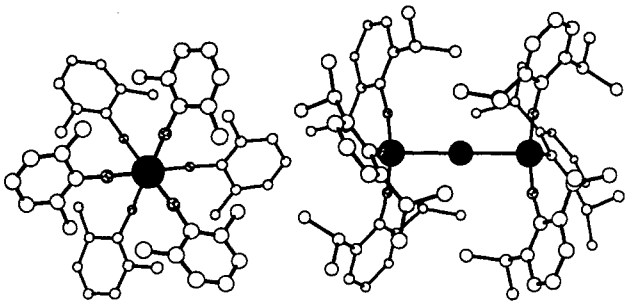
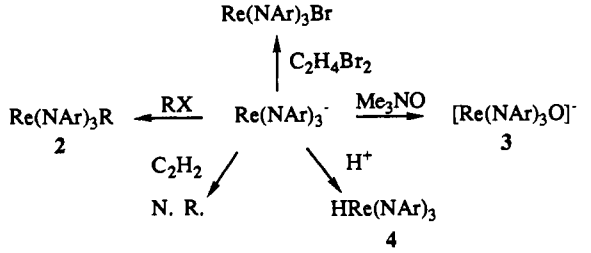


Figure 1. Two views of the structure of $Hg[Re(NAr)_3]_2$ (**1a**). Re-Hg-Re = 180.00°, Hg-Re-N = 97.4 (4)°, N-Re-N = 118.4 (2)°, Re-N-C(1) = 173 (1)°, Hg-Re = 2.621 (1) Å, Re-N = 1.76 (1) Å.

Scheme I



fact that Hg-Re-N = 97.4 (4)°, between the 90° expected for purely ionic bonding of Hg to an unperturbed trigonal-planar anion and the 109° expected for tetrahedral coordination, is evidence that the structure of the free anion probably is trigonal planar.[7] The HOMO in such a trigonal-planar species is likely to be a d_{z^2} orbital, and one pair of electrons should be in a nitrogen-centered nonbonding molecular orbital (A_2 in C_{3v}), is in $Os(NAr)_3$.[1,2]

Some reactions of **1a** or **1b** are summarized in Scheme I. Alkylations with MeI and 2,4,6-trimethylbenzyl chloride to give $Re(NAr)_3(Me)$ (**2a**) and $Re(NAr)_3(CH_2\text{-}2,4,6\text{-}C_6H_2Me_3)$ (**2b**) are very fast (~30 s at 25 °C) and take place in high yield (>90%). Although **1b** reacts with Me_3NO to give $NEt_4[Re(NAr)_3O]$ (**3**), no reaction with ethylene, acetylene, or acetone is observed. **1b** does not oxidize phosphines to give $[Re(NAr)_2(PR_3)_2]^-$ and $R_3P{=}NAr$, as does $Os(NAr)_3$,[1] consistent with the greater oxidizing ability of Os(VI) compared to Re(V). The greater nucleophilicity of $[Re(NAr)_3]^-$ compared to $Os(NAr)_3$ can be ascribed to its overall negative charge, as well as the greater ease of forming Re(VII) from Re(V) versus Os(VIII) from Os(VI).

Addition of H^+ to **1b** (as 2,6-di-*tert*-butylpyridinium triflate) affords $HRe(NAr)_3$ (**4**). In the ^1H NMR spectrum of **4** at temperatures as low as −85 °C, the imido ligands are equivalent and a sharp singlet resonance of area 1 is observed at 7.3 ppm. Upon addition of CCl_4, that resonance disappears and $Re(NAr)_3Cl$ and $CHCl_3$ are formed, a reaction typical of a transition metal hydride complex. No ν(ReH) absorption has yet been identified in the IR spectrum of **4**. Compound **4** reacts only very *slowly* with acetylene, 2-butyne, and norbornene to give $Re(NAr)_2(NHAr)(C_2H_2)$ (**5a**), $Re(NAr)_2(NHAr)(C_2Me_2)$ (**5b**), and $Re(NAr)_2(NHAr)$(NBE) (**5c**), respectively, perhaps because the reactive intermediate is "$Re(NAr)_2(NHAr)$", which is in equilibrium with **4**. NMR data for complexes of type **5** are consistent with a rigid pseudotetrahedral core geometry in which the π-bonding ligand does not rotate about the ligand(centroid)-metal axis, the two carbon atoms lie in the Re-C-C-N(amido) plane, and rotation about the Re-N bond is relatively fast on the NMR time scale. Compound **4** also reacts with PMe_3 to give $Re(NAr)_2(NHAr)(PMe_3)$ (**6**). **5** and **6** are analogous to recently reported d^2 bisimido complexes of W(IV),[8] Re(V),[3] and Os(VI).[2]

