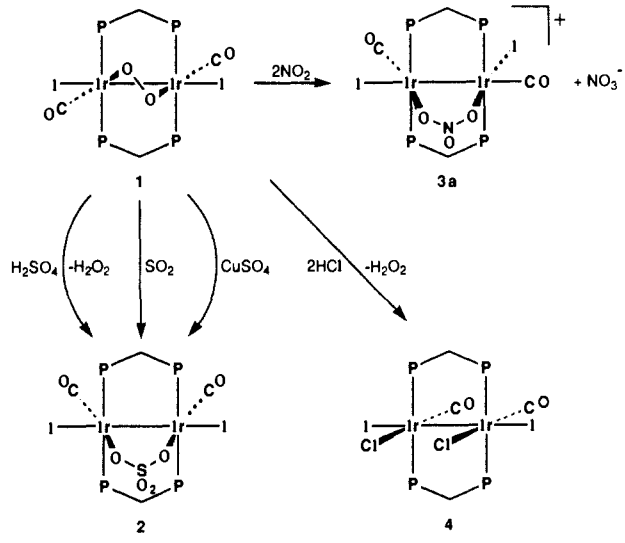
Scheme I



Ir-O(2)-O(2)' angle (102.0 (4)°) is smaller than observed (ca. 120°) in other μ-peroxo compounds,[9] probably because of the strain introduced by the presence of the Ir-Ir bond. As in most such complexes, the Ir-O(2)-O(2)'-Ir' moiety is not planar but displays a torsion angle about the O(2)-O(2)' bond of 34.6°; again, this twist is less than in other bridged cases owing to the metal-metal bond. It is to be emphasized that compound **1** represents a new type of μ-peroxo compound in which the two metal centers are not independent but are connected by a metal-metal bond. It is significant that a related peroxo-bridged complex containing two Ir(II) centers has been postulated as an intermediate in an oxygen-atom transfer to an olefin.[8] Although this intermediate was shown without a metal-metal bond, the present study suggests that it could be reformulated as having an accompanying Ir-Ir bond.

The long O(2)-O(2)' separation in **1** suggests that this bond is weak and should be readily cleaved. Consequently the reactions of **1** with several small molecules have been investigated, and the preliminary results are summarized in Scheme I; in all cases the reactions are characterized by a rapid color change from deep purple to yellow or orange. Compound **1** reacts with SO_2 to yield the sulfate-bridged product $[Ir_2I_2(CO)_2(\mu\text{-}SO_4)(dppm)_2]$ (**2**)[16] through facile oxygen transfer to the SO_2 molecule. This product appears to be quite analogous to **1**, containing two Ir(II) centers linked by an Ir-Ir bond, and with the bridging peroxo group replaced by sulfate. Similarly, reaction of **1** with 2 equiv of NO_2 yields the nitrate-bridged species $[Ir_2I_2(CO)_2(\mu\text{-}NO_3)(dppm)_2][NO_3]$ (**3a**);[17] the $^{31}P\{^1H\}$ NMR spectrum suggests that a rearrangement between carbonyl and iodo ligands at one of the metal centers may have occurred to give an asymmetric species as shown in the scheme. Confirmation of the ionic nature of **3a** is obtained from conductivity measurements and by replacement of the NO_3^- anion by BF_4^- to give $[Ir_2I_2(CO)_2(\mu\text{-}NO_3)(dppm)_2][BF_4]$ (**3b**).[18] Compound **1** also reacts with the protic acids HCl and H_2SO_4 to yield $[Ir_2I_2Cl_2(CO)_2(dppm)_2]$ (**4**)[19] and **2**, respectively, with simultaneous formation of H_2O_2, which can be detected with use of aqueous KI solution in the presence of starch. Attempts to observe intermediates in which protonation of the coordinated O_2 moiety has occurred were unsuccessful. The sulfate-bridged product **2** can also be prepared through reaction of **1** with $CuSO_4$. Compound **1** also reacts with nitric oxide, hexafluoroacetone, and much more slowly (several days), with carbon monoxide, and also with acids such as $HBF_4 \cdot Et_2O$ having only weakly coordinating conjugate bases; these and other reactions are being investigated.

