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Overcrowded Molecules. IV. Synthesis and Properties of Some Highly Strained 1-(2-Pyridyl)-9-oxa-9a-azoniabenzo[*b*]phenanthro[4,3-*d*]furans

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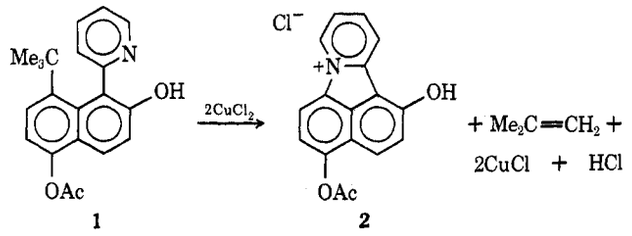
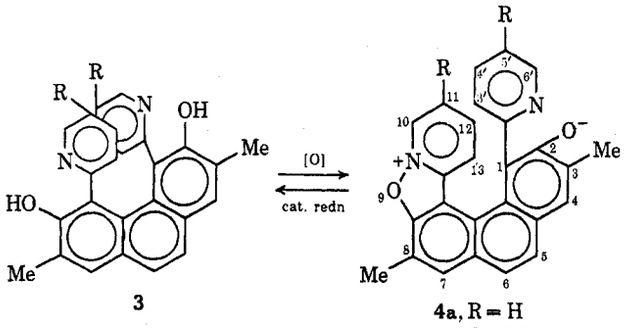
Oxidation of the overlapped pyridyl compounds **3** yields the even more highly overcrowded isoxazolium zwitterions, **4**, whose spectral properties indicate them to be intramolecular charge transfer complexes. Unusual, largely unexplained, chemical shifts and coupling constants occur in the nmr spectra of **4**. Reaction of **4** with several "hard" nucleophiles gives products resulting from addition at C-8a (BH_4^-, OH^-, OMe^-), or substitution at C-7 (CN^-) *via* an apparent 1,6 addition–elimination. In contrast, reaction of the closely related deoxy isoxazolium salt **8** with nucleophiles gives products resulting from the more common reduction (BH_4^-), or substitution (CN^-) of the pyridinium ring. The difference in reactivity is ascribed to the charge transfer character of the zwitterion.

The novel intramolecular cyclization reaction following oxidation of **1** with $CuCl_2$ was reported recently.[1]



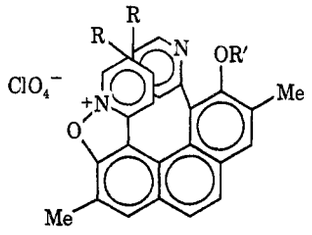
1 **2**

Since we had in hand other highly strained molecules with similar substituent placements (*e.g.*, **3**)[2] whose oxidation potentials[3] were even more favorable for reaction, we subjected **3a** and **3b** to the oxidizing conditions using *N*-chlorobenzotriazole in CH_2Cl_2. A red crystalline product was isolated in each case in 65–70% yield.[4] These compounds have been characterized as isoxazolium betaines **4a,b** based on spectral and chemical evidence, and their formation represents a new type of intramolecular oxidative cyclization reaction. A number of unusual chemical transformations are also recorded, related to the atypical behavior of **4a** toward a few selected nucleophilic reagents.



3 **4a**, R = H; **b**, R = Me

Isoxazolium Betaine (4a).—Elemental analysis and molecular weight determinations of **4a** (390 from mass spectrum, 387 ebullioscopic) established it to be monomeric with respect to **3a** with two less hydrogens in accord with a $C_{26}H_{18}N_2O_2$ formulation. Catalytic reduction (Pd/C) regenerated starting diol **3a**. Treatment of **4a** with dilute perchloric acid gave a yellow perchlorate salt, **5**, and with acetic anhydride–sulfuric acid followed by anion exchange, a monoacetyl perchlorate derivative, **6a**.



	R	R′
5	H	H
6a	H	Ac
6b	Me	Ac

The mass spectral fragmentation of **4a** was dominated by two ions, M^+ and $(M - \text{pyridyl})^+$, this un-

(1) (a) D. L. Fields and T. H. Regan, *J. Org. Chem.*, **36**, 2986 (1971); (b) see also G. Popp, *ibid.*, **37**, 3058 (1972).

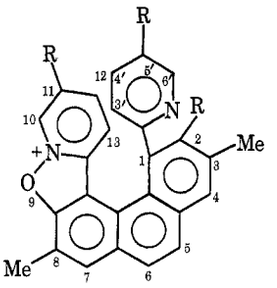
(2) D. L. Fields and T. H. Regan, *ibid.*, 2991 (1971).

(3) $E_{1/2}$ for **3a** = +0.75 V; $E_{1/2}$ for **1** = +1.00 V *vs.* sce in CH_3CN (TBAP as supporting electrolyte).

(4) $CuCl_2$ oxidation of **3a,b** followed by basification with 5% $NaHCO_3$ produced these same compounds, but this is not a preferred procedure, owing to difficulty in ridding the product of trace amounts of copper impurities.

TABLE I

NMR CHEMICAL SHIFTS[a] FOR 9-OXA-9a-AZONIABENZO[*b*]PHENANTHRO[4,3-*d*]FURANS

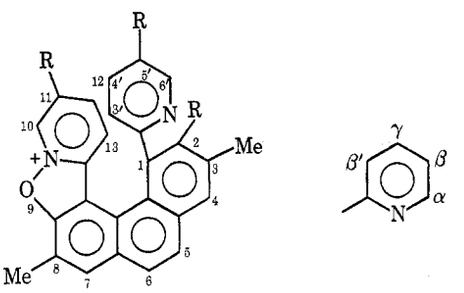


Compd	R-2	Me-3	H-4	H-5	H-6	H-7	H-8	H-9	R-11	H-12	H-13	H-3′	H-4′	R-5′	H-6′
4a[b]		2.30	7.39	6.76	7.30	6.60	1.99	8.43	6.71	7.60	10.12	6.93	7.50	7.14	8.50
[c]		2.30	7.42	6.92	7.38	6.87	2.02	8.36	6.85	7.66	10.00	6.90	7.67	7.24	8.47
4b[b]		2.32	7.44	6.81	7.37	6.60	2.02	8.22	2.24	7.50	10.17	6.84	7.48	2.21	8.30
5[d,e]		2.48	7.91	7.30	7.79	6.94	2.03	9.43	8.45	7.75	9.04	6.50	7.59	7.33	8.44
6a[e]	2.51	2.43	8.30	7.64	8.09	7.32	2.08	9.04	8.78	8.16	9.26	6.44	7.76	7.46	8.61
6b[e]	2.50	2.25	8.00	7.44	7.88	6.90	2.08	8.82	2.59	8.76	9.04	6.23	7.23	2.40	8.36
8[e]	8.65	2.52	8.06	7.56	7.99	7.16	2.06	9.22	8.68	8.06	9.04	6.59	7.71	7.44	8.65

[a] δ values in parts per million downfield from internal TMS. Obtained with a Bruker 90-MHz spectrometer using 1–4% solutions in DMSO-d_6 unless otherwise specified. [b] $CDCl_3$ solvent. [c] Spectrum recorded at 100°. [d] CD_3OD–CD_3CN solvent. [e] Counterion ClO_4^-.