(7) An X-ray study of the PPN^+ salt of **1** is in process.
(8) Williams, D. S.; Schofield, M. H.; Anhaus, J. T.; Crowe, W. E.; Schrock, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6728.
(9) Reference deleted in press.

Hydrido/imido complexes are extremely rare. We believe $Cp^*_2Ta(NH)(H)$ to be the only other d^0 example; it is the product of oxidative addition of ammonia to "$Cp^*_2Ta(CH_3)$", which is present in small equilibrium concentration in a solution of $Cp^*_2Ta(CH_2)H$.[10]

The chemistry reported here provides further evidence for the enhanced stability of d^2 trigonal-planar trisimido species and pseudotetrahedral 14-electron molecules containing the $M(NAr)_2$ core. Other d^2 trigonal-planar molecules that have been observed or isolated recently include $Ta[OSi(t\text{-}Bu)_3]_3$[11] and W(N-*t*-Bu)$[OSi(t\text{-}Bu)_3]_2$.[12] $M(NAr)_2$ species show some characteristics of being 18-electron "metallocene-like" complexes, members of a potentially large class of species containing combinations of $2\pi,1\sigma$ ligands (η^5-C_5R_5, NR, O, and CR). Further studies will be aimed at developing the chemistry of these and other d^2 systems.

Acknowledgment. We thank the National Science Foundation (CHE 88-22508) for research support.

Supplementary Material Available: Experimental procedures, NMR data, and analytical data, a labeled ORTEP drawing of **1a**, experimental details of the X-ray study of **1a**, and tables of final positional parameters and final thermal parameters for **1a** (10 pages); table of final observed and calculated structure factors for **1a** (5 pages). Ordering information is given on any current masthead page.

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(11) LaPointe, R. E.; Wolczanski, P. T.; Mitchell, J. F. *J. Am. Chem. Soc.* **1986**, *108*, 6382.
(12) Eppley, D. F.; Van Duyne, G. D.; Wolczanski, P. T., submitted for publication.

DNA Photodamage Mechanistic Studies: Characterization of a Thietane Intermediate in a Model Reaction Relevant to "6-4 Lesions"

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The (6-4) pyrimidine-pyrimidinone photoproducts and cis-syn cyclobutane dimers are the major photolesions occurring at dipyrimidine sequences in DNA when exposed to the UV portion of sunlight.[1] Whereas the mechanism of solar-induced skin cancers remains only partially understood, these lesions are widely recognized as causative of tumor development.[2] Although no experimental proof was ever produced, the mechanism of (6-4) photoproduct formation, such as in dideoxynucleotide model systems,[3] is thought to proceed via a short-lived oxetane,[4] azet-

(1) (a) Mitchell, D. L.; Nairn, R. S. *Photochem. Photobiol.* **1989**, *49*, 805-819. (b) Cadet, J.; Vigny, P. In *The Photochemistry of Nucleic Acids*; Morrison, H., Ed.; Wiley and Sons: New York, 1990; Vol. 1, pp 79-94.
(2) Brash, D. E. *Photochem. Photobiol.* **1988**, *48*, 59-66.
(3) (a) Haseltine, W. A.; Franklin, W. A.; Lo, K. M. *J. Biol. Chem.* **1982**, *257*, 13535-13543. (b) Franklin, W. A.; Doetsch, P. W.; Haseltine, W. A. *Nucleic Acids Res.* **1985**, *13*, 5317-5325. (c) Rycyna, R. E.; Alderfer, J. A. *Nucleic Acids Res.* **1985**, *13*, 5949-5963. (d) Fourrey, J.-L.; Gasche, J.; Fontaine, C.; Guittet, E.; Favre, A. *J. Chem. Soc., Chem. Commun.* **1989**, 1334-1336. (e) Douki, T.; Voituriez, L.; Cadet, J. *Photochem. Photobiol.* **1991**, *53*, 293-297.

