Table I. Electrolysis of Allyl Quaternary Salts

reactant	concn, M	current, A	no. of Faradays passed	solvent	electrolyte	% yield of dimer 3
2	0.6	0.25	0.014	DMF		26.3
2	0.6	0.5	0.015	DMF		21.1
2	0.6	1.0	0.012	DMF		28.0
2	0.6	0.5	0.019	DMF	NH_4NO_3	32.0
2	0.6	0.5	0.028	DMF	$Et_4N^+NO_3^-$	11.3
2	0.6	0.5	0.019	Me_2SO	NH_4NO_3	24.3
2	0.6	0.5	0.028	CH_3CN		6.0[a]
2	0.6	0.5	0.028	CH_3CN		trace[b]
2	0.3	0.5	0.009	DMF	NH_4NO_3	26.3
2	1.2	0.5	0.040	DMF	NH_4NO_3	32.6
1	0.3	0.5	0.026	DMF		3.7[c]
1	0.3	0.25	0.031	DMF	NH_4NO_3	23.8
1	0.3	0.5	0.028	DMF	NH_4NO_3	23.0

[a] Temp 15 to 34 °C. [b] Temp -30 to -16 °C. [c] Moisture present.

without added electrolyte in order to investigate the effect of added electrolyte. The presence of ammonium nitrate generally resulted in higher yields of the coupled product. At constant current, the voltage increases considerably as the electrolysis proceeds when no electrolyte is present. In the presence of added electrolyte, however, the voltage remains relatively constant, thus decreasing the possibility of side reactions. The fact that tetraethylammonium nitrate is hygroscopic may account for the lower yield when this electrolyte was used.

In conclusion, this investigation has shown that a coupling reaction does in fact occur in the electrolysis of allyl quaternary ammonium and phosphonium salts at an aluminum cathode in nonaqueous solvents to form 1,5-hexadiene. The coupling reaction is favored by the use of relatively high concentrations of the allyl quaternary salt with ammonium nitrate as the added electrolyte and DMF as the solvent.

Experimental Section

Gas-liquid chromatography (GLC) was carried out with a Varian Aerograph Model 90-P with a CDS 111 integrator and a 6-ft column of Carbowax 1500 on Chromosorb W. NMR spectra were obtained with a Varian Model A-60 and IR spectra were recorded on a Beckman Acculab 1 spectrophotometer. A Hewlett-Packard 0-60V DC power supply, Model 6274B, was used in the electrolyses.

Materials. Allyltriphenylphosphonium nitrate (1), mp 164-165 °C, was prepared by the reaction of allyl bromide with triphenylphosphine in acetone followed by treatment of the resulting allyltriphenylphosphonium bromide with aqueous $AgNO_3$. The product was recrystallized from methyl ethyl ketone/DMF. 1 and 2 (Eastman) were dried in vacuo over P_2O_5. DMF and Me_2SO were dried by refluxing over calcium hydride followed by distillation in vacuo and final drying over molecular sieves. Acetonitrile was dried by distillation from P_2O_5.

Electrolysis Procedure. A water-jacketed polarographic cell of 60-mL capacity was used which was fitted with a rubber stopper through which a capillary tube for the passage of nitrogen, a platinum wire anode, and two aluminum cathodes were inserted. The Pt wire was centered between the two Al cathodes which were placed 1.5 cm apart. The immersed area of the each cathode was 3 cm^2 (2 cm high and 1.5 cm wide) and the anode was also immersed to a depth of 2 cm.

The allyl quaternary ammonium or phosphonium salt was dissolved in 40 mL of the solvent and cold water was circulated through the jacket of the cell throughout the electrolyses. The electrolyses were conducted at constant current which was provided by the variable voltage power supply. When an added electrolyte was used, its concentration was 0.1 M. Samples were withdrawn at regular intervals from the electrolysis solution and analysed by GLC at 75 °C. When 2 was electrolyzed three peaks, other than that of the solvent, were observed. They were found to be due to propene, 1,5-hexadiene, and triethylamine, in order of increasing retention time. When 1 was electrolyzed propene and 1,5-hexadiene were detected. The concentration of 1,5-hexadiene in each sample was found by integration and comparison with a standard containing a known concentration of 1,5-hexadiene in the solvent. Electrolyses were discontinued when no further increase in concentration occurred (generally after 1-3 h).

