acid/H_2O_2[13] were for target·I (lane 4) and target·III (lane 8) fully consistent with the results of sequence-specific cleavage. For target·II, sequence-random cleavage afforded approximately equimolar quantities (densitometry) of radiolabeled fragments shorter than full-length target strand representing cleavage at and to the radiolabeled side of T13 (lane 6).[12] This suggests that T13 is the predominant site of cross-linking in target·II, implying that this lesion must be resistant to $NaBH_4/C_6H_5NH_2$ cleavage.[14]

These data demonstrate conclusively that a psoralen can be targeted to react with a selected thymidine in a target single strand. With the present system, it is apparent that the first extrahelical residue in the target strand to the 3'-side of the hybrid duplex is especially susceptible to photoreaction. The absence of appreciable photoreaction at the proximal 5'-TA site in the hybrid of probe I with the target DNA is especially impressive. Furthermore, this study demonstrates that the $NaBH_4/C_6H_5NH_2$-promoted cleavage reaction of the photoadducted thymidine is a preparatively useful reaction.[15] The combination of these two selective processes renders psoralen–oligonucleotide conjugates sequence-tunable, site-specific endonucleases.

The results herein pinpoint for the first time at nucleotide resolution the sites of photo-cross-links afforded by a psoralen covalently tethered to the terminus of a probe oligodeoxynucleotide. Although demonstrated with a single-stranded-DNA target, the methods herein, with minor modification, should be applicable to the definition of cross-link location in DNA–RNA hybrid structures of interest in studies of antisense repression of mRNA translation[16] and cross-links or even ternary linkages in triplex structures of interest in repression of gene transcription.[2]

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(14) The relative reactivity of the three cross-linked species toward $NaBH_4/C_6H_5NH_2$ is most consistent with a structural model in which the HMT moiety is stacked on the end of rather than intercalated within the duplex region. Thus, in target·I and target·III the cross-linked thymidines T13 and T15 are extrahelical and presumably readily accessible to incoming chemical reagents. In contrast, in target·II, an HMT "cap" is expected to protect the buried, intrahelical, cross-linked residue T13. Consistent with this model is the observation that a 16-nt duplex cross-linked with HMT at a central 5'-TA sequence was, like target·II, inefficiently cleaved with $NaBH_4/C_6H_5NH_2$ (unpublished observation).

(15) A 5'-^{32}P-radiolabeled analogue of the target strand (lacking the 3'-terminal radioactive 3'-ddAMP residue) which had been photo-cross-linked to probe I was also studied. Random (iron(II) EDTA) cleavage was fully consistent with cross-linking through T15 (as for target·I). The sequence-specific ($NaBH_4/C_6H_5NH_2$) cleavage conditions afforded, in addition to the fragment of electrophoretic mobility consistent with cleavage at T15, comparable quantities of at least three other substances with mobilities 1–2-nt slower, suggesting that the new 3'-terminus is structurally heterogeneous.

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(17) Cross-linked DNA in 50 μL of 5 mM potassium phosphate buffer (pH 8.4), 5 mM NaCl, and 50 mM thymidine at 2 °C was treated with 50 μL of 0.5 M $NaBH_4$ in 5 mM potassium phosphate buffer (pH 8.4), then stored at 2 °C in a vessel open to the atmosphere for 16 h, then treated with 250 μL of 1.2 mM sodium acetate buffer (pH 5.2), and warmed to 25 °C, where it was vortexed periodically for 1 h. DNA was precipitated with ethanol, and the precipitate was washed with 1 mL of 80% aqueous ethanol (−20 °C) and redissolved in 150 μL of 0.6 M sodium acetate buffer (pH 5.2). After 0.5 h at 25 °C, DNA was precipitated with ethanol and dried. DNA was dissolved in 5 μL of water and 30 μL of 1.0 M aniline which had been brought to pH 4.5 with acetic acid. The mixture was heated to 60 °C for 0.5 h, then frozen, and lyophilized. The resulting sample was twice lyophilized from 30 μL of fresh water and then electrophoresed.

