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 σ_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]

(5) Nelsen, S. F.; Blackstock, S. C.; Rumack, D. T. *J. Am. Chem. Soc.* **1983**, *105*, 3115.

(6) We thank the CIC for a fellowship to J. T. C. and the National Institute of Health, under Grant GM-29549, for financial support of this work.

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., **4** → **6** → **7** → **5** (eq 1).

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

(1) Lowe, G.; Yeung, H. W. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2907. Lowe, G.; Ridley, D. *J. Chem. Soc., Chem. Commun.* **1973**, *328*. Stork, G.; Szajewski, R. P. *J. Am. Chem. Soc.* **1974**, *96*, 5787.

(2) Moore, H. W.; Hernandez, L.; Sing, A. *J. Am. Chem. Soc.* **1976**, *98*, 3728.

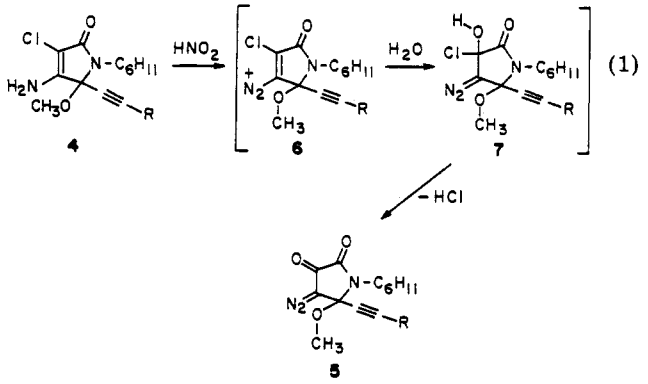
(3) Moore, H. W.; Hernandez, L.; Chambers, R. *J. Am. Chem. Soc.* **1978**, *100*, 2245.

(4) Moore, H. W.; Hernandez, L.; Kunert, D. J.; Mercer, F.; Sing, A. *J. Am. Chem. Soc.* **1981**, *103*, 1769.

(5) Rueppel, M. L.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 3877. Bender, D. R.; Brennan, J.; Rapoport, H. *J. Org. Chem.* **1978**, *43*, 3354.

(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.

0022-3263/83/1948-3365$01.50/0



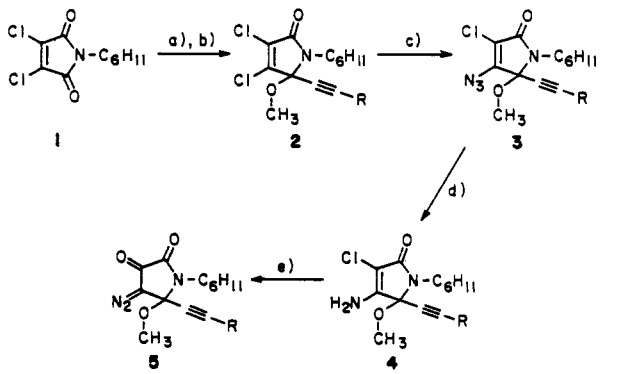
migration) was observed, and respectable yields (63–74%) of the 3-carbomethoxy-2-azetidinones **8a–c** were realized as a mixture of *Z* and *E* isomers (Scheme II). For comparison, the thermolysis (C_6H_6, 80 °C) of the 4-azido-2-pyrrolinones **3a–c** was also investigated, and this gave the 3-cyano-2-azetidinones **9a–c** in yields ranging from 55% to 87%. Here again, mixture of diastereomers resulted. This is of some significance since the previously studied ring contractions of all other 4-azido-5-alkoxy-2-pyrrolinones have been for examples that were monosubstituted at the 5-position; and these nearly always gave only one diastereomer of the corresponding 3-cyano-2-azetidinone.[4]

A typical procedure for the photo ring contraction follows: a solution of 614 mg (1.82 mmol) of **5a** in 500 mL of anhydrous methanol was cooled to −78 °C and subjected to photolysis (Hanovia 450-W lamp, Pyrex filter) under an argon atmosphere. After 1 h the solvent was removed and the crude product was analyzed by ^1H NMR, which revealed the diastereomeric mixture of β-lactams to be present is greater than 80% yield. Rapid filtration through a column of Florisil gave 465 mg (74%) of **8a** as a 5:1 mixture of diastereomers. Characteristic experimental procedures and structural data are available as supplementary material.