The identity of the product was confirmed by fractional distillation of the combined products of several electrolyses of 2. A colorless liquid, bp 60-65 °C, was obtained, shown by NMR and IR to consist of 1,5-hexadiene together with a small amount of triethylamine.

The results of the electrolyses are summarized in Table I.

Registry No. 1, 35171-86-9; 2, 29443-23-0; 3, 592-42-7; allyl bromide, 106-95-6; triphenylphosphine, 603-35-0.

Anti-Bredt Molecules. 2.[1] 1-Azabicyclo[3.3.1]nonan-2-one, a New Bicyclic Lactam Containing Bridgehead Nitrogen

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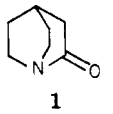
Introduction

Until recently, bicyclic lactams containing bridgehead nitrogen had been very difficult, if not impossible, to synthesize. In 1938, Lukes[3] attributed these difficulties to the lack of resonance stabilization of the N—C=O moiety in the same manner that Bredt's Rule[4] forbids bridgehead olefins. However, this did not deter synthesis chemists from attempting to synthesize these compounds. In 1957, Yakhontov and Rubstov[5] reported the synthesis of 1-azabicyclo[2.2.2]octan-2-one (1).



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More conclusive was the synthesis of 2,2-dimethyl-1-azabicyclo[2.2.2]octan-2-one and 2,2,6-trimethyl-1-azabi-

(1) Paper 1: H. K. Hall, Jr., and R. C. Johnson, *J. Org. Chem.*, 37, 697 (1972).
(2) Department of Nutrition and Food Sciences, College of Agriculture, University of Arizona.
(3) R. Lukes, *Collect. Czech. Chem. Commun.*, 10, 848 (1938).
(4) J. Bredt, H. Thouet, and J. Schmitz, *Justus Liebigs Ann. Chem.*, 437, 1 (1924).
(5) L. N. Yakhontov and M. V. Rubstov, *J. Gen. Chem. USSR (Engl. Transl.)*, 27, 83 (1957).

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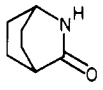
cyclo[2.2.2]octan-2-one by Pracejus[6-8] by reaction of the corresponding acid chloride–amine hydrochloride salts with triethylamine in either. The low-melting lactams were found to have unusually high carbonyl infrared absorption frequencies. They were easily hydrolyzed in water and polymerized on standing.

These investigators stressed the lack of N—C=O resonance interaction as the chief obstacle to synthesis. However, ring strain and H–H crowding should be considered as additional contributors to the unusual properties of these compounds. The polymerizability of 2-azabicyclo[2.2.2]octan-3-one (**2**)[9] and the strain implied thereby, must be due to its rigid two-boat conformation since N—C=O resonance is uninhibited in this structure.

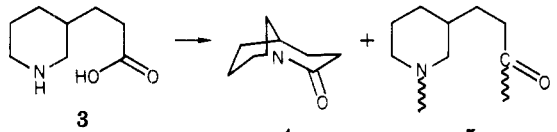


2

Bicyclo[3.3.1]nonanes generally exist in two-chair conformations.[10] The synthesis and properties of 1-azabicyclo[3.3.1]nonan-2-one might shed more light on the relative contributions of resonance stabilization and conformational strain to the properties of N-bridgehead lactams.

Results and Discussion

Synthesis of 1-Azabicyclo[3.3.1]nonan-2-one (4). The dehydration of β-(3-piperidyl)propionic acid (**3**) was studied. The main product, as described earlier,[11] was polyamide **5**. However, bicyclic lactam **4** was also obtained



3 **4** **5**

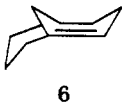
as a waxy solid which sublimed under vacuum during the reaction. Attempts to depolymerize **5** by long heating under vacuum[12] gave no more **4**.

