NaOH (3 × 5 mL). The alkaline solution was acidified with 2 N H_2SO_4, and the solid which precipitated was extracted with ethyl ether (3 × 5 mL). The ethereal solution was washed with brine (3 × 5 mL) and dried over anhydrous Na_2SO_4. The solvent was removed in vacuo, and the crude product was purified by flash column chromatography on silica gel using petroleum ether (60–90 °C)/ethyl acetate (7:3) as the eluent to afford **5** (390 mg, 69% yield): a white solid, mp 140–142 °C; ^1H NMR ($CDCl_3$) δ 3.93 (s, 3 H), 4.49 (q, J_{H-F} = 8.5 Hz, 1 H), 7.50 (m, 6 H); ^{19}F NMR ($CDCl_3$) δ −7.0 (d, J_{H-F} = 8.5 Hz); IR (KCl) 3500, 1710, 1600, 1500, 1358 cm^{-1}; MS *m/z* (relative intensity) 284 (M, 62), 239 (100). Anal. Calcd for $C_{14}H_{11}F_3O_3$: C, 59.16; H, 3.90; F, 20.05. Found: C, 59.27; H, 4.29; F, 20.17.

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Registry No. 1, 1514-82-5; 2, 136476-22-7; 4a, 384-64-5; 4b, 136476-18-1; 4c, 136476-19-2; 4d, 136476-20-5; 4e, 136476-23-8; 4f, 136476-24-9; 4g, 136476-25-0; 4h, 136476-26-1; 4i, 136476-27-2; 4j, 136476-28-3; 4k, 136476-29-4; 4l, 136476-30-7; 5, 87406-13-1; iodobenzene, 591-50-4; *p*-iodonitrobenzene, 636-98-6; *m*-iodonitrobenzene, 645-00-1; *p*-bromoiodobenzene, 589-87-7; *p*-bromonitrobenzene, 586-78-7; *m*-bromonitrobenzene, 585-79-5; *p*-bromoacetophenone, 99-90-1; *o*-bromonitrobenzene, 577-19-5; 2,4-dinitrobromobenzene, 584-48-5; *o*-bromobenzaldehyde, 6630-33-7; *o*-bromophenyl acetate, 1829-37-4; 1-iodonaphthalene, 90-14-2; 2-bromonaphthalene, 580-13-2; 2-bromo-6-methoxynaphthalene, 5111-65-9; silver–zinc couple, 12041-17-7.

Mechanistic Studies on DNA Photolyase. 4. The Enthalpy of Cleavage of a Model Photodimer

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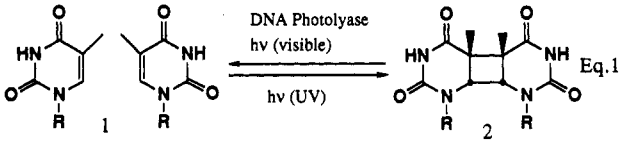
Cyclobutane pyrimidine photodimers constitute the highest quantum yield lethal damage caused to DNA by ultraviolet light.[1] In the cell this lesion can be efficiently repaired by DNA photolyase in a light-dependent reaction (350–450 nm, eq 1).[2] While model studies using quinones



and indoles as sensitizers have demonstrated that both the photodimer radical cation and anion undergo facile fragmentation reactions,[3] the mechanism of this interesting reaction has not yet been clearly established.[4,5]

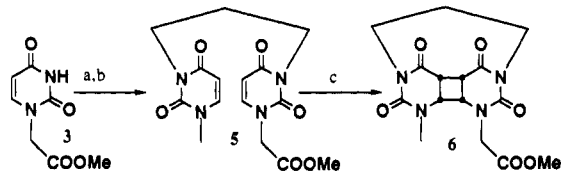
In this paper, we report the enthalpy of cleavage of a model uracil photodimer.[6]

Experimental Section

Melting points were uncorrected. Microanalyses were performed by Guelph Chemical Laboratories. Chromatography was carried out on silica gel.