The structure determination of **1** confirms that this compound is the first member of a new type of species in which a peroxo ligand bridges a metal-metal bond. It will be of interest to determine if the resulting strain introduced in the μ-peroxo unit by this metal-metal interaction, and the exceptionally long O-O distance, will result in unusual reactivity of this species.

Our preliminary studies show that the related dichloro species, $[Ir_2Cl_2(CO)_2(dppm)_2]$, also reacts with O_2, and this reaction is being investigated to determine if a similar metal-metal-bonded, μ-peroxo complex is obtained.

Acknowledgment. We thank the National Science and Engineering Research Council of Canada (NSERC) and the University of Alberta for financial support and NSERC for partial support of the diffractometer and for funding of the PE883 IR spectrometer.

Supplementary Material Available: Tables of X-ray data, atomic coordinates, isotropic thermal parameters, and bond distances and angles for **1** (7 pages). Ordering information is given on any current masthead page.

(15) Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press: Oxford, England, 1986; p 720.

(16) $[Ir_2I_2(CO)_2(\mu\text{-}SO_4)(dppm)_2]$: ^1H NMR (CD_2Cl_2) δ 7.1-7.9 (m, 40 H), 4.9 (m, 4 H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, vs 85% H_3PO_4) δ -17.7 (s); IR (Nujol) ν(CO) 2085, 2037, 2028 cm^{-1}; $\nu(SO_4)$ 1250, 1140, 952, 800 cm^{-1}. Anal. Calcd for $Ir_2I_2SP_4O_6C_{52}H_{44}$: C, 40.06; H, 2.84; I, 16.28; S, 2.06. Found: C, 38.48; H, 2.86; I, 15.13; S, 2.47.

(17) $[Ir_2I_2(CO)_2(\mu\text{-}NO_3)(dppm)_2][NO_3]\cdot CH_2Cl_2$: ^1H NMR (CD_2Cl_2) δ 7.0-8.0 (m, 40 H), 5.9 (m, 2 H), 4.4 (m, 2 H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, vs 85% H_3PO_4) δ -20.0 (m), -26.2 (m); IR (Nujol) ν(CO) 2049 cm^{-1} (br); $\nu(\mu\text{-}NO_3)$ 1518, 1259, 1040, 780 cm^{-1}; $\nu(NO_3)$ 1350, 1023, 700 cm^{-1}. Conductivity Λ (1×10^{-3} M, CH_3NO_2) 81.1 Ω^{-1} cm^2 mol^{-1}. Anal. Calcd for $Ir_2I_2Cl_2P_4O_8N_2C_{53}H_{46}$: C, 37.35; H, 2.66; N, 1.68. Found: C, 37.67; H, 2.78; N, 1.67.

(18) $[Ir_2I_2(CO)_2(\mu\text{-}NO_3)(dppm)_2][BF_4]$: ^1H NMR (CD_2Cl_2) δ 7.0-7.9 (m, 40 H), 5.9 (m, 2 H), 4.3 (m, 2 H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, vs 85% H_3PO_4) δ -20.0 (m), -26.2 (m); IR (Nujol) ν(CO) 2048 cm^{-1} (br); $\nu(NO_3)$ 1519, 1260, 780 cm^{-1}. Anal. Calcd for $Ir_2I_2P_4F_4O_5NC_{52}BH_{44}$: C, 38.75; H, 2.75; N, 0.87; I, 15.75. Found: C, 39.09; H, 2.76; N, 0.99; I, 16.07.

(19) $[Ir_2I_2Cl_2(CO)_2(dppm)_2]$: ^1H NMR (CD_2Cl_2) δ 7.2-7.8 (m, 40 H), 5.7 (m, 2 H), 5.0 (m, 2 H); $^{31}P\{^1H\}$ NMR (CD_2Cl_2, vs 85% H_3PO_4) δ -23.0 (s); IR (Nujol) ν(CO) 2028 cm^{-1}. Anal. Calcd for $Ir_2I_2Cl_2P_4O_2C_{52}H_{44}$: C, 40.71; H, 2.90; Cl, 4.62. Found: C, 40.51; H, 2.95; Cl, 4.59.

