proportion of this endo enol in the gas phase must by very low for **3**. Thus, it appears that the C_7 keto ester **3** exists in the exo enol form in the gas phase to a considerable extent. Previous solution chemistry results on the tautomeric equilibria of the enamines of cyclic β-keto esters and related systems indicate that the C_7 system with an exo double bond is more stable than a C_6 system which prefers an endo double bond.[23,24]

Although the saturated carbocyclic structures of the keto forms of **2**–**4** are favored in the gas phase (see Table V) the extent of methanol elimination from the molecular ions in this tautomeric form is much less for **4** compared to **2** and **3**. This is due to the fact that the energy barrier for the inversion of the equatorially oriented COOMe function to the axial orientation (which is necessary for MeOH loss) is about 7.7 kcal/mol in the case of the cyclooctane system.[15] The conformational free energies for the cyclohexane and cycloheptane systems are 1.2 and 0.9 kcal/mol, respectively.[15]

In conclusion, our study indicates that the tautomeric equilibria of the cyclic β-keto esters **1**–**4** are governed by enthalpy factors both in the solution and gas phases.

Experimental Section

The cyclic β-keto esters **1**–**4** were synthesized by treating the appropriate cyclic ketones with dimethyl carbonate in the presence of sodium hydride, according to the conditions previously described.[25]

The ^{13}C NMR spectra were recorded on a Varian XL-200 NMR spectrometer in deuterated chloroform solution at a concentration of 0.1 M. The solutions were equilibrated for 48 h at room temperature before recording the spectra.

The infrared spectra were recorded on a Nicolet 5-DX FTIR instrument as thin liquid films.

Metastable ion spectra of the molecular ions were examined by the MIKES technique[26] using a reverse-geometry VG Analytical ZAB-2FQ mass spectrometer at a 8-keV ion accelerating potential and a source temperature of 200 °C. Samples were introduced through a heated inlet system at 100 °C. The low-resolution spectra and the deuterium exchange experiments were also performed on the same instrument.

Supplementary Material Available: Tables containing the FTIR, normal mass spectra, and metastable ion spectra of compounds **1**–**4** and references on the keto–enol equilibria and the effect of solvent and temperature (4 pages). Ordering information is given on any current masthead page.

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An Efficient Synthesis of [8-^{13}C]Adenine

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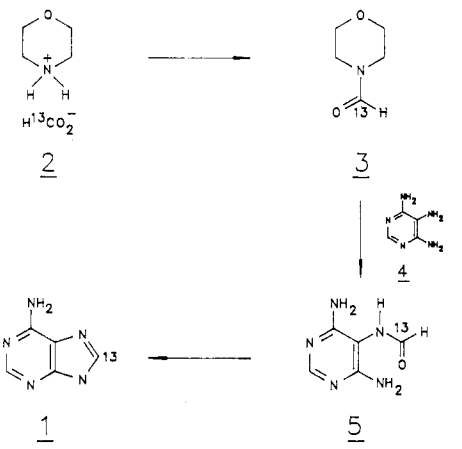
The increasing availability of sensitive, high field nuclear magnetic resonance spectrometers and the development of selective two-dimensional proton-heteronuclear pulse sequences make site-specific incorporation of magnetically active nuclei, especially ^{13}C and ^{15}N, an important technique for studying structure and dynamics of nucleic acids and proteins.[1,2] One can simultaneously take advantage of the high sensitivity inherent in ^1H signals, the chemical shift dispersion of directly attached ^{13}C or ^{15}N, and the suppression of signals for protons not bonded to labeled nuclei to provide important simplifications of complex spectra.[3-6]

Although uniformly labeled biopolymers can be obtained by growing microorganisms on minimal media supplemented with sources of labeled carbon or nitrogen, the use of recombinant plasmids[6] and auxotrophic strains[3-6] makes it possible to construct proteins or nucleic acids with labels positioned at specific locations within selected amino acids or nucleotides. Since incorporation experiments often consume substantial amounts of expensive labeled precursors, it is essential to have efficient syntheses of these materials from readily available sources. We now describe a synthesis of [8-^{13}C]adenine from sodium [^{13}C]formate based on formyl transfer from morpholine that uses equimolar quantities of formate and 4,5,6-triaminopyrimidine. The method is amenable to production of multigram quantities of material in good yield by a simple one-pot procedure.

The synthesis of [8-^{13}C]adenine (**1**) is outlined in Scheme I. Morpholinium [^{13}C]formate (**2**) was prepared from sodium [^{13}C]formate (99%) according to the procedures of Sharma and co-workers[7] and was then converted to the corresponding formamide **3** derivative. Upon heating a mixture of 4,5,6-triaminopyrimidine (**4**) and **3** in 1 N hydrochloric acid at 95 °C, **4** was slowly converted to **1**. When the progress of the reaction was monitored by HPLC, an intermediate, **5**, was observed. Compound **5** was isolated and determined to be the symmetric 5-formyl derivative of triaminopyrimidine (**4**) on the basis of mass spectral and NMR data. Under normal conditions **4** was converted to **1** without isolation of **5** in 61% overall yield based on sodium [^{13}C]formate.

Scheme I



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The ^1H and ^{13}C NMR spectra of [8-^{13}C]-1 gave doublet patterns at the resonance positions for ^1H and ^{13}C in the ^1H–$^{13}C(8)$ unit, J = 209 Hz. A trio of peaks in the mass spectrum of 1 at m/z 135 (0.05), 136 (1.00), and 137 (0.02), along with the absence of extraneous peaks in the ^1H and ^{13}C NMR spectra, demonstrated that labeling was regiospecific and complete. The good yield of 1 from an available source of ^{13}C makes this procedure attractive for the synthesis of [8-^{13}C]adenine and related derivatives. The base can be used directly in feeding experiments or converted to ribonucleosides or deoxyribonucleosides for synthetic applications.