TABLE II

NMR COUPLING CONSTANTS[a] FOR 9-OXA-9a-AZONIABENZO[*b*]PHENANTHRO[4,3-*d*]FURANS. COMPARISON WITH ANALOGOUS VALUES IN PYRIDINE[b]



	—$J_{\alpha,\beta}$ (5.5)—		——————$J_{\beta,\gamma}$ (7.5)——————				—$J_{\alpha,\gamma}$ (1.9)—		—$J_{\beta,\beta'}$ (1.6)—		—$J_{\alpha,\beta'}$ (0.9)—				
Compd	$J_{5',6'}$	$J_{10,11}$	$J_{3',4'}$	$J_{4',5'}$	$J_{11,12}$	$J_{12,13}$	$J_{4',6'}$	$J_{10,12}$	$J_{3',5'}$	$J_{11,13}$	$J_{3',6'}$	$J_{10,13}$	J_{7,CH_3}	J_{4,CH_3}	$J_{5,6}$
4a[c]	4.7	7.1	7.7	7.5	7.1	9.2	1.8	1.6	1.2	1.7	0.8	0.5	1.5	0.8	8.0
d, e	4.7	7.0	8	7.5	7.0	9.1	1.8	1.6	1.2	1.7	0.8	0.5	1.5	1.0	9.5
4b[c]			8.0			9.2							1.5	1.0	7.8
5[f,g]	4.8	8.5	7.8	7.8	7.2	6.7	1.8	1.6	1.2	1.5	1.0	0.6	1.5	1.0	8.0
6a[d,g]	4.7	8.2	7.6	7.6	7.4	6.5	2.0	1.5	1.2	1.5	1.0	0.5	1.5	0.5	8.3
6b[d,g]		8.2	7.8				1.8						1.5	0.5	8.5
8[d,g]	4.8	5.2	7.4	7.7			1.8		1.4	1.4		0.8	1.0	0.5	

[a] Hertz. [b] Reference 6. [c] $CDCl_3$ solvent. [d] DMSO-d_6 solvent. [e] Spectrum recorded at 100°. [f] CD_3OD–CD_3CN solvent. [g] Counterion ClO_4^-.

usual biphenyl-type cleavage being characteristic of the overlapped pyridine systems.[2] The nmr spectrum (see Tables I and II) showed that only the two exchangeable hydrogens were missing. The chemical shifts of the pyridinium hydrogens were puzzling at first; the low-field shifts expected on introduction of the positive charge were observed but not in the expected manner. The hydrogen α to the ring junction (*i.e.*, H-13) appears at very low field, but this hydrogen is β to the N^+ and, in general, should be least affected by the positive charge. However, removal of the negative charge on oxygen of C-2, either by protonation (**5**) or by forming the acetate ester **6a**, causes H-13 to shift to higher field, even though this shift is still at unusually low field. Molecular models show that the hydrogen in question (H-13) is very close to both the $-O^-$ and the N of the other pyridyl ring. Operation of a steric compression shift analogous to that observed by Anet[5] could account for the observed effect. This cannot be the entire explanation, however, since the unusual shifts in the pyridinium ring are accompanied by significant changes in the magnitude of several coupling constants. For example, $J_{12,13}$ (corresponding to $J_{\beta,\gamma}$ = 7.5 Hz in pyridine[6]) is ~9 Hz in the betaine, and falls to ~6.5 Hz in the protonated or acetylated compound. This probably reflects changes in the degree of bond localization in the pyridinium ring as a result of the high degree of strain, but we have been unable to rationalize all the changes in a coherent manner.

Unequivocal assignment of chemical shifts in **4a** could be made since **4b** and **6b** were synthesized with a

(5) S. Winstein, P. Carter, F. A. L. Anet, and A. J. R. Bourn, *J. Amer. Chem. Soc.*, **87**, 5247 (1965).

(6) R. F. M. White, "Physical Methods in Heterocyclic Chemistry," Academic Press, New York, N. Y., 1963, p 142.

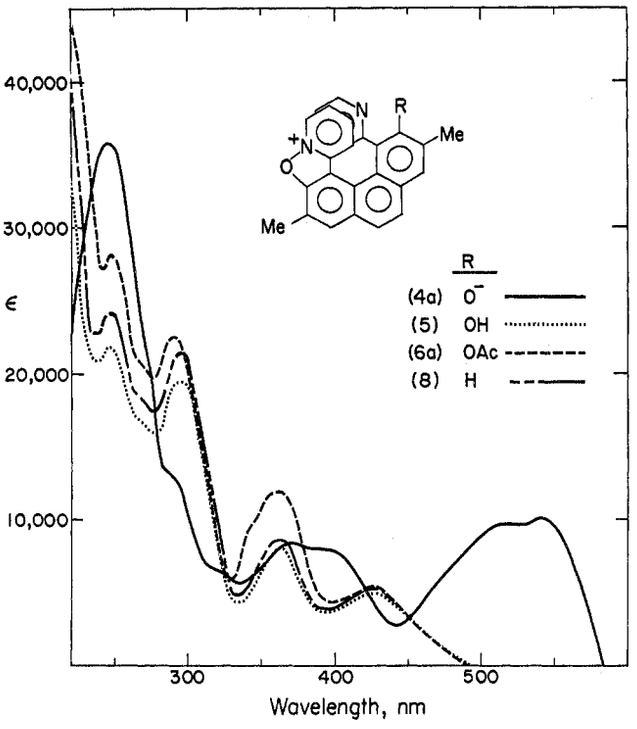
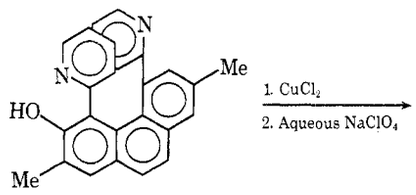


Figure 1.—Electronic spectra of isoxazolium salts **4a, 5, 6a,** and **8**. The counterion for **5, 6a,** and **8** is ClO_4^-.

methyl substituent in each pyridine ring in a known position. Appropriate decoupling experiments served to confirm the assignments.

The electronic spectrum of **4a** (and **4b**) shows a significant long-wavelength shift for the betaine compared to the protonated and acetylated forms (Figure 1). This is interpreted in terms of an intramolecular charge transfer from $-O^-$ to the pyridinium ring, which could contribute to the chemical shift and coupling-constant changes as a result of changes of electron density distribution.

As this study progressed, another particularly useful and closely related isoxazolium salt became available, specifically, **8**. It was prepared by $CuCl_2$ oxidation of phenanthrol **7**, which in turn was obtained by a synthesis which will emerge later. The uv and nmr spectra of **8** bore the expected similarities to those of **5** and



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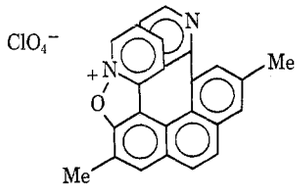


8

6a (see Figure 1 and Tables I and II), its elemental analysis was satisfactory, and the chemistry to be described below was interpretable in terms of the assigned structure.

