Nuclear Magnetic Resonance Spectra of 1-Methyl-2-acetyl-3-phenylperhydrodiazocine

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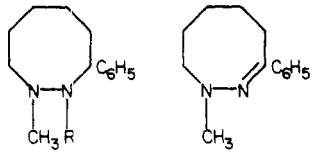
The NMR spectrum of 1-methyl-2-acetyl-3-phenylperhydrodiazocine (**1a**) was investigated to determine whether



1a, R = $COCH_3$ **2**
b, R = H

a similar behavior would exist to that found with its homologue 1-methyl-2-acetyl-3-phenylperhydrodiazepine.[1b] This ring system offers an advantage over the perhydrodiazepine in that the free amine **1b** is stable toward oxidation and can be studied to see whether stable conformers also exist for this structure.

The amine (**1b**) was prepared by the reduction of 1-methyl-3-phenylhexahydrodiazocine **2** using lithium aluminum hydride in dioxane; this method differs from the literature procedure which used catalytic reduction.[2]

The NMR spectrum of **1b** in deuterated chloroform was normal but differed from that reported;[2] a singlet was obtained for the CH_3N group at δ 2.48 instead of the reported doublet. The singlet for the NH appeared at δ 1.98. The spectrum in carbon tetrachloride was similar except the NH absorption was not as well-defined.

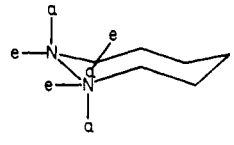
The picrate for this compound melted at 130–132 °C in agreement with the literature value of 130–135 °C[2] and gave a singlet for the NCH_3 group in its NMR spectrum at δ 3.11.

Catalytic reduction of **2** in the presence of acetic anhydride gave **1a**. The NMR spectrum resembled that of its homologue 1-methyl-2-acetyl-3-phenylperhydrodiazepine[1b] and indicated the presence of three stable conformers at room temperature. The perhydrodiazocine **1a** showed at room temperature in carbon tetrachloride two singlets of unequal size at δ 1.88 and 2.07 for the CH_3CO protons and three singlets of unequal size at δ 2.32, 2.38, and 2.57 for the NCH_3 group. The ratio of the intensities for the latter was 1:1.2:4.2, respectively. Raising the temperature to 87 °C coalesced these peaks to one singlet for each group; the singlet for the CH_3CO group appeared at δ 2.02 and that for the NCH_3 appeared at δ 2.50. The ratio of the intensities for the NCH_3 group in **1a** is markedly different from that found for the NCH_3 group in the homologue 1-methyl-2-acetyl-3-phenylperhydrodiazepine in carbon tetrachloride.[1b] The three singlets for this compound at δ 2.71, 2.87, and 3.06 had areas in the ratio of 1.0:1.79:1.40, respectively.

These data indicate that one conformation exists for **1b** and three stable conformations exist for **1a** at room temperature.

The NMR behavior of **1a** and of its homologue, 1-methyl-2-acetyl-3-phenylperhydrodiazepine, is distinctly different from that observed with the open-chain analogue 1,1-dimethyl-2-(*p*-nitrobenzyl)-2-acetylhydrazine which shows a normal behavior at 30 °C and −40 °C; at −83 °C broadening of the three singlets at δ 2.21, 2.49, and 4.62 occurs. This behavior indicates that the rotational barrier for the acetyl group is either low or one rotamer may be strongly preferred. A similar NMR behavior has been observed with *N*-acylhydroxylamines.[3]

Conformational properties of cyclooctane and azocane are similar with the dominant conformation being the boat chair and a minor conformer being the crown.[4] Extensive substitutions and replacement of ring carbon by heteroatoms are reported to favor the crown conformation.[5] With both conformers eight geometrical isomers are possible. On the basis of NMR data only three of these are present at room temperature. Assignment of structures to these possibilities is difficult with one exception. Isomer **3** in which all three groups are equatorial would have the



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least steric hindrance and would probably represent the predominant form. Such an equatorial arrangement would result in the observed greatest deshielding of the CH_3N and CH_3CO groups and these appear further downfield at δ 2.57 and δ 2.07, respectively.

The preponderance of isomer **3** at room temperature may be accounted for by the greater flexibility present in the perhydrodiazocine ring system over that present in the corresponding perhydrodiazepine ring.

Experimental Section

Recording of Spectra. NMR spectra were obtained by using tetramethylsilane as an internal standard with a Varian-A60 NMR spectrometer and JEOL FX90Q Pulse FT NMR spectrometer. IR spectra were recorded with a Perkin-Elmer Infracord spectrometer.