3-(3-Bromopropyl)-1-(carbomethoxymethyl)uracil (4). Three grams (0.016 mol) of **3**[7] was combined with 6.5 mL (13 g, 0.064 mol) of 1,3-dibromopropane and 6.63 g (0.048 mol) of dry finely ground K_2CO_3 in 30 mL of dry DMF and heated at 60 °C for 1.5 h. The reaction mixture was cooled to room temperature and filtered, and the solvent was removed. Chromatography (0.5% CH_3OH in CH_2Cl_2) gave 3.7 g (75%) of **4**: ^1H NMR δ 7.65 (d, J = 9 Hz, 1 H), 5.75 (d, J = 9 Hz, 1 H), 4.6 (s, 2 H), 3.9 (t, J = 6 Hz, 2 H), 3.65 (s, 3 H), 3.5 (t, J = 6 Hz, 2 H), 1.9–2.1 (m, 2 H); HRMS calcd for $C_{10}H_{14}N_2O_4Br$ 305.0143, found 305.0137.

Scheme I[a]



[a] (a) 1,3-Dibromopropane; (b) 1-methyluracil; (c) *hv*.

Bisuracil (5). **4** (2.6 g, 8.5 mmol), 1.0 g (8.5 mmol) of 1-methyluracil,[8] and 3.5 g (25.5 mmol) of K_2CO_3 in 40 mL of dry DMF were heated at 60 °C for 1.5 h. The reaction mixture was filtered, and the solvent was removed. Chromatography (1% CH_3OH in CH_2Cl_2) gave 2.3 g (78%) of **5**: mp 176–178 °C; ^1H NMR δ 7.6 (d, J = 9 Hz, 2 H), 5.75 (d, J = 9 Hz, 1 H), 5.65 (d, J = 9 Hz, 1 H), 4.6 (s, 2 H), 3.75 (t, J = 6 Hz, 4 H), 3.65 (s, 3 H), 3.3 (s, 3 H), 1.6–1.8 (m, 2 H). Anal. Calcd for $C_{15}H_{18}O_6N_4$: C, 51.43; H, 5.18; N, 15.99. Found: C, 51.28; H, 4.91; N, 15.75.

Cis-Syn Photodimer 6. One gram of **5** was dissolved in 500 mL of CH_3CN and degassed by purging with argon for 15 min; 50 mL of acetone was added, and the solution was irradiated in a Rayonet reactor (λ_{max} = 300 nm) for 10 h. The solvent was removed, and the photodimer was purified by chromatography (1% CH_3OH in CH_2Cl_2) to give 0.63 g (63%) of **6**: mp 253–255 °C; ^1H NMR δ 3.65–4.45 (multiplet, 10 H), 3.63 (s, 3 H), 2.8 (s, 3 H), 2.0–2.2 (m, 1 H), 1.4–1.6 (m, 1 H). Anal. Calcd for $C_{15}H_{18}O_6N_4$: C, 51.43; H, 5.18; N, 15.99. Found: C, 51.81; H, 5.35; N, 16.09.

Combustion Calorimetry. The standard enthalpies of formation of bisuracil **5** and its photodimer **6** were measured using a mini rotating-bomb combustion calorimeter suitable for samples of ca. 10–50 mg.[9] The compounds were burned as pellets (ca. 20 mg) under 30 atm of oxygen using *n*-hexadecane (ca. 4 mg) as combustion aid. The bomb was not rotated during the experiments. The HNO_3 formed was determined as NO_3^- using a Dionex 4000*i* ion chromatography apparatus.

Results and Discussion

The model photodimer was synthesized as outlined in Scheme I. The trimethylene linker ensured that only the syn-cis isomer resulted from the photodimerization reaction.[10]

The standard enthalpy of formation of bisuracil **5** and its photodimer **6** were found to be −1116.6 ± 3.7 kJ/mol

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and −1006.6 ± 3.7 kJ/mol, respectively. From these values it can be calculated that the pyrimidine photodimer fragmentation reaction, in the standard state, is exothermic ($\Delta H°_r$ = −110.0 ± 5.2 kJ mol^{-1}). The exothermicity of this reaction, when compared with the endothermic fragmentation of cyclobutane[11] ($\Delta H°_r$ = +76.5 ± 0.8 kJ mol^{-1}), reflects both the release of the additional strain in the pyrimidine photodimer compared to the simple cyclobutane and the formation of the delocalized pyrimidine double bond. Although photoenzymes can catalyze strongly endergonic reactions due to the large amount of energy absorbed by the enzyme substrate complex, this study demonstrates that in the case of DNA photolyase, all of this energy is used for catalysis.

