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(6) The oxide configuration of **8** and **9** was determined by comparison with their α-sulfoxide isomers: α-oxide of **4**, mp 146–148 °C; α-oxide of **5**, mp 183–185 °C, prepared by oxidation with trichloroisocyanuric acid (CH_2Cl_2/acetone/pyridine/H_2O, −20°, 45 min). Details will be dealt with in a forthcoming full paper.
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(12) Cf. (a) B. Fechtig, H. Peter, H. Bickel, and E. Visher, *Helv. Chim. Acta*, **51**, 1108 (1968); (b) F. M. Huber, R. R. Chauvette, and B. G. Jackson, "Cephalosporins and Penicillins: Chemistry and Biology", E. H. Flynn, Ed., Academic Press, New York, N.Y., 1972, pp 39–55, and references therein.
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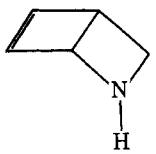
A Synthesis of N-Substituted 1,2-Dihydropyridines

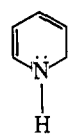
Sir:

Although dihydropyridines have been known since the last century, derivatives without stabilizing electron-withdrawing groups on the ring are very rare and little information is available on their chemistry.[1] There has been recent interest[2] in the synthesis of the 1,2-dihydropyridine ring system because of its implication as a pivotal intermediate in the biosynthesis of indole alkaloids.[3] These biosynthetic studies suggest that 1,2-dihydropyridines may provide a very efficient synthetic route to the indole alkaloids and related compounds.[4]

Previous syntheses of reactive 1,2-dihydropyridines without stabilizing electron-withdrawing groups on the ring essentially have been limited to the *careful* reduction of pyridine or pyridinium ions.[1] We have developed a more versatile nonreductive synthetic method involving 2-azabicyclo[2.2.0]hex-5-ene (**1**) as a key intermediate. Compound **1** is a valence isomer of the parent 1,2-dihydropyridine. In contrast to the parent 1,2-dihydropyridine, which has never been isolated, its valence isomer **1** does not possess the dienamine functionality and is relatively stable to polymerization and oxidation.

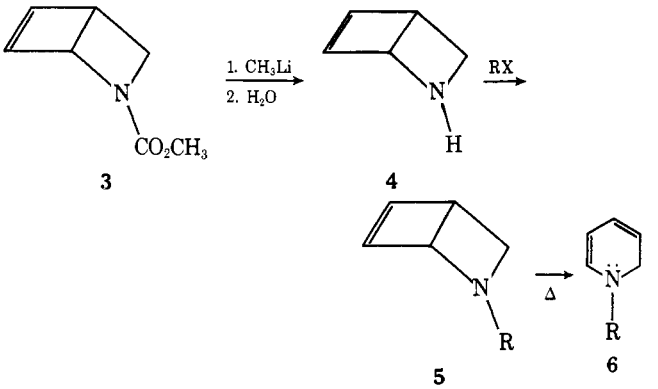


1



2

The preparation of **1** is most conveniently carried out[5] by the slow addition of carbamate **3**[6] to methyllithium in dry tetrahydrofuran at −15°. After 5 min the reaction is quenched by the addition of H_2O. Alkylating agents relatively stable to hydrolysis, e.g., benzyl chloride and 6-bromo-1-hexene, are added in equimolar amounts, and the reaction mixture is allowed to reflux until the disappearance of the alkylating agent ceases. This procedure produces bicyclic amines **5a** and **b** in 40–60% overall isolated yields from carbamate **3**.[7]



3 4 5 6

a, R = $PhCH_2$-
b, R = $CH_2{=}CH(CH_2)_4$-
c, R = $CH_3O_2C(CH_2)_5$-
d, R = $CH_2{=}CHCH_2$-
e, R = $PhCH_2CH_2$-
f, R = $C_2H_5O_2CCH_2$-

If the alkylating agent is sensitive to hydrolysis, e.g., methyl 6-bromohexanoate, then the bicyclic amine **1** is isolated by first extracting the reaction mixture with ether and then by removing most of the solvent by distillation through an efficient column. This procedure produces the bicyclic amine in yields of 20–25%. Treatment of **4** with methyl 6-bromohexanoate and an excess of diisopropylamine produces **4c** in 90–95% yield.