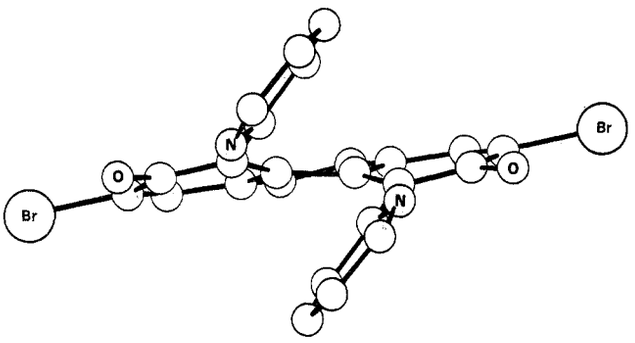


Figure 2.—View of a 4,5-bis(2-pyridyl)phenanthrene-3,6-diol derivative along the twofold symmetry axis.[7]

Reactions with Selected Nucleophiles.—An examination of space-filling models of isoxazolium salts **4** and **8** suggests that they are exceedingly sterically strained compounds, even more so than their phenanthrol precursors, **3** and **7**. It has previously been established by X-ray analysis[7] that the overcrowding found in the latter-type compounds produces a twisting of the phenanthrene skeleton out of its preferred planarity (see Figure 2), with the pyridines located on opposite sides and further rotated by ~40° from the phenanthrene mean plane. As such, the pyridines bear a stepped relationship, are nearly parallel, and are extraordinarily close, having a nonbonded contact of ~2.8 Å between C_2 and C_2' to a more normal 3.45 Å between C_6 and C_6'.

In the oxidative cyclization of these compounds to isoxazolium **4** and **8**, the ~2.6-Å N to O distance must be shortened to within bonding distance (~1.3–1.4 Å), and it would also appear desirable to rotate the pyridine involved in the isoxazolium ring more into the mean plane of the phenanthrene in order to achieve a reasonable degree of N–O bonding overlap and planarity of the atoms of the isoxazolium ring. However, this is not easily accomplished, since any rotation of one pyridine toward greater planarity with the phenanthrene will require displacement of the second pyridine further out of plane if the ~3-Å minimum separation between the pyridines is to be maintained. Therefore, regardless of how adequate bonding overlap is achieved, it seems likely that there will be more pronounced bond-angle deformations and constraint present in **4** than found in the already highly strained **3**, with concomitant higher ring-strain energy. One might expect the isoxazolium ring to reflect this additional strain by showing greater reactivity than is general for isoxazolium ring systems, and it should be quite responsive to interaction, directly or indirectly, with reagents capable of providing relief of this added ring strain.

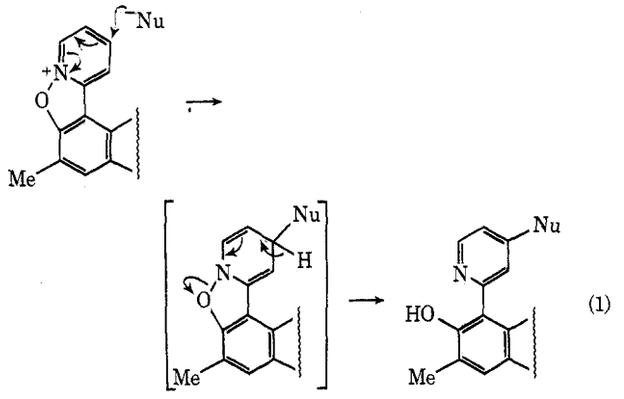
An obvious type of reaction that would achieve this end and one with considerable precedent[8] is a nucleophilic aromatic substitution at the 2 or 4 position of the pyridinium ring, as indicated in eq 1. Indeed, **8** experiences this mode of attack by such "hard" nucleophiles[9] as CN^-, BH_4^-, and probably OH^- and OMe^- as well. However, the closely related zwitterion

(7) D. L. Smith and E. K. Barrett, *Acta Crystallogr., Sect. B*, **27**, 419 (1971).

(8) See, for example, A. R. Katritzky and E. Lunt, *Tetrahedron*, **25**, 4291 (1969); R. Eisenthal and A. R. Katritzky, *ibid.*, **21**, 2205 (1965).

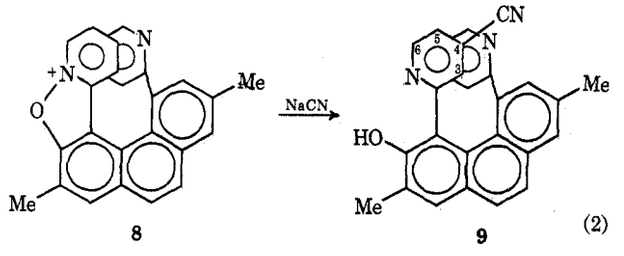
(9) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963); R. G. Pearson and J. Songstad, *ibid.*, **89**, 1827 (1967).

4a differs dramatically from isoxazolium **8** in this respect and is obviously under the influence of strong directive factors not present in **8**. This is illustrated by a comparison of product types from the reactions of **4a** and **8** with cyanide ion.

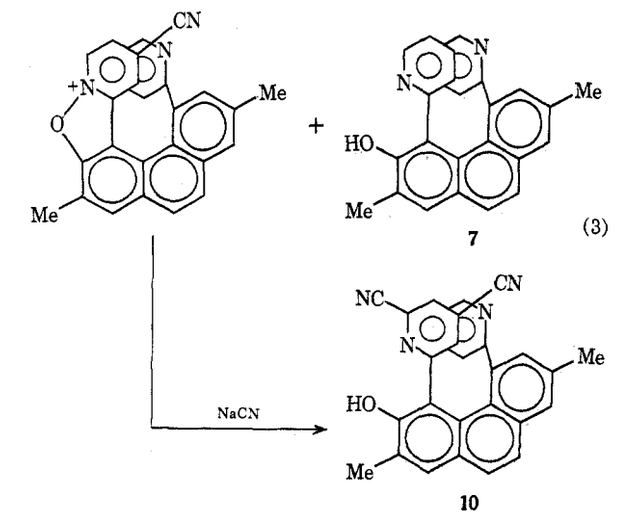


(1)

Treatment of **8** with excess sodium cyanide in DMSO for 5 min at room temperature provided, after work-up and chromatography, three recognizable phenanthrol products: a mono- and a dicyano derivative, **9** and **10**, isolated in 30 and 12% yields, respectively, plus a 28% yield of **7**. Cyanation of one of the pyridines was readily deduced for both **9** and **10** from mass spectroscopic and nmr evidence, wherein **9** displayed *m/e* 401 (9%, M^+), 322 (24%, M − Py), and 298 (100%, M − Py − CN) with a metastable transition 401 → 298, while **10** had *m/e* 462 (10%, M^+), 348 (6%, M − Py), and 298 (100%, M − Py − 2CN), with a metastable transition of 462 → 298. The position or positions of cyano substitution were assigned based on nmr evidence, the pyridine bearing the cyano group of **9** being observed as an AMX pattern [δ 6.88 (d of d, 1, J = 0.9, 1.6 Hz, H-3), 7.20 (d of d, 1, J = 1.6, 5.5 Hz, H-5), and 8.37 (d of d, 1, J = 0.9, 5.5 Hz, H-6)] and in **10**, an AX pattern found at δ 7.08 (d, 1, J = 1.5 Hz, H-3) and 7.58 (d, 1, H-5). The formation of both reduction product **7** and dicyano derivative **10** in this reaction is unexpected, but can be rationalized on the basis that they are a resultant of a redox reaction as indicated in eq 3.

