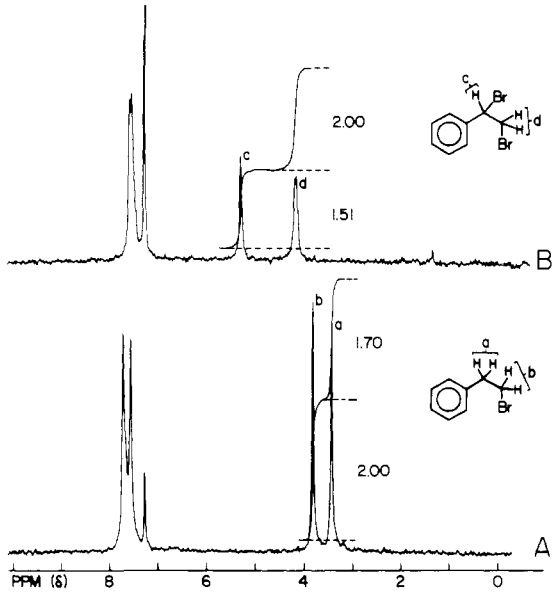

Figure 2. Natural-abundance 38.4-MHz ^2H NMR spectra of (2-bromoethyl)benzene (spectrum A) and styrene dibromide prepared by elimination and bromination of (2-bromoethyl)benzene (spectrum B). The peaks at δ 7.26 are due to chloroform.

analysis of the reaction mixture by GC-MS showed the ratio of protic and deuterated products to be 2.2, in good agreement with the ^2H NMR experiments.

In the preceding example the hydrogen from the broken C-H bond was retained in the product; more typically C-H cleavage results in loss of the hydrogen to the solvent, and in such cases the amount of transferred hydrogen must be obtained indirectly. We illustrate an appropriate method with a simple elimination reaction. The ^2H NMR spectra of (2-bromoethyl)benzene[10a] and the dibromide derivative[10b] of styrene generated by potassium *tert*-butoxide treatment of (2-bromoethyl)benzene[12] are displayed in Figure 2. The reaction was carried to completion, so the C-2 deuterium resonance may be employed as an integration standard in both spectra, and its integral is set to 2.00. Most of the C-1 deuterium has been retained in the course of this reaction: the starting material contains 1.70 units of deuterium at C-1, the product 1.51. The amount of transferred deuterium is given by the difference 1.70 - 1.51 = 0.19, and therefore $k_H/k_D = (1.51/0.19)[1/(2-1)] = 7.9 \pm 0.8$, identical with the literature value of 7.9 ± 0.5 obtained for the elimination reaction of (2-bromo[1,1-$^2H_2$]ethyl)benzene under the same conditions.[12]

Natural-abundance ^2H NMR is a powerful method for the measurement of kinetic isotope effects in a wide variety of chemical reactions without recourse to synthesis of isotopically enriched reactants. However, the present analysis is applicable only when there can be intramolecular competition between hydrogen isotopes. This is true for a great many ordinary chemical reactions, but for enzymatic reactions the method is restricted to hydrogen removal from methyl groups or from substrates containing a proper rotation axis of symmetry.[13] In a future report we will describe our studies of kinetic isotope effects in biological transformations of methyl groups using natural-abundance ^2H NMR.

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(13) For example, there is no possibility of intramolecular competition at the methylene group of ethanol in a reaction catalyzed by alcohol dehydrogenase, since this enzyme acts on only one of the two enantiotopic hydrogens.

Isolation and Structural Analyses of Two Conformers of the Eight-Membered Lactam on 1-Benzazocinone Derivatives

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In general, the conformational interconversions of medium- and large-membered cyclic compounds are so fast at room temperature[1] that it is very hard to isolate their conformers in two isomeric forms.[2]

Eight-membered lactams of 1-benzazocinone skeleton have been efficiently synthesized through the newly developed "*controlled crissocross annulation*"[3] as part of our synthetic approaches to mitomycins. These lactams have been found to consist of two conformers, and we report the first isolation and structural analyses of these conformers of benzazocinone derivatives at ordinary temperatures.