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Chromium-Mediated Cyclizations of Cross-Conjugated Ketoketenes in 8- and 10e⁻ Processes

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The reaction of Fischer carbene complexes with alkynes is one of great utility in the synthesis of substituted quinones and phenols.[1] Recently we reported that the reactions of ketoalkynes with alkoxyalkenyl carbene complexes of the type **1a** give bicyclic lactones of the type **3a** (Scheme I) that arise from double cyclizations of cross-conjugated ketoketene intermediates in an overall process that involves an 8e⁻ reorganization.[2] We report here a demonstration that these cyclizations can be effected in other possible 8e⁻ configurations, the first examples of 10e⁻ processes in this system, and evidence which suggests that the selectivity for the formation of the two possible isomeric η^1,η^3-vinyl carbene and η^4-vinyl ketene complexed intermediates is under stereoelectronic control.[3]

A possible mechanism for the formation of lactones of the type **3** has been previously proposed to involve cross-conjugated ketoketenes of the type A that is complexed to chromium.[2,4] The overall process for the formation of lactone **3a** can be envisioned as the stitching together of the carbene ligand, a CO ligand, and the ketoalkyne as indicated in structure A. Permutation of the vinyl group in A about the cross-conjugated ketoketene unit produces four configurations that would be expected to lead to bicyclic lactones in similar 8e⁻ ring closures. These are indicated by structures A–D (Chart I) where the labels R_1–R_4 define the

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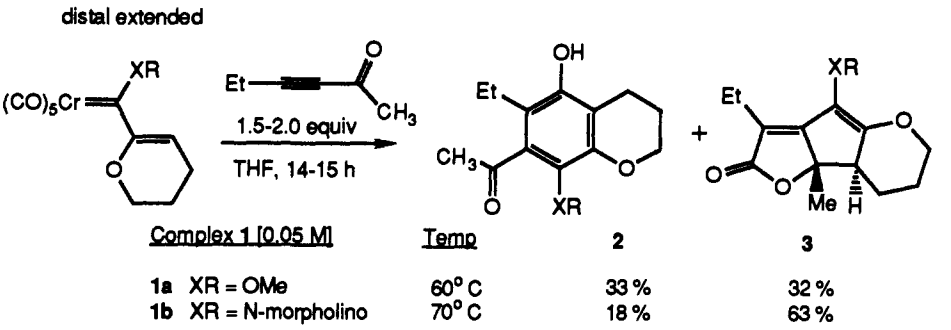
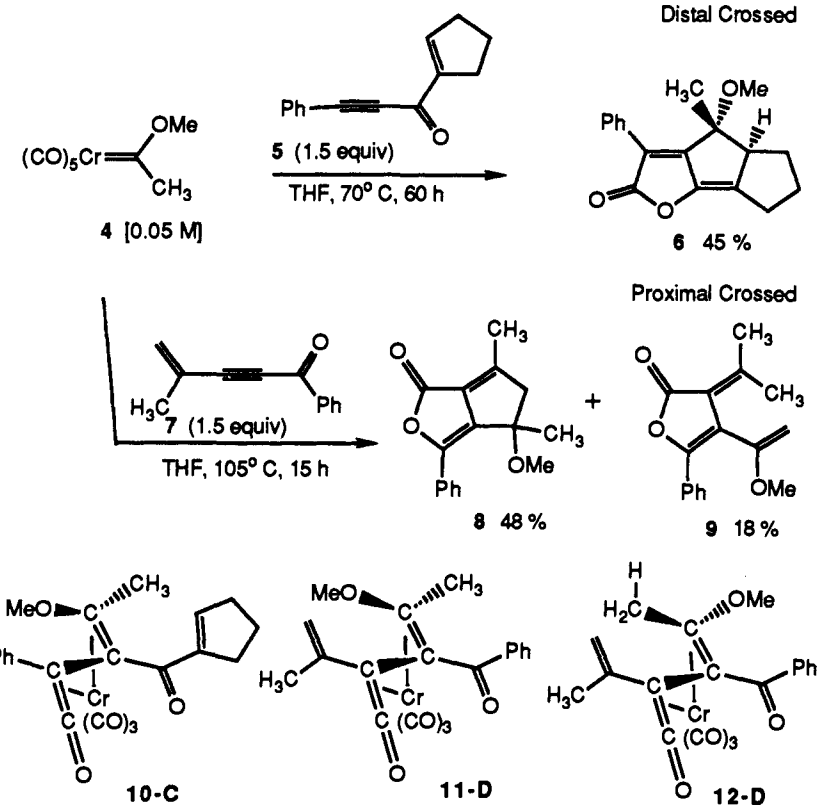
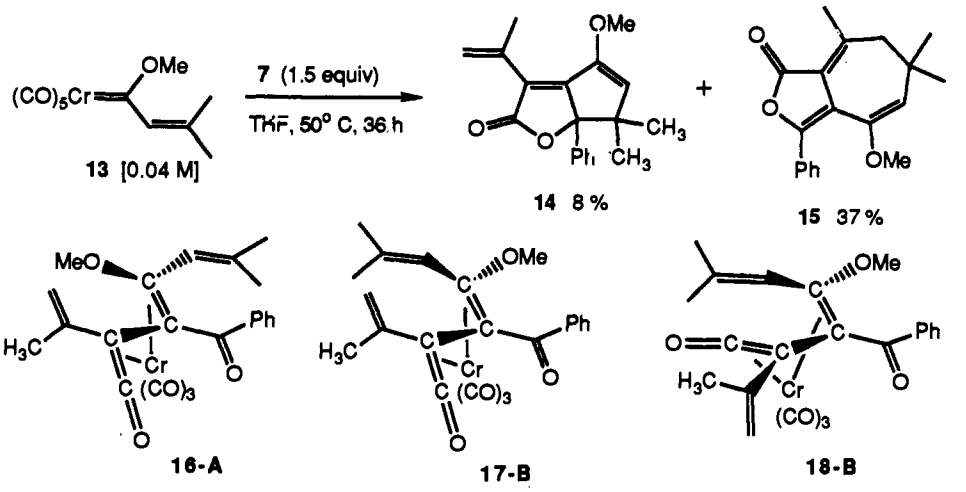
Scheme I