Unusual Reactions of Amino Acid Derivatives: *N*-Nitrooxazolidones and *N*-Nitroamino Acids

Emil H. White,* Seunguk Paik, L. J. Todaro,† and Timothy A. Marean

Department of Chemistry, The Johns Hopkins University Baltimore, Maryland 21218

Received July 23, 1990

Amides are "activated" to attack by nucleophiles via N-nitrosation;[1] the resulting nitrosoamides ($\lambda_{max} \sim 400$ nm) have proved to be useful substrates for enzymes, particularly since suitably constructed ones can also serve as irreversible inhibitors.[2] The present study is based on examining *N*-nitroamides[3] as

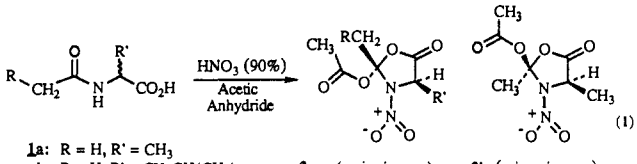
†Physical Chemistry Department, Chemistry Research, Hoffman-LaRoche, Inc., Nutley, NJ 07110.

(1) For example, the facile conversion of *N*-nitrosoamides with base into diazotate salts or diazoalkanes (Thiele, J. *Justus Liebigs Ann. Chem.* **1910**, *376*, 239. Hantzsch, A.; Lehmann, M. *Chem. Ber.* **1902**, *35*, 897. Moss, R. A. *J. Org. Chem.* **1966**, *31*, 1082); also, the references listed in footnote 2.

(2) (a) White, E. H.; Roswell, D. F.; Politzer, I. R.; Branchini, B. R. *J. Am. Chem. Soc.* **1975**, *97*, 2290-2291. (b) White, E. H.; Roswell, D. F.; Politzer, I. R.; Branchini, B. R. *Methods Enzymol.* **1977**, *46*, 216. (c) White, E. H.; Jelinski, L. W.; Perks, H. M.; Burrows, E. P.; Roswell, D. F. *J. Am. Chem. Soc.* **1977**, *99*, 3171. (d) White, E. H.; Perks, H. M.; Roswell, D. F. *J. Am. Chem. Soc.* **1978**, *100*, 7421. (e) White, E. H.; Jelinski, L. W.; Politzer, I. R.; Branchini, B. R.; Roswell, D. F. *J. Am. Chem. Soc.* **1981**, *103*, 4231-4239. (f) Donadio, S.; Perks, H. M.; Tsuchiya, K.; White, E. H. *Biochemistry* **1985**, *24*, 2447-2458. (g) White, E. H.; Li, M.; Cousins, J. P.; Roswell, D. F. *J. Am. Chem. Soc.* **1990**, *112*, 1956-1961. (h) Gold, B.; Linder, W. B. *J. Am. Chem. Soc.* **1979**, *101*, 6772-6773.

0002-7863/90/1512-9426$02.50/0

substrate/inhibitors since, among other advantages, nitroamides are more thermally stable than the analogous nitroso derivatives.[4] The nitration of simple amides and esters of *N*-acylamino acids with nitric acid–acetic anhydride mixtures proceeds readily to yield the expected *N*-nitroamides.[5] We now find, however, that nitration of the acylamino acids themselves is more complex, yielding instead nitrooxazolidones (**2**).[6] These compounds possess a unique structural feature in that three conjugate bases of carboxylic acids and other acids of comparable strength are attached to the same carbon atom;[7] unusual chemical reactions result from this disposition of functional groups and the presence of a nitroamino group.

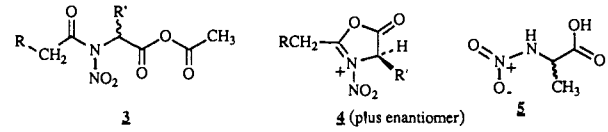


1a: R = H, R' = CH_3
b: R = H, R' = $CH_2CH(CH_3)_2$
c: R = R' = CH_3

2a (major isomer)
2b, c (probable major isomer)

2'a (minor isomer)