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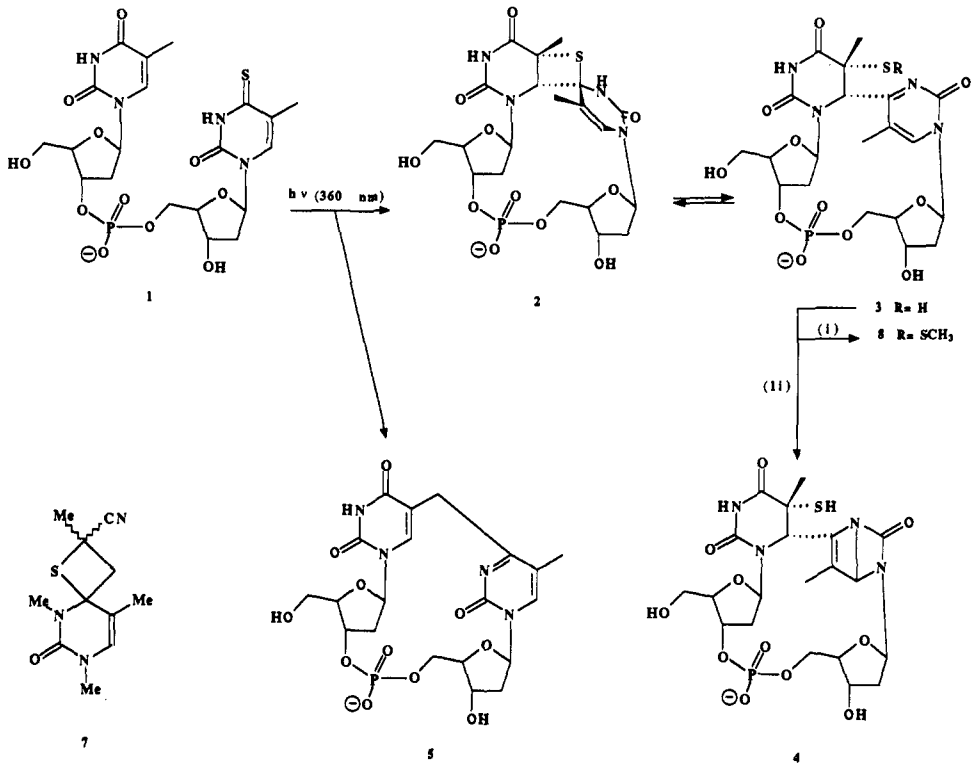
Scheme I[a]



[a] (i) Methyl methanethiosulfonate; (ii) *hν* (360 nm).

idine,[4] or thietane[3d] intermediate arising from (2 + 2) cycloaddition between the C_5–C_6 double bond of the base on the 5′ side (thymine, cytosine) and the C_4 carbonyl (thymine), imine (cytosine), or thiocarbonyl (4-thiouracil) of the base on the 3′ side (Figure 1).

Reported herein is the characterization of the thietane intermediate **2**, formed by 360-nm irradiation of thymidylyl(3′–5′)-4-thiothymidine (**1**),[5] which is indisputably relevant to the mechanism and to the stereochemical course of the reaction leading to (6–4) photoproducts.

