than that of the alkenic group (CH_2=, 0.80 kcal/mol). The repulsion of ethenylidene, as measured by the 0.45 kcal/mol free energy difference, is comparable to that of an axial proton within the CH_2 group in methoxycyclohexane, as measured by the 0.55 kcal/mol free energy difference.

These results indicate that the ethenylidene group is less repulsive than the *exo*-methylene group but that its dipolar repulsion is still substantial.

Experimental Section

***exo*-Methylenecyclohexane** was prepared by the method of Cope and Ciganek.[7]

Ethenylidenecyclohexane was prepared by the method of Moore and Ward.[8]

3-Methoxy-1-methylenecyclohexane was prepared by the method of Lambert and Clikeman.[2] 2-Cyclohexenone was treated with an excess of CH_3OH to form 1,1,3-trimethoxycyclohexane in 80% yield. Acidic hdyrolysis produced 3-methoxycyclohexanone quantitatively. This two-step procedure is superior to that previously reported.[2,3] Conversion to 3-methoxy-1-methylenecyclohexane by the Wittig reaction occurred as reported.

3-Methoxy-1-ethenylidenecyclohexane (2). A three-necked, 100-mL round bottomed flask was charged with 3-methoxy-1-methylenecyclohexane (0.94 g, 0.0075 mol), CBr_4 (2.50 g, 0.0075 mol), and 50 mL of anhyrous diethyl ether. The flask, under N_2, was fitted with a water-cooled condenser, a low-temperature thermometer, and a rubber septum cap. The stirred solution was cooled to −78 °C (dry ice/methanol), and CH_3Li (5 mL of a 1.6 M solution in diethyl ether) was introduced dropwise via a syringe needle placed through the septum. The addition, which took 5 min, was carried out so that the temperature of the mixture did not exceed −50 °C. After 20 min, a second equivalent of CH_3Li (5 mL of a 1.6 M solution in diethyl ether) was added. The orange or dark red solution was allowed to warm to room temperature and was stirred overnight. The reaction was then quenched with 25 mL of H_2O. The contents of the flask were placed in a separatory funnel, and the layers were separated. The ether layer was removed and dried over Na_2CO_3. The material was filtered, and the ether was distilled under N_2 at atmospheric pressure. GC analysis of the remaining red oil showed that the reaction had proceeded in only about 38% yield, the remainder of the mixture being starting material. The allene was isolated by preparative GC (column 100 °C, 25% DEGS, $^1/_4$ in. × 8 ft, He flow 7.5 mL/min): ^{1}H NMR (CF_2Cl_2) δ 4.57 (m, 2, =CH_2), 3.30 (s, 3, OCH_3), 3.20 (m, 1, CH), 2.50 (dd, 1, 2-CH_2), 1.70–2.20 (br m, 5, ring CH_2), 1.40 (br m, 2, ring CH_2); ^{13}C NMR δ 204.7 (sp carbon), 98.0 (ring sp^2 carbon), 81.5 ($COCH_3$), 73.3 (exocyclic sp^2 carbon), 60.5 (OCH_3), 36.0, 33.0, 30.8, and 29.0 (ring methylenes). Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.05; H, 10.43.

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Evaluation of Lithium Amide Base Formation at Low Temperature via ^{13}C NMR Spectroscopy

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Lithium amide bases are a group of reagents widely used in organic synthesis.[1] Examples of these lithium amide bases include lithium diisopropylamide (LDA), lithium bis(trimethylsilyl)amide (LBTSA), and lithium 2,2,6,6-tetramethylpiperidide (LTMP) to name a few. The usefulness of lithium amide bases in carbanion formation is well established.[2] As a result of their popularity, the preparation of each respective base has been accomplished by a wide variety of experimental conditions. For instance, LDA has been prepared by the addition of *n*-butyllithium in hexane to a solution of diisopropylamine in tetrahydrofuran (THF) at 0 °C with stirring for 5–30 min.[3] In a few recent papers, the formation of LDA at −78 °C is indicated in the experimental section; however, the amount of time allowed to form LDA at that temperature varied or was not indicated.[4] The formation of LBTSA, utilizing bis(trimethylsilyl)amine and *n*-butyllithium, has been accomplished at 0 °C in a similar fashion to LDA.[5] LTMP, formed by the reaction of 2,2,6,6-tetramethylpiperidine with methyllithium, reportedly requires room temperature conditions for best results.[6] In all cases, the formation of the lithium amide base was confirmed only by the success of the subsequent anion reaction.