The ring opening of the bicyclic amines is induced thermally.[8] Initial studies on the gas phase ring opening indicated the reaction rate to be sensitive to the substituent on nitrogen. In contrast to the *N*-carbomethoxy derivative **4d** (R = CO_2CH_3, $t_{1/2} \simeq 0.5$ h at 165°), the *N*-methyl derivative **4e** (R = CH_3) exhibits a $t_{1/2} \simeq 0.5$ h at only 122°. Compounds **4a–c** showed similar kinetic behavior to the *N*-methyl derivative **4e.** A more detailed kinetic study of the ring opening of **4a** and **d** in benzene solution gives results similar to the above.[9]

This synthetic scheme has many advantages over the direct reduction of pyridine and its derivatives as an entry into the 1,2-dihydropyridine ring system. Whereas the reduction of pyridine derivatives can produce both 1,4- and 1,2-dihydropyridines,[1] as well as tetrahydropyridines,[10] the ring opening is efficient in giving only the 1,2-dihydropyridine free of side products. Finally, the 2-azabicyclo[2.2.0]hex-5-ene ring system present in **4a–c** is a masked 1,2-dihydropyridine. The greater chemical stability of the 2-azabicyclo[2.2.0]hex-5-enes (**4a–c**) compared to the isomeric dihydropyridines will allow for the development of synthetic schemes leading to biologically interesting molecules that normally would be prohibited using the more reactive 1,2-dihydropyridines.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (MPS74-23700).

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(5) The 2-azabicyclo[2.2.0]hex-5-ene ring system has been reported previously but this method is not readily applicable to the preparation of gram quantities needed in our scheme. (K. E. Wilzbach and D. J. Rausch, *J. Am. Chem. Soc.*, **92**, 2178 (1970).)
(6)(a) Carbamate **3** can be prepared in large quantities (ca. 30 g) by irradiating 5% solutions of the *N*-carbomethoxy-1,2-dihydropyridine in acetone using a Rayonet 208 photochemical reactor (Southern New England Ultraviolet Co., Middletown, Conn.) equipped with RUL-3000 lamps. The product is further purified by first passing it through aluminum oxide with a pentane–ether gradient followed by a bulb-to-bulb distillation; (b) F. W. Fowler, *J. Org. Chem.*, **37**, 1321 (1972).
(7) The N-substituted bicyclic amines and 1,2-dihydropyridines are easily identified because they have very characteristic spectral properties (see ref 5 and 6). We have further characterized the 1,2-dihydropyridines by reduction to the 1,2,5,6-tetrahydropyridines. These were compared to authentic samples prepared by the reaction of 1,2,5,6-tetrahydropyridine with the appropriate alkylating agent.
(8) The ring opening reaction to the dihydropyridine has been carried out in solution using an inert solvent such as benzene at 120° and in the gas phase using a sealed evacuated bulb or flow system. The 1,2-dihydropyridines can be prepared free from solvent using either the static or flow gas phase system. However, the technique we find to be most convenient is to dissolve the bicyclic amine (**5**) in an inert solvent such as benzene and to distill the mixture through a hot quartz tube (24 × 1.0 cm) at 300°. The solution phase pyrolysis is not as clean as in the gas phase and the sealed evacuated bulb (345 ml) can be used only for small quantities (50–100 mg).
(9) The disrotatory concerted ring opening reaction of the cyclobutenes **5a–c** is clearly not an allowed process according to the principles of orbital symmetry. However, the nitrogen atom introduces a considerable electronic perturbation in these ring systems. The lone pair of electrons on nitrogen can have a stablizing interaction with the transition state for a nonconcerted ring opening of these cyclobutenes. In fact, when the lone pair of electrons is more available for a bonding interaction (**3**), the activation energy for the ring opening reaction is indeed available. (The E_a values for carbamate **3** and amine **5a** are 32.0 and 30.6 kcal/mol, respectively.)
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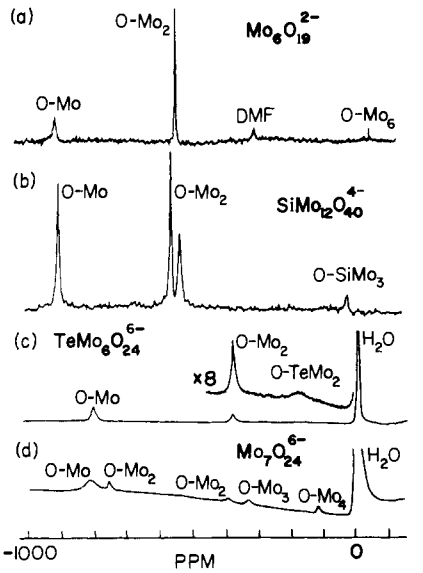