Irradiation of **1**, monitored and optimized by HPLC and NMR spectroscopy, led to the formation of four products, **2**–**5**[6] (Scheme I). Structures **4** and **5** were evident from the interpretation of their spectral data. The main fraction consisted of a mixture of two slowly interconverting compounds **2** and **3** in a 3/1 ratio (water). Its FAB mass spectrum (negative mode) exhibited a unique peak at m/z 561 corresponding to M − H, and its UV spectrum showed an absorption maximum (320 nm) expected for a pyrimidinone chromophore as in **3**. The key NMR spectroscopic evidence for the thietane **2** structure is as follows: in the ^{1}H NMR spectrum of the mixture, the characteristic signals due to **2** and **3** are easily recognized (Figure 2); the chemical shift of the H_6 proton of the pT unit of **2** is at 6.30 ppm, which is 1.70 ppm upfield from that of the corresponding proton of the (6–4) adduct **3** but very similar to the value (6.10 ppm) of the H_6 proton of a model thietane **7** obtained by irradiation of 1,3-dimethyl-4-thiothymine (**6**) in the presence of methacrylonitrile.[7] The signal of the spiro pTC_4 carbon of **2** was identified from its scalar correlation (^3J) with the methyl and H_6 protons of the pT part of the molecule. It appears at 73.7 ppm, which is 103.3 ppm upfield from the signal of the corresponding carbon in **3**. This chemical shift value corresponds well with that of the C_4 carbon of **7** (88.9 ppm), considering the substitution difference at the N^3 position. To a lesser extent the chemical shift values of the C_6 and C_5 carbons of the pT part of **2** are shifted upfield with regard to those of its related (6–4) isomer **3** (146.5 to 123.8 ppm and 118.0 to 111.6 ppm, respectively). They are similar to those of the reference thietane **7** (127.3 and 109.7 ppm).

Chemical confirmation of the interpretation of these spectral observations was obtained by increasing the pH (by controlled addition of K_2CO_3 or NaOH) of the aqueous solution containing the **2** + **3** mixture. This led to the complete displacement of the equilibrium toward the opened form **3**, whereas neutralization of the alkaline solution regenerated the original mixture of compounds. Moreover, addition of methyl methanethiolsulfonate to the mixture of **2** and **3** was followed by the immediate disappearance of the two latter bipyrimidines to give the methyl disulfide **8** (FAB MS: m/z 631; M + Na^+). Finally, when a solution of **2** and **3** was further irradiated at 360 nm until their complete disappearance, a single compound **4** was formed which is the Dewar valence isomer[8,3e] of the (6–4) bipyrimidine **3**.

The characterization of thietane **2** definitively establishes the stereochemical course of the reaction leading to (6–4) photoproducts. In particular, the cis relationship that has been found between the C_5 hydroxyl, amino, or thiol groups and the C_6 pyrimidinone rings of the (6–4) photoproducts, respectively, is governed by the stereochemistry of the four-membered-ring intermediate which in the case of the thietane **2** was determined by 2D phase sensitive NOESY experiments. The configurations at C_5 and C_6 of the Tp part were found to be *R* and *S*, respectively, and the two bases were shown to be in an anti conformation[9] as observed for related (6–4) bipyrimidine adducts.[3c,10] This implies

(4) Wang, S. Y. In *Photochemistry and Photobiology of Nucleic Acids*; Wang, S. Y., Ed.; Academic Press: New York, 1976; Vol 1, pp 326–351.

(5) For the preparation of **1**, see ref 3d.

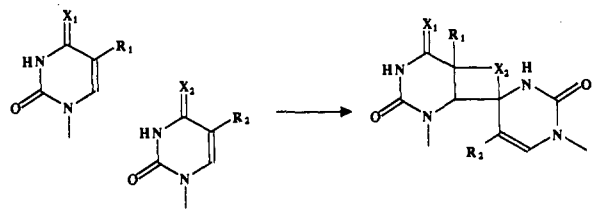
(6) Under our best irradiation conditions, the respective product proportions for compounds **1**, **2**, **3**, **4**, and **5** were found to be 12, 52, 17, 10, and 9% as estimated by NMR measurement. The isolated yields for (**2** + **3**), **4**, and **5** were 35, 5, and 5%, respectively, after preparative HPLC (C18 RP).

(7) Fourrey, J.-L.; Jouin, P.; Moron, J. *Tetrahedron Lett.* **1974**, 3005–3006.

