Tetrahedron Letters, Vol. 34, No. 36, pp. 5673-5676, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Synthesis and Reactions of 2,3-Diazabicyclo[2.2.1]hept-5-ene

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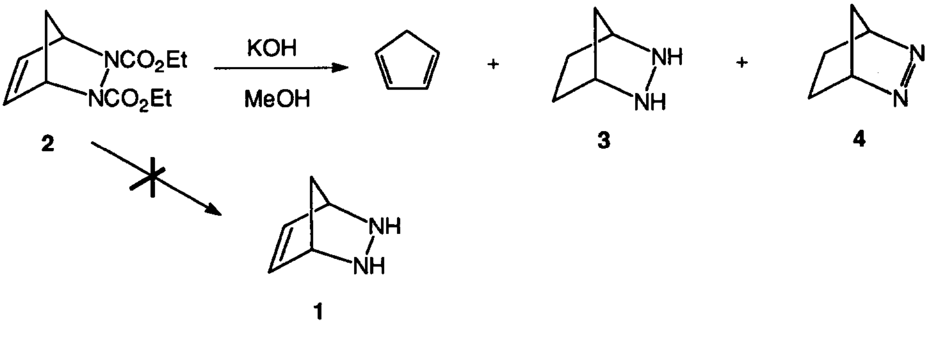
Abstract: The first synthesis of 2,3-diazabicyclo[2.2.1]hept-5-ene is reported. The generation of this molecule is facilitated by the isolation of the bis-carboxylate salt formed on hydrolysis of the corresponding biscarbamate. The retro-Diels-Alder generation of diimide and cyclopentadiene is explored.

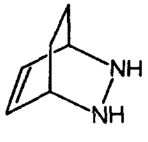
In investigations revolving around the synthesis of energy-rich molecules, we required isolable quantities of 2,3-diazabicyclo[2.2.1]hept-5-ene (**1**), and ring-substituted derivatives of this hydrazine. Although N,N'-dialkyl derivatives of this molecule have long been known,[1] the isolation of the parent hydrazine has, surprisingly, not been described in the literature. In the most extensive attempts reported to date at generating this compound, Cohen and co-workers[2] investigated methanolic basic hydrolysis of the azodicarboxylate-cyclopentadiene adduct **2**, at both room temperature and reflux. In all cases, they were only able to isolate cyclopentadiene, the fully reduced hydrazine **3**, and azo compound **4** (Scheme I).

Scheme I



The following possibilities[2] were suggested for the origin of these products, and the absence of desired **1**: (1) hydrazine **1** might directly reduce the π-bond of starting material **2** or another molecule of **1**, to give the saturated derivative **3** (directly or indirectly via the biscarbamate) and the unstable 2,3-diazabicyclo[2.2.1]hepta-2,5-diene, which would spontaneously denitrogenate to give cyclopentadiene; (2) **1** might intramolecularly transfer two hydrogens to its own π-bond, giving **4** directly; (3) **1** might undergo retro-Diels-Alder reaction, producing cyclopentadiene and diimide. The diimide, in turn, would reduce starting material or another molecule of **1**. The azo compound **4** would then presumably be produced by adventitious oxidation during workup. Several other groups[3-5] have attempted the generation of **1** via the acidic hydrolysis of **2** (or the corresponding di-*t*-butoxy derivative), with no success. Under acidic conditions, the bis-carbamates are labile toward rearrangement or fragmentation.

It is not obvious why **1** should be so difficult to produce. Askani was able to synthesize the corresponding bicyclo[2.2.2] hydrazine **5**,[6] and related molecules, via saponification of the corresponding diethyl azodicarboxylate Diels-Alder adducts. The diimide-anthracene adduct **6** can be isolated by similar procedures.[7] Acyclic analogs have also been synthesized.[8] Nelsen[9] has shown that the rate of cycloreversion of the 2,3-dimethyl derivative of **1** to cyclopentadiene and azomethane is somewhat slower than that of the N,N'-dimethylated analog of the Corey-Mock diimide precursor, **6**. Hence, retro-Diels-Alder fragmentation of **1** should not preclude its synthesis. We now wish to report the successful isolation of the parent hydrazine **1**, and a preliminary investigation of its chemistry.



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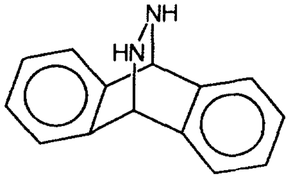