With the increased emphasis on asymmetric synthesis and stereoselective reactions, the use of low-temperature (−78 °C) anion reactions has increased. However, for low-temperature work the optimal conditions required to form the lithium amide bases used to generate the anion have not been evaluated. In this paper, we describe the use of ^{13}C NMR to evaluate the formation of lithium amide bases at low temperature. ^{13}C NMR was chosen because of its previous success in distinguishing dialkylamines from lithium dialkylamides[7] and for its ability to be used under conditions in which lithium amide bases will be formed in the reaction vessel. Evaluation of the formation of three of the most commonly used bases, lithium diisopropylamide, lithium bis(trimethylsilyl)amide, and lithium 2,2,6,6-tetramethylpiperidide, will serve to illustrate the method.

The synthesis of lithium diisopropylamide was conducted at −73 °C by the rapid addition of an *n*-butyllithium hexanes solution to a solution of diisopropylamine in tetrahydrofuran (THF) containing a trace of tetramethylsilane (TMS). The Experimental Section contains the details of this procedure. The ^{13}C NMR spectrum, obtained at −73 °C within 2 min, indicated complete conversion of diisopropylamine (α carbon 45.0 ppm) to LDA (α carbon 52.3 ppm). The peaks corresponding to the α carbon in diisopropylamine (45.0 ppm) and in LDA (52.3 ppm) were readily distinguishable, although many additional peaks were present in the spectrum between 12.2 and 42.3 ppm. The additional peaks were a result of the various hexanes in the *n*-butyllithium reagent. However, it should be emphasized that the presence of the additional peaks had no adverse effect on the ^{13}C NMR method.

The synthesis of lithium bis(trimethylsilyl)amide was examined by the reaction of bis(trimethylsilyl)amine with the *n*-butyllithium hexanes solution in the THF/TMS solvent system. The reaction was complete within 2 min after the reagents were mixed at −73 °C. This result was

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evident by the loss of the bis(trimethylsilyl)amine methyl signal (2.6 ppm) and the formation of LBTSA methyl signals (5.7 and 6.4 ppm). Warming the sample to room temperature resulted in coalescence of the methyl resonances at 6.0 ppm. It is known that a monomer–dimer equilibrium of LBTSA exists in THF.[8] Presumably, at −73 °C, the exchange rate between the monomer and dimer is slow on the NMR time scale, and the nonaveraged, different environments of the two species result in two signals being observed for the methyl groups. At room temperature the exchange rate is rapid so that only one averaged signal is observed for the methyl groups.[9]

The final example studied was the synthesis of lithium 2,2,6,6-tetramethylpiperidide. The spectral data for the reaction of 2,2,6,6-tetramethylpiperidine with the *n*-butyllithium hexanes solution at −73 °C revealed that the reaction was complete within 2 min. This result was concluded from the loss of the 2,2,6,6-tetramethylpiperidine α-carbon signal (49.8 ppm) and the formation of the LTMP α-carbon signal (52.7 ppm). When the reaction was warmed to room temperature, a change in peak shape was observed for several of the peaks. However, when the solution was cooled again to −73 °C, the spectrum was identical with the low-temperature spectrum taken within the first 2 min. The change in peak shape may be attributed to an equilibrium between complexing species of LTMP.[9]

Several different lithium reagents were also examined. The reaction of 2,2,6,6-tetramethylpiperidine with a methyllithium ether solution in the THF/TMS solvent system was investigated at −73 °C. LTMP was formed to a major extent, although not completely, after 15 min at −73 °C. When the sample was warmed to 0 °C, the spectrum, taken within 5 min, revealed complete formation of LTMP. This result indicates that room temperature conditions are not required to rapidly form LTMP from the reaction of methyllithium with 2,2,6,6-tetramethylpiperidine.

