Furthermore, *in vitro* iron chelation studies carried out in the present work were of necessity performed in partly aqueous media and at low pH. These conditions differ widely from the environment of the reduced coenzyme Q–cytochrome c reductase particle where pH has little or no meaning in the absence of water. The stability of the antimycin A–iron chelates described in this study may, however, be compared with the stability of similar chelates of other electron transport inhibitors, such as those described by Tappel.[12]

Estabrook[27] has demonstrated that high concentrations of ferrous iron do not prevent electron transport inhibition or compete for antimycin. It might be possible to test the hypothesis that antimycin A inhibition is due to binding of nonheme ferric iron by adding the purified antimycin–iron(III) chelate to the reaction medium. If the purified chelate failed to show electron transport inhibition, the possibility of an iron(III) binding mechanism by antimycin would be considerably strengthened.

(23) M. E. Loomans, Ph.D. Thesis, University of Wisconsin, 1962, p. 26.
(24) E. E. van Tamelen, *et al.*, ref. 5, p. 1641.
(25) P. Pfeiffer, *Angew. Chem.*, **53**, 93 (1940).

(26) H. W. Moore and K. Folkers, *J. Am. Chem. Soc.*, **86**, 3393 (1964).
(27) R. W. Estabrook, *Biochim. Biophys. Acta*, **60**, 246 (1962).

Communications to the Editor

The Neighboring Anthryl Group in Solvolysis[1]

Sir:

2-Phenyl-1-ethyl systems[2] (I) are marginal with respect to the competition in solvolysis between anchimerically unassisted ionization (k_s) and anchimerically assisted ionization (k_Δ). The latter leads to the "nonclassical" phenyl-bridged or "ethylenephenonium"[3] cation. The two modes of ionization are associated with characteristically different ΔS^*,[2c] β-D isotope ef-

fects[4] and response to solvent nucleophilicity and ionizing power.[2] From kinetic criteria the k_Δ/k_s ratio in solvolysis of I-OTs is judged[2b,c] to be low in EtOH and AcOH and substantial in HCOOH. For 2-p-anisyl-1-ethyl p-toluenesulfonate (2-An-EtOTs), with a p-MeO group accelerating k_Δ but not k_s, the kinetic criteria[2c] indicate k_Δ/k_s is *ca.* 1 in EtOH and high in both AcOH and HCOOH. In typical solvolysis of such simple primary systems leakage from any intermediate III associated with k_s to the bridged ion II or the rearranged open ion IIIa is negligible, so that product composition[2d,5] from suitably labeled starting

(1) (a) Reported in summary at the Japanese–American Seminar in Physical Organic Chemistry, Kyoto, Japan, April 6–10, 1965; (b) research sponsored by the U. S. Army Research Office (Durham).
(2) S. Winstein, *et al.*: (a) *Bull. soc. chim. France*, **18**, 55 (1951); (b) *J. Am. Chem. Soc.*, **75**, 147 (1953); (c) *ibid.*, **78**, 4801 (1956); (d) *Helv. Chim. Acta*, **41**, 807 (1958).
(3) (a) D. J. Cram, *J. Am. Chem. Soc.*, **71**, 3863 (1949); (b) *ibid.*, **86**, 3767 (1964).

(4) (a) W. H. Saunders, *et al.*, *ibid.*, **80**, 242 (1958); (b) *ibid.*, **82**, 3586 (1960).
(5) C. C. Lee, *et al.*, *Can. J. Chem.*, **35**, 1417 (1957); *Tetrahedron*, **7**, 206 (1959).

Solvent	I-OTs	$(\%k_\Delta)^a$	2-An-EtOTs[2b-d]	$\%k_\Delta$	IV-OTs	$\% k_\Delta{}^a$
60% dioxane	11.2 ± 0.2	ca. 2			36.5 ± 0.2	ca. 100
EtOH	7.43 ± 0.02	0.6^b	13.6	47^c	8.52 ± 0.05	
AcOH	0.288^{2b}	10.8^b	9.8	99^c	11.6^d	100
HCOOH	41^{2c}	90^b	1770	100^c	4000 ± 500	100