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Registry No. 3, 5236-60-2; 4, 135790-03-3; 5, 137394-53-7; 6, 137394-54-8; 1,3-dibromopropane, 109-64-8; 1-methyluracil, 615-77-0; DNA photolyase, 37290-70-3.

Supplementary Material Available: NMR spectrum for 4 and details of the calorimetric measurements (7 pages). Ordering information is given on any current masthead page.

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Diastereoselective Electrophilic Addition Reactions to Chiral β-Dimethylphenylsilyl Ester Enolates. Synthesis of 2,3-Anti-α-substituted-β-silyl-(*E*)-hex-4-enoates

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Current efforts in our laboratory are focusing on the development of optically active (*E*)-crotylsilane reagents for their use as carbon nucleophiles in asymmetric addition reactions.[1,2] In this regard, we have recently reported the stereoselective synthesis of α-substituted β-silyl-(*E*)-hex-4-enoates **3** through the use of the Ireland–Claisen rearrangement on esters of optically active (*E*)-vinylsilanes **1**.[3,4] The process is illustrated with the *R* stereoisomer in Scheme I. This strategy is particularly useful for the construction of the syn diastereomers $\mathbf{3}_{syn}$, derived from the corresponding glycolate (X = OMe, OH) and propionate esters (X = Me). Thus, by using enolization conditions that permit the near exclusive formation of the chelated *Z* O-enolate, high levels of syn diastereoselection (16 to >25:1 syn/anti) were achieved.

In connection with studies directed toward the asymmetric synthesis of trans olefin dipeptide isosteres we required functionalized β-dimethylphenylsilyl (*E*)-hex-4-enoates that possess large alkyl substituents (e.g., ^{i}Pr, benzyl, cyclohexylmethyl) and an amine precursor (azide) α to the ester group with anti stereochemistry relative to the silicon group. In these cases the Claisen strategy was plagued by the fact that the desired anti diastereomer could only be isolated in low yield with considerable amounts of 1-(dimethylphenylsilyl)-1-buten-3-ol produced presumably via the hydrolysis of the intermediate silylketene acetal. Furthermore, for cases employing glycolate esters of **1** (X = OR) the configuration of the enolate had to be reversed from *Z* O- to the *E* O-ester enolate, a situation where the strong chelating ability of the glycolate oxygen made it difficult to achieve useful levels of selectivity resulting in only moderate levels of diastereoselection for the anti product.[3] In an effort to develop a more efficient method for the production of $\mathbf{3}_{anti}$ with high levels of diastereoselection, we investigated the potential of the derived β-silyl ester enolate of **2** to participate in diastereoselective electrophilic addition reactions (Scheme I). As first documented by Fleming,[5a,b] useful levels of diastereoselection were achieved in alkylation reactions of racemic β-silyl enolates derived from the conjugate addition of a silyl cuprate to an α,β-unsaturated carbonyl compound. The sense of asymmetric induction is the same as the well-established anti stereospecifity observed in the addition of electrophiles to allylsilanes.[6]

In this paper, we wish to report the results of our experiments on the electrophilic additions to chiral β-(dimethylphenylsilyl)lithium ester enolates of (*R*)-**2a** and (*S*)-**2b**. The reactions constitute a viable approach for the synthesis of the 2,3-anti diastereomers in nearly optically pure form. The (*E*)-crotylsilanes **2** are derived from an Ireland–Claisen reaction on the acetate of (*S*)-**1a** or (*R*)-**1b** (X = H) as previously reported.[3] A variety of carbon electrophiles and the azide doner, 2,4,6-triisopropylbenzenesulfonyl azide (trisyl-N_3),[7] were examined. The

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