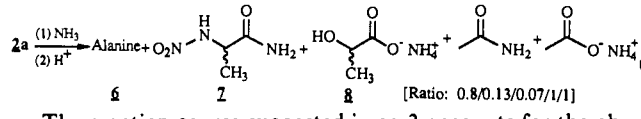
The structure of **2a** was determined by X-ray crystallography. Interestingly, some of the physical data *appeared* to support anhydride structure **3** more so than oxazolidone structure **2**: IR (KBr) ν(CO) 1825 cm^{-1}; ^1H NMR ($CDCl_3$) δ of both non-alanine CH_3 groups for compound **2a** had the same chemical shift, located at 2.12 ppm.[6,8,9] However, the inertness to hydrolysis, the finding of only two ^{13}C NMR resonances for CO groups (168.8 and 166.5 ppm), and certain chemical reactions firmly supported structure **2** for the nitration products. Actually, two isomers are formed in the nitration of acetylalanine, the major one being cis isomer **2a** (about two-thirds of the product). The reactions probably proceed via cyclization of **1** to the corresponding oxazolinone, nitration to yield intermediate **4**, and finally, addition of the acetate moiety preferentially from the less hindered side (nitration of the oxazolinones also produces **2**). The unusual IR and NMR frequencies measured for the nitrooxazolidones referred to above can be accounted for in terms of ring strain and dipole–dipole interactions.[9]



3 **4** (plus enantiomer) **5**

A few of the chemical reactions of nitrooxazolidone **2** are straightforward. For example, heating nitrooxazolidone **2a** in methanol produced methyl *N*-nitroalaninate, and treatment with sodium hydroxide led predominantly to *N*-nitroalanine (**5**). Only *N*-nitroglycine—in the class of *N*-nitroamino acids—had been hitherto reported in the chemical literature;[10-13] it was examined for its antibiotic properties,[11] its plant growth stimulating activity,[12] and its ability to inhibit succinate dehydrogenase.[13]

Reactions of the nitrooxazolidones (**2**) in ether with ammonia (30 min, 25 °C) or with ammonium hydroxide led to some unexpected products. While the ammonolysis of nitroamides normally leads simply to the ammonium salt of the *N*-nitroamine moiety,[5] that reaction applied to nitrooxazolidones **2a** and **2c** led, predominantly, to the amino acid alanine (**6**) (eq 2; 60% isolated)! Ammonolysis of optically active **2a** produced alanine with ~90% retention of configuration. With benzylamine as the base, *N*-benzylalanine[2g,14] was produced, eliminating the possibility that a direct denitration had occurred in the ammonia reaction.



(2)

6 **7** **8** [Ratio: 0.8/0.13/0.07/1/1]

The reaction course suggested in eq 3 accounts for the observations listed and also for the facts that nitrous oxide, *N*-nitroalaninamide (**7**), and ammonium lactate (**8**) are also produced in the ammonolyses.

Precedent exists for the acylation of nitroamine anions (step 2 of the reaction; path b),[16] for the ionization of nitronic carboxylic anhydrides (step 3),[3a,c,16] for displacement of a stable molecule by a neighboring α-carboxylate ion with inversion of configuration

(3) (a) White, E. H.; Grisley, D. W., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1191. (b) White, E. H.; Chen, M. C.; Dolak, L. A. *J. Org. Chem.* **1966**, *31*, 3038. (c) White, E. H.; McGirk, R. H.; Aufdermarsh, C. A., Jr.; Tiwari, H. P.; Todd, M. J. *J. Am. Chem. Soc.* **1973**, *95*, 8107. (d) White, E. H.; Field, K. W. *J. Am. Chem. Soc.* **1975**, *97*, 2148–2153. (e) White, E. H.; Lewis, C. P.; Ribi, M. A.; Ryan, T. J. *J. Org. Chem.* **1981**, *46*, 552–558. (f) White, E. H.; Ryan, T. J.; Hahn, B. S.; Erickson, R. H. *J. Org. Chem.* **1984**, *49*, 4860–4866.

(4) White, E. H.; Dolak, L. A. *J. Am. Chem. Soc.* **1966**, *88*, 3790.

(5) (a) Campbell, R.; Peterson, C. J. *J. Org. Chem.* **1963**, *28*, 2294. (b) Garcia, J.; González, J.; Segura, R.; Urpí, F.; Vilarrasa, J. *J. Org. Chem.* **1984**, *49*, 3322–3327. (c) Curry, H. M.; Mason, J. P. *J. Am. Chem. Soc.* **1951**, *73*, 5041–5042, 5043–5046.

