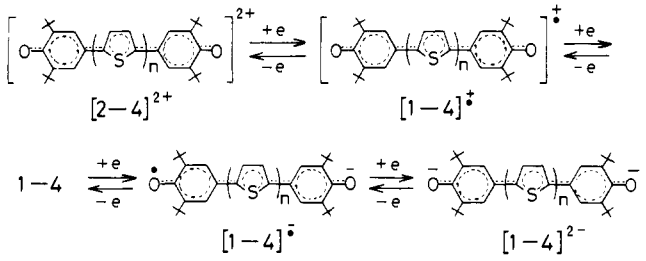
Table I. Oxidation and Reduction Potentials, Their Numerical Sums, and the Longest Wavelength Absorption Maximum of Quinones **1**, **2**, **3**, **4** Compared with a Reference Compound, Tetra-*tert*-butyldiphenoquinone (**11**)

quinone	electrochemical properties[a]						absorptn max[b] λ nm (log ε)
	E_2^{ox}	E_1^{ox}	E_1^{red}	E_2^{red}	E_1^{sum}	E_2^{sum}	
11			−0.52	−0.89			420 (4.85)
1		+1.20	−0.46	−0.60	1.65	1.81	558 (4.90)
2	+1.44	+0.91	−0.31	−0.39	1.22	1.83	678 (4.50)
3	+1.07	+0.63	−0.26	−0.30	0.89	1.37	785 (4.77)
4	+0.89	+0.55	−0.20	−0.26	0.75	1.15	830 (4.45)

[a] Obtained by cyclic voltammetry vs SCE with 0.1 M Et_4NClO_4 at room temperature (scan rate, 50 mV/s; solvent, **1**, **11** in MeCN, **2** in CH_2Cl_2; **3**, 4 in EtCN); E^{ox} and E^{red} values were calculated by averaging the anodic and cathodic peak potentials: $E = E_p^a + E_p^c)/2$. [b] In MeCN.

Scheme II



(**1** < **2** < **3** < **4**) is given by the first excitation band in the electronic absorption spectra of these quinones, namely, the bands of **1**, **2**, **3**, and **4** show a bathochromic shift by 138, 258, 365, and 410 nm, respectively, from that of **11** in acetonitrile (Table I). The X-ray crystallographic analysis of these quinones and synthesis of other correlated systems exhibiting small E^{sum} values are in progress.

Acknowledgment. This work was supported by a Grant-in-aid from the Ministry of Education, Science and Culture, Japan.

Supplementary Material Available: IR, UV-vis, MS, and ^1H NMR and ^{13}C NMR spectral data of **1-4**, **10a-d**, and **9a-d**, including elemental analysis (6 pages). Ordering information is given on any current masthead page.

High Diastereofacial Selectivity in the Additions of the Enolates of Aminocarbene Complexes to Chiral Aldehydes without the Assistance of a Lewis Acid

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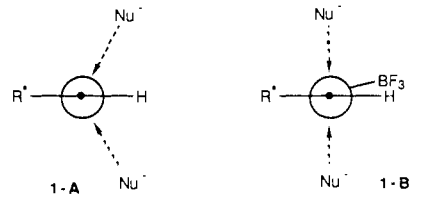
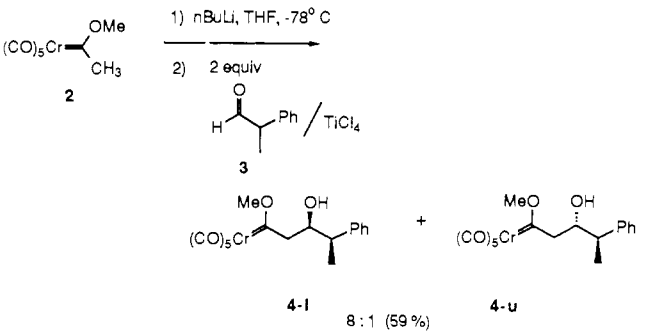
The diastereofacial additions of nonchiral enolates to chiral aldehydes can be quite selective, but in the case of α-unsubstituted enolates the facial selection is not significant enough to be practically useful.[1,2] The best solution involves the Lewis acid mediated addition of enolsilanes to chiral aldehydes.[3-6] Heathcock proposes that the Lewis acid complex **1-B** enhances facial selectivity by favoring approach of the nucleophile on a trajectory that brings it in greater proximity to the chiral substituent than in the case of the uncomplexed aldehyde (**1-A**).[3] This same kind of analysis has been successfully applied to the addition of nucleophiles to chiral ketones[6b] and chiral thionium ions.[6c]