Scheme II



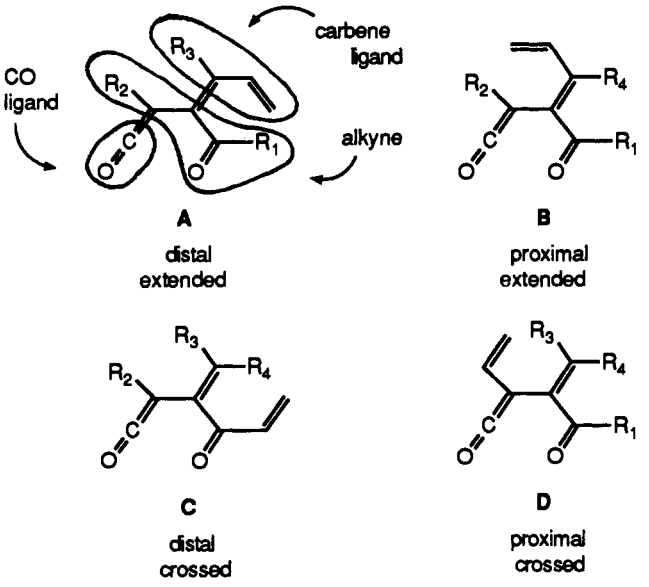
Scheme III



positions available for the vinyl group (the metal has been omitted for clarity). In principal, it should be possible to access all four of these configurations with the proper choice of carbene complex and alkyne.

It was possible to access the distal-crossed and proximal-crossed configurations from the reaction of the alkyl carbene complex **4** and the ketoalkynes **5** and **7**, respectively. The reaction with alkyne **5** produced the tricyclic lactone **6** as a single diastereomer in which