(6) The *N*-acylamino acid (2.5 mmol) was added to a mixture of 1 mL of fuming 90% nitric acid (sp gr 1.5) (commercial sample used without purification) and 3 mL of acetic anhydride at −20 °C. The solution obtained after ~10 min was warmed to 0 °C for ~5 min and then worked up with ice and methylene chloride. **2a**: 51% (from ether), mp 87–88 °C; IR (KBr) 3068, 1825, 1766, 1555, 1443 cm^{-1}; 400-MHz ^1H NMR ($CDCl_3$) δ 4.92 (q, J = 7.0 Hz, 1 H), 2.12 (s, 6 H, $C(O)CH_3$, CCH_3), 1.67 (d, J = 7.0 Hz, 3 H); ^1H NMR (DMSO-d_6) δ 4.98 (q, J = 7.0 Hz, 1 H), 2.15 (s, 3 H), 2.13 (s, 3 H) (CCH_3 and $C(O)CH_3$), 1.62 (d, 7.0 Hz, 1 H); ^{13}C NMR ($CDCL_3$) δ 168.8, 166.5, 108.4, 56.6, 25.9, 20.9, 16.1; UV (ether) λ_{max} 237.5 nm (ϵ = 3980); MS (70 eV), *m/e* 159 $(M - CH_3CO_2)^+$, 90, 43; CI MS, *m/e* 236 $(M + NH_4)^+$, 219 $(M + H)^+$, 159 $(MH - CH_3CO_2H)^+$. Anal. ($C_7H_{10}N_2O_6$) C, H, N. Chromatography of the mother liquors (SiO_2) yielded ca. 20 mg of **2'a** as an oil: ^1H NMR ($CDCl_3$) δ 4.72 (q, J = 6.64 Hz, 1 H), 2.14 (s, 3 H), 2.12 (s, 3 H) (CCH_3 and $C(O)CH_3$), 1.55 (d, J = 6.6 Hz, 1 H); ^1H NMR (DMSO-d_6) δ 5.21 (q, J = 6.6 Hz, 1 H), 2.14 (s, 3 H), 2.12 (s, 3 H) (CCH_3 and $C(O)CH_3$), 1.55 (d, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.9, 165.9, 108.9, 55.8, 22.9, 21.5, 13.7. **2b**: 50% from pentane, mp 78–79 °C; IR ($CHCl_3$) 1829, 1768, 1558 cm^{-1}; ^1H NMR ($CDCl_3$) δ, 4.93 (m, 1 H, CH_2CHN), 2.13 (s, 6 H, $C(O)CH_3$ + CCH_3), 2.02–1.89 [m, 3 H, $CH_2CH(CH_3)_2$], 0.99 [d, 6 H, J = 5.6 Hz, $CH(CH_3)_2$]; ^{13}C NMR ($CDCl_3$) δ 168.6, 166, 108.4, 59.1, 38.6, 25.4, 24.2, 22.9, 21.5, 20.9; UV (ether) λ_{max} 237.5 mm (ϵ = 3980). Anal. ($C_8H_{14}N_2O_5$) C, H, N. **2c**: 46% from hexane, mp 72 °C; IR (KBr) 1832, 1768, 1552 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.95 (q, J = 7.0 Hz, 1 H), 2.44 (m, J = 7.5 Hz, 2 H), 21.3 (s, 3 H), 1.66 (d, J = 7.0 Hz, 3 H), 1.03 (t, J = 7.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 168.9, 166.8, 111.2, 56.7, 30.4, 21.2, 16, 6.9; UV (ether) λ_{max} 237 nm (ϵ = 3900). Anal. ($C_8H_{12}N_2O_6$) C, H, N. (**7**): mp 88.5–90 °C; IR (KBr) 1723, 1589, 1466 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.61 (q, J = 7.4 Hz, 1 H), 1.45 (d, J = 7.4 Hz, 3 H). Anal. ($C_3H_6N_2O_4$) C, H, N. (**9**): mp 144–145 °C; ^1H NMR (D_2O) δ 4.31 (q, J = 7.2 Hz, 1 H), 1.38 (d, J = 7.2 Hz, 3 H); IR (KBr) 1689, 1413, 1360 cm^{-1}. Anal. ($C_3H_7N_3O_3$) C, H, N.