1-Methyl-3-phenylperhydro-1,2-diazocine (1b). A solution of 1,4,5,6,7,8-hexahydro-1-methyl-3-phenyl-1,2-diazocine (**2**)[2] (7.0 g, 0.035 mol) in dioxane (50 mL) was added dropwise to a suspension of lithium aluminum hydride (1.5 g, 0.40 mol) in dioxane (100 mL) at 112 °C under nitrogen with vigorous stirring over a 45-min period. The resulting mixture was heated under reflux for 19 h and cooled and the excess hydride was decomposed with aqueous sodium hydroxide. Removal of the dioxane and water under reduced pressure followed by distillation of the resulting oil gave 1-methyl-3-phenylperhydro-1,2-diazocine (5.51 g, 78% yield): bp 92–94 °C (0.3 torr); n^{20}_D 1.537; IR (film) 3.05, 3.43, 3.52, 6.90, 14.25 μm; NMR ($CDCl_3$) δ 1.08–2.27 (m, 8 H, 4-, 5-, 6-, 7-CH_2), 1.98 (s, 1 H, NH), 2.48 (s, 3 H, CH_3N), 2.46 (t, 2 H, CH_2N, J = 5 Hz), 4.02 (t, 1 H, CH, J = 5 Hz), 7.05–7.57 (m, 5 H, aromatic H). The singlet at 1.98 ppm underwent exchange with D_2O.

Anal. Calcd for $C_{13}H_{20}N_2$: C, 76.42; H, 9.87; N, 13.7; mol wt 204. Found: C, 75.95; H, 9.79; N, 13.56; mol wt 204 (mass spectrum).

The picrate was formed by treating the diazocine **1b** in ethanol with picric acid and after two crystallizations from absolute ethanol melted at 130–132 °C (lit.[2] mp 130–135 °C); NMR ($CDCl_3$) δ 1.27–2.37 (m, 8 H, 4-, 5-, 6-, 7-CH_2), 3.11 (s, 3 H, NHC_3), 3.47 (t, poorly defined, 2 H, CH_2N, J = 7 Hz), 4.50 (t, 1 H, C H, J = 6 Hz), 7.37 (s, 5 H, C_6H_5), 8.90 (s, 2 H, $C_6H_2(NO_2)_3$). The two NH signals were broad and not distinguishable.

1-Methyl-2-acetyl-3-phenyloctahydro-1,2-diazocine (1a). A solution of **2** (1.43 g, 0.007 mol) in acetic anhydride (30 mL) was treated with hydrogen and platinum oxide (0.1 g) at at-

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mospheric pressure for 72 h. Removal of the catalyst by filtration and the solvent by distillation gave an oil which was dissolved in methylene chloride and washed with sodium carbonate solution. Removal of the methylene chloride gave an oil which was purified by chromatography on silica gel using chloroform as an eluant. The acetyl derivative (**1a**, 0.69 g) is a liquid: n^{20}_D 1.5454; IR (film) 3.44, 6.06, 14.24 μm; NMR (CCl_4, 29 °C) δ 0.65–3.32 (m, 8 H, 4-, 5-, 6-, 7-CH_2), 1.88, 2.07 (2 s, 3 H, CH_3CO), 2.32, 2.38, 2.57 (3 s, 3 H, NCH_3), 2.57–3.10 (m, 2 H, CH_2N), 3.32–5.73 (m, 1 H, CH), 7.00–7.67 (m, 5 H, C_6H_5); at 87 °C the two singlets for the CH_3CO became one singlet at δ 2.02 and the three singlets for the NCH_3 became a singlet at δ 2.50.

Anal. Calcd for $C_{15}H_{22}N_2O$: C, 73.13; H, 9.00; N, 11.37; mol wt 246. Found: C, 73.48; H, 9.05; N, 11.40; mol wt 246 (mass spectrum).

1,1-Dimethyl-2-(*p*-nitrobenzyl)-2-acetylhydrazine:[6] NMR ($CDCl_3$, 30 °C) δ 2.27 (s, 3 H, CH_3CO), 2.50 (s, 6 H, 2 CH_3), 4.67 (s, 2 H, CH_2), 7.45 (d, 2 H, *o*-H's, J = 9 Hz), 8.15 (d, 2 H, *m*-H's, J = 9 Hz); NMR (−40 °C) δ 2.25 (s, 3 H, CH_3CO), 2.50 (s, 6 H, 2 CH_3), 4.65 (s, 2 H, CH_2), 7.45 (d, 2 H, *o*-H's, J = 9 Hz), 8.13 (d, 2 H, *m*-H's, J = 9 Hz); NMR ($CDCl_3$–CS_2, −83 °C), broadening of all three singlets.