Purification of **4** by resublimation at room temperature under high vacuum was rapid and afforded pure material, mp 83 °C, in 2.5% yield.

We were unsuccessful in synthesizing **4** by the acyl chloride hydrochloride–triethylamine route.[5-8]

Physical Properties of 4. The lactam was soluble in the usual organic solvents and in water and was somewhat hygroscopic.

The NMR spectrum was consistent with the structural assignment. The most remarkable feature was a doublet, representing one hydrogen, centered at δ 4.10. Wiseman and Marshall[13-15] showed that the homomorphic bridged olefin bicyclo[3.3.1]non-1-ene (**6**) existed in the chair–boat conformation in order to place the trans double bond in the largest ring. Accordingly we write **4** in the chair–boat conformation. The downfield absorption of one hydrogen



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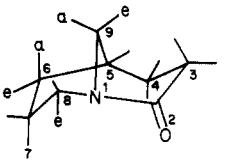

4

is then explained by its assignment to the equatorial hydrogen at C8. In the chair–boat conformation, this hydrogen is in the anisotropic cone of the C=O group.

The infrared spectrum showed a sharp, strong carbonyl absorption at 1680 cm^{-1}. This is not far from the absorption expected for a tertiary amide and suggests substantial π character in the N—C=O bond. This again supports the chair–boat assignment for **4**. This conformation is energetically reasonable, in that the amide resonance stabilization energy, about 20 kcal mol^{-1}, is greater than that, about 12 kcal mol^{-1}, required to force a cyclohexane ring into the boat form.

Finally, the mass spectrum of **4** showed the parent molecular ion and a cracking pattern consistent with the assigned structure.

Chemical Properties. Once prepared, lactam **4** was reasonably stable and could be stored at 0 °C without change. No reaction was observed upon heating with water at 100 °C. It hydrolyzed rapidly when HCl was added to the D_2O solution at 28 °C. The product was the hydrochloride of amino acid **3**.

Polymerizability is a powerful tool for the detection of ring strain.[1,9,11,16] Oligomerization of **4** occurred immediately on treatment with 85% phosphoric acid, and heating this reaction mixture to 100 °C resulted in formation of polyamide **5**.

Heating **4** at 125 °C with either *p*-toluenesulfonic acid monohydrate or potassium *tert*-butoxide gave no polymer.

Accordingly **4** is not greatly different from ordinary lactams but does possess enough strain to polymerize with the very active initiator phosphoric acid.[16] Because the N—C=O overlap is reasonably complete in monomer **4** (as in polymer **5**), the strain presumably resides in the boat portion of the chair–boat conformation. It is this boat strain energy which is relieved on ring-opening polymerization, just as in **1**.

Lactam **4** is the only bicyclo[3.3.1]nonane monomer yet reported to polymerize.

Experimental Section

All infrared spectra were recorded on a Perkin-Elmer 710 spectrophotometer. NMR spectra were taken on a Varian T-60 spectrometer. Evaporations under vacuum were carried out with a Buchi Rotoevaporator-R apparatus. Melting points were recorded on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Elemental analyses and mass spectra were obtained from the University Analytical Center at the University of Arizona.

1-Azabicyclo[3.3.1]nonan-2-one (4). Amino acid **3**, 1.0 g (0.0064 mol), was dried under vacuum in a 50-mL round-bottom flask at 65 °C. The flask was connected to two receiving flasks in series and placed in a Buchi Kugelrohr oven. The temperature was raised to 180 °C in 14 min after which a vacuum of 0.05 torr was applied while the flask was rotated. The second receiving flask was cooled by bathing it in acetone. The oven temperature was raised slowly to 285 °C over 1 h. After a total of 2.5 h, the vacuum was released and the two receiving flasks were placed immediately under a dry nitrogen atmosphere. In the sublimation flask was hard, glassy polyamide.[11] In the second receiving flask