In a previous report from our laboratory,[7] it was observed that the enolate of methoxyl stabilized carbene complex **2** would add to *dl*-2-phenylpropanal that had been pretreated with titanium tetrachloride to give the aldol adduct **4** as an 8:1 mixture of diastereomers (l:u).[8-11] The carbene complex **2** can serve as a



synthon for methyl acetate since the products **4** can be oxidatively converted to their corresponding methyl esters, however, for the purposes of diastereoselection appeared not to be practical since the selectivity is only slightly better than is observed for methyl acetate.[3] One approach to the search for the greater expression of this asymmetric induction with the enolates of carbene complexes is to consider variations in the ancilliary substituent of the carbene carbon, and in this regard our attention was first turned to the (dimethylamino)carbene complex **5**.

The aldol reactions of aminocarbene complexes have not been previously reported, and very quickly it was found that there is a major difference between the aldol reactions of alkoxy- and aminocarbene complexes.[9] Whereas the enolates derived from

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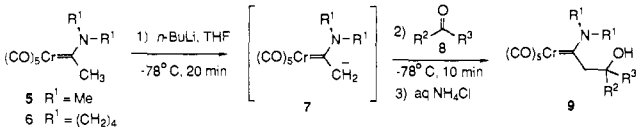
Table I. Aldol Reactions of Aminocarbene Complexes **5** and **6**[a]

series	complex	carbonyl **8** R^2	carbonyl **8** R^3	equiv of **8**	yield of **9**[b] (%)	% recovery of **5** or **6**
a	**5**	Ph	H	5.6	81	17
b		*n*-Pr	H	1.7	73	16
c		Me	H	4.3	81	
d	**6**	Ph	H	1.1	96	
e		*n*-Pr	H	2.0	76	18
f		Me	H	3.0	79	
				10.0	94	
g		*i*-Pr	H	1.5	81	
h		Me	Me	1.7	58	32
				1.0	53	26
				1.7[c]	59	28
				1.7[d]	54	40
i		$(CH_2)_5$		1.7	66	24
				1.1	89[e]	

[a] Unless otherwise specified all reactions were run at 0.1–0.2 M in **5** or **6** in THF at −78 °C for 10 min. [b] Unless otherwise indicated, all yields are the average of at least two runs. [c] This reaction was quenched by addition of a solution of 0.2 mL of acetic acid (3.8 equiv) in 1.0 mL of THF which had been precooled to −78 °C. [d] 0.33 M in 6. [e] Isolated by rapid chromatography on silica gel.

alkoxycarbene complexes fail to give aldol products unless the aldehyde or ketone is activated by precomplexation with a Lewis acid, the aldol reactions of the enolates of aminocarbene complexes fail only if the carbonyl compound is precomplexed with a Lewis acid. The (dimethylamino)carbene anion **7** (from **5**[12]) leads only

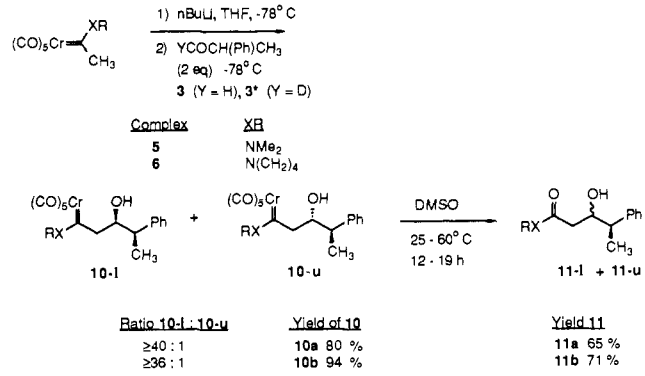


to recovered **5** upon addition to a variety of Lewis acid carbonyl complexes (benzaldehyde and *dl*-2-methyl-3-phenylpropanal); however, this and the pyrrolidinocarbene complex anion **7** (from **6**[13]) react directly with a variety of aldehydes and ketones to give aldol adducts **9** in good to excellent yields.