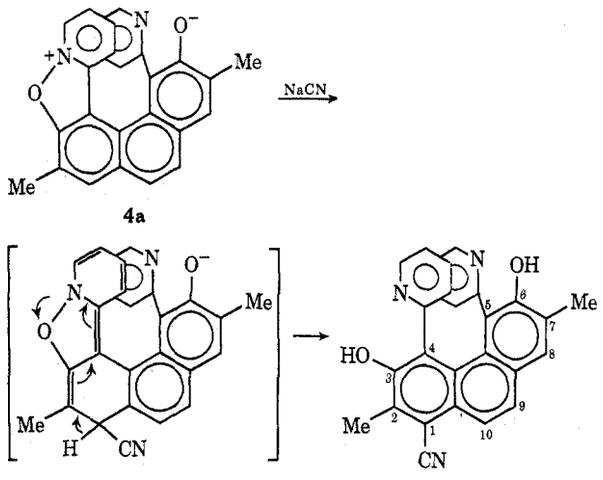


8 **9** (2)

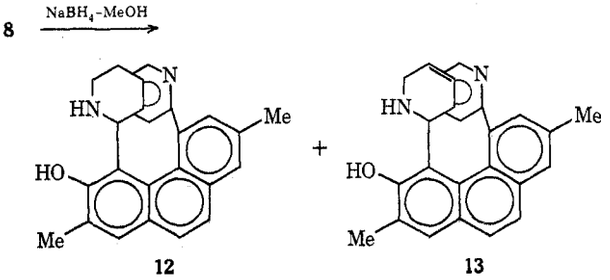


(3)

In contrast to these results, a single product, 1-cyano-2,7-dimethyl-4,5-bis(2-pyridyl)phenanthrene-3,6-diol (**11**), was obtained in virtually quantitative yield from the reaction of **4a** with NaCN under reaction conditions comparable to those employed in the conversion of **8** to **7**, **9**, and **10**. The very close similarity of the uv spectrum of **11** to that of **3a** strongly suggested it to also be a 4,5-bis(2-pyridyl)phenanthrene-3,6-diol and its mass spectrum was also characteristic, having only two significant fragments, that of the parent ion (*m/e* 417, 27%) and M − pyridyl (*m/e* 341, 100%). The complete absence of a *m/e* 314, which would represent the loss of a cyanopyridyl group from the parent, as found in the fragmentation of **9**, suggested that cyanation of the phenanthrene rather than the pyridine ring had occurred, and this was confirmed by nmr results which completely supported the 1-cyano derivative assignment. Two prominent features of the nmr spectrum are the absence of a signal from H-1 and 0.5-ppm shift downfield for H-10, consistent with the presence of the CN at C-1, peri to H-10.



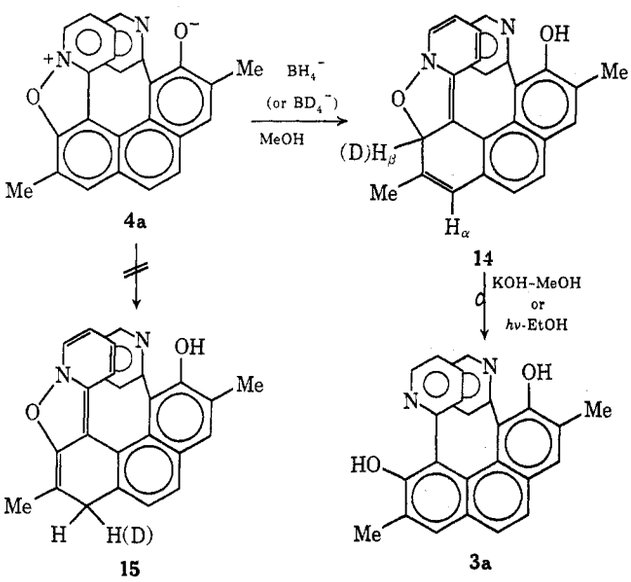
The difference in modes of reaction of **4a** and **8** with $NaBH_4$ is equally striking. A complex mixture of products resulted from the reaction of **8** with excess methanolic $NaBH_4$ for 5 min at room temperature. The two major components were isolated by Florisil chromatography as a difficultly separable mixture and are assigned the hexa- and tetrahydropyridylphenanthrol structures **12** and **13**, respectively, based on



spectral evidence presented in the Experimental Section.

On the other hand, treatment of **4a** with methanolic $NaBH_4$ under identical conditions resulted in the immediate discharge of its deep red color to a light orange followed by separation of a highly insoluble bright orange crystalline product, **14**, in essentially quantitative yield. This compound was not the known diol **3a**, which might be anticipated from our experience with the **4a**–cyanide reaction. However, it could be readily isomerized to **3a**, either by photolysis in ethanol or by heating at reflux temperature with methanolic KOH followed by neutralization.

Its mass spectrum has two dominant peaks, a parent *m/e* 392 (60%, M^+) and M − pyridyl *m/e* 314 (100%), establishing it to be isomeric with **3a**. The analogous product from a $NaBD_4$ reduction in CH_3OD has *m/e* 394 and 316, and that from $NaBD_4$ in CH_3OH has *m/e* 393 and 315, showing that one of the hydrogens (or deuteriums) provided by the reducing agent was incorporated into the product in a nonreadily exchangeable position.

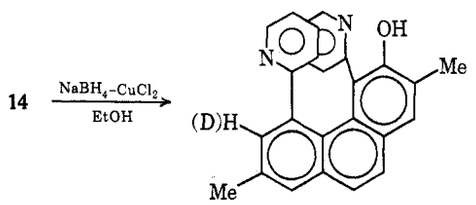


4a **14** **15** **3a**

Unfortunately, the very low solubility of **14** in all of the common nonacidic nmr solvents prevented its nmr examination *per se*. However, the nmr spectrum of a solution of it in CD_3OD acidified with DCl was obtained, and provided the desired information as to the site of BH_4^- (BD_4^-) attack, and a firm basis for its structure assignment as the 3-isoxazoline **14**.[10] Most noteworthy, double irradiation experiments showed one of the two methyls (at δ 2.05) now to be weakly coupled to *two* protons found at δ 5.93 (H_β) and 6.54 ppm (H_α), and they themselves coupled (J = 2.5 Hz) to each other. The absence of the upfield multiplet at δ 5.93 in the spectrum of the deuterio derivative identifies the signal as that associated with the hydrogen derived from the BH_4^- reagent. The 2.5-Hz spin coupling observed for these two protons is compatible with their having an allylic–axial relationship rather than the geminal one found in an alternative structural possibility, **15**.

(10) See I. Adachi and H. Kano, *Chem. Pharm. Bull.*, **17**, 2201 (1969), for an analogous example of reaction of Grignard reagents with a 5-unsubstituted isoxazolium salt to give 5-substituted 3-isoxazoline derivatives.

As additional support for the structural assignment, **14** was further reduced with resulting aromatization by $NaBH_4$–$CuCl_2$ in refluxing ethanol[11] to the aforementioned phenanthrol **7**. Its structure rests on correct elemental analysis, the usual spectral evidence (uv, ir, nmr, mass spectrometry), and its chemistry, which we have already mentioned.



