sertion[5] are in fact secondary products which can be eliminated by scavenging for iodine and hydrogen iodide.

(8) The alternative possibility of direct formation of the carbene–iodine complex from *gem*-diiodides is less consistent with the presence of competing elimination and nucleophilic substitution reactions and with the fact that scavengers for hydrogen iodide resulted in substantially decreased carbenoid behavior by 1.

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Figure 1.

Stereoelectronic Control in the Base-Catalyzed H–D Exchange Reaction of Twistan-4-one

Sir:

Recent research activities in a number of areas have added to our understanding of the sensitivity of reaction rates to stereochemical influences. Both x-ray data[1] and theoretical calculations[2] indicate a clearly defined path of minimum energy for the attack of a nucleophile on a carbonyl group. The stringent constraints upon this reaction have led to Baldwin's approach vector analysis method of predicting the stereochemistry of the addition products.[3] In amide and ester hydrolysis, the selective cleavage of the tetrahedral intermediates has been shown by the extensive studies of Deslongchamps and co-workers[4] to be controlled by stereoelectronic[5] effects. Their work was also reinforced by theoretical calculations.[7] In contrast, one of the earliest proposals of stereoelectronic control remains a subject of controversy. The preference for axial over equatorial attack in the protonation of cyclohexenols was attributed by Corey and Sneen[8] to the necessity for proper orbital alignment in the enol fragment during protonation. Subsequent work has both reinforced[9-11] and contradicted[12-15] this interpretation. Perhaps the strongest evidence against stereoelectronic control has been the lack of selectivity in the base-catalyzed H–D exchange of conformationally biased ketones, the axial:equatorial rate ratio being between 5:1[11] and 3.5:1[15] for exchanges of 4-*tert*-butylcyclohexanone. Work in our laboratories showed much greater selectivity (75:1) in the exchange of the bridged biaryl ketone 1 as a conformationally fixed substrate,[16] although some ambiguity in the interpretation arises from the possibility of selective stabilization by the benzene rings.
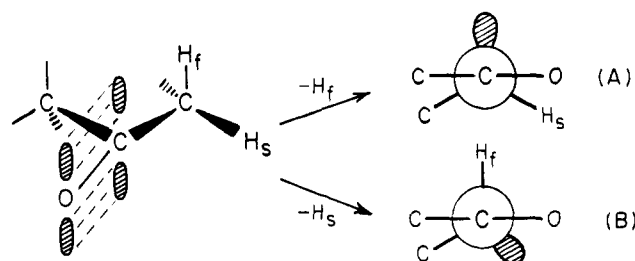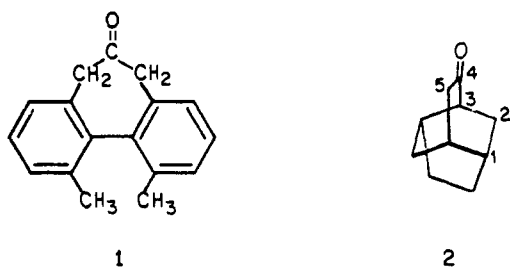

1   2

In this paper, we wish to describe the observation of a kinetic selectivity of 290:1 in the base-catalyzed exchange of the diastereotopic protons α to the carbonyl group in twistan-4-one (2[17]). The observation of such a highly selective exchange process clearly shows that the principle of stereoelectronic control can be of major importance in the reaction of an α ketocarbanion.

The conformational properties of twistan-4-one make it an interesting subject for this stereochemical investigation. A Dreiding model of 2 shows the CH_2–CO fragment oriented so that one of the C–H bonds is aligned to permit maximum overlap with the adjacent π orbital of the carbonyl function, while the other C–H bond is held 60° out of this alignment as in the perspective formula in Figure 1. When a sample of twistanone[18] was treated with sodium methoxide (0.093 M) in methanol-*O-d*, the relative rates of exchange of the diastereotopic protons α to the carbonyl were found to be in the ratio 290:1. The rate data is given in Table I.

The assignment of the more rapidly exchanging proton to that labeled H_f (H_{fast}) in Figure 1 was made by ^{1}H NMR. A Dreiding model indicates a dihedral angle of 80° between H_f and the bridgehead proton at C-6. According to the Karplus equation,[19] a coupling constant of <1 Hz would be expected between these protons. For its diastereotopic partner (H_s), a coupling of at least 4 Hz would be anticipated. The 100-MHz spectrum of 2 (0.2 M in furan) shows a doublet at δ 2.35 (J = 15 Hz) and a quartet at δ 1.95 (J = 15 and 4 Hz) for the protons at C-5. It is the doublet at δ 2.35 with no observable vicinal coupling which first disappears on deuteration and is thus assigned to H_f as in Figure 1.