(8) (a) Taylor, J.-S.; Cohrs, M. P. *J. Am. Chem. Soc.* **1987**, *109*, 2834–2835. (b) Taylor, J.-S.; Garrett, D. S.; Cohrs, M. P. *Biochemistry* **1988**, *27*, 7206–7215. (c) Taylor, J.-S.; Lu, H.-W.; Kotyk, J. J. *Photochem. Photobiol.* **1990**, *51*, 161–167.

(9) The C_5(*R*) and C_6(*S*) configurations and the anti conformations of **2** were established from the following sets of NOEs: TpH_6–$TpH_{2'}$; TpH_6–$TpH_{3'}$; pTH_6–$pTH_{2'}$; pTH_6–$pTH_{3'}$; TpH_6–$Tp(CH_3)$; TpH_6–$pT(CH_3)$.

(10) (a) Taylor, J. S.; Garrett, D. S.; Wang, M. J. *Biopolymers* **1988**, *27*, 1571–1593. (b) Kan, L.; Voituriez, L.; Cadet, J. *Biochemistry* **1988**, *27*, 5796–5803.



X_1 = O, NH X_2 = O, NH, S

R_1 = CH_3, H R_2 = CH_3, H

Figure 1. Presumed precursors of (6-4) bipyrimidines.

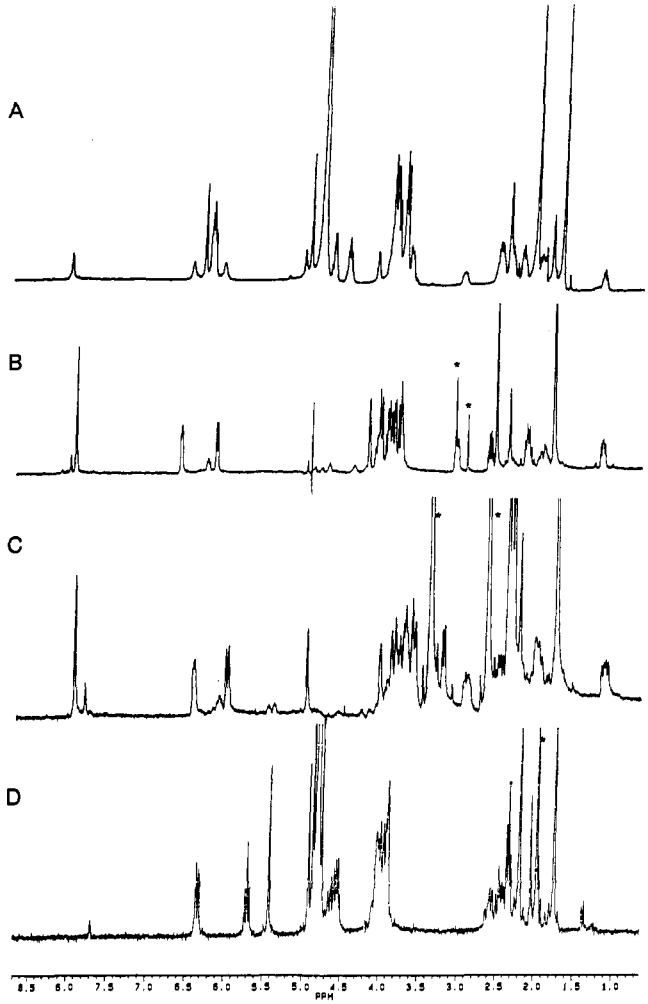


Figure 2. ^1H NMR spectra (D_2O) of photoproducts and derivatives: spectrum A, **2** + **3**; spectrum B, **3** (* denotes impurities); spectrum C, **8** (* denotes methyl methanethiosulfonate signals); spectrum D, **4** (* denotes ammonium acetate).

that the (2 + 2) cycloaddition proceeds with the two bases in an anti conformation, despite the proximity between the two bulky methyl substituents, and that the anti conformation of the pT part is retained during and after ring opening as it is also the case for the Dewar isomer **4**.