One of the prime objectives of this work was to investigate the possibility of utilizing the 4-diazopyrrolidine-2,3-dione ring contraction for the synthesis of bicyclic β-lactams. Our efforts were encouraged by the earlier report of Wasserman, Precopio, Liu,[7] who showed that the pyrrolinone **10** was available in one step from the condensation of mucochloric acid with penicillamine (Scheme III). Thus, a slight modification of this condensation was repeated with (±)-penicillamine to give a racemic mixture of **10** (R = H, 80%), and this was converted to the methyl esters in 80% yield.[8] Treatment of **10** (R = CH_3) with KN_3 in CH_3CN containing a trace of dibenzo-18-crown-6 gave the azide **11** in 40% yield. Azide **11** gave a complex mixture of products upon thermal decomposition. However, it was converted to the diazopyrrolinone **12** in 62% overall yield by the method utilized in the synthesis of the monocyclic series. The structure and relative stereochemistry of **12** were established by a complete X-ray analysis, which revealed the indicated trans relationship between the methine protons.[9] Photolysis of **12**, as a dilute THF solution in the presence of 1 equiv of diisopropylamine at −78 °C, gave the β-lactam **13** in 72% isolated yield:[10] mp 138–139 °C; IR ($CHCl_3$) cm^{-1} 1781, 1760, 1645; ^1H NMR ($CDCl_3$) δ 5.83 (d, J = 4 Hz, 1 H), 4.48 (s, 1 H), 4.30 (d, J = 4 Hz, 1 H), 4.25 (hep, J = 9 Hz, 1 H), 3.78 (s, 3 H), 3.45 (hep, J = 9 Hz, 1 H), 1.74 s, 3 H), 1.48 (s, 3 H), 1.40 (d, J = 9 Hz, 6 H), 1.23 (d, J = 9 Hz, 6 H); mass spectrum (CI), m/e M + 1 = 343. The H^1NMR spectrum of **13** reveals a trans relationship between the methine protons at positions 6 and 7.[11] This observation, in conjuction with the established stereochemistry of **12**, allows the complete stereochemical assignment of this new β-lactam to be as represented by structure **13**.

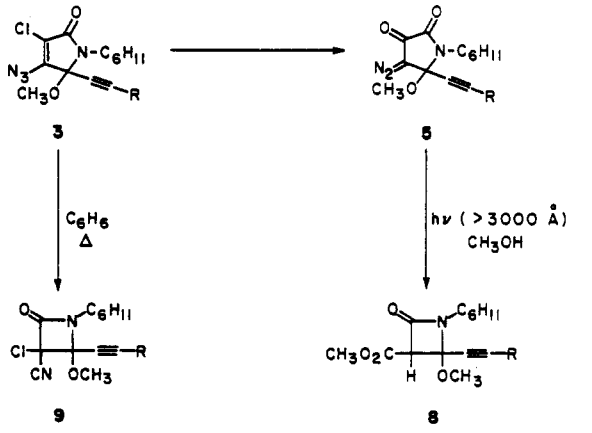
Even though the trans relationship between the protons at positions 6 and 7 in **13** is opposite to that of penicillin, the potential utilization of this methodology for the conversion of mucochloric acid or maleimide to a variety of other synthetic and natural bicyclic β-lactams presents a potentially important area for subsequent studies. This is of particular interest with regards to thienamycin and

Scheme I



(a) Li−≡−R, THF, −78°
(b) CH_3I, K_2CO_3, acetone
(c) KN_3, CH_3CN, (1eq.) 18-crown-6
(d) $NaBH_4$, C_2H_5OH, 0°
(e) $NaNO_2$, aq HCl, CH_2Cl_2, 0°