^{a} $100k_\Delta/(k_\Delta + k_s)$. ^{b} Based on data in ref. 5. ^{c} Based on data in ref. 2d. ^{d} Downward drifting first-order rate constant.

material correlates with the proportions of k_Δ and k_s deduced from kinetics.[6,7]
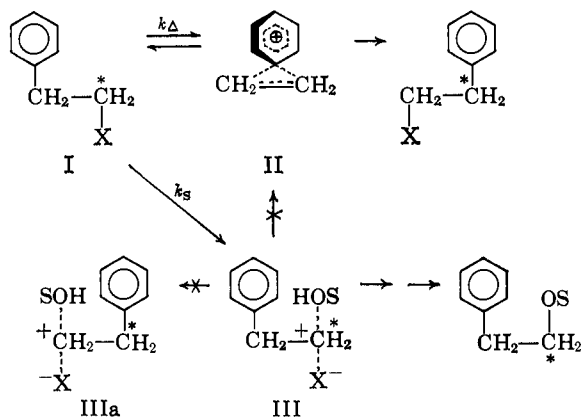
On the basis of theoretical considerations and the known behavior of anthracene and some of its derivatives, we can predict greater k_Δ values for the 9-anthrylethyl derivative IV-OTs than for I-OTs and anticipate the possibility that kinetic control of product from the corresponding bridged ion V might lead to substantial amounts of isolatable spiro alcohol VI-OH. In this communication we can now report the striking behavior of the anthrylethyl system in solvolysis and in a following communication[8] we describe the direct observation of the aryl-bridged anthrylethyl cation V by n.m.r. technique.

Hydrolysis of IV-OTs,[9a] m.p. 117–119°, in refluxing 60% aqueous dioxane in the presence of $NaHCO_3$ did indeed lead to a nearly quantitative yield of an alcohol mixture containing 15% of the known[9b] 9-anthrylethanol (IV-OH), m.p. 106–108°, and 85% of a new very reactive alcohol, m.p. 80–82°, whose chemical behavior and n.m.r. spectrum was consistent with the VI-OH structure. This spiro alcohol[10] VI-OH was separately prepared by lithium aluminum hydride reduction of the known spiro ketone[9c] VII. In its n.m.r. spectrum in $CDCl_3$, VI-OH displayed a singlet at τ 4.36 for the α-proton, a multiplet at τ 2.3–3.2 for the eight aromatic protons, and an A_2B_2 multiplet centered at τ 8.55 for the 4 cyclopropane

(6) See S. Winstein, et al., Experientia, 12, 138 (1956); J. Am. Chem Soc., 79, 3105, 3114 (1957), for the analogous correlation between rates and products in Ar₁-5 and Ar₂-6 solvolyses.

(7) In our opinion, H. C. Brown has given a poor perspective on this competition between k_Δ and k_s in solvolysis of I-OTs and related systems [H. C. Brown, Special Publication No. 16, The Chemical Society, London, 1962, pp. 140–157; H. C. Brown, K. J. Morgan, and F. J. Chloupek, J. Am. Chem. Soc., 87, 2137 (1965)]. See ref. 3b and S. Winstein and R. Baker, ibid., 86, 2071 (1964).

(8) L. Eberson and S. Winstein, ibid., 87, 3506 (1965).

(9) (a) W. A. Waters, J. Chem. Soc., 1108 (1956); (b) B. M. Mikhailov, Izv. Akad. Nauk SSSR, Otdel. Khim. Nauk, 420 (1948); (c) A. Mustafa and M. K. Hilmy, J. Chem. Soc., 1434 (1952).

(10) This and other new compounds gave satisfactory carbon and hydrogen analyses.