Our results demonstrate that **1** undergoes a very efficient photochemical conversion into a bipyrimidine of the (6-4) type. It is likely that this will prove useful for the study of the chemical behavior of related adducts in model systems and more particularly in double-stranded oligodeoxynucleotides. In the latter case we are currently interested in raising antibodies that could detect the (6-4) lesions of cellular DNA.[11] Finally, this work also supports the mechanism of (5-4) bipyrimidine formation in tRNAs containing 4-thiouridine.[12]

Supplementary Material Available: Experimental conditions, ^1H NMR spectra of **1** and **5**, and ^{13}C NMR chemical shifts of **1-7** (4 pages). Ordering information is given on any current masthead page.

(11) Mitchell, D. L.; Allison, J. P.; Nairn, S. N. *Radiat. Res.* **1990**, *123*, 299-303.

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Lewis Acid Induced Internal Proton Return: Enantiocontrolled Protonation of an Amide Enolate

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We report a new technique for enantiocontrolled amide enolate protonation in the enolate complex with a chiral secondary amine. We have found that $BF_3{\cdot}Et_2O$ and certain other Lewis acids induce the protonation of amine-containing enolates derived from acids, esters, and amides. Under these conditions, there can be no competition from enolate quenching by external proton sources, and proton transfer is more likely to occur within a specific, highly chirotopic environment. Our experiment is an example of the internal proton return process (IPR).[1-3] This phenomenon was encountered early in the LDA era, usually as an undesired side reaction in the attempted deuterium labeling of LDA-derived lithium enolates.[1,2] Evidence for IPR has also been detected in the course of certain alkylation experiments.[2c] We are not aware of prior studies designed to maximize and exploit this process, but pioneering work by Seebach et al. reveals a close relationship between IPR and aggregate structures in amine-containing lithium enolates.[3,4] The most relevant X-ray analogy (Figure 1) has a secondary amine ligand N-H proton within H-bonding distance of the amide enolate nitrogen. As noted by Seebach et al., a relatively small geometrical change is needed for internal transfer of this proton from nitrogen to carbon if ligand N-H acidity is increased by the interaction of the enolate-amine complex with an electrophile.

Our experiments were designed to maximize the IPR process by using electrophilic quenching agents that might attack amine ligand nitrogen in the amine-enolate complex in preference to enolate carbon or oxygen. Naproxen amides **1** were chosen for the initial optimization study because the α-substituents differ sufficiently in size to allow reasonable control for one major enolate isomer. Thus, treatment of racemic **1a** with *sec*-BuLi (2 equiv, 10 min in THF, -78 °C) afforded a yellow anion **2**, and quenching with TMSCl gave 14:1 *Z*:*E* mixture of enol silanes **3Z**:**3E**.[5] We

(1) Creger, P. L. *J. Am. Chem. Soc.* **1970**, *92*, 1396.

(2) (a) Seebach, D.; Boes, M.; Naef, R.; Schweizer, W. B. *J. Am. Chem. Soc.* **1983**, *105*, 5390. (b) High internal return from a chiral amine has been demonstrated in the enolate of 2,2,6-trimethylcyclohexanone enolate, resulting in a solvent-dependent 15-46% ee: Eleveld, M. B.; Hogeveen, H. *Tetrahedron Lett.* **1986**, *27*, 631. (c) Aebi, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1507. El Achqar, A.; Roumstant, M. L.; Villefont, P. *Tetrahedron Lett.* **1988**, *20*, 2441. Polt, R.; Seebach, D. *J. Am. Chem. Soc.* **1989**, *111*, 2622.

(3) For an excellent review of the role of the coordinating amine in enolate chemistry and a number of examples of chiral diamine induced asymmetric transformations, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624. Further examples of chiral diamine or triamine modified enolate reactions are discussed by Hansen: Hansen, J. Ph.D. Dissertation No. 7863, ETH, Zürich, 1985.

(4) Seebach, D.; Laube, V. T.; Dunitz, J. D. *Helv. Chim. Acta* **1985**, *68*, 1373.

(5) NMR (200 MHz, $CDCl_3$): major (**3Z**) δ 2.07 (3 H, s), 1.16 (12 H, d, J = 6.0 Hz), -0.26 (9 H, s); minor (**3E**) δ 2.04 (3 H, s), 0.96 (12 H, d, J = 6.0 Hz), 0.30 (9 H, s).

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