(6) H. Pracejus, *Chem. Ber*, **92**, 988 (1959).
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(9) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **80**, 6412 (1958).
(10) J. A. Peters, *Synthesis*, 321 (1979).
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(12) W. H. Carothers, *Chem. Rev.*, **8**, 353 (1931).
(13) J. R. Wiseman, *J. Am. Chem. Soc.*, **89**, 5966 (1967).
(14) J. R. Wiseman, *J. Am. Chem. Soc.*, **92**, 956 (1970).
(15) J. A. Marshall and H. Faubl, *J. Am. Chem. Soc.*, **92**, 948 (1970).
(16) H. K. Hall, Jr., *J. Am. Chem. Soc.*, **80**, 6404 (1958).

was the desired lactam **4**. This waxy solid, 70 mg, mp 77–79 °C, was removed with a spatula and stored under dry nitrogen. Two successive sublimations at 25 °C (0.05 torr) yielded 25 mg of **4**: mp 82–83 °C; IR (film) 2915 (s, CH_2), 2860 (m, CH_2), 1680 (s, C=O), 1460 and 1370 (s), 1245, 1020 (s), no OH or NH; NMR ($CDCl_3$) δ 1.53 (6 H, br m, methylene H's at C_4, C_6, C_7), 2.35 (4 H, one peak, CH_2 at C_3 and axial H's at C_8 and C_9), 3.10 (2 H, two peaks, equatorial H at C_9 and C_5), 4.10 (1 H, br d, equatorial H at C_8); mass spectrum, *m/e* 139 (parent; calcd 139.2), 111 (M − C=), 83 [base, M − CH_2CH_2C=O (leaving the positively charged piperidine ring)], 55 (M − CH_2CH_2C=O − CH_2=CH_2). Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.15; H, 9.62; N, 9.89.

Hydrolysis Studies. Lactam **4** was unchanged after 1 week at 28 °C in D_2O (by NMR) or after 6 h at 100 °C.

Lactam **4** was dissolved in D_2O and gaseous hydrogen chloride was passed in. An exothermic reaction occurred. The NMR spectrum of the resulting solution was identical with that of an authentic sample of β-(3-piperidyl)propionic acid hydrochloride, and the doublet at δ 4.40 in the spectrum of **4** had vanished.

Polymerization Studies. Lactam **4**, 35 mg, was placed in a vial to which was added 20 mg of 85% phosphoric acid (1 drop) by pipet. Infrared analysis immediately after mixing afforded a spectrum with broad absorption at 1640 cm^{-1}, indicating rapid oligomerization of the lactam. An identical mixture was heated to 100 °C in 20 min and formed polyamide **5**.

Heating **4** with either *p*-toluenesulfonic acid monohydrate or potassium *tert*-butoxide at 125 °C for 6 h gave no polyamide.

Registry No. **3**, 1822-31-7; **4**, 74331-49-0; **5** homopolymer, 74331-33-2; **5** repeating unit, 74331-34-3.

O-(2-Acetoxycyclohexyl)-*N*-isopropylhydroxylamine: A Striking Inertness of Acyl Carbon toward an Intramolecular Hydroxylamine Function

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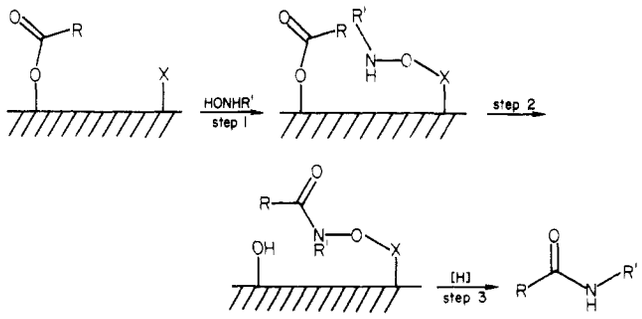
Received September 18, 1979