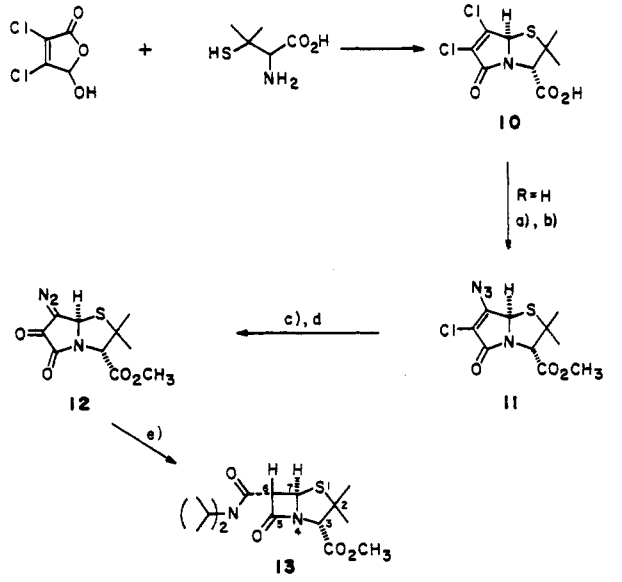
Scheme II



R	9	8
(a) $-C_6H_5$	87(3:1)	74(5:1)
(b) $-CH_2-O-CH_2C_6H_5$	60(5:1)	57(6:1)
(c) $-(CH_2)_2-CH_2-OTHP$	55(1:1)	63(>10:1)

(7) Wasserman, H. H.; Precopio, F. M.; Liu, T. C. *J. Am. Chem. Soc.* **1952**, *74*, 4093.
(8) The condensation was accomplished by using 1 equiv each of penicillamine, sodium chloride, and acetic acid in ethanol to give 80% of the δ-lactam thiazolidine **10**. The yield reported previously was 52% when the reaction was carried out by using penicillamine hydrochloride and sodium acetate as a buffer.
(9) We acknowledge Professor Robert Doedens for aiding in obtaining the X-ray structure of **12**.
(10) An analogous photolysis of **12** in the presence of benzylamine gave a lower yield of the corresponding β-lactam. When the trap was methanol rather than an amine, only a product corresponding to methanolysis of the β-lactam was isolated.
(11) The relative configuration at positions 6 and 7 was assigned on the basis of the coupling constants for the methine protons. See, for example: Banrow, K. D.; Spotswood, T. M. *Tetrahedron Lett.* **1965**, 3325.

Scheme III



its derivatives since the 6,7-trans stereochemistry is desirable in these cases.

Acknowledgment. We thank the National Institutes of Health (Al-15651) and the National Science Foundation (CHE-8025567) for financial support of the work.

Registry No. 1, 50343-26-5; **2a**, 86900-90-5; **2a**-ol, 86901-16-8; **2b**, 86900-91-6; **2c**, 86900-92-7; **3a**, 86900-93-8; **3b**, 86900-94-9; **3c**, 86900-95-0; **4a**, 86900-96-1; **4b**, 86900-97-2; **4c**, 86900-98-3; **5a**, 86900-99-4; **5b**, 86901-00-0; **5c**, 86901-01-1; *cis*-**8a**, 86901-02-2; *trans*-**8a**, 86901-03-3; *cis*-**8b**, 86901-04-4; *trans*-**8b**, 86901-05-5; *cis*-**8c**, 86901-06-6; *trans*-**8c**, 86941-19-7; *cis*-**9a**, 86901-07-7; *trans*-**9a**, 86901-08-8; *cis*-**9b**, 86901-09-9; *trans*-**9b**, 86901-10-2; *cis*-**9c**, 86901-11-3; *trans*-**9c**, 86941-20-0; (±)-**10**, 86901-12-4; (±)-**10** (methyl ester), 86901-13-5; (±)-**11**, 86901-17-9; (±)-**11** (amine), 86901-18-0; (±)-**12**, 86901-14-6; (±)-**13**, 86901-15-7; $LiC{\equiv}CC_6H_5$, 4440-01-1; $LiC{\equiv}CCH_2OCH_2C_6H_5$, 64080-63-3; $LiC{\equiv}C(CH_2)_3O$-THP, 85168-38-3; *dl*-penicillamine, 52-66-4; mucochloric acid, 766-40-5; diisopropylamine, 108-18-9.

Supplementary Material Available: Full experimental procedures and spectral data for compounds **2–5** and **8–13** (12 pages). Ordering information is given on any current masthead page.

