Acknowledgment. We thank the National Science Foundation for their generous support of our programs.

Registry No. 1, 109468-75-9; **2**, 112713-31-2; **3**, 109468-77-1; **4**, 109468-82-8; **7** (R = H), 112713-14-1; **7** (R = D), 112713-17-4; **8** (R = H), 112713-15-2; **8** (R = D), 112713-18-5; **9** (R = H), 112713-16-3; **9** (R = D), 112713-19-6; **10** (R′ = H), 112739-95-4; **11**, 112713-32-3; **12**, 112713-20-9; **13**, 112713-21-0; **14** (R = H), 109468-75-9; **14** (R = CO_2CH_3), 112713-33-4; **15a** (R = H), 112713-22-1; **15a** (R = CO_2CH_3), 112713-25-4; **15b** (R = H), 112713-23-2; **16** (R = H), 112713-24-3; **17** (R = CO_2CH_3), 112739-96-5; **18**, 112713-26-5; **19a**, 112713-27-6; **19b**, 112713-28-7; **19c**, 112713-29-8; **20**, 112713-30-1; DMAD, 762-42-5; methyl 2-butynoate, 23326-27-4.

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Nonpeptide Mimetics of β-Turns: A Facile Oxidative Intramolecular Cycloaddition of an Azodicarbonyl System

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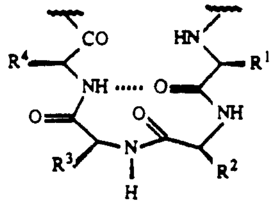
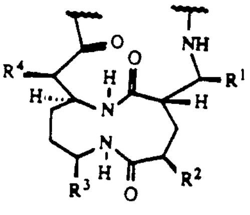
As part of our program to utilize conformationally restricted nonpeptide mimetics to investigate the relationship between peptide structure and function,[2] we have designed system **1**[3] as a mimetic of a type I beta turn.[4] An efficacious and versatile retrosynthetic strategy is outlined in Scheme I. The key transformation involves the previously unreported intramolecular Diels–Alder reaction of an azodicarbonyl system.[5,6] We wish to disclose the success of a model study of this key cycloaddition reaction (Scheme II), the facility with which this reaction proceeds, despite the unusual bridging between diene and dienophile, and the strained tricyclic system which is produced.[7] We envisioned that the requisite precursor **2** could be generated in situ via oxidation of the diacylhydrazide **3**, which would subsequently undergo cycloaddition through a less encumbered exo transition state. The synthesis of **4** commences with the readily available ethyl 5-phenyl-4-pentenoate (**5**) (Scheme III).[8] Cyclocondensation with *N*-chlorosulfonyl isocyanate (18 h, room temperature) proceeds smoothly providing trans β-lactam **6** in 72% yield.[9] Benzylation using the