For the present work, compound **2** was obtained by the above-mentioned synthesis in one pot from **1** (Scheme I).[3]

When the keto group of **2** was protected by reaction with ethylene glycol at 80-90 °C, the resulting ketal **3** was found to consist of two stereoisomers, **3a** and **3b**, in the ratio of about 8:1, though it has only one asymmetric center in the molecule. Similar phenomena were also observed with other ketals (**4**, **5**). The isomers were separated at room temperature by conventional chromatography.[4] The most easily separable sulfonamides, **5a** and **5b** obtained in the ratio of 10.8:1, were chosen as the representative of the above ketals of detailed structural analysis. The interconversion between each **5a** and **5b** was investigated by comparison of the respective integrations of 6-methyl signals [**5a**, δ 0.68 (d); **5b**, δ 1.13 (d)] of ^1H NMR spectra at elevated temperatures. From the equilibrium ratio of the resulting mixture, the major isomer **5a** was proved to be the thermodynamically preferred one, since the spectrum of **5b** at 180 °C (Me_2SO-d_6) showed to isomerize mainly into **5a** in the ratio of 8.6:1 (**5a**:**5b**) while **5a** was slightly converted into **5b** (**5a**:**5b** = 10:1) at the same temperature.

From the ^1H NMR spectral data and NOE's of **5a**, the following important facts were revealed: two benzylic protons (11-H) had very different chemical shifts [δ 4.22 (d) and 5.62 (d)], caused by restricted rotation of the benzyl group; an NOE of 4% was observed only for the 6-Me signal on saturation of the 7-H signal.

The molecular structure of **5a** was finally established by X-ray crystal analysis as shown in Figure 1.

The aromatic proton (7-H) lies closer to 6-Me than to 6-H, which well explains the observed NOE's on **5a**. Also it is particularly noteworthy that both 6-H and 6-Me are close to the face of the benzene ring of the *N*-benzyl group. Thus, the above-described upfield shift of the 6-methyl signal can be ascribed to the shielding effects of this benzene ring.

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(4) All new compounds gave satisfactory spectral and analytical data. In a typical example, the amine **4** (37.0 mg, a 10:1 mixture of **4a** and **4b**) was led to **5a** (44.7 mg, 86%, mp 216-217 °C) and **5b** (4.2 mg, 8%, mp 183-184 °C).

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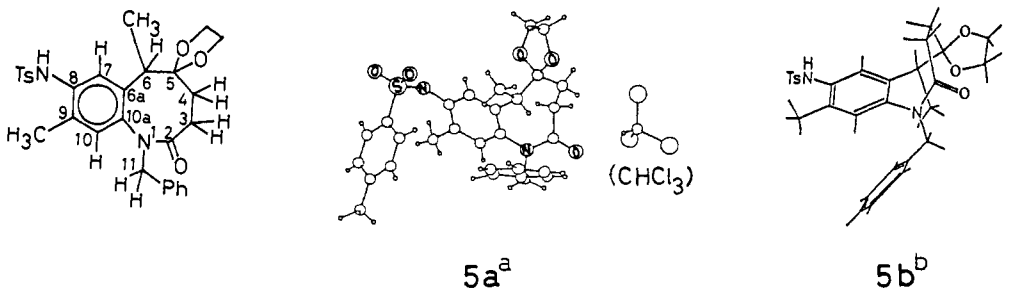
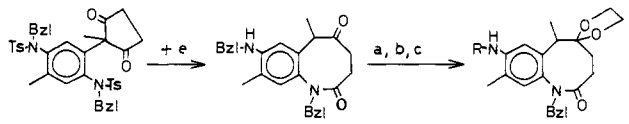


5a[a] 5b[b]

Figure 1. (a) X-ray crystal structure of **5a** (twist-boat-chair), (b) Presumed structure of **5b** (twist-boat, Dreiding model).