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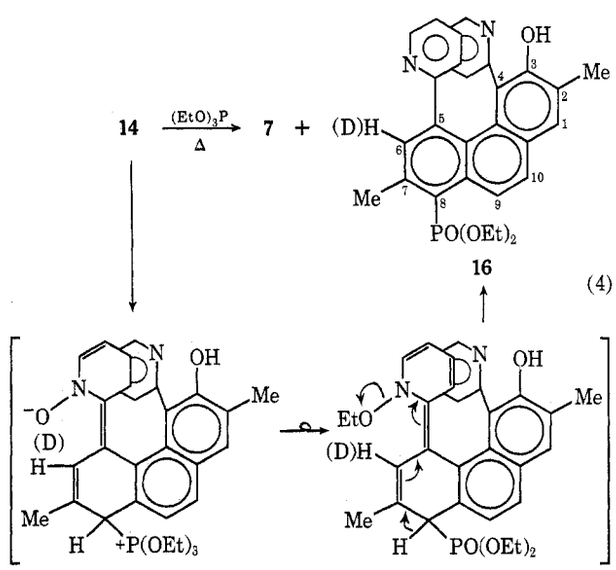
An alternative approach to **7** which proved much less successful, but nonetheless interesting, was an attempted deoxygenation involving heating **14** with triethyl phosphite at reflux temperature (*ca.* 160°) until the starting material was consumed (2 hr, by tlc). At least four products were formed, two of which were isolated on a crystalline basis and identified. Phenanthrol **7** was one of these, but was obtained in only 4% yield. The other product, **16** (23%), also proved to be a 4,5-bis(2-pyridyl)phenanthren-3-ol, but was further substituted by a diethyl phosphonate group in the 8 position. The position of substitution of the phosphonate moiety was apparent from nmr spectral results, wherein half (H-9) of the AB pattern of H-9,10 was found at an unusually low-field position at 8.78 ppm, approximately 1.2 ppm lower field than that of H-9 of **7**, and is attributed to the deshielding influence of the peri phosphonate group.

A possible reaction path for the formation of this product is suggested in eq 4.



(4)

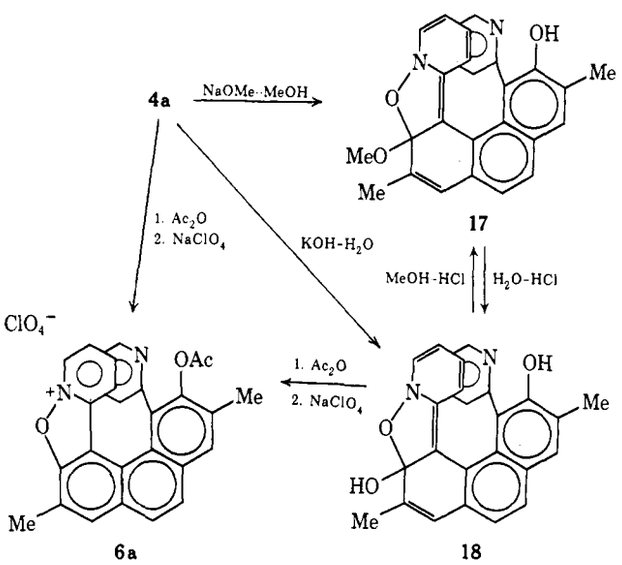
One final set of comparisons of reactivity behavior of **4a** and **8** has been determined using OH^- and OMe^- reagents. Isoxazolium **8** is transformed almost immediately into a dark, multicomponent mixture of products of undefined composition when treated with either aqueous NaOH or methanolic NaOMe at room

(11) See C. A. Brown, *J. Org. Chem.*, **35**, 1900 (1970); T. Satoh, S. Suzuki, T. Kikuchi, and T. Okada, *Chem. Ind. (London)*, 1626 (1970).

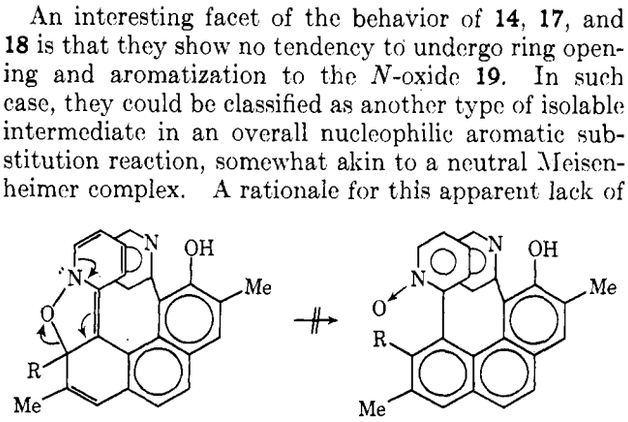
temperature. Isoxazolium **4a** also reacts with these reagents, but much more slowly over a 20–30-min period at 60° to yield after work-up in each case a single crystalline compound believed to be isoxazolines **17** and **18**, respectively.

Elemental analysis and mass spectral evidence establishes **17** to be a 1:1 adduct of **4a** with MeOH, and the marked resemblance of its uv spectrum to that of the BH_4^- product, **14**, suggests that they are closely related structurally. Particularly compelling spectral evidence is found in the high-resolution mass fragmentation of **17**, which displays a metastable transition for *m/e* 422 (M^+) → 363 ($M - CO_2CH_3$), indicative that one of the carbons of **17** attached to oxygen also bears the methoxyl group. The chemical interconversions of **4a**, **17**, and **18** outlined in Chart I lend further credence to the structural assignments.

CHART I



An interesting facet of the behavior of **14**, **17**, and **18** is that they show no tendency to undergo ring opening and aromatization to the *N*-oxide **19**. In such case, they could be classified as another type of isolable intermediate in an overall nucleophilic aromatic substitution reaction, somewhat akin to a neutral Meisenheimer complex. A rationale for this apparent lack of



a driving force toward rearomatization can be advanced based on steric arguments. Dreiding-model representations of **14**, **17**, and **18** show their benzisoxazoline moieties to be inclined somewhat away and reasonably separated from the neighboring pyridine, so that steric overcrowding is not a dominant structural concern. This suggests that they possess relatively negligible ring strain, epecially when compared to either *N*-oxide **19** or starting isoxazolium **4**, evidently to an extent that the gain in phenanthrene resonance energy derived from such an aromatization is not sufficient to compensate for the concomitant increase in steric strain.

At this point, it is a matter of conjecture as to why **4a** and **8** differ so in their reactions with these nucleophilic reagents. It certainly appears that the presence of an $-O^-$ at the seemingly remote 2 position of **8**, *i.e.*, **4**, inhibits the normal attack of the pyridinium ring by nucleophiles. The intramolecular charge-transfer properties of **4** may strongly contribute to a lessening of the electrophilic character of the pyridinium ring. Certainly the delocalization of electrons from the adjacent negatively charged oxygen into the pyridine positioned very close and directly behind the pyridinium ring should have a detrimental effect through electrostatic repulsive interactions on the approach of nucleophilic species.

Experimental Section[12]

Isoxazolium 4a, b.—A solution of 8.00 g (53 mmol) of *N*-chlorobenzotriazole[13] in 150 ml of methylene chloride was introduced into a mechanically stirred solution of 15.60 g (40 mmol) of 2,7-dimethyl-4,5-bis(2-pyridyl)phenanthrene-3,6-diol (**3a**)[2] in 150 ml of methylene chloride, and the mixture was stirred for 15 min at autogenous temperature. The resulting light red solution was extracted with 100 ml of 5% aqueous sodium bicarbonate solution, giving a deep red methylene chloride layer which was separated, dried over Na_2SO_4, and introduced onto the top of a Florisil column (5 × 85 cm). A yellow zone containing 0.89 g of starting **3a** was eluted with methylene chloride, followed by a deep red product zone which was eluted with methylene chloride–acetone (1:1, v/v). This was collected and concentrated to a red crystalline residue.

One recrystallization from CH_2Cl_2–Et_2O gave 10.40 g (71%) of **4a** as deep red plates, mp 242–243°.[14]

Anal. Calcd for $C_{26}H_{18}N_2O_2$ (**4a**): C, 80.0; H, 4.7; N, 7.2. Found: C, 80.1; H, 5.0; N, 7.2.