Experimental Section

[8-^{13}C]Adenine (1). Sodium [^{13}C]formate (1.0 g, 14.49 mmol, 99%) was converted to morpholinium formate according to the procedure of Sharma.[7] The low melting salt was then heated to 95 °C under nitrogen for 45 min, during which time moisture was observed to form on the walls of the flask. 4,5,6-Triaminopyrimidine sulfate hydrate (Aldrich) (3.5 g, 14.5 mmol) was dissolved in 10 mL of 1 N HCl with gentle heating and added to the flask. The resulting mixture was allowed to stir under nitrogen at 95 °C. The progress of the reaction was monitored by HPLC on a Waters ACCELL CM cation exchange column using 0.02 M ammonium formate, pH 4.5, as the eluting buffer. After 36 h the reaction was complete. The solution was allowed to cool to room temperature, neutralized with 6 N NaOH, and allowed to stand at 4 °C for 24 h. Crystals were collected on a glass frit, washed thoroughly with water, and dried over P_2O_5. The mother liquor was lyophilized. The residue was recrystallized from hot water and dried over P_2O_5. The combined crystallizations gave 1.2 g (61%) of a white solid; UV λ_{max} (H_2O) 261 nm (ϵ 1.32 × 10^4); EI-MS (relative intensity), m/z at 136 (M^+, 100), 135 (4.5), 109 (17.7), 54 (5.1), 53 (2.8); ^1H NMR (400 MHz, DMSO) δ 8.25 (1 H, d, J = 209 Hz, H8), 8.24 (1 H, s, NH), 7.89 (1 H, s, H2), 7.05 (2 H, br s, NH_2); ^{13}C NMR (DMSO) δ 140.9 (d, J = 209 Hz).

Anal. Calcd for $C_5H_7N_5O$ (adenine monohydrate): C, 39.6; H, 4.5; N, 45.4. Found: C, 39.3; H, 4.4; N, 45.0.

A separate reaction was interrupted after 12 h, and three UV-active components were separated by HPLC on an ACCELL CM cation exchange column upon elution with 20 mM ammonium formate, pH 4.5. Two of the materials, unreacted 5 and 1, were identified from their ^1H and ^{13}C NMR spectra. The third component, 5, was a white solid; EI-MS (relative intensity), m/z at 154 (M^+, 100) 125 (73), 124 (5), 98 (4), 97 (9), 71 (14), 70 (7); ^1H NMR (DMSO, 300 MHz) δ 9.22 (1 H, s, amide H), 8.20 (1 H, s, H6), 8.09 (1 H, d, J = 199 Hz, formamide), 7.70 (4 H, br s, amino H); ^{13}C NMR (^1H decoupled, DMSO) δ 161.54, 147.4, 143.3, 91.4. Formamide 5 was converted to 1 when heated at 95 °C in 1 N hydrochloric acid.

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Photodesulfurization of Indoline-2-thiones: A Facile Synthesis of Indoles

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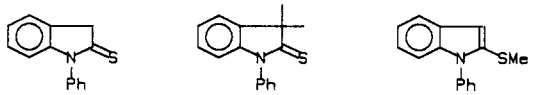
The photochemistry of thiones has been extensively studied over the past 2 decades.[1] However, relatively few reports have dealt with the photochemical properties of thioamides[2] and the major photochemical processes of the thioamides are largely limited to intra- or intermolecular cycloaddition to alkenes. Das et al. reported that on irradiation indoline-2-thiones reacted with methyl methacrylate to give a mixture of isomeric 2-substituted indoles.[2c] One of these isomers has been employed as a key intermediate in a synthesis of indole alkaloids. In continuation of our work on the photochemistry of cyclic conjugated nitrogen–thiocarbonyl systems,[2g] we have studied the photochemical behavior of the indoline-2-thiones 1.

Due to the ambident nature of the indoline-2-thiones 1, either thione 1 or thiol 1′ forms are possible. Thus UV and ^{13}C NMR spectra of 1-phenylindoline-2-thione (**1a**) were compared with those of the 3,3-dimethyl-1-phenylindoline-2-thione (**1m**) (thione form) and 2-(methylthio)-1-phenylindole (**6**) (thiol form). The UV spectrum of **1a** [λ_{max} (EtOH) 225 (ϵ 13400), 294 (7900), and 321 nm



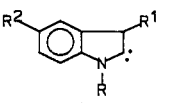
(1a) (1m) (6)

λ_{max}(EtOH) λ_{max}(EtOH) λ_{max}(EtOH)

225 nm (ε 13400), 294 (7900), 321 (12800)

226 nm (ε 14700), 294 (8400), 317 (13900)

219 nm (ε 29400), 260 sh (12500), 283 (16000), 290 (15900)



(7)

(12800)] is similar to that of 3,3-dimethyl-1-phenylindoline-2-thione (**1m**, thione form)[3] but different from that of 2-(methylthio)-1-phenylindole (**6**, thiol form).[3] Furthermore, the ^{13}C NMR spectrum of **1a** showed signals at δ 49.7 (t) and 202.5 (s), assignable to methylene at C-3 and thiocarbonyl carbon at C-2, respectively. Consequently, the indoline-2-thione **1a** is present preferentially in the thione form in the ground state.[4]

Irradiation of 1-phenylindoline-2-thione (**1a**) in benzene in a Pyrex vessel with a high-pressure mercury lamp under

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(3) The UV spectrum of **1m**: λ_{max} (EtOH) 226 (ϵ 14700), 294 (8400), and 317 nm (13900). The UV spectrum of **6**: λ_{max} (EtOH) 219 (ϵ 29400), 260 sh (12500), and 283 (16000), and 290 nm (15900).

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