Chart I



the relatively stereochemistry was assigned by X-ray diffraction.[5] The lactone **6** has the methoxyl group and methine hydrogen cis and this requires that the cross-conjugated ketene complex **10-C** cyclizes to **6** via the indicated *Z* isomer. Although the mass balance is not high, the apparent preference for the formation of the *Z* isomer of **10-C** which has the methoxyl anti to the ketone function may be due to an electronic interaction that favors a trans relationship of the methoxyl and the carbonyl.[6] In support of this idea is the observation that the reaction of the amino complex **1b** with 3-hexyn-2-one shifts the product partition in favor of the lactone product **3** relative to the methoxyl complex **1a**. The formation of **2** requires the intermediacy of a ketoketene complex in which the group XR is syn to the keto group of the alkyne, and for the formation of the lactone **3** this relationship must be anti as it is for example in **10-C**.[2] Whether or not the product distribution for these reactions are under stereoelectronic control remains to be established, nonetheless, this result extends the synthetic utility of the lactone-forming reactions in the distal-extended mode in our original observations.[2]

The reaction of **4** with the alkyne **7**[7] produces two compounds, **8** and **9**, both of which arise from the proximal-crossed configuration. However, these two products are apparently derived from the two stereoisomeric cross-conjugated ketoketene complexes **11-D** and **12-D**. The lactone **8** is thought to arise from the isomer **11-D**, but the monocyclic lactone **9** can only arise from the isomer **12-D**.[8] The formation of **9** requires a 1,6-hydride shift that involves an unprecedented 10e⁻ reorganization in the overall process. If the product ratio reflects the stereochemistry of the reaction intermediates, then the vinyl ketene complex **11-D** with the methoxyl anti to the ketone carbonyl is preferred by a factor of 2.7:1 over the syn isomer **12-D**.

The final example illustrated in Scheme III was examined in an effort to document the fourth cyclization mode for these reactions (proximal-extended). The lactone **14** was the minor product and arises from the cross-conjugated ketoketene complex **16-A** in which the distal-extended closure wins out over the proximal-crossed closure. A similar competition exists in the intermediate **17-B** where both a proximal-extended and a proximal-crossed closure is possible. However, this intermediate leads to a bicyclization involving an unprecedented 10e⁻ reorganization that produces a seven-membered ring into which both vinyl groups have been incorporated.[9]

That a variety of configurations of cross-conjugated ketoketenes complexes can be easily generated from the reaction of carbene complexes and alkynes should serve to stimulate the general class of 8- and 10e⁻ bicyclization reactions that are inherent to these intermediates.

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Supplementary Material Available: Spectral data for all new compounds (**2b**, **3b**, **5-10**, **14**, and **15**) and X-ray crystallographic data for compound **6** including tables of fractional coordinates, isotropic and anisotropic thermal parameters, bond distances, and bond angles (9 pages); a listing of F_o and F_c for compound **6** (11 pages). Ordering information is given on any current masthead page.

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(8) Compound **9** appears not to be a fragmentation product of **8** as **9** can be recovered in high yield after heating in THF for 105 °C for 15 h with no detectable formation of **8**.

(9) No cyclohexadienone products were observed in this reaction.[10]

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Persistent Triplet Diradicals from the Dimerization of Silacyclobutadienes

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Silacyclobutadiene, SiC_3H_4, is a molecule of great interest because of its unusual electronic structure and novel reaction chemistry.[1-5] The formal Hückel antiaromaticity of its π system suggests that the HOMO-LUMO gap in this molecule should be small. Ab initio calculations predict a singlet-triplet splitting of only 5 kcal/mol for silacyclobutadiene,[6] a value significantly less than the 23.0 kcal/mol calculated for cyclobutadiene, C_4H_4.[7] Due to closely spaced frontier orbitals, diradicaloid behavior should be important in some chemical reactions involving silacyclobutadienes. We now report that persistent triplet diradicals arise from the dimerization of two highly hindered silacyclobutadiene analogues (Scheme I).

When a 3-methylpentane (3-MP) glass containing either **1-Mes** or **1-Trip** at 77 K is warmed in the cavity of an EPR spectrometer and refrozen at 77 K, strong well-resolved features indicative of triplet species appear (Figure 1). In the case of **1-Mes**, two triplets initially appear at ~100 K: a major triplet (A), with $|D|/hc = 0.0243$ cm^{-1} and $|E|/hc < 0.000\,01$ cm^{-1}, and a minor triplet (B), with $|D|/hc = 0.0138$ cm^{-1} and $|E|/hc = 0.000\,47$ cm^{-1}. If the

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