the percentage composition listed in Table I. Small amounts of *p*-tolyl disulfide and benzophenone ketazine were also formed.

Reaction of 6.—A similar decomposition of **6** (50 mmol) in NMP (100 ml) at 160–180° for 1 hr gave a combined yield of 70% of product, isolated exactly as above and with the composition given in Table I.

Registry No.—2, 883-40-9; *p*-toluenesulfinic acid, 536-57-2; **6**, 17447-59-5; NMP, 872-50-4.

Transannular Nitrogen–Carbonyl Interaction. Generation of an α-Acetoxy Quaternary Ammonium Salt

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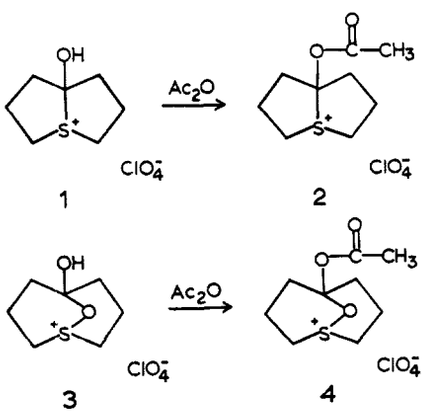
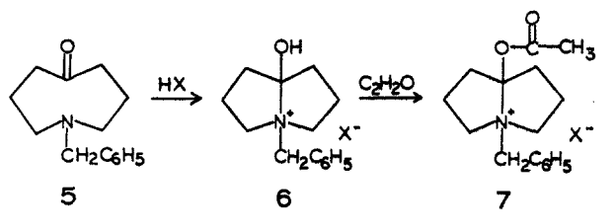
Earlier work on transannular interactions and reactions in this laboratory provided examples of α-acetoxysulfonium salts[1] and -oxosulfonium salts.[2,3]

For example, it was found that the perchlorate salt of 1-thiacyclooctan-5-one, which is in the transannular form 5-hydroxy-1-thioniabicyclo[3.3.0]octane perchlorate (1),[4] was converted with acetic anhydride into 5-acetoxy-1-thioniabicyclo[3.3.0]octane perchlorate (2).[1] The salt of 1-thiacyclooctan-5-one 1-oxide, also in the transannular form 5-hydroxy-9-oxa-1-thioniabicyclo[3.3.1]nonane perchlorate (**3**), gave 5-acetoxy-9-oxa-1-thioniabicyclo[3.3.1]nonane perchlorate (**4**) with acetic anhydride at room temperature.[2]



The salts of 1-alkyl-1-azacyclooctan-5-ones generally exist in the transannular form,[5,6] and we have now been able to acetylate the α-*t*-hydroxyl group of the transannular salt of an eight-membered-ring amino ketone by means of ketene.[7] Specifically the perchlorate and picrate salts of 1-benzyl-1-azacyclooctan-5-one (**5**)[8] are in the transannular form (**6a, b**), as evidenced by their infrared and nmr spectra. Neither salt exhibits ir absorption in the region 1620–1800 cm^{-1}, and both show hydroxyl absorption. The nmr spectrum of the perchlorate shows a singlet for the benzyl CH_2 protons in both acetonitrile-d_3 and trifluoroacetic acid. Splitting of



a, X = ClO_4; b, X = $C_6H_2N_3O_7$

these protons would be expected if the salt were in the alternative N-protonated form. The hydroxy proton of **6a** is observed in acetonitrile-d_3 as a broad singlet, δ 5.1–5.7, which disappears upon the addition of deuterium oxide.

The reaction of 1-benzyl-5-hydroxy-1-azoniabicyclo[3.3.0]octane perchlorate (**6a**) and of the picrate (**6b**) in acetonitrile with ketene led to 5-acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane perchlorate and picrate (**7a, b**). The structure proof was based on elemental analyses and on ir and nmr spectral evidence. Each compound exhibits only one ir absorption maximum in the carbonyl region (ν_{max}^{KBr} 1746 cm^{-1} for **7a**, 1750 cm^{-1} for **7b**) corresponding to an ester function. The nmr spectrum of the perchlorate **7a** is much like that of its precursor **6a** with the exception of a new sharp singlet at δ 2.20 (CD_3CN) and loss of the signal for the hydroxyl proton. For comparison, the corresponding 1-thionia analog **2** had ν_{max}^{Nujol} 1737 cm^{-1} (C=O)[1] and δ 2.33 in CF_3COOH (CH_3CO).[2]

The prediction that 5-acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane perchlorate (**7a**) would behave as a powerful acetylating agent was verified qualitatively in two rather extreme examples. Acetylation of piperidine with **7a** at −20° in methylene chloride solution was complete in less than 2 min. Acetylation of potassium acetate to give acetic anhydride was accomplished in a melt of the two solids within a total manipulation time of less than 5 min.