(7) For example, 1,1,1-triacetoxyethane has not been reported in the chemical literature. In the absence of the carbonyl group, such a substitution pattern is not a rarity, however: 1,1,1-trialkoxy- and trinitroalkanes, e.g., are known compounds.

(8) For acetic anhydride, ν(CO) = 1820 cm^{-1} (neat) and δ ($CDCl_3$) = 2.21 ppm (Pouchert, C. J. *The Aldrich Library of Infrared Spectra*, 2nd ed.; Aldrich Chemical Co., Inc.: Milwaukee, 1975; p 368. Pouchert, C. J. *The Aldrich Library of NMR Spectra*, 2nd ed.; Aldrich Chemical Co., Inc.: Milwaukee, 1983; p 601).

(9) ν(CO) = 1800 cm^{-1} (KBr) for 4-acetoxy-4-methyl-γ-butyrolactone (i) (compound **2a** with CH_2 replacing the nitroamino group) (Wineburg, J. P.; Abrams, C.; Swern, D. *J. Heterocycl. Chem.* **1975**, *12*(4), 749–754); the value in $CHCl_3$ is 1795 cm^{-1} (Dolphin, D.; Wick, A. *Tabulation of Infrared Spectral Data*; John Wiley & Sons, Inc.: New York, 1977; p 369). For solutions in $CDCl_3$, δ = 1.8 ppm (Wineburg et al.). From the effect of an NNO_2 group on methyl groups β to it in methyl *N-tert*-butyl-*N*-nitrocarbamate (ref 3b), it can be estimated that the nitroamino group of **2a** (absent in i) should be responsible for a downfield shift of ~0.2–0.3 ppm.

(10) Hantzsch, A.; Metcalf, W. V. *Chem. Ber.* **1896**, *29*, 1680–1685.

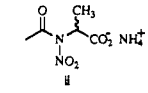
(11) Miyazaki, Y.; Kono, Y.; Shimazu, A.; Takeuchi, S.; Yonehara, H. *J. Antibiot.* **1968**, *21*, 279–282.

(12) Borer, K.; Hardy, R. J.; Lindsay, W. S.; Spratt, D. A.; Mees, G. C. *J. Exp. Bot.* **1966**, *17*(51), 378–389.

(13) Suggested, in this connection, to be a suicide inhibitor, a transition-state analogue, and/or a substrate (Alston, T. A.; Seitz, S. P.; Porter, D. J. T.; Bright, H. J. *Biochem. Biophys. Res. Commun.* **1980**, *97*, 294–300).

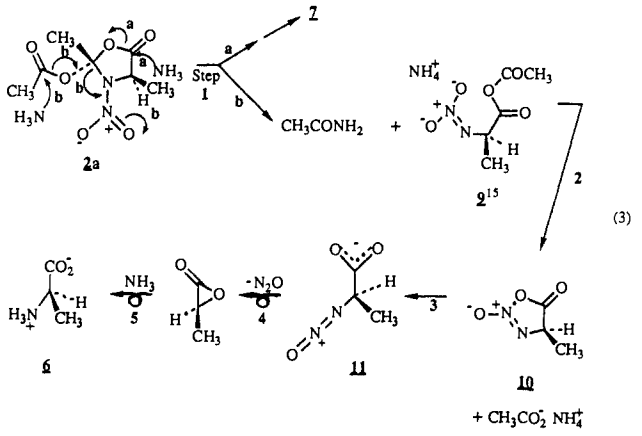
(14) Quitt, P.; Hellerbach, J.; Vogler, K. *Helv. Chim. Acta* **1963**, *46*, 327–333.

(15) Step 1 (path b) of eq 3 could occur in an alternate sense to yield ii. The parent acid of ii can be made (in low yield) from the nitration of acylamino acid **1a** with nitronium tetrafluoroborate; on treatment with ammonia, it does not produce alanine, however.



ii

(16) White, E. H.; Aufdermarsh, C. A. *J. Am. Chem. Soc.* **1958**, *80*, 2597.



(step 4),[17] and for the reaction of strained lactones with ammonia at an sp^3 carbon (step 5)[18] (with inversion of configuration).[19] The extension of the nitration outlined in eq 1 to *N*-acyldipeptides and proteins could, in principle, yield polyspiro analogues of the nitrooxazolidones (**2**).