Figure 1. ^{17}O NMR spectra of (a) $[(n\text{-}C_4H_9)_4N]_2Mo_6O_{19}$, (b) α-$[(n\text{-}C_4H_9)_4N]_4Si_{12}O_{40}$, (c) $Na_6TeMo_6O_{24}$, and (d) $Na_6Mo_7O_{24}$, [Mo] = 2.8 M. See Table I for details regarding experimental conditions.

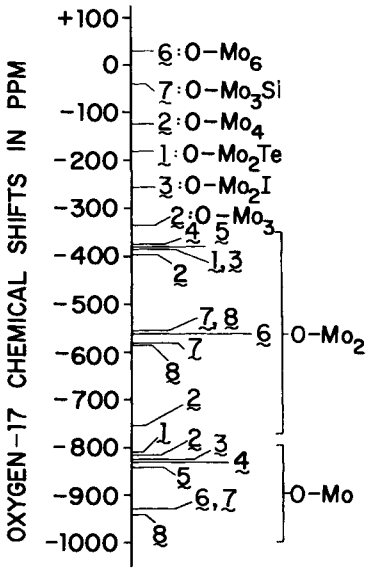

Figure 2. Assignments of ^{17}O NMR shifts given in Table I.

An ^{17}O Nuclear Magnetic Resonance Chemical Shift Scale for Polyoxomolybdates

Sir:

The feasibility of observing ^{17}O NMR spectra of large group 5a and 6a polyoxoanions was demonstrated recently.[1,2] In order to determine the factors which influence chemical shifts and line widths, we have examined the spectra of a number of polyoxomolybdates under various experimental conditions.

All spectra were measured on a JEOL JMN-PS-100 spectrometer at 13.5 MHz in the Fourier mode using a Nicolet 1085 data system. Samples were pulsed at 0.33 s^{-1} utilizing 4096 data points over 15 152 Hz. An external proton lock provided frequency stabilization.

The samples studied are described in Table I and representative spectra shown in Figure 1. All of the compounds have known structures,[3,4] and chemical shift assignments given in Figure 2 are based on the previously established qualitative correlation between downfield shift and decreasing number of metals to which an oxygen atom is bonded. Compounds **1**, **3**, **4**, and **5** all have 12 symmetry equivalent terminal oxygens (O-Mo), 6 equivalent doubly bridging oxygens ($O\text{-}Mo_2$), and 6 oxygens bonded to two molybdenums and the heteroatom. Thus the resonances near −825 and −380 ppm are assigned to the terminal and doubly bridging oxygens, respectively. The very broad resonances observed for **1** and **3** at −180 and −256 ppm are assigned to the triply bridging oxygens, while the corresponding resonances in **4** and **5** are presumably too broad to observe or obscured by the solvent resonance. Compound **2** contains 12 terminal oxygens, 8 doubly bridging oxygens, 2 equivalent triply bridging oxygens, and 2 equivalent quadruply bridging oxygens. Although the terminal oxygens are not all symmetry equivalent, they have similar local environments and collectively yield a broad resonance at −814 ppm. Two of the doubly bridging oxygens, however, are distinguished from the remaining doubly bridging oxygens by unusually short bond distances to a molybdenum which has no terminal oxygens. The resonance at −757 ppm is assigned to these oxygens and the resonance at −395 ppm is assigned to the "normal" doubly bridging oxygens. Assignments for compounds **6**, **7**, and **8** have been discussed previously,[1] but the narrow line widths observed here allow the resonances