Phenyllithium in ether/cyclohexane was examined in the THF/TMS solvent system with 2,2,6,6-tetramethylpiperidine at −73 °C. After 10 min essentially no reaction had occurred. The sample was warmed to 0 °C and after 10 min only a slight increase in LTMP was observed. Therefore, the reaction was warmed to room temperature. A slight increase in LTMP was indicated after 15 min; however, the majority of 2,2,6,6-tetramethylpiperidine was left unreacted.

The difference in the rate of LTMP formation, depending on the lithium reagent used, is believed to be due to the difference in base strength of the particular lithium reagent.[2] The most basic lithium reagent, *n*-butyllithium, generated LTMP rapidly at −73 °C while the least basic reagent, phenyllithium, was slow even at room temperature. Methyllithium, being intermediate in base strength, required an intermediate temperature, 0 °C, for rapid complete formation of LTMP.

In conclusion, we have confirmed the low-temperature formation of several lithium amide bases. LDA, LBTSA, or LTMP was quantitatively generated at −73 °C in THF within 2 min of mixing *n*-butyllithium with diisopropylamine, bis(trimethylsilyl)amine, or 2,2,6,6-tetramethylpiperidine, respectively. The fact that LDA, LBTSA, and LTMP are rapidly formed at low temperature indicates that current experimental manipulations can be simplified and that the time required to conduct a procedure utilizing one of these lithium amide bases can be shortened. This method should be applicable in determining the effect reaction conditions have on the formation of other lithium amide bases and may prove especially useful when examining hindered lithium amide base formation.[10]

Experimental Section

Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian XL-400 spectrometer. Tetrahydrofuran was used as the solvent, with tetramethylsilane as the internal reference. Spectrometer shimming was optimized with THF-d_8/TMS at −73 °C prior to running the actual reaction samples. The chemical shift assignments were referenced to internal tetramethylsilane. The lithium reagents were purchased from Aldrich and were titrated before use. Tetrahydrofuran was distilled from lithium aluminum hydride, and diisopropylamine, bis(trimethylsilyl)amine, and 2,2,6,6-tetramethylpiperidine were distilled from calcium hydride under nitrogen.

Evaluation of LDA Formation. Typical Procedure. A standard 5-mm NMR tube containing 0.07 mL (0.5 mmol) of diisopropylamine in 0.5 mL of THF was chilled to −73 °C in the NMR probe.[11] A ^{13}C NMR spectrum was recorded.[12] By syringe, 0.22 mL of *n*-butyllithium (2.3 M *n*-butyllithium in hexanes, 0.5 mmol) was rapidly added to the chilled solution. The tube was then shaken and reinserted in the NMR probe, all within approximately 30 s. The ^{13}C NMR spectrum was acquired within 2 min of addition of the lithium reagent, followed by additional data collection at 5-, 10-, and 15-min intervals. After the 15-min measurement, the NMR tube was removed from the probe and allowed to warm to room temperature, and the room temperature ^{13}C NMR spectrum was recorded.

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Registry No. LDA, 4111-54-0; LBTSA, 4039-32-1; LBTSA (dimer), 97587-69-4; LTMP, 38227-87-1; diisopropylamine, 108-18-9; bis(trimethylsilyl)amine, 999-97-3; 2,2,6,6-tetramethylpiperidine, 768-66-1.

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Transannular Cyclizations in the Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione System: A Reinvestigation

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As part of an ongoing program that is involved with the synthesis and chemistry of polycyclic "cage" compounds,[1] we have examined some interesting imine and ketone reductions in the pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane ring

(1) See: Marchand, A. P. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI: Greenwich, CT; Vol. 1, in press and references cited therein.

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