Acknowledgment. This research was supported by Grant 21450 from the Institute of General Medical Sciences of the U.S. Public Health Service. We thank Dr. C. C. Wei, Hoffman-La Roche, Inc., for arranging for the X-ray structure determination.

Supplementary Material Available: Experimental details concerning the X-ray structure determination of **2a**, crystal data, atomic parameters, thermal parameters, bond distances, bond angles, perspective drawings, torsion angles, and out-of-plane distances (10 pages). Ordering information is given on any current masthead page.

(17) Brewster, P.; Hiron, F.; Hughes, E. D.; Ingold, C. K.; Rao, P. A. D. S. *Nature* **1950**, *166*, 179. Yamada, S.-i.; Taniguchi, M.; Koga, K. *Tetrahedron Lett.* **1969**, 25-28.

(18) Gresham, T. L.; Jansen, J. E.; Shaver, F. W.; Frederick, M. R.; Fiedorek, F. T.; Bankert, R. A.; Gregory, J. T.; Beears, W. L. *J. Am. Chem. Soc.* **1952**, *74*, 1323-1325. Gresham, T. L.; Jansen, J. E.; Shaver, F. W.; Bankert, R. A.; Fiedorek, F. T. *J. Am. Chem. Soc.* **1951**, *73*, 3168-3171.

(19) In the deamination of amino acids, a displacement reaction of water on an α-lactone intermediate proceeds with inversion of configuration.[17]

Sequence-Specific Alkylation of Double-Helical DNA by Oligonucleotide-Directed Triple-Helix Formation

Thomas J. Povsic and Peter B. Dervan*

Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology
Pasadena, California 91125

Received July 2, 1990

Affinity cleaving, a method that relies on the attachment of a nonspecific cleaving moiety, such as EDTA·Fe(II), to a DNA binding molecule, facilitates the elucidation of the structural principles for DNA recognition.[1-4] The determination of the sequence specificities, groove locations, and binding orientations of peptide analogues,[2] protein-DNA binding motifs,[3] and oligonucleotide-triple-helix motifs[4] has provided reliable models for the sequence-specific recognition of double-helical DNA. It now becomes possible to combine these binding molecules with domains capable of base-specific and quantitative modification of DNA (Figure 1).[5] We report the design and synthesis of an oligodeoxyribonucleotide equipped with an electrophile at the 5'-end that binds to double-helical DNA by triple-helix formation and alkylates predominantly at a single guanine base adjacent to the target DNA sequence in high yield.[8]

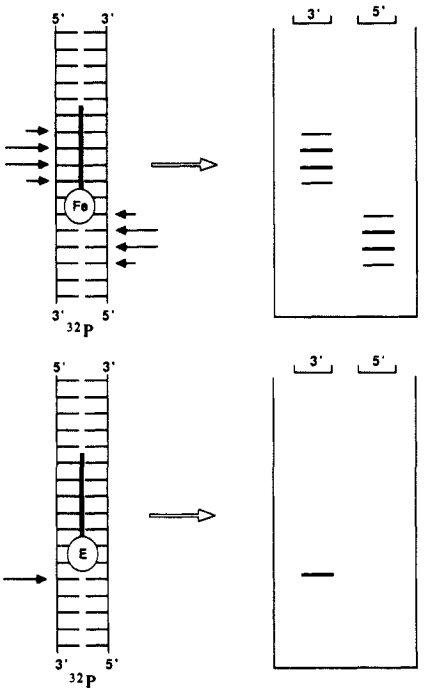


Figure 1. Replacement of a *diffusible nonspecific* DNA cleaving moiety generated by EDTA·Fe(II) (hydroxyl radical) useful for studying DNA recognition (affinity cleaving) to a *nondiffusible base-specific* moiety.[6,7] This is a key issue with respect to the design of sequence-specific DNA cleaving molecules. Sequence-dependent recognition is coupled with sequence-dependent cleavage.

