Communications

Long-Lived Trialkylhydroxylamine and *N*-Acyldialkylhydroxylamine Radical Cations

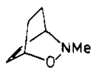
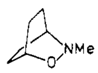
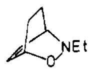
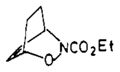
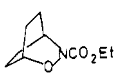
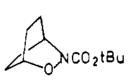
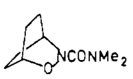
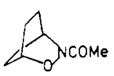
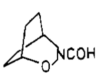
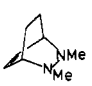
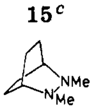
Summary: In contrast to other trialkyl- and *N*-acyldialkylhydroxylamines, 3-substituted-3-aza-2-oxabicyclo[2.2.2]octanes give long-lived radical cations.

Sir: Cyclic voltammetry (CV) studies of heteroatom-substituted dialkylamines R_2NX have shown that the thermodynamically significant formal potential for one-electron oxidation ($E^{\circ\prime}$) can be measured when $R_2NX^{+\cdot}$ is long-lived enough in the presence of neutral R_2NX. When the substituent is a powerful enough cation-stabilizing group, as for hydrazines ($X = NR'_2$)[1] and sulfenamides ($X = SR'$),[2] $E^{\circ\prime}$ measurements can be made with most alkyl groups R and R′. When less cation-stabilizing X groups are attached, $(R_2NX)^{+\cdot}$ decomposes too rapidly and $E^{\circ\prime}$ cannot be measured. α-Deprotonation at nitrogen is successfully blocked by using bicyclic alkyl groups which force the α-hydrogens to lie in the nodal plane of the partially filled p orbital at nitrogen of $R_2NX^{+\cdot}$. The most generally successful such Bredt's rule protected dialkylamino group is the 9-azabicyclo[3.3.1]nonyl group.[3] For example, both amine 1 (X = *t*-Bu) and chloroamine 2 (X = Cl) exhibit no cation radical decompostion by CV ($i_{ox}/i_{red} = 1$, even at slow scan rates), so their radical cations must last seconds under CV conditions. No cation radical decomposition was observed for 3 either, although sulfenamides with unprotected *N*-alkyl groups require rapid scan rates for detection of the reduction wave.[2] In contrast, hydroxylamine 4 showed no radical cation reduction wave, even at a 20-V/s scan rate.[3] Because the irreversible oxidation wave for 4 is near $E^{\circ\prime}$ for 3, we suggested that the thermodynamic ease of oxidation of sulfenamides and hydroxylamines is similar and that $4^{+\cdot}$ is only kinetically much less stable than $3^{+\cdot}$.[2]

1, X = *t*-Bu
2, X = Cl
3, X = SMe
4, X = OMe

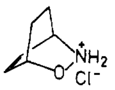
In this work we prepared oxygen Bredt's Rule protected hydroxylamine derivatives by employing the 3-aza-2-oxobicyclo[2.2.2]octyl system and report that this lengthens the trialkylhydroxyamine radical cation lifetime enough that the thermodynamics of electron loss may be studied.

Table I. CV Data[a] for Some 2-Oxa-3-azabicyclo[2.2.2]octane Derivatives

compound	$E^{\circ\prime}$ (ΔE_{pp}), V	scan rate, V/s
 6	0.78 (0.10)	5
 7	0.67 (0.09)	0.5
 8	0.75 (0.09)	0.2
 9	irrev ($E_p^{ox} = 1.45$)[b]	0.2
 10	1.38 (0.09)	0.2
 11	1.32 (0.08)	0.2
 12	1.15 (0.07)	0.2
 13	1.36 (0.07)	0.2
 14	1.52 (0.07)	0.2
 15[c]	0.17	0.2
 16[c]	0.07 (0.09)	0.2

[a] For acetonitrile solutions containing 0.1 M tetrabutylammonium perchlorate, vs. SCE, at 23 ± 1 °C, Pt, or Au electrode. [b] No reduction wave observed even at 10 V/s. [c] From: Nelsen, S. F.; Hollinsed, W. C.; Grezzo, L. A.; Parmelee, W. P. *J. Am. Chem. Soc.* **1979**, *101*, 7347.