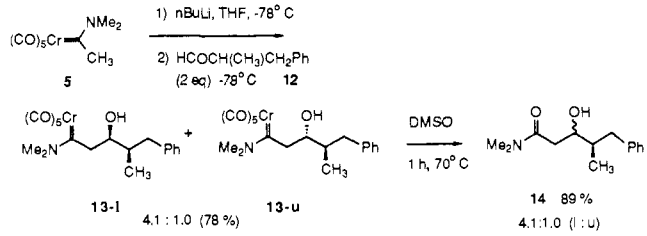
The ketone aldol adducts **9h** and **9i** have been observed to undergo retro-aldol on silica gel during purification; however, if the chromatography is performed rapidly, the cyclohexanone adduct **9i** can be cleanly isolated in 89% yield. Although the aldehyde adducts have not been observed to undergo retro-aldol reaction, the fact that the ketone adducts **9h** and **9i** do, causes some concern with regard to the initial anticipation of increased diastereofacial selection in the addition of enolates of **5** and **6** to chiral aldehydes. There is further concern over the degree of the diastereofacial selectivity to be expected for complexes **5** and **6** since any facial differentiation must be made without the steric influence of the Lewis acid coordinated carbonyl.

These concerns proved to be ill founded as it was found that the anion from the dimethylamino complex **5** will react with *dl*-2-phenylpropanal under the conditions described in Table I to give an 80% yield of the aldol adduct **10a** in which the ratio of the **10a**-l to the **10a-u** diastereomer is 40:1.[10] Furthermore, it was demonstrated that the high selectivity observed with *dl*-2-phenylpropanal is due to the kinetic addition of the enolate of the aminocarbene complex. The adduct **10a-l** was treated with *n*-butyllithium and then exposed to 3 equiv of 1-deutero-2-phenylpropanal **3*** under the reaction conditions, the recovered adduct **10a**-l (65%, isolated) was found not to have incorporated deuterium (<5% by crude ^{1}H NMR), and additionally, the formation of **5** could not be detected.

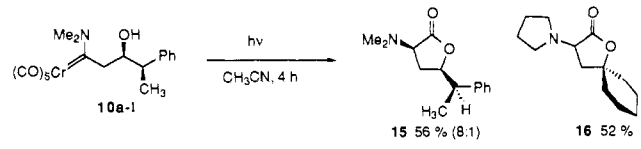
The ratios of the u- and l-diastereomers of the carbene complex aldol adducts **10a** and **10b** were determined by oxidation of the crude aldol reactions mixtures with DMSO[14] and analysis of the



crude mixtures from these oxidations by capillary GC. The stereochemical assignments were made by GC with the co-injection of authentic samples of mixtures of the u- and l-diastereomers of the amides **11a** and **11b**. Oxidation of the purified adducts **10b** (SGC) with DMSO and then purification of the amide **11b** led to a much cleaner GC trace, and the ratio of **11b**-l to **11b-u** can be set at ≥200:1 by capillary GC. This is significant diastereofacial selectivity when it is considered that the highest selectivity observed for α-unsubstituted ketone, ester, or amide enolates is 4:1, and the highest selectivity reported for the Lewis acid mediated addition of an α-unsubstituted silyl ketene acetal or silyl enol ether to this aldehyde was 36:1 (l:u).[3] A more difficult test of the diastereofacial selectivity of the aminocarbene complexes would involve addition to *dl*-2-methyl-3-phenylpropanal (**12**), an aldehyde that resists any significant facial differentiation.[3] The selectivity observed for the addition of the anion of **5** to this aldehyde is modest (4.1:1.0) but other α-unsubstituted enolates give essentially a 1:1 mixture with this aldehyde.[3,6c,10]



There are a variety of methods known for removal of the metal unit from transition-metal carbene complexes which make them uniquely versatile synthons in organic synthesis.[15] An important new method is the carbonylative cleavage recently reported by Hegedus, de Weck, and D'Andrea.[16] Photolysis of **9i** gives the spirolactone **16** in 52% yield, and photolysis of the l-isomer of **10a** gives the lactone **15** as an 8:1 mixture of isomers (cis:trans). Derivatives of 2-amino-γ-butyrolactones have biologically interesting properties and have been used as intermediates in prostaglandin synthesis.[17]



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The finding that complexes **5** and **6** give high diastereofacial selectivity in their aldol reactions with chiral aldehydes should encourage the continued investigation of the origins of the selectivity and the synthetic applications of the reactions of aminocarbene complexes.

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Supplementary Material Available: Spectral data (^{1}H NMR, ^{13}C NMR, and IR) for all new compounds (6 pages). Ordering information is given on any current masthead page.