Zwitterion **4a** was converted to perchlorate **5**, mp 275° dec, by treatment with 10% perchloric acid.[14]

Anal. Calcd for $C_{26}H_{19}ClN_2O_6$: C, 63.6; H, 3.9; Cl, 7.2. Found: C, 63.3; H, 4.0; Cl, 7.1.

Isoxazolium **4b**, prepared by analogous oxidative procedure from **3b**,[2] had mp 254–256°.

Anal. Calcd for $C_{28}H_{22}N_2O_2$ (**4b**): C, 80.4; H, 5.3; N, 6.7. Found: C, 80.2; H, 5.2; N, 6.8.

A mixture of 200 mg of **4a**, 300 mg of 10% palladium/charcoal, and 200 ml of ethanol was hydrogenated at 60 psi (initial pressure) for 2 hr in a Parr shaker, giving (after standard work-up of the reaction mixture and Florisil chromatography) 120 mg (60%) of **1a** and 20 mg (10%) of a hexahydro derivative of **4a**: mass spectrum *m/e* 396 (M^+), 318 (M – pyridyl).

Acetate **6a** was prepared by dissolving **4a** (0.20 g, 0.51 mmol) in a mixture of acetic anhydride (20 g) and concentrated sulfuric acid (1.0 g). The solid produced by the addition of 75 ml of Et_2O was collected, dissolved in 20 ml of water, and treated with sodium perchlorate to give 0.24 g (84%) of **6a** as a yellow crystalline precipitate, mp 265–270° dec after one recrystallization from acetonitrile–ether.[14]

Anal. Calcd for $C_{28}H_{21}ClN_2O_7$: C, 63.0; H, 3.9; N, 5.2. Found: C, 63.0; H, 4.2; N, 5.4.

2,7-Dimethyl-4,5-bis(2-pyridyl)phenanthren-3-ol (7).—To a suspension of **14** (4.40 g, 11.2 mmol) and $NaBH_4$ (1.50 g) in 200 ml of refluxing ethanol was added dropwise, over a 4-min period, a solution of 350 mg of anhydrous cupric chloride in 15 ml of ethanol. The cupric chloride was immediately reduced to a

(12) Melting points (uncorrected) were determined on a Thomas-Hoover apparatus. Ultraviolet absorption spectra were recorded by a Cary Model 14 recording spectrophotometer. Nmr spectra were determined with a Bruker HX-90 spectrometer. Peak positions are reported in parts per million downfield from tetramethylsilane, followed by (in parentheses) multiplicity, relative area, and assignment. The mass spectra were determined on a Du Pont 21-110B mass spectrometer. Samples were analyzed *via* direct inlet at 70 eV.

(13) C. W. Rees and R. C. Storr, *J. Chem. Soc.*, 1474 (1969).

(14) For spectral data, see Tables I and II (nmr) and Figure 1 (uv).

black, insoluble substance, while starting **14** disappeared more slowly. After being heated at reflux for 15 min, the mixture was filtered, the filtrate was diluted with 600 ml of H_2O, and the resulting tan precipitate was collected and dried. The four major components of this mixture were easily separated by silica-gel column chromatography (3 × 50 cm column) into four product zones, the development of the chromatogram being followed visually using a 3660-Å light source.

In the order of elution there was isolated 100 mg (2%) of **1a** (nonfluorescent at 3660 Å), eluted with CH_2Cl_2; 510 mg (12%) of an isomerization product of **14** (bright yellow fluorescence at 3660 Å), eluted with CH_2Cl_2–EtOAc (20:1, v/v); 2.11 g (50%) of **7** (nonfluorescent at 3660 Å), CH_2Cl_2–EtOAc (10:1, v/v); and 350 mg (8%) of a tetrahydro derivative of **14** (blue fluorescence at 3660 Å, CH_2Cl_2–acetone (2:1, v/v).

Phenanthrol **7**, recrystallized from methylcyclohexane, had mp 256–257°; uv max (CH_3CN) 232 nm (log ε 4.67), 297 (4.39), 316 sh (4.33), 375 (3.48), 394 (3.54); mass spectrum (70 eV) *m/e* 376 (M^+), 298 (M − pyridyl); nmr ($CDCl_3$) δ 2.40 (d, 3, methyl), 2.50 (broadened s, 3, methyl) 6.57–7.67 (m, 11, aromatic), 8.00 (d of m, 1, pyridyl H-6), 8.21 (d of m, 1, pyridyl H-6), 13.17 (broadened s, 1, –OH).

Anal. Calcd for $C_{26}H_{20}N_2O$: C, 83.0; H, 5.3; N, 7.4. Found: C, 82.7; H, 5.3; N, 7.0.

The material eluted second is isomeric with **14**, and was purified by rechromatographing on silica gel. It was crystallized as stubby yellow needles from methylcyclohexane, mp 198–205° dec, mol wt 392 (mass spectrum).[15]

Anal. Calcd for $C_{26}H_{20}N_2O$: C, 78.7; H, 5.2; N, 7.1. Found: C, 78.8; H, 5.1; N, 7.3.

The tetrahydro derivative of **14** was recrystallized from methylcyclohexane: mp 243–250° dec; mass spectrum (70 eV) *m/e* (rel intensity) 396 (100) (M^+), 368 (18), 339 (37), 318 (15), 311 (62). Its structure has not been established nor was it further characterized.

The 6-deuterio derivative of **7** was obtained in analogous fashion starting with monodeuterated **14**, mass spectrum (70 eV) *m/e* 377 (M^+), 299 (M − pyridyl).

Isoxazolium 8.—The initially dark brown solution resulting from dissolving phenanthrol **7** (2.50 g, 6.7 mmol) and anhydrous $CuCl_2$ (2.50 g) in 150 ml of ethanol lightened to yellowish-green after heating at reflux for 5 min. The solution was filtered and diluted with ether to give 2.50 g of yellow crystals. These were collected, dissolved in 200 ml of methylene chloride, and passed through a silica gel column (3 × 50 cm), using CH_2Cl_2–methanol (5:1, v/v) as eluent. The yellow crystals obtained after concentrating the eluate were dissolved in aqueous methanol (1:1, v/v) and filtered, and the filtrate was treated with sodium perchlorate to give 1.80 g of **8**. Analytically pure **8** was obtained as yellow plates after one recrystallization from acetonitrile–ether, mp 275° dec.[14]

Anal. Calcd for $C_{26}H_{19}ClN_2O_5$: C, 65.8; H, 4.0; N, 5.9. Found: C, 65.8; H, 4.2; N, 5.9.

Phenanthrols 9 and 10.—A mixture of **8** (400 mg, 0.84 mmol) and sodium cyanide (400 mg) was dissolved in 10.0 g of dry DMSO. After standing for 5 min, the dark yellow solution was diluted with 5 ml of water, acidified with 5% HCl, and basified with 5% $NaHCO_3$ to yield a yellow multicomponent precipitate. The three major products were easily separated by silica gel chromatography using CH_2Cl_2–EtOAc (10:1, v/v) as eluent, and identified in order of elution. Phenanthrol **10** (40 mg, 12%) had mp >300° dec; uv max (CH_3CN) 227 nm (log ε 4.73), 236 sh (4.71), 290 (4.42), 314 sh (4.33), 400 sh (3.49); mass spectrum (70 eV) *m/e* (rel intensity) of major peaks 426 (10) (M^+), 348 (5) (M − pyridyl), 298 (100) (M − dicyanopyridyl); nmr ($CDCl_3$) δ 2.43 (d, 3, *J* = 1 Hz, Me) coupled to poorly resolved quartet at 7.70 (1, H-1), poorly resolved triplet at 2.53 (3, Me) coupled to multiplets at 7.22 (1, H-7) and 7.73 (1, H-8), AB quartet centered at 7.63 (2, *J* = 8 Hz, H-9,10), AX pattern at 7.08 (d, 1, *J* = 1.5 Hz, pyridyl H-3), and 7.58 (d, 1, *J* = 1.5 Hz, pyridyl H-5), typical 2-substituted pyridine pattern at 6.83 (H-3), 7.50 (H-4), 7.20 (H-5), 8.18 (H-6).