Experimental Section

1-Benzyl-5-hydroxy-1-azoniabicyclo[3.3.0]octane Perchlorate (6a).—This salt was obtained quantitatively from 1-benzyl-1-azacyclooctan-5-one[8] and was recrystallized as colorless needles from acetone–ether: mp 144–145.5°; $\nu_{max}^{Fluorolube}$ 3260 cm^{-1}; ν_{max}^{KBr} 3290 cm^{-1}; ν_{max}^{Nujol} 3280 (OH), no absorption 1620–2000 cm^{-1}; nmr (CD_3CN) δ from TMS 2.0–2.6 (8 H), 2.85–3.4 (2 H), 3.5–4.0 (2 H) (all series of multiplets, ring protons), 4.25 (2 H, s, benzyl CH_2), 5.1–5.7 (1 H, br s, OH, disappears with D_2O), 7.74 (5 H, s, C_6H_5). In trifluoroacetic acid the nmr spectrum was similar except that no signal for the OH proton was observable.

(1) N. J. Leonard, T. W. Milligan, and T. L. Brown, *J. Amer. Chem. Soc.*, **82**, 4075 (1960).
(2) N. J. Leonard and C. R. Johnson, *ibid.*, **84**, 3701 (1962).
(3) N. J. Leonard and W. L. Rippie, *J. Org. Chem.*, **28**, 1957 (1963).
(4) For current nomenclature, see IUPAC 1957 Rules, *J. Amer. Chem. Soc.*, **82**, 5545 (1960), especially p 5572.
(5) (a) N. J. Leonard, J. A. Adamcik, C. Djerassi, and O. Halpern, *ibid.*, **80**, 4858 (1958); (b) N. J. Leonard, D. F. Morrow, and M. T. Rogers, *ibid.*, **79**, 5476 (1957), and earlier papers in the series.
(6) (a) N. J. Leonard, *Rec. Chem. Progr.*, **17**, 243 (1956); (b) N. J. Leonard and M. Ōki, *J. Jap. Chem.*, **10**, 1003 (1956).
(7) NOTE ADDED IN PROOF.—R. A. Johnson, M. E. Herr, H. C. Murray, and G. S. Fonken [*J. Org. Chem.*, **33**, 3187 (1968)] have converted **6** into **7** by warming with acetic anhydride on the steam bath.
(8) N. J. Leonard and T. Sato, *ibid.*, in press.

Anal. Calcd for $C_{14}H_{20}ClNO_5$: C, 52.91; H, 6.34; N, 4.41. Found: C, 52.87; H, 6.34; N, 4.20.

5-Acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane Perchlorate (7a).—To a solution of 0.50 g (0.16 mmol) of 1-benzyl-5-hydroxy-1-azoniabicyclo[3.3.0]octane perchlorate in 75 ml of anhydrous acetonitrile was added ketene at 0°, with stirring, by passing a dry nitrogen stream over liquid ketene at −20°. After addition of ketene for 15 min, during which the colorless solution turned yellow-orange. The solution was treated with charcoal, filtered, and concentrated to give a light yellow oil. Recrystallization from acetonitrile–ether gave colorless needles: mp 194–195° (reported[7] mp 190–195°, then mp 203–204°); yield 0.31 g (53%); ν_{max}^{KBr} 1746 cm^{-1}; ν_{max}^{Nujol} 1755, 1080, 710 cm^{-1}; nmr (CD_3CN) δ 2.20 (3 H, s, CH_3CO), 1.9–2.8 (8 H, series of multiplets, ring protons), 2.9–4.0 (4 H, series of multiplets, ring protons), 4.50 (2 H, s, benzyl CH_2), 7.53 (5 H, s, C_6H_5).

Anal. Calcd for $C_{16}H_{22}ClNO_6$: C, 53.41; H, 6.16; N, 3.89. Found: C, 53.49; H, 6.17; N, 3.98.

1-Benzyl-5-hydroxy-1-azoniabicyclo[3.3.0]octane Picrate (6b).—This salt was obtained from 1-benzyl-1-azacyclooctan-5-one:[8] mp 207–208°; ν_{max}^{Nujol} 3100, 1625, 1607, 1565, 1462, 710 cm^{-1}; ν_{max}^{KBr} 3180, 1620, 1580, 1430, 1320, 710 cm^{-1}.

Anal. Calcd for $C_{20}H_{22}N_4O_8$: C, 53.81; H, 4.97; N, 12.55. Found: C, 54.04; H, 4.88; N, 12.21.

5-Acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane Picrate (7b).—The picrate was prepared from **6b** and ketene in the same manner as described for the perchlorate salt to yield yellow needles: mp 124–125°; yield 50%; ν_{max}^{KBr} 1750 cm^{-1}; nmr (CD_3CN) δ 2.21 (3 H, s, CH_3CO), 2.05–2.83 (8 H, series of multiplets, ring protons), 3.0–4.0 (4 H, series of multiplets, ring protons), 4.49 (2 H, s, benzyl CH_2), 7.53 (5 H, s, C_6H_5), 8.58 (2 H, s, picrate H's).

Anal. Calcd for $C_{22}H_{24}N_4O_9$: C, 54.10; H, 4.95; N, 11.47. Found: C, 54.37; H, 5.05; N, 11.77.