We have previously outlined a new strategy for peptide bond formation in which the amide function is generated by an intramolecular acylation, preceded by trapping of the nitrogen component of the amide at an electrophilic site of an ester of the acyl component (prior amine capture).[1] Rapid intramolecular O,N acyl transfer is a necessary condition for any structure that can be used with this strategy, and as we have reported for a number of peptide-derived model systems, this condition is difficult to achieve.[2] Accordingly, we are screening a variety of structures that place acyloxy and amino functions in proximity. A structure that allows rapid and clean intramolecular acyl transfer (1) in an unhindered case and (2) in hindered cases[2] (Ala-Val or Val-Val couplings) gives us a promising lead for developing the remaining chemical features that are required for a successful prior amine capture system. In this note we report that a candidate involving N-oxygenated derivatives fails a first test of rapid acyl transfer in an unhindered model case.

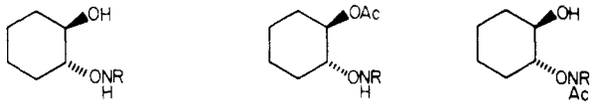
Derivatives of *N*-hydroxy-α-amino acids have been reported.[3] Hydroxylamine itself is noted for the rapidity

Scheme I



of its reactions with both activated and simple esters;[4] moreover, both the nitrogen and oxygen of hydroxylamine exhibit enhanced nucleophilic reactivity. We envisaged a reaction sequence similar to that of Scheme I, in which a capture step (step 1) involves reaction of the unhindered oxygen with an electrophilic site and a cleavage step (step 3) is carried out reductively. Before considering means of achieving these steps, we had to establish that the nucleophilic reactivity of hydroxylamines toward simple esters is retained for an intramolecular reaction involving an *O*,*N*-dialkylhydroxylamine.

Ideally, a model for step 2 of Scheme I should position the carbonyl of the ester function five or six atoms removed from the nitrogen of the hydroxylamine function, which should bear the side-chain residues of a simple amino acid derivative. Since species **1** were expected to be available from the reactions of cyclohexene oxide with oxime salts, followed by reduction, the *O*-acyl derivatives (**2**) were natural choices for models.[5]



1a, R = *i*-Pr
b, R = $CHMeCO_2Et$

2a, R = *i*-Pr
b, R = $CHMeCO_2Et$

3, R = *i*-Pr

Reactions of cyclohexene oxide with the oxime of ethyl pyruvate failed to give the desired product under a variety of reaction conditions. However, acetoxime was found to react under basic conditions with cyclohexene oxide to give the desired *O*-alkyl oxime, which was hydrogenated to yield **1a** (59%, overall). The *O*-acetyl derivative, **2a**, was obtained in a novel two-step procedure in which **1a** is first N-acetylated to form **3**, which is isomerized by treatment with 12 N HCl to the hydrochloride salt of **2a**. The latter is expected to approximate the steric features of an alanine derivative, **2b**.

Neutralization of this salt with triethylamine provided the desired hydroxylamine derivative, **2a**, which proved to be surprisingly resistant to O,N acyl transfer. No transfer was observed in $CDCl_3$ or Me_2SO-d_6 within 24 h, and the substance was recovered unchanged from a Kugelrohr distillation at 100 °C for 30 min (0.001 mm). Although there is clearly a mechanism that allows rapid equilibration of **2a** and **3** under strongly acidic conditions, the nitrogen of **2a** shows no hint of nucleophilicity toward the neighboring ester carbonyl under neutral or mildly basic conditions.

It is clear that this hydroxylamine derivative shows none of the special reactivity exhibited by hydroxylamine itself toward acyl carbon.[4] Instead, the oxygen of this derivative

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(3) For examples, see (a) T. Polański and A. Chimiak, *Tetrahedron Lett.*, 2453 (1974); (b) T. Kolasa and A. Chimiak, *Tetrahedron*, **30**, 3591 (1974); (c) E. Buehler and G. B. Brown, *J. Org. Chem.*, **32**, 265 (1967).
(4) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 1778 (1960).
(5) Inspection of models indicates that the tetrahedral intermediate for O → N acyl transfer can assume a strain-free *trans*-decalin-like conformation.

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