Anal. Calcd for $C_{28}H_{18}N_4O$: C, 78.9; H, 4.3; N, 13.1. Found: C, 79.3; H, 4.7; N, 13.1.

Phenanthrol **9** (100 mg, 30%) had mp 250–252°; uv max (CH_3CN) 233 nm (log ε 4.67), 289 (4.37), 318 (4.32), 395 (3.53); mass spectrum *m/e* (rel intensity) 401 (9) (M^+), 323 (24) (M − pyridyl), 298 (100) (M − cyanopyridyl); nmr ($CDCl_3$) AMX of cyanopyridyl at δ 6.88 (d of d, 1, *J* = 0.9, 1.6 Hz, H-3), 7.20 (d of d, 1, *J* = 1.6, 5.5 Hz, H-5), 8.37 (d of d, 1, *J* = 0.9, 5.5 Hz, H-6), AKMX of pyridyl at δ 6.88 (H-3), 7.40 (H-4), 7.06 (H-5), 8.07 (H-6), phenanthrene protons at δ 7.64 (H-1) coupled to Me at 2.42 (*J* = 1 Hz), 7.18 (H-6) and 7.68 (H-8) coupled to each other and to Me at 2.50 and AB pattern of H-9,10 at 7.53 and 7.63 (*J* = 8 Hz).

Anal. Calcd for $C_{27}H_{19}N_3O$: C, 80.8; H, 4.8; N, 10.5. Found: C, 80.6; H, 5.2; N, 10.4.

Phenanthrol **7** was also eluted, 90 mg (28%).

1-Cyano-2,7-dimethyl-4,5-bis(2-pyridyl)phenanthrene-3,6-diol (11).—A mixture of finely divided **4a** (100 mg, 0.26 mmol) and sodium cyanide (100 mg) was dissolved in 2.5 g of dry DMSO. After standing for 5 min, the dark yellow solution was diluted with 5 ml of water, acidified with 5% HCl, and basified with 5% $NaHCO_3$ to yield a yellow, crystalline precipitate consisting of a single product (tlc). One recrystallization from methylcyclohexane afforded 100 mg (94%) of analytically pure **11**: mp 281–283° dec; uv max (CH_3CN) 242 nm (log ε 4.72), 318 (4.46), 420 (3.64); nmr ($CDCl_3$) δ 2.40 (d, *J* = 0.5 Hz, 3, Me), 2.62 (s, 3, Me) 6.60 (m, 2, pyridyl H-3, H-3′), 6.94 (m, 2, pyridyl H-5, H-5′), 7.43 (pyridyl H-4, H-4′), 7.64 (d, 1, *J* = 8.5 Hz, H-9), 7.65 (q, 1, H-8), 7.94 (d, 1, *J* = 8.5 Hz, H-10), and 8.04 (m, 2, pyridyl, H-6, H-6′).

Anal. Calcd for $C_{27}H_{19}N_3O_2$: C, 77.7; H, 4.6; N, 10.1. Found: C, 77.9; H, 4.7; N, 10.3.

Borohydride Reduction of 8.—Isoxazolium **8** (300 mg) reacted immediately when treated with 500 mg of sodium borohydride in 15 ml of methanol to give a yellow solution. A multicomponent amorphous solid was precipitated from this solution by the addition of 450 ml of water. The two main constituents of this mixture were separated from the other products by silica gel chromatography (eluent CH_2Cl_2–EtOAc, 1:1 v/v), but even with repeated recrystallization we were unable to completely separate them from one another: mp 234–238°; mass spectrum (70 eV) *m/e* 382 (M^+ of **12**), 380 (M^+ of **13**), 326, 325, 304 (382 − pyridyl), 302 (380 − pyridyl), 298 (382 − hexahydropyridine and/or 380 − tetrahydropyridine), 286, 284, 282, 269; nmr ($CDCl_3$) δ 1.80 (t, 3, methyl), 2.48 (broadened s, 3, methyl), 2.61–4.10 (m, ~4), 4.96–6.27 (m, ~4), 6.40–7.76 (m, 8, aromatic), 8.56–8.70 (d of m, 1, pyridyl H-6). The position of the tetrahydropyridyl double bond of **13** is undefined.

Borohydride Reduction of 4a, *i.e.*, Isoxazoline 14.—To a stirred suspension of finely powdered **4a** (0.78 g, 2.0 mmol) in 25 ml of MeOH was added 0.26 g of $NaBH_4$, producing rapid dissolution of **4a** followed immediately by the separation of flocculent orange needles. The mixture was refrigerated for 1 hr at 5° and the crystals (0.75 g, 96%) were collected by filtration and washed with cold methanol: mp 160–171°, partially solidified and melted at 236°; uv max (MeOH) 258 nm sh (log ε 4.22), 279 (4.31), 317 sh (3.75), 383 (3.66), 487 (3.94); mass spectrum of major peaks (70 eV) *m/e* (rel intensity) 392 (64) (M^+), 314 (100) (M − pyridyl), 297 (58); partial nmr (CD_3OD + one drop of 5% DCl in D_2O) δ 2.04 (poorly resolved triplet, 3, Me), 5.93 (broad q, 1, H_β), 6.54 (broad q, 1, H_α). Double irradiation at δ 2.04 converts the 5.92 and 6.54 multiplets each to doublets (*J* = 2.5 Hz). Irradiation of either the 5.93 or 6.54 signal converts the other to a quartet and the methyl at δ 2.03 to a doublet (*J* = 1 Hz).

Anal. Calcd for $C_{26}H_{20}N_2O_2$: C, 79.6; H, 5.1; N, 7.1. Found: C, 79.7; H, 5.5; N, 6.9.

An analogous procedure using $NaBD_4$ gave the monodeuterio derivative, mass spectrum *m/e* (rel intensity) 393 (46), 315 (100), 298 (46).

Isomerizations of 14a to 3a. A. Photochemically.—A suspension of 100 mg of **14** in 250 ml of ethanol was irradiated over a 2-hr period using a Philips HPK 125-W source with Pyrex filter. Tlc analysis of the crystalline residue isolated after removal of solvent indicated the presence of only one product and it proved identical in every respect with authentic **3a**. A repeat of the above experiment, substituting THF for ethanol as solvent, produced no reaction after 24-hr irradiation.

B. By Base.—A mixture of 300 mg of **14** and 0.5 g of NaOMe in 15 ml of methanol was heated at reflux temperature for 3 hr, cooled, acidified with 5% HCl, and basified with 5% $NaHCO_3$, giving 280 mg of essentially pure **1a** as a yellow, crystalline precipitate.