protons. The spiro alcohol was converted to the thermodynamically favored IV structure with a half-life of ca. 40 min. at ca. 30° in 95% ethanol 10^{-4} M in $HClO_4$. On the other hand, VI-OH was completely stable under the conditions for solvolysis of IV-OTs in aqueous dioxane when excess $NaHCO_3$ was present.
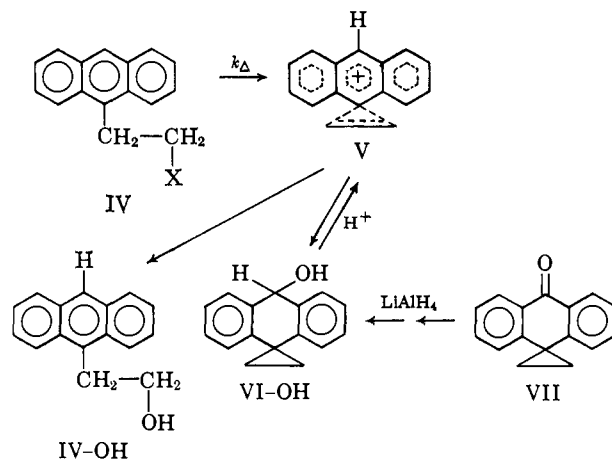
That even the 15% of IV-OH obtained in hydrolysis of IV-OTs in 60% dioxane arises essentially entirely from the k_Δ route was shown by n.m.r. examination of the product from α-d_2-labeled IV-OTs. The IV-OH component of the product was within experimental error completely scrambled. The competition between k_Δ and k_s in solvolysis of IV-OTs in a variety of solvents is further elucidated by the comparison of titrimetric solvolysis rate constants (k_t) with those of I-OTs and 2-An-EtOTs in Table I. As usual,[2] the EtOH:AcOH: HCOOH solvent rate sequences are quite instructive, these being 26:1:142 for I-OTs, 1.39:1:180 for 2-An-EtOTs, and 0.73:1:345 for IV-OTs.

From the data we conclude that k_s for IV-OTs is considerably smaller than for I-OTs or 2-An-EtOTs, probably largely for steric reasons. On the other hand, k_Δ for IV-OTs is larger than that for I-OTs in all four solvents by factors of the order of 10^2. As regards rate of anchimerically assisted ionization, IV-OTs is similar to 2-An-EtOTs, neighboring anthryl being slightly superior to p-anisyl. Even in EtOH k_Δ/k_s is quite high for IV-OTs, the product from buffered ethanolysis of IV-OTs containing 75% VI-OEt and 25% IV-OEt.

It is evident that a bridged cationic intermediate, most simply written as V, is preferred in the usual solvolytic reactions of the IV- and VI-type structures.

Kinetic control tends to favor spiro-VI products, while thermodynamic control gives the IV type. Presumably because of such thermodynamic control, acetolysis of IV-OTs leads entirely to IV-OAc, and we have so far obtained only IV-RCl,[10] m.p. 93–96°, from various treatments of VI-OH with HCl or SOCl₂.

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Direct Observation of the Anthrylethyl Bridged Cation[1]

Sir:

Solvolysis and deuterium scrambling studies[2] of I-OTs show that the 9-anthryl group is a better participating group than phenyl. Even in 60% aqueous dioxane under conditions of kinetic control, essentially all of the product is formed through an aryl-bridged cation (II), the product being partly I-OH (15%) but mainly the spiro-III-OH (85%). We now report that II is sufficiently stable for direct observation in SO₂–SbF₅, in which a number of chemically unstable cations have recently become accessible for n.m.r. spectroscopy.[3]
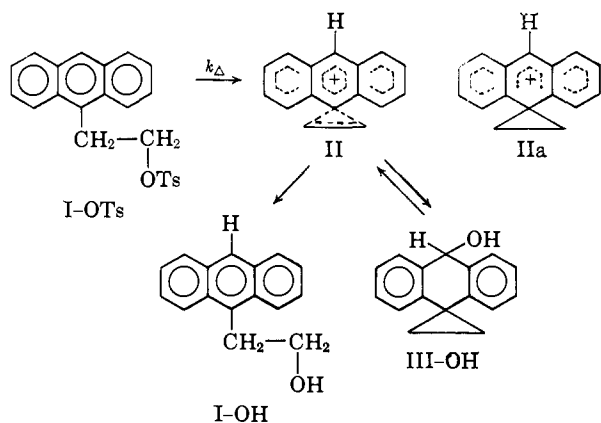
Since we have so far been unable to convert III-OH into a halide (III-Cl or III-F) because of the extreme ease of rearrangement, III-OH was used directly for n.m.r. studies in SO₂–SbF₅. Careful addition of III-OH at −80° to a 2.5 M excess of SbF₅ dissolved in SO₂ gave a brown solution having signals[4] (at −55°) at 3.44 (sharp singlet), 7.73 (triplet), 8.20 (triplet), and 9.64 (sharp singlet) p.p.m. with integrated band areas in the proportions 4:4:4:1. Two other singlets at 10.0 and 8.80 p.p.m. (area ∼1) broadened and finally