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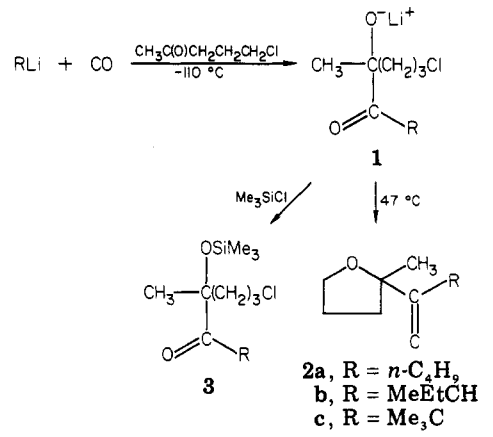
High-Yield Acyl Anion Trapping Reactions. Synthesis of Acyltetrahydrofurans

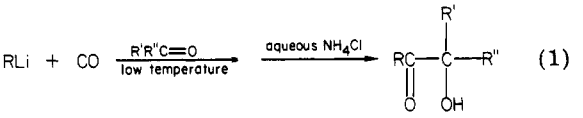
Summary: In situ generated acyllithium reagents add to the carbonyl function of lactones, usually with retention of the ring structure.

Sir: We have reported recently the nucleophilic acylation of ketones and esters by means of in situ generated

Scheme I



acyllithium reagents.[1] The latter were prepared by the carbonylation of alkyllithium reagents at low (−110 °C) temperature. Such reactions provided a facile, high-yield route to α-hydroxy ketones (eq 1). In the case of esters, α-diketones were the final products obtained.



(1)

In order to demonstrate that this novel chemistry may be applied to the synthesis of organic compounds other than simple α-hydroxy ketones and α-diketones, we have used our in situ direct nucleophilic acylation technique to prepare acyltetrahydrofurans by two different routes.

In one of these routes, the acyllithium reagent was generated at −110 °C in the presence of 2 molar equiv of 5-chloro-2-pentanone in a 4:4:1 THF/Et_2O/pentane solvent system.[2] The reaction mixture subsequently was heated at reflux (47 °C) for 2 h. The mixture was concentrated, treated with pentane to precipitate lithium salts, and filtered. The filtrate was concentrated and the residue examined by GLC. When *n*-butyllithium was the lithium reagent that was used, one product was present in 92% yield. This was identified as 2-pentanoyl-2-methyltetrahydrofuran (**2a**).[3] Scheme I summarizes the chemistry involved in this simple one-pot process. Intermediate **1** could be intercepted by adding trimethylchlorosilane to the reaction mixture at −110 °C to give **3**. Similar reactions in which *sec*-butyllithium and *tert*-butyllithium were used gave **2b** (95%) and **2c** (80%), respectively. This concept should be extendable to the preparation of other cyclic ethers containing an acyl function in the 2-position.

(1) Seyferth, D.; Weinstein, R. M.; Wang, W.-L. *J. Org. Chem.* **1983**, *48*, 1144.
(2) For details of the general procedure, see ref 1.
(3) Anal. Calcd for $C_{10}H_{18}O_2$: C,70.55; H, 10.66. Found: C, 70.46; H, 10.52. IR (film) ν(C=O) 1708 (s); ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, 3 H, CH_3 of the *n*-C_4H_9 group, J = 7.35 Hz), 1.21–1.35 (m, 5 H, contains a singlet at δ 1.30 for the $CH_3(H_c)$ group), 1.45–1.94 (m, 5 H), 2.19 (m, 1 H), 2.58 (complex m, 2 H, H_b (diastereotopic)), 3.96 and 3.82 (m, 1 H each, 2 H_a); ^{13}C NMR (gated decoupled, 67.5 MHz, $CDCl_3$) δ 13.8 (q, C_d, J = 124 Hz), 22.3, 23.8, 25.2, 25.7 (unresolved multiplets in the ^1H-coupled spectrum, includes the three CH_2s of the *n*-C_4H_9 group and the 2-methyl substituent), 35.0 (t, C_c, J = 129 Hz), 36.3 (t, C_c, J = 129 Hz), 68.7 (t, C_b, J = 145 Hz), 88.5 (s, C_a), 215 (s, C=O).