Acetylation of Piperidine with 5-Acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane Perchlorate (7a).—To 24 mg (0.28 mmol) of piperidine in 60 ml of methylene chloride was added 50 mg (0.14 mmol) of 5-acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane perchlorate at −20° with magnetic stirring. After 2 min, the solution was concentrated under vacuum pump pressure at 0° to a yellow oil. The time for concentration was less than 6 min. The presence of N-acetylpiperidine and 1-benzyl-1-azacyclooctane-5-one was evidenced by both thin-layer chromatography and by comparison of the nmr spectrum of the mixture with the spectra of the authentic samples. No starting material (**7a**) was found in the reaction mixture by either method of analysis.

Acetylation of Potassium Acetate with 5-Acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane Perchlorate (7a).—A sealed capillary tube containing 6 mg (16.7 μmol) of 5-acetoxy-1-benzyl-1-azoniabicyclo[3.3.0]octane perchlorate and 3 mg (30.6 μmol) of vacuum dried potassium acetate[9] was heated at 195° for 1 min, during which melting occurred. The end of the tube containing the melt was cooled to −78°, and the upper two-thirds of the tube was heated with an electric dryer to cause volatile materials to condense in the lower part of the tube.

Heating of the lower third of the capillary tube then served as a gas chromatograph inlet system. Analysis of the volatile components using an 8 ft, 20% diisodecyl phthalate column on Chromosorb W led to identification of acetic anhydride as the major volatile component of the reaction mixture. Comparison of the peak areas of the reaction mixture with peak areas of known amounts of acetic anhydride generated using a similar capillary inlet system indicated that greater than 90% of the acetic anhydride expected was produced in the acetylation reaction. The presence of 1-benzyl-1-azacyclooctane-5-one was shown by thin-layer chromatographic analysis of the less volatile residue in the capillary tube.

Registry No.—**6a**, 16853-07-9; **6b**, 17555-90-7; **7a**, 16853-91-1; **7b**, 17555-92-9.

Acknowledgment.—The authors are grateful for the support of this research by the National Science Foundation (Grant GP-2012, currently GP-8407X).

(9) Attempts to powder the reagents finely prior to insertion into the capillary led to brownish mulls. This could indicate that reaction is occurring even under these conditions.

Improved Synthesis of *anti*-Benzaldoxime. Concomitant Cleavage and Formylation of Nitrones

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Recent interest in alkylation of *anti*-benzaldoxime[1] to form nitrones[2,3] and in the hydrolysis of nitrones to N-hydroxyamino compounds[3,4] has emphasized the fact that no satisfactory procedure is available in the literature for the preparation of this starting material. The published procedures[5-7] involving sodium carbonate neutralization of the oxime hydrochloride have not been successfully carried out on a large scale[2] and are suitable only for the preparation of a few grams of transiently stable[6] *anti*-oxime, rapid reversion to the low-melting *syn*-oxime occurring during work-up and handling.

In connection with our synthetic program on hadacidin, a growth inhibitor isolated from *Penicillium frequentans* Westling,[8] it was necessary to develop a procedure for the preparation and use of *anti*-benzaldoxime on a large scale.

The *syn*-oxime, obtained by conventional means from benzaldehyde and hydroxylamine, is converted into a hydrochloride on treatment with anhydrous hydrogen chloride in a variety of solvents. Brady and Dunn described[6] the preparation of two isomeric hydrochlorides, the β hydrochloride, prepared at higher temperatures, affording the very unstable *anti*-oxime on neutralization.

We have developed a procedure in which the hydrochloride is prepared in refluxing benzene to ensure complete conversion into the β form, which is isolated with exclusion of atmospheric moisture and is then neutralized in a rapid sequence of dissolution in excess caustic, reacidification with ammonium chloride, and extraction with ethyl ether. Both the preparation of the hydrochloride in hot solvent and the particular mode of neutralization are critical to the process. By this means, *anti*-benzaldoxime can be prepared conveniently in large quantities in 88% over-all yield from benzaldehyde. The method is described below on a 2-mol scale and has been carried out on a scale many fold larger. Oxime so produced is free of *syn* isomer and has remained stable for several weeks. The nmr spectrum in tetrahydrofuran showed the —CH=N— proton as a singlet at 7.27 ppm relative to TMS, a value identical

(1) *anti*-Benzaldoxime has been referred to as β-benzaldoxime in the older literature. The name (Z)-benzaldoxime has been proposed by *Chemical Abstracts Service* [J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968)].

(2) E. Buehler, *J. Org. Chem.*, **32**, 261 (1967).

(3) E. Falco and G. B. Brown, *J. Med. Chem.*, **11**, 142 (1968).

(4) E. Buehler and G. B. Brown, *J. Org. Chem.*, **32**, 265 (1967).

(5) E. Beckmann, *Chem. Ber.*, **23**, 1684 (1890).

(6) O. Brady and F. Dunn, *J. Chem. Soc.*, 1783 (1923). In this reference, the designations *syn* and *anti* are interchanged.

(7) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed., Longmans, Green and Co., Ltd., London, 1956, p 719.

(8) E. A. Kaczka, C. O. Gitterman, E. L. Dulaney, and K. Folkers, *Biochemistry*, **1**, 340 (1962).