Scheme I[a]



1 2 3;(3a,3b); R=Bzl
4;(4a,4b); R=H
5;(5a,5b); R=Ts

[a] (a) $(CH_2OH)_2$, CSA, 80–90 °C, 92%; (b) H_2/Pd-C, catalytic AcOH, AcOEt, quantitative; (c) TsCl, pyridine, 94%.

The rotation of the benzyl group is restricted mainly by the steric hindrance in the structure of **5a** (Figure 1). Furthermore, the interesting folded conformation is also presumed to be caused by the spatial "attractive interaction" between the benzene ring and 6-H and also between the benzene ring and 6-Me due to the CH/π[5] or the van der Waals' attraction.[6]

The structure of **5b** was determined from the ^{1}H NMR spectral data and NOE's because of the difficulty of preparing a single crystal suitable for X-ray diffraction. Both 9-Me and 10-H signals were observed to be upfield compared to the case of **5a**. One of the four methylene protons (3-H, 4-H) was observed at higher field (δ 1.7–1.9) and distinct from the others (δ 2.1–2.4). Moreover a large NOE of 23% was observed for the 6-H signal, and none for the 6-Me signal on saturation of the 7-H signal.

Considering these data and the steric strain of the molecule, the structure of **5b** should be represented by the twist-boat form (TB, Figure 1), which has been known to be the metastable conformer of *cis,cis*-1,3-cyclooctadiene.[7] The 7-H is in close proximity to 6-H, and both the 9-Me and 10-H are close to the face of the benzene ring of the N substituent, probably caused by the CH/π interaction as discussed for **5a**. One 4-H (see **5b** in Figure 1) is situated directly over the benzene ring of the fundamental framework, accounting for the observed shielding. Thus, the signal at δ 1.7–1.9 is assigned to the endo-4-H.

The other conformers, e.g., twist-chair, boat, and twist-boat-chair[7] with the hindered oriented 6-Me (which was generated by the ring inversion of **5a**, TBC, Figure 1), were excluded for the following reasons. First, they seemed to be of high energy, labile because of the strain caused by the nonbonded interactions and/or by the large torsion of the lactam bond. Moreover, they could not explain the ^{1}H NMR spectral data and NOE's of **5b**.

Thus, there is no doubt that the two isomers (**5a**, **5b**) are not simply a pair of rotamers based on the restricted rotation of the benzyl group but a pair of conformational diastereoisomers of the eight-membered ring. The rates of interconversion between **5a** and **5b** were measured in Me_2SO-d_6 by monitoring the relative intensities of the 6-Me signals in the ^{1}H NMR spectra as a function of time. The free energies of activation for the interconversion were estimated to be 26.6 ($\Delta G^{\ddagger}_{5a\rightarrow 5b}$) and 25.2 kcal/mol ($\Delta G^{\ddagger}_{5b\rightarrow 5a}$) at 25 °C.

Further studies on the conformational interconversions of **5** are in progress.

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Supplementary Material Available: Crystal data and tables of atomic coordinates, thermal parameters, bond angles, bond lengths, and structure factors for **5a** (7 pages). Ordering information is given on any current masthead page.

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Synthesis and Structure of a Stable Complex Featuring an S-Bound Dibenzothiophene Ligand: $RuCl_2(4\text{-}R_2P(DBT))_2$ (DBT = Dibenzothiophene)

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This report describes the preparation and structural characterization of the first coordination complex of a dibenzothiophene (DBT) derivative. Dibenzothiophenes[1] are among the most abundant and refractory organosulfur compounds found in fossil fuel feedstocks, and the interaction of these aromatic heterocycles with metals is widely assumed to be central to the mechanisms of both catalytic desulfurization[2] and the poisoning of noble metal catalysts.[3] Given the deteriorating quality of available feedstocks, these mechanistic issues are of considerable current interest.

In 1975 Kuehn and Taube reported the isolation of $[Ru(NH_3)_5(thiophene)](PF_6)_2$ wherein the thiophene is probably S bound to the ruthenium(II) center.[4] Although the instability of the Kuehn–Taube complex ($K_{H_2O} \approx 10$) limited its characterization, this report suggested that ruthenium(II) would be a good starting point for the preparation of more stable derivatives of

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