We used the readily available cyclohexadiene, chloronitrosocyclohexane condensation product 5,[4] converting it to the N_3 alkylated and acylated hydroxylamines 6–14 shown in Table I by routine methods. The size of the reduction wave for 6–8 decreases with increasing concentration, indicating that the cation radicals are being de-



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(2) Nelsen, S. F.; Steffek, D. J.; Cunkle, G. T.; Gannett, P. M. *J. Am. Chem. Soc.* **1982**, *104*, 6641.
(3) Nelsen, S. F.; Kessel, C. R.; Brien, D. J. *J. Am. Chem. Soc.* **1980**, *102*, 702.
(4) (a) Arbuzov, Yu. A.; Markovskaya, A. *Bull Akad. Sci. USSR., Div. Chem. Sci.* **1952**, 355. (b) For a review, see: Hamer, J.; Mushtaq, A. in "1,4-Cycloaddition Reactions": Hamer, J., Ed.; Academic Press: New York, 1967; Chapter 12, p 419.

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protonated by neutral compound. Similar behavior was observed for unprotected trialkylsulfenamides.[2] More difficult oxidation of the unsaturated compound **6** than its saturated analogue **7** by 0.11 V is paralleled in the tetraalkylhydrazine series, where **16** oxidizes 0.10 V more easily than **15**. The fact that **6–8** give radical cations that are rather long-lived on the CV time scale verifies our previous contention that the problem with observing a reduction wave for **4**$^{+\cdot}$ was entirely kinetic and resulted from deprotonation α to oxygen. The data of Table I show that hydroxylamine **7** is 0.60 V (13.8 kcal/mol) thermodynamically harder to oxidize than is hydrazine **16**. Our previous study of 9-azabicyclo[3.3.1]nonyl derivatives suggests that about 0.32 ± .05 V of this increase in $E^{\circ\prime}$ can be assigned to the inductive effect of replacing the NR_2 group of hydrazine **16** by the OR group of hydroxylamine **7** (using $\sigma_I = 0.06$ for NR_2, 0.27–0.34 for OR). The rest of the increase in $E^{\circ\prime}$ presumably represents lowered resonance energy in the hydroxylamine radical cation compared to the hydrazine radical cation. Because steric factors favor hydroxylamine oxidation relative to hydrazine oxidation (**16**$^{+\cdot}$ has a methyl,methyl eclipsing interaction that is absent in **7**$^{+\cdot}$; and two nitrogens flatten in **16**$^{+\cdot}$, but only one in **7**$^{+\cdot}$), the resonance stabilization of a trialkylhydroxyamine radical cation is probably less than that of a hydrazine radical cation by more than the 6–7 kcal/mol estimated above.

Despite the thermodynamic difficulty of oxidizing the acylated compounds **10–14**, no radical cation decomposition was detected by CV. This result parallels the behavior of certain *N,N′*-diacylated dialkylhydrazines, which also show electrochemically reversible oxidation.[5] The $E^{\circ\prime}$ values of hydroxylamine derivatives **10–14** are far easier to consider than those of any acylated hydrazines, because of much decreased steric interactions in the oxidized form (the oxygen of **10–14** has no alkyl substituent syn to the nitrogen substituent, but all hydrazines must). Replacement of the N_3 methyl of **7** by C(=O)NMe$_2$ increased $E^{\circ\prime}$ 0.48 V, by C(=O)Me and C(=O)OR increased $E^{\circ\prime}$ 0.65–0.69 V, and by a formyl group increased $E^{\circ\prime}$ 0.85 V. Although these *N*-acylhydroxylamines probably exist in two conformations (*s*-cis and *s*-trans at the N_3—C(=O) bond), we have not as yet succeeded in observing splitting of the oxidation wave, which would be possible if *s*-cis and *s*-trans radical cations had significantly different energies and interconverted slowly. Rotation about the N—(C=O) bond is slow in the neutral compounds but probably much faster in the radical cations. We will consider these questions in detail in subsequent studies. The unsaturated alkoxycarbamate **9** gave only totally irreversible oxidation. We suggest that the allylic nature of the C_1–O_2 and/or C_4–N_3 bonds is responsible for the rapid radical cation decomposition, because **10**$^{+\cdot}$–**14**$^{+\cdot}$ are long-lived.