The specificity of oligonucleotide-directed triple-helix formation is imparted by Hoogsteen base pairing between a pyrimidine oligonucleotide and the purine strand of the Watson-Crick duplex DNA.[4,9] The discovery of other base triplets, such as G·TA, and the development of 3'-3'-linked oligonucleotides for alternate-strand triple-helix formation has greatly extended the number of sites capable of being recognized by this motif.[4c,d] Model building of a triple-helical complex indicated that a pyrimidine oligo-

(1) (a) Hertzberg, R. P.; Dervan, P. B. *J. Am. Chem. Soc.* **1982**, *104*, 313. (b) Hertzberg, R. P.; Dervan, P. B. *Biochemistry* **1984**, *23*, 3934.

(2) (a) Schultz, P. G.; Taylor, J. S.; Dervan, P. B. *J. Am. Chem. Soc.* **1982**, *104*, 6861. (b) Taylor, J. S.; Schultz, P. G.; Dervan, P. B. *Tetrahedron* **1984**, *40*, 457. (c) Dervan, P. B. *Science* **1986**, *232*, 464, and references cited therein. (d) Wade, W. S.; Dervan, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 1574. (e) Griffin, J. H.; Dervan, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 6840. (f) Youngquist, R. S.; Dervan, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 7564.

(3) (a) Sluka, J. P.; Bruist, M.; Horvath, S. J.; Simon, M. I.; Dervan, P. B. *Science* **1987**, *238*, 1129. (b) Sluka, J. P.; Griffin, J. H.; Mack, J. P.; Dervan, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 6369, and references cited therein.

(4) (a) Moser, H. E.; Dervan, P. B. *Science* **1987**, *238*, 645. (b) Povsic, T. J.; Dervan, P. B. *J. Am. Chem. Soc.* **1989**, *111*, 3059. (c) Griffin, L. C.; Dervan, P. B. *Science* **1989**, *245*, 967. (d) Horne, D. A.; Dervan, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 2435.

(5) Two early examples were the conversion of distamycin-EDTA·Fe to bromoacetyldistamycin[6] and FeEDTA-Hin(139-190) to Cu/Ni·GGH-(Hin139-190).[7]

(6) (a) Baker, B. F.; Dervan, P. B. *J. Am. Chem. Soc.* **1985**, *107*, 8266. (b) Dervan, P. B.; Baker, B. F. *Ann. N.Y. Acad. Sci.* **1986**, *471*, 51. (c) Baker, B. F.; Dervan, P. B. *J. Am. Chem. Soc.* **1989**, *111*, 2700.

(7) (a) Mack, D. P.; Iverson, B. L.; Dervan, P. B. *J. Am. Chem. Soc.* **1988**, *110*, 7572. (b) Mack, D. P.; Dervan, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 4604.

(8) For reaction of single-stranded DNA with oligodeoxyribonucleotides containing electrophiles, see: (a) Vlassov, V. V.; Zarytova, V. F.; Kutiavin, I. V.; Mamaev, S. V.; Podyminogin, M. A. *Nucleic Acids Res.* **1986**, *14*, 4065. (b) Iverson, B. L.; Dervan, P. B. *J. Am. Chem. Soc.* **1987**, *109*, 1241. (c) Iverson, B. L.; Dervan, P. B. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 4615. (d) Vlassov, V. V.; Zarytova, V. F.; Kutyavin, I. V.; Mamaev, S. V. *FEBS Lett.* **1988**, *231*, 352. (e) Boutorin, A. S.; Gus'kova, L. V.; Ivanova, E. M.; Kobetz, N. D.; Zarytova, V. F.; Ryte, A. S.; Yurchenko, L. V.; Vlassov, V. V. *FEBS Lett.* **1989**, *254*, 129. (f) Meyer, R. B., Jr.; Tabone, J. C.; Hurst, G. D.; Smith, T. M.; Gamper, H. *J. Am. Chem. Soc.* **1989**, *111*, 8517.

(9) (a) Praseuth, D.; Perrouault, L.; Le Doan, T.; Chassignol, M.; Thuong, N. T.; Lhomme, J.; Helene, C. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 1349. (b) Rajagopal, P.; Feigon, J. *Nature* **1989**, *239*. 637. (c) de los Santos, C.; Rosen, M.; Patel, D. *Biochemistry* **1989**, *28*, 7282, and references cited therein.

0002-7863/90/1512-9428$02.50/0