The observed selectivity of 290:1 could, in principle, be the result of (a) steric effects, (b) stereoelectronic control, or (c) preferential internal return.[20] To test for a steric effect, the rates of exchange of H_f and H_s in 2 were also determined using sodium phenoxide as catalyst. Involvement of the bulkier phenoxide base[16,21] would be expected to alter the selectivity if a steric effect were present. As the data in Table I show, there is no change in selectivity when sodium phenoxide is used as base. This indicates the absence of any significant steric effect.[22]

To test for the presence of internal return is more difficult. Although the probability of internal return occurring in methanol appears slight,[23] any discussion of the observed

Table I. Rates of Exchange of Diastereotopic Protons of 2

Ketone	Base (solvent)	Concn, M	$k_f{}^a$ (h^{-1})	$k_s{}^a$ (h^{-1})	k_f/k_s (± estd error)
2	CH_3ONa (CH_3OD)	0.093	1.99	0.0068	293 ± 20
2	C_6H_5ONa (CH_3OD)	0.380	0.87	0.0031	280 ± 20
2-5,5-$d_2{}^b$	CH_3ONa (CH_3OH)	0.100	0.114	0.0018	63 ± 5

a All rate constants are reported as pseudo-first-order rate constants, measured at 29.0 °C. Each reported constant is the average of two determinations on quenched aliquots which were purified by sublimation prior to analysis for deuterium by mass spectral analysis. The fast reaction was followed by monitoring loss of starting material, the slow reaction by monitoring formation of d_2 species, all measurements being made by determination of P, P + 1, and P + 2 peak height ratios (average of ten spectra) after correction for natural isotopic abundances. The absence of any fragmentation pathway involving loss of deuterium or the carbon bearing the deuterium justifies the use of peak height ratios. The precision in rate constants is considered to be ±4%. *b* This dideuterio derivative, prepared by exchange of 2 in CH_3OD (1.46 M in CH_3ONa) for 4 days, showed no evidence of formation of 2-d_3 (≤2% by mass spectral analysis).

relative rates is meaningful only if it is absent. An unambiguous test would require detailed isotope effect measurements as outlined by Streitwieser.[24] A simpler qualitative test used by us in the study of sulfoxide exchanges[25] requires measurement of the rates of dedeuteration in light methanol for comparison with the deuteration rates. If internal return plays a significant role, one would expect small primary isotope effects and possibly an unusual change in the relative rates of the diastereotopic protons. In fact, the backward exchange of H_f showed isotope effects of the order expected for a rate-determining proton abstraction accompanied by a solvent isotope effect of ~2.[26] The reverse exchange of H_s showed a smaller overall decrease as has been observed in several exchanges of ketones. Both Werstiuk[28] and Lamaty[15] have confirmed the original observations of Thomas et al.[29] that the stereoselectivity is much less in the reverse than forward (deuteration) exchange. This effect has been attributed to reversibility during exchange in the light solvent, a conclusion which appears qualitatively correct.[30] Thus, the relative rates of deuteration give no indication of the presence of internal return.

The only reasonable explanation for the observed 290:1 rate ratio in the exchange of **2** is the effect of stereoelectronic control. The stereoselectivity is in marked contrast to its virtually negligible magnitude in the studies involving cyclohexanones. The contrast arises not from a failure of the principle of stereoelectronic control in the latter instance, but a difference in the ability of the ketones to reveal its importance. In any organic reaction involving a stereochemical effect, its presence is usually revealed by those molecules having structural constraints which allow only certain specific conformations in the transition states. As both Valls and Tomaranoff[31] and House[10] have pointed out, the reaction of a cyclohexanone enolate can proceed by two transition states, both of which involve perpendicular attack[32] of the electrophile, and their energy differences result from the differences in strain in the chair and boat conformers produced therefrom. In the exchange of **2**, the enolate involved is constrained in a twist–boat conformation and its protonation from either side must lead to the single product **2**. This prescribed course of reaction will require the transition states to contain some of the sp^3 character of the two carbanions A and B.[33] In A, maximum overlap of the carbanion with the carbonyl occurs while, in B, overlap will be much decreased by the near orthogonality of the sp^3 and π orbitals. Thus, resonance stabilization of A will be much greater than that of B as is reflected experimentally in the stereoselectivity.

This effect has been predicted in a recent paper by Wolfe, Schlegel, Csizmadia, and Bernardi.[34] Using ab initio MO calculations, they calculated A to be more stable than B by 18 kcal/mol.[35] The qualitative agreement between experiment and theory provides an indication of the real potential of stereoelectronic control. Its influence on the rates of exchange could, in principle, result in much larger stereoselectivities, provided the ketone structure or its macroscopic environment[36] produces the requisite geometry in Figure 1, as well as a greater resistance to any change in geometry.

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Continuous Wave CO_2 Laser Induced Chemistry of Diborane. A Thermal Reaction

Sir:

The idea of using lasers in chemical synthesis to open reaction channels not accessible at thermal equilibrium is attractive. Bachmann, Nöth, Rinck, and Kompa[1] generated con-