Registry No. **5a**, 88-27-7; **5b**, 13086-92-5; **5c**, 42900-95-8; **6a**, 94817-72-8; **6b**, 102392-51-8; **6c**, 94817-75-1; **6d**, 102392-50-7; **7**, 95423-30-6; **8**, 114199-90-5; 2,6-dimethylphenol, 576-26-1; 2-methyl-6-*tert*-butylphenol, 2219-82-1; 1,3-butadiene, 106-99-0; 2,6-di-*tert*-butylphenol, 128-39-2; 2,6-diisopropylphenol, 2078-54-8.

A Comparison of the Through-Space, Dipolar Repulsion of Alkenic and Allenic Groups

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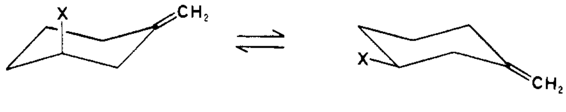
The double bond exerts a repulsive dipolar interaction with polar groups across a six-membered ring. We have documented this phenomenon in 3-substituted *exo*-methylenecyclohexanes (eq 1), in which there is less axial conformer for polar X groups (OH, OCH_3, SCH_3) in low polarity solvents than there is in the corresponding monosubstituted cyclohexanes.[2] These observations have provided a superb opportunity for studying the dipolar interactions of double bonds, because the equilibrium of eq 1 is extremely sensitive to these effects. There have been no such studies of the cumulated double bond (the allenic functionality). Consequently, we have prepared ethenylidenecyclohexane (**1**) and its 3-methoxy derivative (**2**) and have explored the conformational properties of the ethenylidene group by low-temperature NMR experiments. The barrier to ring reversal in **1** provides information about deformation of the six-membered ring by the ethenylidene group. The axial–equatorial equilibrium constant in **2** (eq 2) provides information about the dipolar repulsion between the ethenylidene and methoxy groups. We report herein the synthesis and conformational analysis of **1** and **2**.



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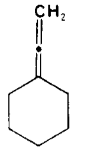

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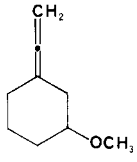

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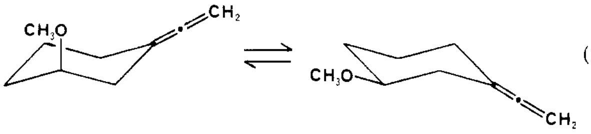

(2)

Results

exo-Methylenecyclohexane was converted to ethenylidenecyclohexane (**1**) by treatment with carbon tetrabromide and, sequentially, 2 equiv of methyllithium.[3] Reaction of CBr_4 with the first equivalent of CH_3Li resulted in addition of dibromocarbene to the double bond to form the dibromocyclopropane. The second equilvalent of CH_3Li removed the two bromine atoms to form a carbene that rearranged to the ethenylidene product **1**. Treatment of 3-methoxy-1-methylenecyclohexane[2] in the same fashion with CBr_4 and CH_3Li produced 3-methoxy-1-ethenylidenecyclohexane (**2**).

The ^{1}H NMR spectrum of ethenylidenecyclohexane (**1**) was measured as a function of temperature at 500 MHz.[3] Measurements were carried out in CF_2Cl_2, a nearly nonpolar solvent that minimizes solute–solvent interactions. At room temperature, the C2 and C6 resonances occurred at δ 2.28 the C3 and C5 resonances at δ 1.74, and the C4 resonances at δ 1.68. The latter two resonance groups overlapped at lower temperatures. The two broad peaks at 193 K passed through decoalescence at 180 K, from slowing of ring reversal, and produced two peaks apiece at 153 K for the separate axial and equatorial protons. From k_C at coalescence ($\pi\Delta\nu/\sqrt{2}$, in which $\Delta\nu$ is the slow exchange shift difference), the free energy of activation for ring reversal was calculated to be 8.3 kcal/mol, compared with 8.4 kcal/mol for *exo*-methylenecyclohexane.[4]

The proton geminal to methoxyl (3H) provides the best probe for the conformational equilibrium of 3-methoxy-1-ethenylidenecyclohexane (eq 2), since its resonance is well removed from the other ring proton resonances. Lowering the temperature should result in slowing of ring reversal and doubling of the 3H signal. Unfortunately, the 3H resonance is only slightly upfield of the methoxy resonance. The resonance, however, may be followed through its low-temperature decoalescence into two peaks, one above and the other below the methoxy resonance.[3] Direct integration of these peaks yielded a free energy difference of 0.45 kcal/mol at 143 K.