(1) (a) Reported in summary at the Japanese-American Seminar in Physical Organic Chemistry, Kyoto, Japan, April 6–10, 1965; (b) research sponsored by the U. S. Army Research Office (Durham).
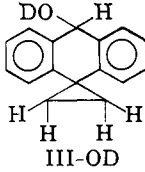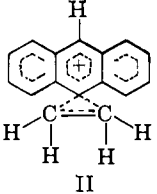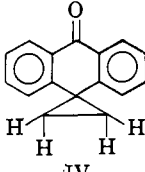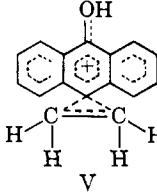
(2) L. Eberson, J. P. Petrovich, R. Baird, D. Dyckes, and S. Winstein, *J. Am. Chem. Soc.*, 87, 3504 (1965).

(3) (a) G. A. Olah, *ibid.*, 86, 932 (1964); (b) G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyesi, J. S. McIntyre, and I. J. Bastien, *ibid.*, 86, 1360 (1964).

(4) Unless otherwise stated, all n.m.r. band positions are given in p.p.m. downfield from external (CH₃)₄Si.

almost disappeared as the temperature was gradually raised to −15° (the rest of the spectrum remained unchanged). By using III-OD these signals were eliminated from the spectrum, showing their origin from the removed OH group. Positions and assignments of n.m.r. signals in the spiro alcohol III-OD and its solution in SO₂–SbF₅ are summarized in Table I.

Table I. Proton Signals in p.p.m. Downfield from $(CH_3)_4Si$

SO₂, −20°	SO₂–SbF₅, −55°
III-OD: 5.37 sharp singlet; 6.6–8.0 multiplet; 1.20 A₂B₂ multiplet	II: 9.60 sharp singlet; 7.7, 8.2 2 triplets; 3.44 sharp singlet

CDCl₃[a]	H₂SO₄
IV: 6.9–8.4 multiplet; 1.84 sharp singlet	V: 7.7–9.2 multiplet; 3.18 singlet

[a] Me₄Si as internal standard.

By treatment of the carbonium ion solution with excess methanol at −80° there was obtained a 79% yield of crude I-OCH₃, identified by comparison with authentic I-OCH₃, m.p. 69–69.5°, prepared from I-ONa and methyl iodide. This is the product of thermodynamic control as would be expected from the strongly acidic nature of the medium.

The observed n.m.r. spectrum of the carbonium ion obtained from the spiro alcohol III-OH is in excellent agreement with that expected for a symmetrical bridged ion[5] II. The proton in the 10-position of II displays a signal (9.60 p.p.m.) at nearly the same chemical shift as that of the analogous α-proton in the benzhydryl cation[3a] (9.80 p.p.m.), and the aromatic protons in this latter cation are deshielded to approximately the same extent as are those in II. The sharp singlet signal from the "cyclopropane" protons in II is appropriate for a symmetrical structure, and the chemical shift for these protons is very far from that which would be expected for rapidly equilibrating classical ArCH₂CH₂⁺

(5) Attempts to prepare the ion II from derivatives of the I series and SbF₅ failed since I-OH and I-Cl gave σ-complexes with SbF₅. The n.m.r spectra of these solutions were like that of 9-ethylanthracene (I–H) under the same conditions. Unchanged starting materials were recovered almost quantitatively by water quenching of the SO₂–SbF₅ solutions. Anthracene is known to give σ-complexes with strong Lewis acids [W. I. Aalbersberg, G. J. Hoijtink, E. L. Mackor, and W. P. Weijland, *J. Chem. Soc.*, 3055 (1959)]. 2-Phenylethyl fluoride and 2-(α-naphthyl)ethyl fluoride were also investigated but did not give solutions stable enough for n.m.r. measurements.