Registry No. 1a, 75299-33-1; **1b**, 79868-87-3; **1b** picrate, 75299-34-2; **2**, 75311-36-3.

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Preparation and Some Properties of 4-Chloro-2-(and -4-) methyl-2-pentenes

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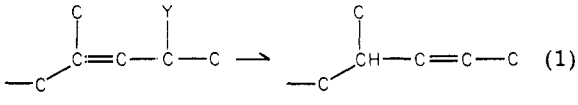
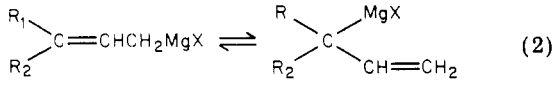
One sequence in a synthesis required the overall reductive process illustrated in eq 1. While a direct S_N2'



(1)

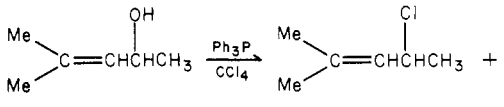
reduction might prove feasible, we considered the known protonation of an allylic Grignard, which generally leads to a less substituted olefin as the major product,[2] as a viable alternative. However, the mechanism of this protonation is not known and might reasonably bear a relation to the structure of the allylic Grignard reagent. These reagents are known to be equilibrating mixtures of the two covalent isomers (eq 2)[3] and when R_1 = Me, R_2 = H, or



(2)

R_1 = R_2 = Me, the primary reagent is the dominant form.[4] However, no example of a secondary vs. tertiary system has been studied, and we decided to examine the protonation process in such a system, i.e., the simplest case possible—the Grignard from 4-chloro-2-methyl-2-pentene. When we initiated this project, the chloride had been reported as the main product (80%—along with 20% of its allylic isomer) from addition of hydrogen chloride to trimethylallene.[5] The mixture was described as being heat labile but capable of distillation under reduced pressure. While our studies were in progress a further report appeared which indicated that attempts to prepare the chloride gave 4-methyl-1,3-pentadiene from spontaneous loss of hydrogen chloride.[6] Since we have successfully prepared the chloride and have studied some of its properties, we report our results at this time.

Mesityl oxide was reduced to 4-methyl-3-penten-2-ol by LAH according to the established procedure.[7] Initially we attempted to prepare the chloride using triphenylphosphine and carbon tetrachloride.[8] The reaction mixture, freed from triphenylphosphine oxide, gave an NMR spectrum indicating the presence of 4-chloro-2-methyl-2-pentene (**1**) and 4-chloro-4-methyl-2-pentene (**2**). How-



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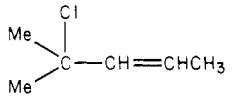

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ever, attempted separation of the chlorides from the carbon tetrachloride either by distillation, column chromatography, or TLC led to either codistillation or decomposition. Treatment of the alcohol with concentrated hydrochloric acid gave a good yield of 2,4-dichloro-2-methylpentane. Hoping that the allylic chloride was generated initially in this reaction and the addition of hydrogen chloride was a subsequent reaction, we followed the course of the reaction with GLC. This showed that the postulated course was indeed correct and we were able to develop a satisfactory procedure, albeit of low isolated yield, for preparation of this rather unexpectedly difficult compound.

The chlorides **1** and **2** were always obtained as a mixture containing about 84% **1** and 16% **2** (by NMR). They can be isolated as a clear liquid by reduced-pressure distillation or by GLC. Structural assignments are based purely on the NMR and infrared data. The infrared spectrum shows the complete absence of hydroxyl, and the NMR spectrum closely resembles that of 4-methyl-3-penten-2-ol. The two spectra differ slightly in chemical shifts and the CHCl proton shows a clean pair of overlapping quartets instead of the broadened near quintet of the CHOH proton. The NMR spectrum of the allylic chloride also contains two new peaks, a very tight AB pattern with further splitting which is centered at ca. 5.70 and a singlet at 1.65. For the AB pattern J_{AB} is 15 Hz, reasonable for a *trans*-CH=CH system. We attribute these new bands to the presence of some 16% **2** in the mixture. The position of the doublet for the CH_3CH methyl group is apparently hidden under the peaks for **1**. However, the total integration accords well with the expectations of the 84:16 mixture.

The mass spectrum of the mixture proved surprising and quite interesting. For $C_6H_{11}Cl$ the molecular ions should be at m/z 118 and 120, but the major peaks in that area

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