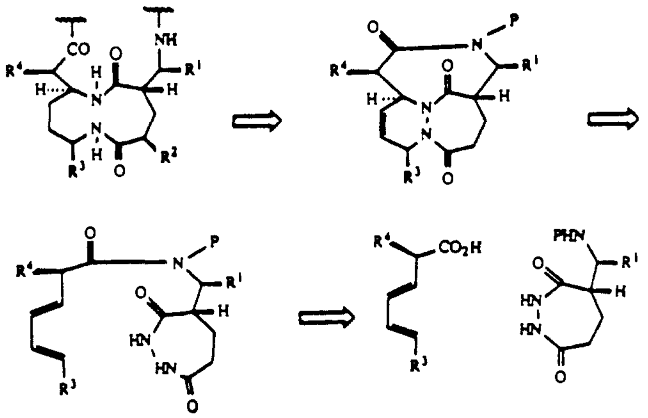


Type I β-turn

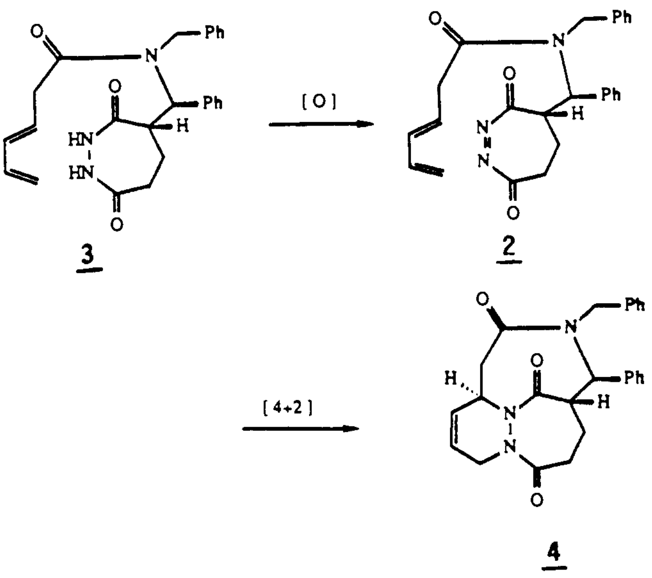


1

Scheme I



Scheme II



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[1] Recipient of a Dreyfus Young Faculty Grant (1985–1990), Searle Scholars Award (1986–1989), Presidential Young Investigators Award (1987–1992), and an American Cancer Society Junior Faculty Fellowship (1987–1990).

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(3) Details of the design and modeling will be published separately: Kahn, M.; Johnson, M.; Lee, Y.; Wilke, S.; Chen, B. *J. Biomol. Recogn.*, in press.

(4) For an excellent review on turns, see; Rose, G. D.; Gierasch, L. M.; Smith, J. A. *Adv. Prot. Chem.* **1985**, *37*, 1–104.

(5) Despite the long history of azodienophiles (for a recent review, see: Adam, W.; DeLucchi, O. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 762 and references therein), until the recent report of Medina et al. (Medina, J. C.; Cadilla, R.; Kyler, K. S. *Tetrahedron Lett.* **1987**, 1059) which appeared during the course of our investigation, the intramolecular version of this reaction remained unprecedented.

(6) For a recent review on the intramolecular Diels–Alder reaction, see: Fallis, A. *Can. J. Chem.* **1985**, 4297.

(7) For examples of intramolecular Diels–Alder reactions leading to strained ring systems, see: Shea, K. J.; Gilman, J. W.; Huffner, C. D.; Dougherty, T. K. *J. Am. Chem. Soc.* **1986**, **108**, 4953 and references therein.

(8) Prepared by vinyl Grignard addition to benzaldehyde and subsequent ortho ester Claisen rearrangement.

(9) For recent reviews on the use of CSI, see: Rasmussen, J. K.; Hassner, A. *Chem. Rev.* **1975**, 389. Kamal, A.; Sutter, P. B.; *Heterocycles* **1987**, **26**, 1051.

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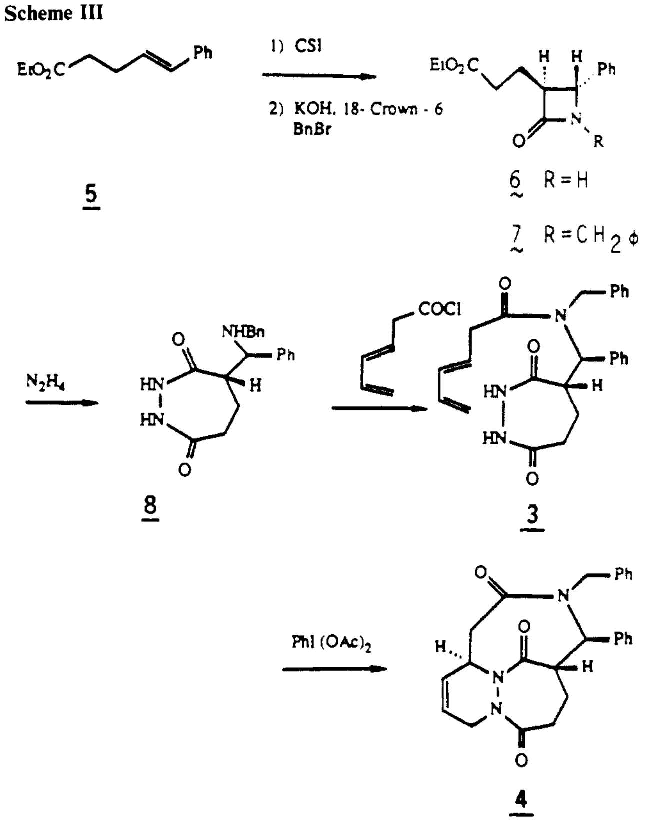
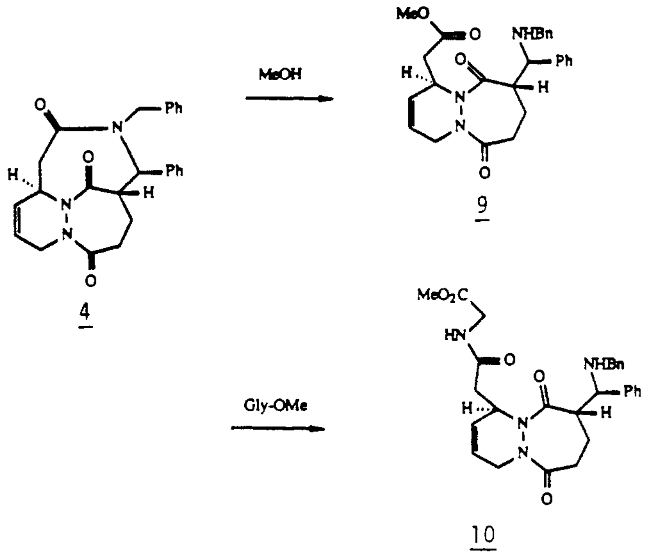
Scheme III