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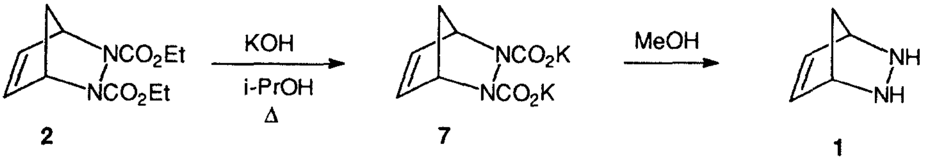
Our initial attempts confirmed the observations of previous workers[2] that basic ethanolysis of **2**, even with the Corey-Mock procedure,[7] does not give isolable amounts of **1**. However, isopropanol was found to be a more successful solvent for the saponification (Scheme II). Adduct **2** was heated in a solution of 1.2 M KOH in isopropanol for 2 h at 55 °C, under N_2. During this period, a white solid formed, which after cooling of the reaction mixture was collected, washed with cold isopropanol, and dried in vacuo. We believe this material to be bis-salt **7**, based on its subsequent chemistry. Dissolution of this solid in water at room temperature produced the immediate evolution of gas, which we presume to be CO_2. To isolate the hydrazine **1**, a methanol solution of **7** was attached to a series of two traps held at - 20 °C and - 78 °C, respectively, and vacuum was applied (0.1 torr). The temperature of the solution was held at 0 °C until most of the solvent had collected in the - 78 °C trap. The solution temperature was then raised gradually to 40 °C, during which time a white solid collected in the - 20 °C trap. The NMR spectra and reactivity of this solid, isolated in 40 % yield, are consistent with the hydrazine structure **1**: ^{1}H NMR ($CDCl_3$) δ 6.2 (2H, s), 4.2 (2H, s), 3.3 (2H, br s), 1.6 (1H, d, J = 8.4 Hz), 1.4 (1H, d, J = 8.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, ^{1}H coupled multiplicities and coupling constants in parentheses) δ 133.6 (d, J = 173 Hz), 61.5 (d, J = 157 Hz), 49.1 (t, J = 137 Hz) ppm.

Scheme II



Hydrazine **1** is extremely labile to oxidation. Exposure of a $CDCl_3$ solution of **1** to air at room temperature causes complete oxidation in several minutes to give cyclopentadiene and H_2O, as monitored by ^{1}H

NMR. Similarly, oxidation/trapping with excess 4-methyl-1,2,4-triazolinedione (MTAD) produces exclusively the corresponding cyclopentadiene/MTAD Diels-Alder adduct. Other oxidants give similar results. It has been previously shown that dihydropyridazines undergo spontaneous denitrogenation, even at extremely low temperatures.[8,10]

As suggested by previous workers,[2] **1** undergoes retro-Diels-Alder reaction readily to give cyclopentadiene and diimide. A solution of **1** in $CDCl_3$ or C_6D_6 at room temperature, under inert atmosphere, shows obvious decomposition in the NMR spectra after one hour at room temperature. As **1** decays, cyclopentadiene and the reduced adduct **3** both grow. With rigorous exclusion of air, no oxidation product **4** is observed. That diimide is produced, and is the progenitor of reduction product **3**, can be confirmed by decomposition of **1** in the presence of excess bicyclo[2.2.1]hepta-2,5-diene. Under these conditions, only cyclopentadiene and bicyclo[2.2.1]hept-2-ene are formed on thermolysis of **1**. The decomposition of **1** follows first order kinetics which can be monitored by NMR. At 45 °C, the rate of retro-Diels-Alder reaction is 1.02×10^{-4} s^{-1} in $CDCl_3$. For comparison, the rate of decomposition of the Corey-Mock[7] diimide precursor **6** is slightly higher, 3.28×10^{-4} s^{-1}, under identical conditions. These results rule out the other, more exotic, mechanistic proposals[2] for reaction of **1** (vide supra). In particular, the rate of decomposition of **1** is independent of the concentration of the diene, as long as enough diene is present to overcome reduction of **1**.

It is not clear why it is difficult to produce **1** with methodology effective for **5** and **6**. It is possible that the intermediate bis-CO_2 adduct of **1** formed during the saponification process is more labile than those of the [2.2.2]-hydrazines. The rapid generation of CO_2 on reaction of **7** with water is consistent with this possibility.[11] Once **1** is formed it decomposes fairly rapidly and would not survive the hydrolysis conditions. Our success at generating **1**, in contrast to previous attempts by others,[2-5] is apparently linked to the isolation of the bis-potassium salt **7**. This might be attributable to a lower solubility of **7** in isopropanol compared to methanol or ethanol. An alternative or additional factor might be the greater basicity of KOH in isopropanol than in the more polar alcohols. This procedure to prepare **1** should be generally useful for the synthesis of other sensitive cyclic hydrazines.[12] The bis-salt **7** can be kept at room temperature under N_2 without decomposition for at least one month, providing convenient storage of the hydrazine.

In principle, **1** represents an addition to the long list of diimide precursors available.[13] Nelsen has also shown that the dimethyl derivative of **1** produces primarily *cis*-azomethane on thermolysis.[9] A similar stereoselectivity in fragmentation of **1** would give *cis*-diimide, the reductively effective geometric isomer of this species. In addition to bicyclo[2.2.1]hepta-2,5-diene (vide supra), we have found that heating a methanol solution of bis-salt **7** at 55°C with azobenzene gave the reduction product hydrazobenzene. To obtain complete reduction of the substrate, however, a four-fold excess of **7** had to be added. Hence, the convenience of having a storable precursor from which diimide can easily be thermally generated must be balanced with problems in efficiency. It should be noted, however, that we made no attempts to optimize these reductions.

Acknowledgment. We thank the National Science Foundation (CHE 9215177) for generous support of this work.

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(11) Unfortunately, **7** is not soluble in D_6-DMSO, or other aprotic solvents that would permit the measurement of an NMR spectrum.

(12) Hydrazines **3** and **6**, as well as the 3-methyl and the 7-methyl derivatives of **1**, could be generated from the bis-salts by similar procedures.

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(Received in USA 14 June 1993; accepted 15 July 1993)