These results are consistent with the hypothesis that spin density at oxygen causes significantly more $C_\alpha H$ bond weakening than spin density at nitrogen or sulfur[2] and shows that Bredt's rule protection increases radical cation lifetime enough to make thermodynamic studies feasible on hydroxylamine derivatives. The limits of Bredt's rule protection in kinetically stabilizing radical cations which usually decay rapidly remain to be determined, but the bicyclo[2.2.2]octyl system is clearly a good one for protecting two centers simultaneously.[6]

Supplementary Material Available: Preparations and ^1H and ^{13}C NMR data for **5–14** (4 pages). Ordering information is given on any current masthead page.

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Photolysis of 4-Diazopyrrolidine-2,3-diones. A New Synthetic Route to Mono- and Bicyclic β-Lactams

Summary: A new synthesis of mono- and bicyclic β-lactams by the photorearrangement of 4-diazopyrrolidine-2,3-diones is described.

Sir: We report a new synthetic route to β-lactams that utilizes readily available precursors and is applicable to the synthesis of monocyclic as well as strained bicyclic examples; it involves the photolytic ring contraction of 4-diazopyrrolidine-2,3-diones to 3-carboxy-2-azetidinones. This new β-lactam synthesis is directly analogous to the Photo-Wolff rearrangement of 3-diazopyrrolidine-2,4-diones[1] and more remotely related to the pyrrolytic ring contraction of 4-azido-2-pyrrolinones[2-4] and the oxidative rearrangement of pyrrolidine-2,3-diones.[5] However, it appears to have the advantage of being more applicable to the synthesis of strained bicyclic β-lactams than are the analogies. In addition, the synthesis of 4-diazopyrrolidine-2,3-diones, as outlined here, is experimentally simple and starts with readily available precursors.

The starting 5-alkynyl-4-diazo-5-methoxypyrrolidine-2,3-diones (**5**) are conveniently prepared from 3,4-dichloro-*N*-cyclohexyldichloromaleimide (**1**; Scheme I). Alkynylation of **1** gave the corresponding 5-alkynyl-5-hydroxy derivatives in >80% yields. It should be noted that this route to 2-pyrrolinones introduces the synthetically versatile alkynyl group into the 5-position, and thus a variety and 4-alkylated derivatives of 2-azetidinones can be envisaged as arising via the methodology outlined here. Treatment of **2** with KN_3 in acetonitrile/18-crown-6 (1 equiv) for 10 days gave the azidopyrrolinones **3** in 58–63% yield. The amino derivatives *4* were then obtained by reduction of the azides (BH_4^-, C_2H_5OH, 0 °C) in 80–90% yield. The only step deserving of any detailed comment is the conversion of the aminopyrrolinones **4** to the diazo derivatives **5** (50–55%), which was accomplished by treating a biphasic mixture (0 °C) of CH_2Cl_2 and dilute HCl (1%) with $NaNO_2$ followed by the aminopyrrolinones. This is an unusual transformation for which little precedent exists[6] and is viewed as proceeding by the following sequence of steps: i.e., $\mathbf{4} \rightarrow \mathbf{6} \rightarrow \mathbf{7} \rightarrow \mathbf{5}$ (eq 1).

These cyclic diazo ketones were then subjected to photolysis (λ > 3000 Å) in methanol. Ring contraction (acyl

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(6) This transformation was suggested by our previous observation that 2-amino-3-chloro-1,4-naphthoquinone gives 2-diazobenzocyclohexa-1,3,4-trione upon treatment with sodium nitrite in aqueous acetic acid. See: Cajipe, G. J. B.; Landen, G.; Semler, B.; Moore, H. W. *J. Org. Chem.* **1975**, *40*, 3875.