Phosphonate 16.—A solution of **14** (500 mg, 1.27 mmol) in 10 g of triethyl phosphite was heated at reflux for 2 hr, during which

(15) This is an extraordinary rearrangement product of **14**, and is the subject of paper VI of this series to be submitted for publication.

time 14 was consumed (by tlc). The resulting purple solution was concentrated *in vacuo* to a syrup and the syrup was chromatographed on silica gel to yield in order of elution 20 mg (4%) of 7 (CH_2Cl_2–EtOAc, 2:1 v/v, as eluent), 150 mg (23%) of 16 (CH_2Cl_2–Me_2CO, 6:1 v/v, as eluent), and *ca.* 100 mg of purple syrup (Me_2CO eluent) which was discarded.

One recrystallization of 16 from methylcyclohexane provided yellow needles: mp 234–235°; mass spectrum (70 eV) *m/e* (rel intensity) 512 (20) (M^+), 434 (100) (M − pyridyl), 360 (30); nmr ($CDCl_3$) δ 1.40 (d of t, 6, phosphonate methyls), 2.42 (s, 3, 2-Me), 2.87 (d, 3, J = 2 Hz, 7-Me), 4.23 (m, 4, phosphonate $-CH_2-$), 6.56–7.53 (m, 8), 7.56 (d, 1, J = 9 Hz, H-10), 8.06 (d of m, 1, pyridyl H-6), 8.11 (d of m, 1, pyridyl H-6), 8.78 (d, 1, J = 9 Hz, H-9).

Anal. Calcd for $C_{30}H_{29}N_2O_4P$: C, 70.4; H, 5.7; N, 5.5. Found: C, 70.0; H, 6.1; N, 5.3.

By an analogous procedure, starting with 14 (deuterio), the 6-deuterio derivative was obtained, mass spectrum (70 eV) *m/e* (rel intensity) 513 (23) (M^+), 435 (100) (M − pyridyl), 361 (35).

Isoxazoline 17.—A mixture of 4a (800 mg, 2.0 mmol) and sodium methoxide (800 mg) in 50 ml of methanol was heated at reflux for 30 min, until the starting material had disappeared (tlc). The resulting orange solution was concentrated to dryness, and the residue was chromatographed on Florisil using CH_2Cl_2–Me_2CO–MeOH (5:5:1, v/v) as eluent. The single orange zone was eluted and concentrated to a syrup which crystallized. One recrystallization from CH_2Cl_2–ligroin (bp 35°) gave 530 mg (62%) of analytically pure 17 as reddish orange needles: mp 202–210° dec; uv max (MeOH) 264 nm (log ε 4.47), 355 (3.90), 480 (4.13); mass spectrum (70 eV) *m/e* (rel intensity) 422 (46%) (M^+), 407 (1) (M − Me), 391 (1) (M − OCH_3), 363 (1) (M − CO_2CH_3), 344 (100) (M − pyridyl), 335 (6), 284 (7), 270 (6), 256 (3), 254 (4), 242 (4), 241 (5), 167.5 (5), 78 (3), 59 (1); nmr ($CDCl_3$) δ 2.04 (d, 3, J = 2 Hz), 2.28 (d, 3, J = 1 Hz), 3.44 (s, 3), 6.56–7.73 (m, 9), 8.09 (d of m, 1), 8.42 (d of m, 1), 9.88 (d of m, 1).

Anal. Calcd for $C_{27}H_{22}N_2O_3$: C, 76.8; H, 5.2; N, 6.6. Found: C, 76.5; H, 5.3; N, 6.9.

Conversion of 17 to 18.—A solution of 120 mg of 17 in 12.5 ml of 2 *N* HCl was heated at reflux for 3 hr, concentrated to a syrup, and then redissolved in 10 ml of water. The yellow crystals which separated from solution over a 1-hr period proved identical with the hydrochloride of 18 in every respect.

Isoxazoline 18.—A suspension of 800 mg (2.0 mmol) of 4a in 20 ml of methanol and 40 ml of water containing 1.40 g of sodium hydroxide went into solution over a 30-min period at 60° to give an orange solution. The solution was filtered and slowly acidified with 5% HCl, producing an amphoteric, orange, crystalline precipitate. The solid was redissolved with the addition of another 2 ml of 5% HCl and the resulting yellow solution was refrigerated at 5° for 2 hr, during which time 0.84 g (96%) of light yellow crystals of 18, as the hydrochloride salt, separated. This sample initially dissolved readily in 15 ml of methanol, but within 5 min yielded a relatively insoluble yellow crystalline methanol solvate: mp 187–190° dec; uv max (CH_3OH) 261 nm (log ε 4.54), 360 (3.96), 418 (3.76), 480 (4.20); nmr (CD_3OD) δ 2.32 (d, J = 2 Hz, 3), 2.52 (d, J = 1 Hz, 3), 6.82–7.96 (m, 8), 8.30–8.62 (m, 2), 9.22 (d of m, 1), 9.41 (d of m, 1).

Anal. Calcd for $C_{26}H_{21}ClN_2O_3 \cdot CH_3OH$: C, 68.0; H, 5.2; N, 5.9; Cl, 7.5. Found: C, 67.6; H, 5.2; N, 5.8; Cl, 7.7.

Conversion of 18 to 17.—A sample (200 mg) of the above product (18) in 20 ml of 5% methanolic HCl was heated at reflux for 2 hr, cooled, and basified with 5% $NaHCO_3$, yielding an orange, crystalline precipitate. This product, after purification by Florisil chromatography and recrystallization from CH_2Cl_2–ligroin (bp 35°), proved to be identical in every respect with 17.

Conversion of 18 to 6a.—A mixture of 200 mg of 18 in 10 ml of acetic anhydride was refluxed for 2 min, concentrated to a syrup, and then dissolved in 5% $NaHCO_3$. Yellow crystals of 6a (180 mg) immediately separated upon the addition of aqueous $NaClO_4$ solution.

Registry No.—**4a**, 37387-76-1; **4b**, 37413-08-4; **5**, 37413-09-5; **6a**, 37420-75-0; **6b**, 37413-10-8; **7**, 37387-77-2; **8**, 37387-78-3; **9**, 37387-79-4; **10**, 37387-80-7; **11**, 37387-81-8; **12**, 37387-82-9; **13**, 37387-83-0; **14**, 37387-84-1; **16**, 37387-85-2; **17**, 37387-86-3; **18**, 37387-87-4.

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Lead Tetraacetate and Pyridine. New, Mild Conditions for a Hofmann-Like Rearrangement. A New Synthesis of 2-Oxazolidinones

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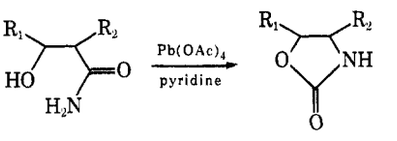
Lead tetraacetate in pyridine has been found to provide a new, mild procedure for effecting a rapid, high-yield, Hofmann-like rearrangement of β-hydroxy primary amides to 2-oxazolidinones. These products in turn give the corresponding β-hydroxy amines so that the reaction can also be used to transform primary amides to amines in high yield.

2-Oxazolidinones have been found useful as drugs and polymer monomers and as such they have attracted considerable attention.[2,3] Not unexpectedly, there are many methods available for their synthesis.[2-4] We would like to report that the reaction of β-hydroxy amides with lead tetraacetate in pyridine constitutes yet another synthetic route to these compounds (eq 1).



(1)

Lead tetraacetate is known to react with primary amides to give isocyanates in a Hofmann-like reaction.[5-7] Typically these reactions are run at 50–60°

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