Ring Opening of Cyclic Pentapeptides by Electron Impact Mass Spectrometry: Correlation with Peptide Bond Nonplanarity

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We have designed and synthesized a series of cyclic pentapeptides as conformational models of reverse turns.[1] These molecules are highly constrained by formation of the cyclic backbone. Consistent with this, we have observed at least one strongly nonplanar peptide bond in crystal structures of these cyclic peptides.[2] As part of our characterization, we have obtained electron impact (EI) mass spectra of these synthetic cyclic peptides. The results of these studies suggest that ring opening of cyclic pentapeptide radical molecular ions, $M^{\bullet+}$s, produced from electron impact occurs preferentially in bonds adjacent to a nonplanar peptide bond in the parent molecule. If general, this mechanism could offer useful information about conformational properties of cyclic peptides.

Early EI studies showed that principal breakdown of linear peptides was by cleavage at peptide bonds.[3] Substantial evidence of rearrangements of fragments and secondary fragmentations[4] contributed to decreasing application of EI methods for sequence determination as the softer methods, principally fast atom bombardment, became available.[5] EI studies of cyclic peptides focused on the first loss process, which requires the cleavage of at least two bonds, the first a ring opening and the second analogous to fragmentation in a linear peptide. Multiple mechanisms have been proposed:[6] (1) Cleavage of a C^{α}—CO bond of a residue in $M^{\bullet+}$, with the loss of a neutral amine fragment carrying the side chain (NH=CHR), (2) cleavage at the peptide bond preceding an aromatic residue with migration of a β-hydrogen atom to the oxygen of the preceding residue, or (3) cleavage of a C^{α}—CO bond of a residue with the loss of neutral NHCO.

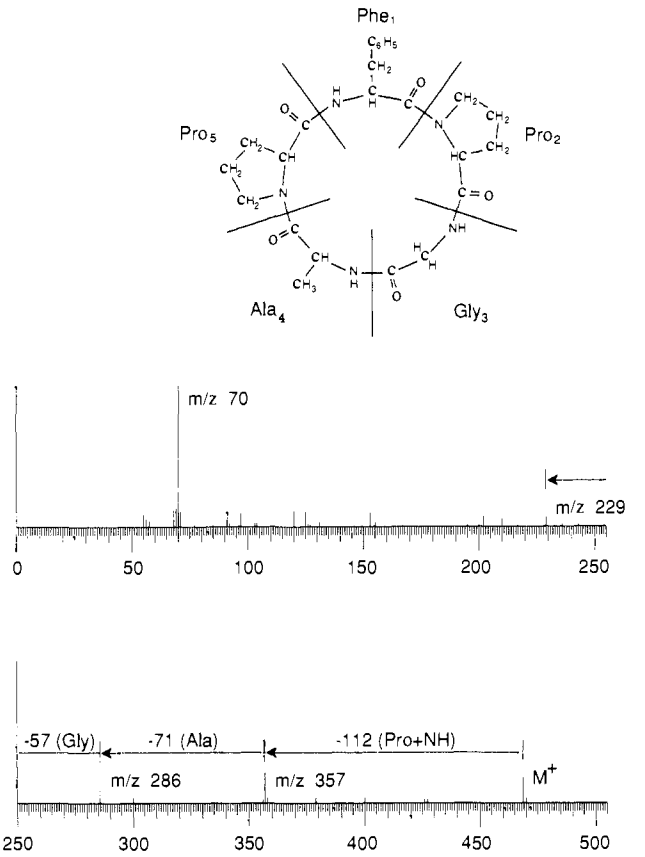

Figure 1. EI mass spectrum of cyclo(D-Phe$_1$-Pro$_2$-Gly$_3$-D-Ala$_4$-Pro$_5$). Data were collected on a DuPont 21-492B double focusing mass spectrometer equipped with a Hewlett-Packard 21MX computer. The samples were prepared by applying the peptide to the Teflon covered direct exposure probe tip: 70 eV.

Figure 1 shows a typical mass spectrum for a cyclic pentapeptide, cyclo(D-Phe$_1$-Pro$_2$-Gly$_3$-D-Ala$_4$-Pro$_5$), I. The peak at m/z 70, $C_4H_8N^+$, is a characteristic ion observed in the EI mass spectra of many proline-containing peptides.[6c,7] The most abundant high mass fragment ions (m/z 357, 286, 229) suggest the sequential losses of proline + NH (112), alanine (71), and glycine (57). Peaks corresponding to the molecular ion minus 43 and minus 69 are also observed, suggesting that the 112 loss may occur as two fragments, a peptide bond unit (CONH, 43), and a proline ring amine (C_4H_7N, 69). From the known sequence of the peptide and the assumption that these ions arise primarily from a single ring opening followed by sequential loss of residues, we infer that the proline lost is Pro$_5$ (not Pro$_2$) and that ring opening occurred

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