Discussion

The barriers to ring reversal are essentially equal in *exo*-methylenecyclohexane[4] and ethenylidenecyclohexane (**1**), 8.3–8.4 kcal/mol. This result suggests that deformations of the six-membered ring by the alkenic and allenic exocyclic unsaturations are the same. Therefore, any differences in substituent preferences for the axial and equatorial positions should not be attributed to changes in the shape of the ring.

In the parent saturated system, methoxycyclohexane, the axial/equatorial free energy difference is 0.55 kcal/mol in CS_2.[5] Introduction of the *exo*-methylene group raises the equatorial preference to 0.80 kcal/mol in the nonpolar solvent CF_2Cl_2.[2] We have attributed this change to the presence of a significant intramolecular dipolar repulsion between the *exo*-methylene double bond and the axial 3-methoxy group. When *exo*-methylene ($CH_2{=}$) is replaced with isopropylidene ($Me_2C{=}$), the free energy difference drops to 0.19 kcal/mol.[6] The tetrasubstituted double bond in the isopropylidene system has little or no dipole, so that electrostatic repulsion with the axial 3-methoxy group is negligible and more axial methoxy is present.

The free energy difference for 3-methoxy-1-ethenylidenecyclohexane (**2**) is 0.45 kcal/mol. Thus the dipolar repulsion of the allenic group is substantially less

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(2) Lambert, J. B.; Clikeman, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 4203–4211. Lambert, J. B.; Taba, K. M. *J. Org. Chem.* **1980**, *45*, 452–455.

(3) Details may be found in D. E. Marko, Ph.D. Dissertation, Northwestern University, Evanston, IL, 1987.

(4) Gerig, J. T.; Rimerman, R. L. *J. Am. Chem. Soc.* **1970**, *92*, 1219–1224.

(5) Jensen, F.; Bushweller, C. H.; Beck, B. H. *J. Am. Chem. Soc.* **1969**, *91*, 344–351.

(6) Lambert, J. B.; Taba, K. M. *J. Am. Chem. Soc.* **1981**, *103*, 5828–5832.

0022-3263/88/1953-2642$01.50/0

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): ^1H 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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(7) Cope, A. C.; Ciganek, E. *Organic Syntheses*; John Wiley and Sons, Inc.: New York, 1963; Collect. Vol. IV, pp 612–615.

(8) Moore, W. R.; Ward, H. R. *J. Org. Chem.* **1960**, *25*, 2073. Moore, W. R.; Ward, H. R. *Ibid.* **1962**, *27*, 4179–4181. Skatteböl, L. *Tetrahedron Lett.* **1961**, 167–172.

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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(1) For many examples, see: Fieser, L. F.; Fieser, M., Eds. *Reagents for Organic Synthesis*; Wiley: New York, 1967–1986; Vols. 1–12.

(2) Stowell, J. C., Ed. *Carbanions in Organic Synthesis*; Wiley: New York, 1979.

(3) (a) Kende, A. S.; Fludzinski, P. *Org. Synth.* **1985**, *64*, 68–72. (b) Marshall, J. A.; Andrews, R. C.; Lebioda, L. *J. Org. Chem.* **1987**, *52*, 2378. (c) Dieter, R. K.; Fishpaugh, J. R. *J. Org. Chem.* **1987**, *52*, 923. (d) Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 3353.

(4) Ireland, R. E.; Wardle, R. B. *J. Org. Chem.* **1987**, *52*, 1780. (b) Radinov, R.; Haimova, M.; Simova, E. *Synthesis* **1986**, 886. (c) Raucher, S.; Gustavson, L. M.; Stenkamp, R. E. *J. Org. Chem.* **1987**, *52*, 2760.

(5) Hart, H.; Love, G. M.; Wang, I. C. *Tetrahedron Lett.* **1973**, 1377.

(6) Dougherty, C. M.; Olofson, R. A. *Org. Synth.* **1978**, *58*, 37–43.

(7) Fraser, R. R.; Baignee, A.; Bresse, M.; Hata, K. *Tetrahedron Lett.* **1982**, 4195.

0022-3263/88/1953-2643$01.50/0