Scheme IV



Yamazaki protocol[10] affords **7** in 79% yield after chromatography. Hydrazine treatment (refluxing methanol, 24 h) generates diacylhydrazide **8** in 84% yield.[11] Acylation of **8** with 3,5-hexadienoyl chloride[12] provides the penultimate intermediate **3**. Oxidation with iodosobenzene diacetate[13] generates the requisite dienophile **2**, which undergoes an extremely facile (15 min, 80 °C) exo cycloaddition to afford **4** in 97% yield.[14] Upon methanolysis (room temperature MeOH, pyridine), amino ester **9** is generated quantitatively[15] (see Scheme IV). Significantly, reaction of **4** with glycine methyl ester in methylene chloride at ambient temperature provides hybrid mimetic **10**.[16]

This intramolecular cycloaddition strategy provides rapid entry into β-turn mimetic systems of type **1**. Extension and utilization of this approach to prepare biologically relevant mimetics and mimetic hybrids are in progress and will be reported in due course.

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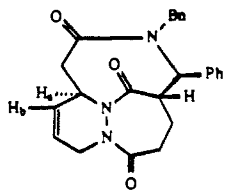
[10] Hirai, Y.; Kamide, I.; Yamazuki, T. *Heterocycles* **1981**, *15*, 1101.

[11] This reaction proceeds via initial formation of the β-lactam acylhydrazide. This is critical in that the cyclization of succinic esters to diacylhydrazides is quite problematic (see, for example: Miller, D. M.; White, R. W. *Can. J. Chem.* **1956**, *34*, 1510). In this instance the β-lactam presumably acts as an activated acyl group and lowers the entropic factors which disfavor the seven-membered ring closure.

[12] Martin, S. F.; Tu, C.-Y.; Chou, T.-S. *J. Am. Chem. Soc.* **1980**, *102*, 5274.

[13] Moriarty, R. M.; Prakash, R. M. I.; Penmasta, R. *Synth. Commun.* **1987**, 409.

[14] Stereochemical assignment was made on the basis of the less than 2 Hz coupling constant between protons H_a and H_b and comparison with molecular modeling.



[15] The extreme mildness of the methanolysis reaction highlights the strain and reactivity of the tricyclic system of lactam **4**.

[16] We define mimetic hybrids as synthetic units coupled to oligopeptides.

The π-Complex Benzene-Ethylene Cation Radical

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Received September 4, 1986

It has been known for some time that under suitable conditions planar conjugated hydrocarbons M upon ionization in solution form π-complexes $(M)_2^{\bullet+}$ consisting of two such species carrying a single charge.[1] Apart from coulombic and dispersive attractions such dimer cations are bound by substantial covalent or resonance contributions ΔH_{res} arising mainly from the interaction between the two HOMOs of M and $M^{\bullet+}$ as depicted in Figure 1a. Spectroscopically, $(M)_2^{\bullet+}$ distinguish themselves from the monomeric constituents by an additional intense absorption in the near-infrared spectral range which is attributed to so called "charge resonance" (CR) transitions of energy E_{CR}.[2] If follows from the qualitative MO diagram in Figure 1a that the energy of these transitions E_{CR} is independent of ϵ_{HOMO} of M involved and should hence be a direct measure of ΔH_{res} between M and $M^{\bullet+}$. Indeed, both E_{CR}[3] and ΔH_{res}[4] are found to decrease slightly with the size

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[1] Badger, B.; Brocklehurst, B. *Trans. Faraday Soc.* **1969**, *65*, 2576, 2582, 2588.

[2] Badger, B.; Brocklehurst, B. *Nature (London)* **1968**, *219*, 263. Badger, B.; Brocklehurst, B. *Trans. Faraday Soc.* **1970**, *66*, 2939.

[3] Kira, A.; Imamura, M. *J. Phys. Chem.* **1979**, *83*, 2267.

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